EVALUATION OF NEUROMUSCULAR CONTROL AFTER ANTERIOR CRUCIATE LIGAMENT RUPTURE

Development of objective criteria to assess sensorimotor competence

Thesis submitted for the degree of Doctor
of Medical Sciences at the University of Antwerp to be defended by

Angela BLASIMANN SCHWARZ

Evaluation of neuromuscular control after anterior cruciate ligament rupture: Development of objective criteria to assess sensorimotor competence

Evaluatie van neuromusculaire controle na voorste kruisbandruptuur: Ontwikkeling van objectieve criteria ter beoordeling van sensorimotorische competentie

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Faculty of Medicine and Health Sciences
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The cover shows a wrestling fight of the Swiss wrestler and physiotherapist Pirmin Reichmuth (upper athlete), who suffered three ACL ruptures in the right knee (2014 – 2017) and one in the left knee (2021). The ACL injuries forced him to adjust his wrestling technique in order to continue competing.

For Stefan,
Elina, Anic and Malin

For my parents, Therese and Beat

“SCIENCE AND EVERYDAY LIFE CANNOT AND SHOULD NOT BE SEPARATED.”

Rosalind Franklin (1920 – 1958)
biochemist and X-ray crystallographer
key role in elucidating the DNA structure

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CONTENT

CHAPTER 1

GENERAL INTRODUCTION

Abstract

What is known

- Rupture of the anterior cruciate ligament (ACL) is a severe knee injury with various, extensive and long-term consequences for the patients regarding functioning, disability, health and participation.
- The rates for return to sport (RTS) are rather low combined with a high risk for re-injury and re-rupture.
- Neuromuscular alterations and biomechanical adaptations occur after ACL rupture.
- Electromyography (EMG) gives insights into the physiology of the neuromuscular system.

Where is the gap

- There is a lack of basic knowledge concerning neuromuscular control for functional stability of the knee during activities of daily living (ADL), at work or in doing sports.
- Current physical performance tests do not give direct insight into neuromuscular control.
- No valid, objective criteria for deficits in neuromuscular control exist.
- It is unknown whether patients after ACL rupture have sufficient neuromuscular control at RTS time point.

Injuries of anterior cruciate ligament (ACL) happen quite frequently and concern athletes[1 2] but also the active part of the general, adult population. ACL rupture rates vary by country, by sport, by sex, and in response to injury-reducing, preventive training programs.[3] Regarding activities or sports in which both sexes participate, females have a significantly higher ACL injury rate than males.[4] An overall age- and sex-adjusted incidence of 68.6/100'000 person-years has been reported, with the highest incidence in males between 19 and 25 years (241.0/100'000) and in females between 14 and 18 years (227.6/100'000).[5]

About 80% of all ACL injuries are due to a non-contact nature (without physical contact by an opponent) with a multiplane mechanism.[6-9] Axial compressive force was identified as the primary component responsible.[6] In addition, deceleration and acceleration motions with excessive quadriceps contraction or insufficient hamstrings activation, and landings at or near full knee extension with dynamic knee valgus have been reported as injury mechanism.[10-12] ACL injuries typically occur within about 50 milliseconds (ms) after initial floor-foot contact,[8] leaving a short time frame for mechano-sensory feedback (e.g., reflex response). Pre-activity and reactive neuromuscular responses regulate muscle and joint stiffness, which is influencing dynamic joint stability.[13]

The rupture of the ACL is often accompanied by concomitant injuries such as meniscal tears, bone bruises or strain of collateral ligaments,[14 15] leading to several weeks or even months of physical impairment with wide consequences for the patients concerning return to work or return to sport (RTS).[16] In the long run, ACL ruptures may lead to anterior knee pain, instability, secondary meniscal injury, graft rupture after ACL reconstruction (ACL-R), or even post-traumatic knee osteoarthritis.[17-19] Within two years following ACL-R, 20 - 40% of athletes sustain a re-injury, either a rupture of the graft, of the contra-lateral ACL, or other structures being affected.[20-25] It is known that ACL ruptures induce altered kinematics and kinetics[26] – these changes are referred to neuro-muscular adaptations due to altered sensorimotor control.[27] Neuromuscular impairments have been shown to be predictive of secondary ACL injuries.[28] Additionally, it is assumed that neuromuscular abilities may play a decisive role in ACL injury prevention.[29]

To assess RTS ability after ACL rupture or reconstruction, mainly a combination of time-based decisions, clinical tests and physical performance test batteries are used.[30-32] Despite great advances in rehabilitation guidelines published, there is still a lack of validity of RTS criteria after ACL-R[33] and consensus about gold standard for reliable RTS assessments and safe RTS cut-off points is missing.[34-36] Unfortunately, current assessments for RTS do not adequately reflect the level of knee stability needed for a safe RTS as no electromyography-based assessments for neuromuscular control are included so far. Another gap is the lack of basic knowledge concerning neuromuscular control of the knee for functional stability during activities of daily life (ADL), at work or in doing sports. Assessing objective neuromuscular outcomes could contribute to decision-making regarding safe RTS and closes the gap between clinical assessments by physicians and physical performance test batteries. Consequently, those outcomes could give insight into neuromuscular control status after ACL rupture or reconstruction. Therefore, it is obvious that meaningful, reliable, valid, and accurate diagnostic tools for neuromuscular control in ACL patients are needed to improve therapy, the determination of the right timing for RTS and secondary prevention.

The following chapters provide a brief overview of the knee anatomy and biomechanics, ACL rupture, management and rehabilitation after rupture including RTS, and neuromuscular control to provide a contextual background for the research conducted during the PhD studies.

1.1 Anatomy and biomechanics of the knee joint

The knee joint allows motion during static and dynamic activities while maintaining stability.[37] It is essential that the knee joint provides a physiological range of motion (ROM) without sacrificing stability during static tasks such as standing to more dynamic activities such as level and stair walking, running, and pivoting.[38] In general, the interaction of the involved bony parts, the capsule, the ligaments, the menisci, joint load, and muscular forces surrounding the knee joint guarantees the balance between stability and motion, allowing function in various ADL and sports under different conditions.[39] Therefore, changes in any of these structures can alter the biomechanics of the knee joint, increase the loads and functional demands placed on the non-affected, remaining structures.[37]

Capsular ligaments

Roughly, the capsule of the knee joint can be divided into thirds (anterior, middle and posterior) on the medial and lateral side: The anterior thirds are components of the extensor mechanism or patellofemoral articulation, and the posterior two-thirds are components of the tibiofemoral articulation (Fig. 1).[39]
Several structures such as muscles, ligaments, and capsule, which interact together in a complex way, guarantee rotational stability of the knee joint.[40] In summary, the ACL, the posterior cruciate ligament (PCL), the medial and lateral collateral ligaments (MCL and LCL), and the antero-lateral ligament (ALL) are defined as passive stabilizers for internal

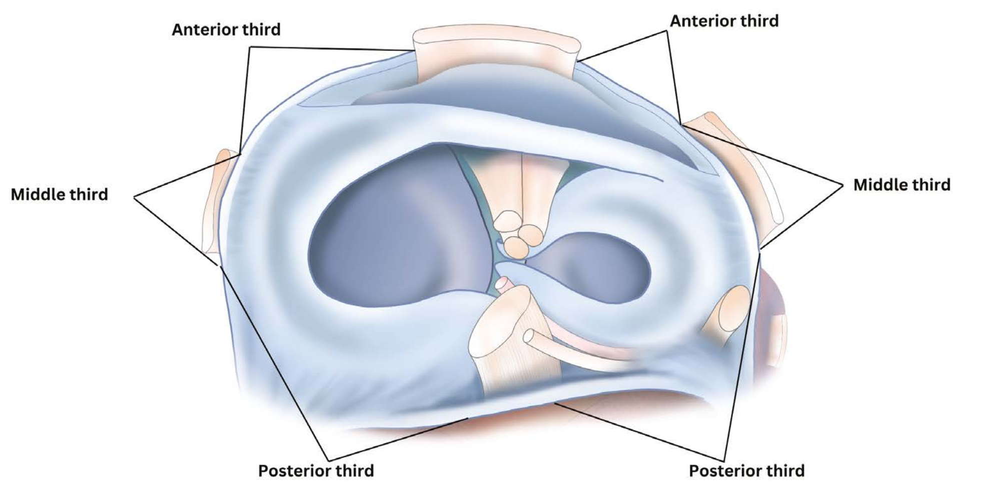

Figure 1: Classification of the capsule of the right knee joint into anterior, middle, and posterior thirds (own drawing, based on Flandry & Hommel, 2011,[39] with permission from Wolters Kluwer Health Inc., license number 5514830183607)

tibial rotation.[40 41] Despite the term MCL is well known and widely used, it is anatomically not correct as it describes one single ligament medially instead of all capsular ligaments in the posterior-medial corner of the knee joint (Fig. 2).[39] Under the aspect of function, the posteromedial or posterolateral corner of the knee are seen as a large aponeurotic expansion of the respective medial or lateral hamstring muscle. The aponeurotic expansion stretches from the muscle belly to the meniscus, including the latter as well.[39]

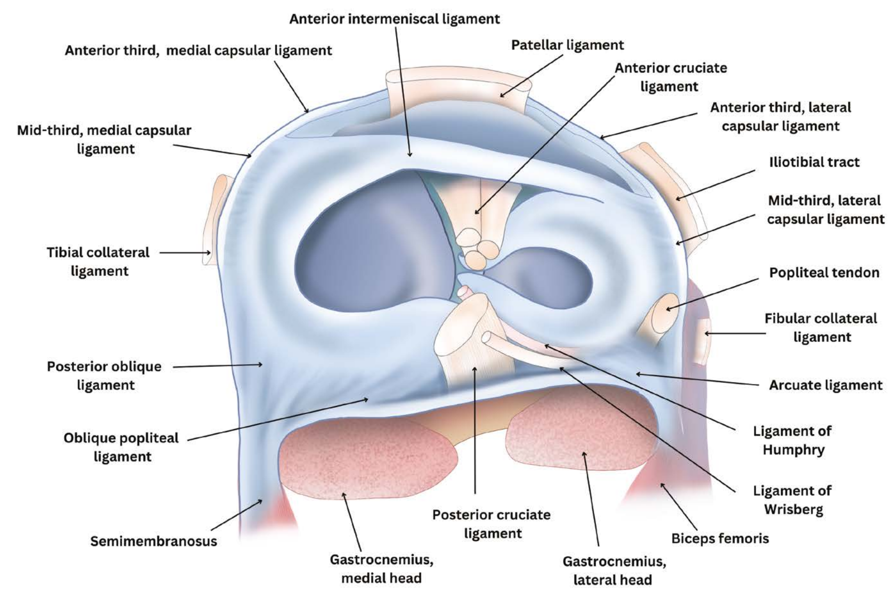

Figure 2: Capsular ligaments of the right knee: Major structures involved in menisco-ligamentous stability (own drawing, based on Flandry & Hommel, 2011[39], with permission from Wolters Kluwer Health Inc., license number 5514830183607)

Regarding rotational stability in knee flexion above 35°, the ALL (Fig. 3) is an isometric structure acting as an antagonist to the ACL.[40-42] Internal tibial rotation at higher flexion angles of the knee joint (above 90°) is not only controlled by either the iliotibial band or the ALL but rather by the interplay of all antero-lateral knee structures (including the mid-third lateral ligament and capsulo-osseous layer) acting synergistically.[40 43] The ACL and the ALL secondarily stabilize each other under dynamic load conditions as indicated by a biomechanical study using computational modeling.[44] With ACL deficiency, the mean force on the ALL increased significantly during gait loading and high degrees of knee flexion during squatting.[44]

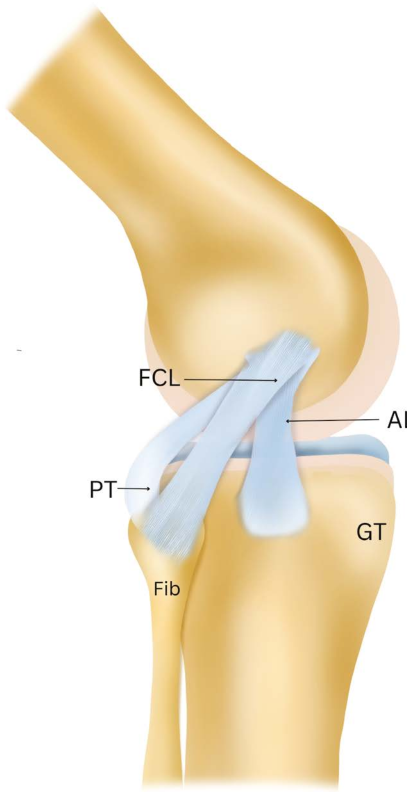

Figure 3: Lateral aspect of the right knee with the antero-lateral ligament (ALL), the popliteal tendon (PT), the fibular collateral ligament (FCL), the fibula (fib) and the Gerdy's tubercle (GT) (own drawing, based on Claes et al., 2013[41])

Menisci

Due to the complex anatomy, the lateral and the medial meniscus have several functions in biomechanics of the knee, namely bearing loads, guiding rotation, stabilizing translation, and constituting a contact area.[39] By their role in guiding rotation and stabilization of translation, they support the ACL in its function.[39] There are close connections between the anterior roots of the menisci and the ACL.[45] In addition, the lateral meniscus supports rotational stability of the knee joint (Pivot Shift).[46] Meniscal injuries, which are common in combination with an ACL injury but often difficult to diagnose preoperatively, lead to altered biomechanics in the knee joint and posttraumatic knee osteoarthritis.[47] However, incidence of meniscal tears is reported to be higher in patients with chronic ACL deficiency, indicating that meniscal injuries could also be a consequence of ACL rupture.[48]

Muscles, fascial connections, and myofascial meridians

The vastus muscles of the quadriceps femoris (QF) are referred to as general joint stabilizers because they show activity regardless of the direction of pull or force application.[49]

The hamstrings can counteract the force of the QF and consequently reduce or even completely cancel out the antagonistic force acting on the ACL.[50] Especially during weight-bearing activities, hamstrings' muscular activity is seen as antagonist activation preventing anterior tibial translation and reducing knee extension moments.[51] In addition, the hamstrings tense the ligaments through their insertion into the medial and lateral capsular ligaments to decrease or even eliminate any laxity present.[39] This mechanism of tension leads to an increase of load on the articular surfaces, contributing to static stability.[39] A relatively high association of semitendinosus (ST) and biceps femoris (BF) muscle with internal and external knee rotation was found, indicating that hamstring activation is essential for stabilizing the knee against torsional loads.[49] This is important for knee extension induced by isolated quadriceps force which leads to an internal rotation of the tibia relative to the femur.[52] A reduction of this internal rotation is only achieved by adding hamstring loads, especially the BF, resulting in knee motion with neutral alignment.[52]

Co-activation of both anterior and posterior thigh muscle groups provides joint stability and occurs during ADL such as walking, standing, getting up, sitting down, going up- and downstairs.[53] Additionally, it is essential during powerful, dynamic movements to reduce shear forces on the ACL.[54]

Muscular co-activation can be elicited as a direct result of a reflex arc peripherally (without integration of the central nervous system (CNS) or – when a movement is too fast for reflexes – be centrally controlled. Central and peripheral control of agonist-antagonist co-activation aims at producing highly regulated, accurate joint motion, and at preserving joint stability.[53]

The iliotibial band and heads of the gastrocnemius muscles can also be seen as specific joint stabilizers for knee rotation as they enhance the stability derived from capsular ligaments of the tibiofemoral joint.[49] The role of the triceps surae muscle in dynamic stability of the knee joint is sparsely documented. Rhim et al.[55] describe that the soleus muscle counteracts anterior sliding of the tibia on the upper ankle joint (articulatio talocruralis), acting as agonist to the ACL.[55]

Most skeletal muscles of the human body are directly linked by connective tissues[56] as proposed as myofascial meridians[57] or shown in anatomical studies.[58-60] In the last years, the paradigm regarding myofascial meridians shifted from being "kinetic chains" as conceptual pathways only to physical entities which determine viscoelastic tension in the body.[56] A better insight into strain transmission along myofascial meridians could "provide a rationale for the development of more holistic treatment approaches".[56] This is represented in therapeutic approaches such as Anatomy Trains Structural Integration or movement concepts such as Slings Myofascial Training®.[61 62] So far, strong evidence was found for the existence of three myofascial meridians: the superficial back line, the functional back line, and the functional front line, moderate-to-strong evidence for parts of the spiral line and the lateral line, and no evidence for the superficial front line.[56] Hamstrings and gastrocnemii are fascially connected via the superficial back line.[57] In upright standing body position with extended knee joints, the superficial back line acts as a myofascial continuum.[57] Regarding links between myofascial meridians and knee ligaments, no connections of the ALL to the iliotibial band were found.[41]

Anterior and posterior cruciate ligaments

The ACL (Fig. 4) and the PCL do not differ histologically but in function:[63 64] The primary function of the PCL is to prevent posterior translation, but also any translation or rotation in the transversal plane.[39] The two main functions of the ACL are to prevent hyperextension and anterior tibial translation, although biomechanically the ACL does this best at approximately 20° to 30° of knee flexion.[37 65-67] This position – standing with knee flexion of 30° - was chosen to assess reflex activity induced by anterior tibial translation in this PhD project.

Figure 4: Arthroscopy of an intact ACL: standard image in 90° knee flexion (©PD Dr. med. Philipp Henle, with permission)

Furthermore, the ACL has an important role in guiding the tibia during rotational movements when the knee joint comes into full extension, and in coupling translational movements with axial rotation of the tibia.[39] The ACL serves as secondary stabilizer to internal tibia rotation, in particular near full extension of the knee joint, and to external rotation and knee varus-valgus, especially under weight-bearing conditions.[68-70] These securing movements by the intact ACL are possible thanks to the insertion sites, the tensile characteristics of the ACL and the complex oval-like shape of the condyles.[71] The ACL also allows for normal biomechanical knee motion, normal helicoid knee action respectively, preventing from meniscal pathology.[37 38] In summary, the ACL is a key structure in the knee joint.[68 70 72 73]

It is generally accepted that the ACL functionally consists of two distinct bundles (Fig. 5): the antero-medial bundle (AMB) and the postero-lateral bundle (PLB), named after their attachments on the tibia.[74-80] On average, the anterior fibers of the ACL are longer than the posterior fibers.[78 79] During all degrees of flexion of the tibiofemoral joint, parts of the fiber bundles of the ACL are under tension which guarantees stability in posterior-anterior direction and in rotation.[81]

In the sagittal plane (Fig. 5), the fascicles of the ACL are approximately parallel during knee extension. In flexion, the two bundles are no longer parallel: there is a slight lateral rotation of the ACL as a whole about its longitudinal axis, and the AMB begins to wrap around the rest of the ligament.[72] This relative, spiral movement of one bundle around the other is due to the orientation of the osseous attachment sites of the ACL.[78 82]

In the transversal plane, the two bundles wrap upon themselves as they spiral from lateral to medial which consequently increases tension during internal rotation of the tibia.[39 72] Internal rotation of the tibia leads to a slightly increased lengthening of the ACL, which is most noticeably at 30° knee flexion, compared to external rotation.[72] However, the cruciate ligaments play only a secondary role to secure the knee joint in the transversal plane: Twisting is mainly resisted by a combination of capsular shearing, by the geometry of the menisci and joint surface, and the impact of collateral ligament action.[84]
Like the ACL, there are two distinct bundles forming the PCL: an antero-lateral bundle, which is under tension during flexion, and a postero-medial bundle being stretched in extension.[39] The two bundles wrap upon themselves during internal tibia rotation leading to a wrapping around each other of the ACL and PCL.[39]

Regarding biomechanical properties, it has been demonstrated that the AMB of the ACL experiences significantly larger maximum stress compared to the PLB.[85] Structural properties of the femur-ACL-tibia complex in human cadaveric knee joints, as represented by the linear stiffness and ultimate load, decreased significantly with specimen age and repetitive loads.[86] The tensile strength, ultimate load respectively, was 2160(±157) Newton (N) and values for linear stiffness were 242(±28) Newton/millimeter (N/mm) in younger age (<35 years), both tested in 30° knee flexion.[86] For normal level walking, in situ forces of 169 N were reported for the ACL.[87] During stair descent, increased in situ forces of 445 N were measured, which have been explained by the complementary effects of knee extensor muscles.[88]
During knee extension, anterior tibial translation is low, with a maximum scope of 2 mm, providing support during stance.[14] During walking and with knee flexion, anterior tibial translation may be up to 3 mm, and up to 5.5 mm when applying external load.[66] After ACL rupture, anterior tibial translation may be up to 10 to 15 mm with 30° knee flexion and anterior load of 134 N.[89-91]

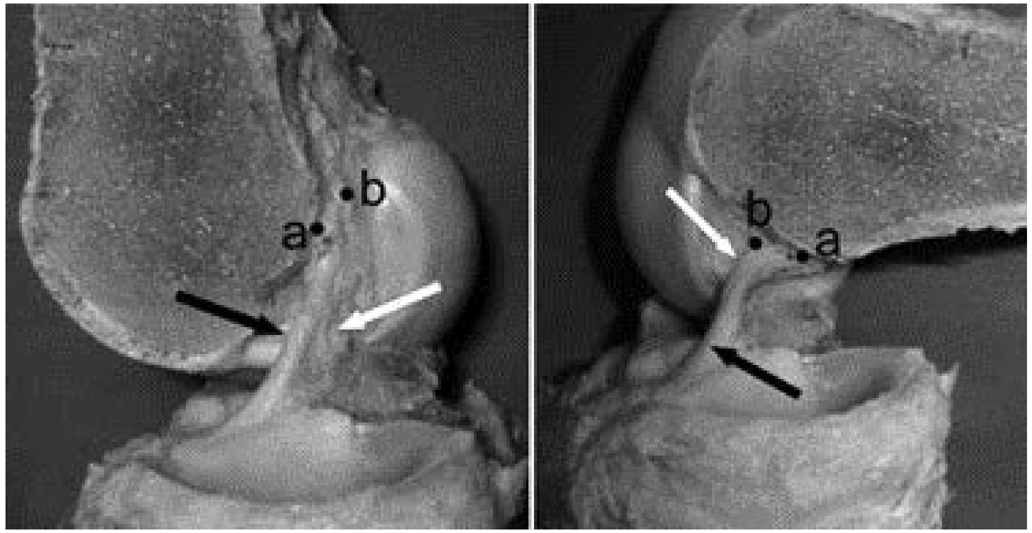

Figure 5: Fiber arrangements of the AMB (a, black arrow) and the PLB (b, white arrow) of the ACL in full extension and 90 degrees of flexion (from Dargel et al., 2007[83], distributed under the terms of the Creative Commons Attribution 2.0 International License CC-BY 2.0 (https://creativecommons.org/licenses/by/2.0/)

Innervation of the ACL and its role in proprioception

In addition to its mechanical function of securing translational and rotational movements contributing to passive stability of the tibiofemoral joint, the ACL has an important proprioceptive function, controlled by an extensive network of intraligamentary nerves.[92] This proprioceptive function is central also for this PhD topic, as it is all about neuromuscular control in participants with a ruptured, reconstructed, or healthy ACL.

Nerval fibers from the posterior articular branches of the tibial nerve supply the ACL.[93] Additionally, there have been described smaller myelinated and unmyelinated nerve fibers lying alone among the ACL fascicles.[93] These nerves terminate in so-called mechanoreceptors, which are in the collagen structures of the ACL on the one hand and in the connective tissue surrounding the ACL on the other,[93 94] predominantly at the femoral and tibial end of the ACL.[95] As specialized afferent end organs, the morphologically different mechanoreceptors convert the physical stimulus of muscle tension into neural signals.[95] In addition to the perception of movement, their physiological characteristics include adaptation to external circumstances.[96] During a movement of the knee joint, those mechano-receptors provide information about speed, acceleration, direction of movement and exact position of the knee joint.[92 93 96-98] The stronger the stimulus, the higher the discharge rate, e.g., the more signals are sent which are analyzed by the CNS.[95]

The following four distinct types of receptors have been described for the ACL:

- Ruffini corpuscles or receptors, which respond to static and dynamic tensile stress in the joint, are located at the surface of the ACL and predominantly found on the femoral end of the ligament where deformations are greatest.[92 96]
- Vatter-Pacini corpuscles, which are sensitive to fast movements,[97] are situated at the femoral and tibial end of the ACL.[92 95 96] However, one research group did not find any Pacini corpuscles in the ACL.[99]
- Golgi-like tension receptors, located near the insertions of the ACL and at its surface, are one of the static receptors that provide information about knee position together with the Ruffini corpuscles.[93 96 98]
- Free-nerve endings, serving as local effectors by releasing neuropeptides with vasoactive function, probably have a modulatory effect in normal homeostasis of ligamentous tissue or in late remodeling of grafts.[92 100]

Ruffini, Pacini and Golgi receptors as mechanoreceptors have a proprioceptive function and form the afferent arc for signaling postural changes of the knee.[72] Within-ligament deformations affect the performance of muscle spindles via the fusimotor system.[96 100] Activation of afferent nerve fibers in the proximal portion of the ACL influences motor activity in the muscles surrounding the knee; the so-called "ACL reflex" phenomenon".[72 101] Electrical stimulation of the ACL during arthroscopy has been shown to generate electromyography (EMG) signals in the BF and ST muscles.[101] These findings were in line with observations of Beard et al., according to which the ischiocrural musculature is activated when an „anterior drawer" occurs.[102] Stimulation of group II or III fibers (e.g., mechanoreceptors) triggers those responses of muscles around the knee joint.[72] Consequently, this reflex is absent in patients with ACL rupture.[81]

1.2 Rupture of the anterior cruciate ligament (ACL)

Epidemiology

In general, the ACL is the most injured ligament in the body (Fig. 6), however, incidence rates for ruptures are difficult to assess because some ACL ruptures are not diagnosed.[103] In most of the cases, both bundles of the ACL are completely ruptured.[91] In contrast, 12% of these patients show an intact PLB.[91] Other ligamentous injuries, such as a (partial) rupture of the MCL, meniscal lesions, compression of the lateral condyle with a bone bruise or chondral lesions are often associated with ACL ruptures.[14]

It is assumed that passive as well as active joint stability of the knee have a decisive influence on the injury rate.[53] Passive stability of the knee joint is mainly determined by the geometry of the joint, the joint surfaces and the laxity of the ligamentous complex as a major factor.[13] Active stability of the knee joint is determined by the angle between the patellar tendon and the tibial shaft, neuromuscular activity (reflex-induced, voluntary activation), muscular reaction times, the increase in rate of force during muscle contractions, and muscular stiffness.[13]

Rates for ACL rupture vary by country, sport, sex, as well as in response to injury-reducing training programs,[104] and concern athletes but also the active part of the general population.[1 2] Regarding activities or sports in which both sexes participate and when the rate has been normalized to sports exposures, females have a significantly higher ACL injury rate than males.[4 105] A large variability in different outcomes reporting numbers of ACL injuries is found in the literature, making it difficult to compare between various populations and sport groups.[106]

Figure 6: ACL rupture as seen during arthroscopy (©PD Dr. med. Philipp Henle, with permission)

The incidence for ACL ruptures is estimated to lie between 30 and 85/100'000 person-years.[5 107-113] Especially professional athletes in football, basketball, soccer, rugby, skiing, handball, volleyball, and professional dancers, have a higher risk for ACL injuries, likely due to the increased exposure to intense training and frequent competition.[106 114]

For the United States of America (USA), up to 250'000 people suffer from an ACL injury each year,[2 103 115 116] meaning an annual incidence of 3.2% for men and 3.5% for women.[117] ACL injuries are mainly reported in high school and college students and with an increasing tendency especially for females, probably since female students more and more participate in high school and other organized sports.[2] Data collected over 21 years revealed an overall age- and sex-adjusted annual incidence of ACL ruptures of 68.6/100'000 person-years, with the highest incidence in males between 19 and 25 years (241.0/100'000) and in females between 14 and 18 years (227.6/100'000).[5] For Scandinavian countries, an overall annual incidence rate of 85/100'000 people who sustain an ACL injury are reported, with males at a higher risk than females.[110 118 119] The population at the age between 16 and 39 years was most at risk and had an incidence of 85/100'000 inhabitants in Norway,[118] 91/100'0000 inhabitants in Denmark[119] and 71/100'000 inhabitants in Sweden.[118 119] In Germany, an incidence of 46/100'000 inhabitants[120] or 70'000 – 80'00 ACL injuries per year were reported.[120 121] In Belgium, the annual incidence rate was reported to be around 40/100'000 inhabitants.[122] In Switzerland, about 10 000 to 12 000 ACL injuries happen each year.[123] Current incidence rates for Switzerland are not available because ACL injuries are not systematically recorded in a national registry so far.

Sex-specific differences

Women have a higher injury risk to sustain an ACL rupture than men,[7 124] with adolescent females at highest risk.[2 125] The ACL injury risk for women can be three and a half times bigger for non-contact injuries.[104 126 127] When playing high-risk sports such as soccer or basketball, women even have a two to eight times higher risk to rupture the ACL compared to men.[104 128] Other authors reported injury rates for ACL in female athletes to be between two and six times higher than the rate in male athletes, depending on the type of sports.[7 105 129 130] Regarding sex-based incidence and sports participation, an annual rate for ACL ruptures of 5% for females participating in soccer and basketball was found.[131] In contrast, some authors stated a greater incidence of ACL injuries for male athletes, based on increased exposure to higher risk sports.[106]

Injury mechanism

The reasons for ACL injuries are multifactorial.[132] Most ACL injuries – 70 to 80% – are due to a multiplane mechanism without physical contact by an opponent.[6-9] Thereby, the proportions of so called "non-contact" ACL ruptures account for 67% of all cases in men and nearly 90% in women.[103] ACL injuries usually happen during activities such as side cuttings, plant and cut situations, and (one-leg) landings after a jump.[8 10 133] The mechanism involves a forceful valgus and an internal or external tibial rotation in combination with only moderate knee flexion, resulting in a valgus collapse of the knee[7 9] (Fig. 7), being highly positive predictive to sustain an ACL injury.[28 134]

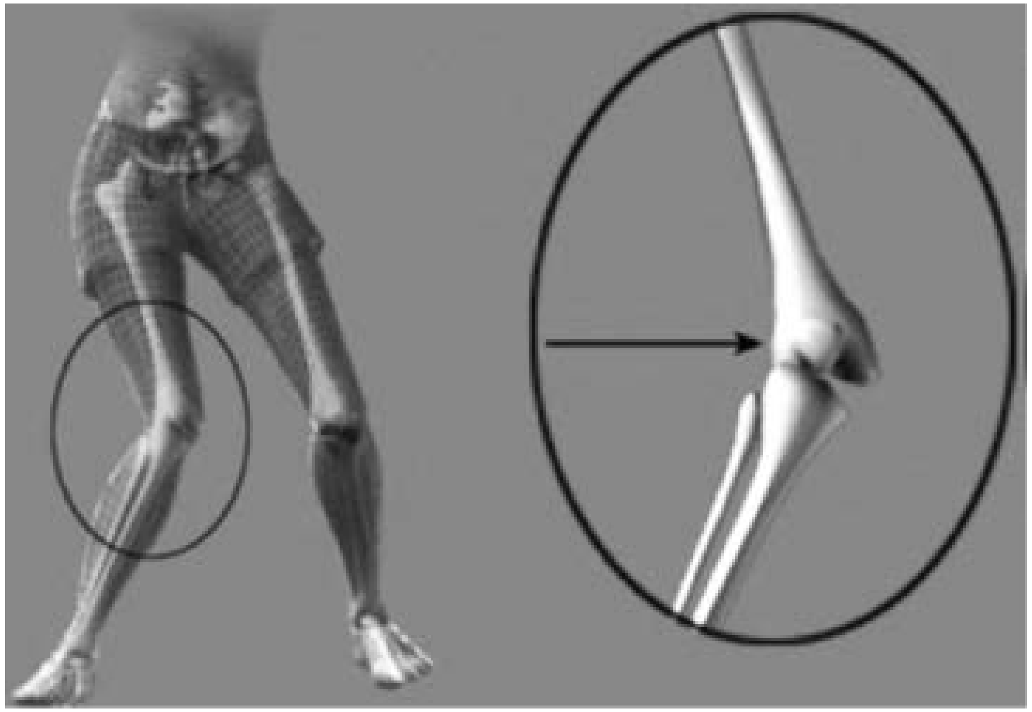

Figure 7: Dynamic knee valgus, potentially combined with hip adduction and internal rotation, knee abduction, external rotation and anterior translation of the tibia, and ankle eversion (from Hewett et al., 2006,[7] with permission by SAGE Publishing)

Deceleration and acceleration motions with excessive quadriceps contraction or insufficient hamstrings activation at or near full knee extension play a role in ACL injury mechanism.[10 12] Thereby, the tibia is translated anteriorly relatively to the femur and stresses the ACL. With an intact ACL, the hamstring muscles act synergistically to this translational movement.[135]

"Non-contact" ACL injuries typically occur immediately after initial foot-ground contact with the knee almost fully extended during sudden deceleration or single-leg landing[11] without extreme rotational component of the trunk over the lower extremity.[10] Findings of a two-dimensional video analysis revealed that ACL injured athletes landed with the hindfoot or flatfooted in contrast to non-injured athletes having ground contact with the forefoot first.[136] Moreover, ACL-injured athletes showed a trend towards less knee flexion, significantly more hip flexion and a significantly more posterior trunk position to the base of support.[136] However, a multifaceted approach including qualitative questionnaires from athletes after ACL injury, quantitative video analysis, magnetic resonance imaging (MRI) and cadaver studies revealed axial compressive force being the primary component and critical factor responsible for non-contact ACL injury (Fig. 8).[6] Apparently, knee flexion angles alone do not significantly affect the risk of rupture, but a "provocative" combined landing posture does (Fig. 8).[6]

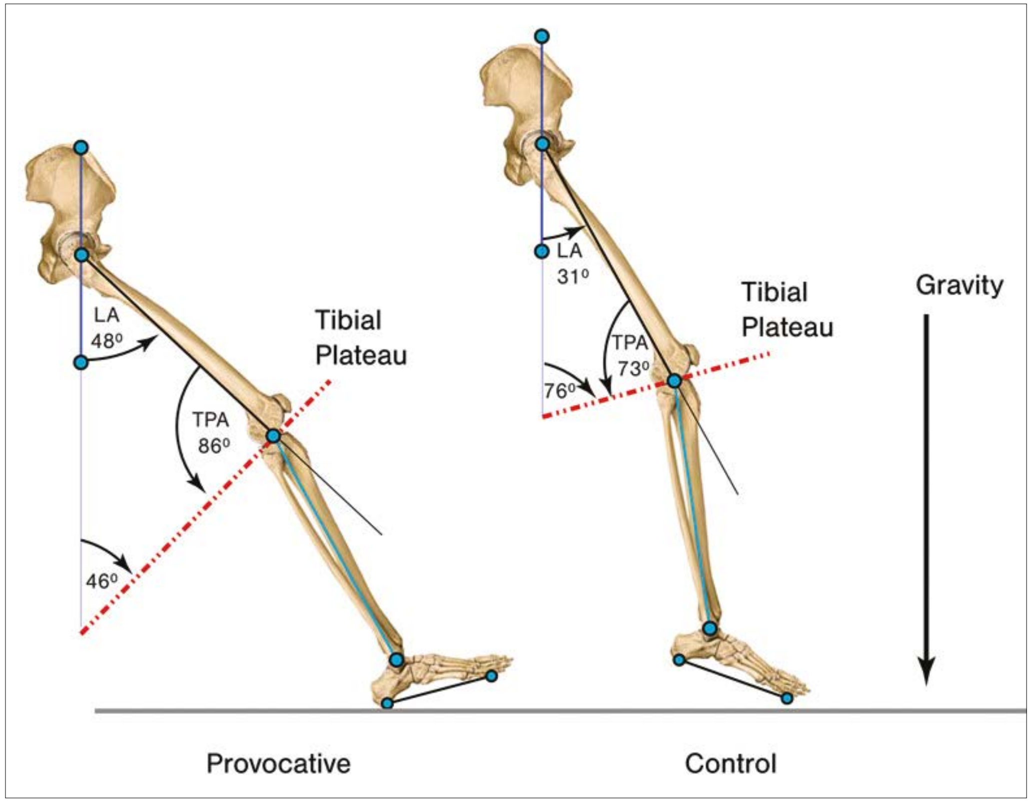

Figure 8: Two different single-leg landing strategies: provocative for an ACL injury (left) versus the control position (right) with knee and ankle placed in the average provocative and safe positions at initial contact.[136 137] (from Boden & Sheehan, 2022[6] with permission, license number 5504830011924).
Abbreviations: LA = limb angle; TPA = tibia plateau angle

Sex-specific differences

When playing the same landing and cutting sports, the increased knee valgus is supposed to be one of the reasons why female athletes have a 4- to 6-fold greater incidence to sustain an ACL injury in comparison to males.[128 138] Adequate neuromuscular activation of the medial hamstrings and the vastus medialis (VM) muscle in females can limit knee valgus by generating medial joint compression to absorb valgus forces.[134 139] Four times greater firing of the lateral hamstrings in females in comparison to male athletes was found.[134] Consequently, it may be assumed that enhanced hamstring activation in women reflects an active compensation mechanism to prevent from excessive valgus loading. Additional sex-specific neuromuscular adaptations such as activation timing, differences in force intensity of knee stabilizing muscles[140-145] and a dominance of the quadriceps over the hamstring muscles in women, which could increase anterior tibia translation, had been reported previously.[143 144 146 147]

In addition, females showed a significantly larger lateral flexion of the trunk during landing compared to male injured individuals.[136] However, these findings had been contradicted by a systematic review about sex differences in landing and cutting maneuvers.[148] The authors reported that no proof for quadriceps dominance during the described activities was present.[148] Furthermore, neither sex-specific differences in the explosive quadriceps-hamstrings ratio[149] nor significant differences in neuromuscular activity were found.[150]

Risk factors for ACL injury

As extrinsic or external, controllable risk factors for ACL injury, the type of competition,[151] position of play[152] and shoe/surface interface[153-155] are proposed among others. As intrinsic, internal and not controllable risk factors a narrow femoral intercondylar notch,[156 157] an increased posterior tibial plateau slope,[157 158] hormonal variation,[159 160] and biomechanical factors related to neuromuscular control[146 161] are reported among others. Among the proposed internal risk factors, biomechanics related to neuromuscular control can be seen as modifiable factors for primary and secondary injury prevention through appropriate training programs.[162] Initial theories discussed a lack of dynamic knee joint stability as predisposing factor[12 163 164] leading to a dynamic knee valgus.[165] Eccentric, vigorous contraction of the quadriceps leading to anterior translation of the tibia and consequently putting strain on the ACL was also attributed to non-contact ACL injuries.[166] Furthermore, high abduction moments or excessive valgus torque were reported as causative factors for non-contact ACL ruptures.[138] However, later studies stated that knee valgus and knee internal rotation moments were not likely to significantly contribute to ACL injury but appeared post-injury.[11 167] In addition, only weak evidence was found for decreased vision affecting knee biomechanics[152] and for fatigue reducing vertical ground reaction force of the hip and knee joint moments causing increased anterior tibial translation.[164 168] Regarding landing biomechanics, initial contact with flat foot was identified as one component of faulty dynamics as risk factor for a non-contact ACL injury (Fig. 8).[6]

In summary, degrading weather conditions, decreased intercondylar notch index or width, increased lateral or posterior tibial plateau slope, decreased core and hip strength and potential genetic influence were reported as risk factors for a non-contact ACL injury in both, females and males.[9]

Sex-specific risk factors

The increased risk for females to suffer from an ACL injury is probably multifactorial.[125] Anatomical factors such as leg alignment, an increased rate of valgus deformity among women, narrower notch width with possibly less space for the ACL are discussed among others.[169-171]
Sex-specific neuromuscular factors, such as neuromuscular adaptation and biomechanically different landing techniques,[172] are considered as the most likely ones for the increased risk of injury in women.[7 159] Altered biomechanics can be observed as different motion and loading of the knee joint in women during performance:[134 138 152] Female athletes typically perform movements in sports with a greater knee valgus angle in frontal plane than men. Therefore, the amount of stress on the ACL in these situations is higher due to high activation of the quadriceps despite limited knee and hip flexion, greater hip adduction and a large knee adduction moment.[173 174] Moreover, females typically land with an internally or externally rotated tibia,[175] leading to an increased knee valgus stress due to greater and more laterally orientated ground reaction forces.[176] In addition, female athletes move into greater hip internal rotation and decreased hip flexion during side-step cutting maneuvers which may influence loading of the knee joint.[177] Other studies described differences in timing of muscular activation or force intensity of knee stabilizing muscles of females.[140-145] Additionally, women have a larger quadriceps to hamstrings ratio compared to men which could be a risk factor for ACL injuries as it may foster anterior tibial translation.[143 144 146 147] This female quadriceps dominance over the hamstrings was found in various activities such as jumps, cutting and swerving maneuvers.[161 178 179] Furthermore, several studies indicate that hormonal factors play a role[160 164 170 180 181] contributing to an increased laxity of ligaments and increasing the risk especially during the preovulatory stage of the menstrual cycle.[170] However, various biomechanical, hormonal, and neuromuscular aspects for the increased risk of ACL injury in women are controversially discussed: A systematic review summarizing sex-specific alterations in landing and cutting maneuvers reported that biomechanical differences were based on questionable clinical relevance and that no quadriceps dominance for the activities described could be found in the included studies.[148] Similarly, no sex-specific differences were found for either the explosive quadriceps-hamstrings ratio[149] or strength-paired differences in neuromuscular activity.[150] Moreover, a recent systematic review from our research group, reported controversial findings regarding sex-specific neuromuscular activation of knee stabilizing muscles.[182]

1.3 Management, rehabilitation and return to sport (RTS) after ACL rupture

Diagnosis

Patient history, especially regarding injury mechanism, clinical examination and imaging are combined to diagnose an ACL rupture.[30] MRI is the standard imaging technique used also to diagnose indirect signs of the rupture such as bone bruises in the lateral compartment and any concomitant injures of meniscus, cartilage, and ligaments (Fig. 9).[15]

Figure 9: MRI of an ACL rupture in the sagittal plane (©PD Dr. med. Philipp Henle, with permission)

Clinical tests such as the Anterior drawer test, the Lachman and the Pivot-Shift test and laxity measurements with different devices[183] are often used to assess passive stability of the knee joint, either after the accident for diagnostic purposes or as outcome measure after reconstruction/rehabilitation. The Lachman test is the most accurate diagnostic test in clinics (85% sensitivity, 94% specificity).[184] The Anterior drawer test shows high sensitivity (92%) and specificity (91%) for patients suffering from a chronic ACL deficiency, but lower accuracy for patients with an acute ACL injury.[184] A positive Pivot-Shift test has a very high specificity (98%), but a low sensitivity (24%), and should therefore not be used to exclude an ACL rupture.[184]

Participants in our cross-sectional studies were assessed either by the orthopedic surgeon using the Rolimeter™ (Aircast®, Europe) or by an experienced sports physical therapist using the Lachmeter – The digital Rolimeter® (digital arthrometer, www.newarthrometer.com), both devices measuring the extent of passive anterior tibial translation in (mm). In addition, we measured active and passive ROM of the femorotibial joint with a goniometer, evaluated passive mobility of the patella and passive stability of the knee joint with the Anterior drawer test in 90° knee flexion, the Lachman and the Pivot-Shift test.

Treatment options and outcomes

Optimal treatment of an ACL rupture, a complex knee injury, is challenging and subject to debate.[185-190] Nevertheless, an individual patient-centered, decision-making process including the International Classification of Disability and Health (ICF),[191] is needed[192 193] as concomitant injuries (meniscus, cartilage, additional ligaments) and patent-specific factors (e.g., being a coper or a non-coper)[194] play a role and influence the outcomes.[195]

ACL ruptures can be treated either surgically with reconstruction (ACL-R) by an autograft or allograft, with primary repair by dynamic intraligamentary stabilization[196-198] and similar techniques, or with rehabilitation alone, conservative treatment respectively.[185] Physiotherapy plays an important role in rehabilitation of both surgically and non-surgically treated individuals.[199]

Between 50 and 80% of all patients with an ACL rupture are treated with ACL-R.[120 121 123 200] There is consensus that mainly young, highly active athletes and patients who wish to return to jumping, pivoting, and cutting sports such as soccer or handball should have early surgical reconstruction of the ruptured ACL[201] as ACL-R may have a preventive effect on secondary joint damage such as meniscal and cartilage lesions.[201 202] Discussion with the patient regarding graft selection should include complication rate, graft failure, donor site morbidity and patient-reported outcomes.[203] Equal and comparable clinical outcomes have been shown for ACL-R with ST tendon, quadriceps tendon (QT) and bone-patellar-tendon-bone (BPTB) grafts[204-206] despite different surgical techniques and biomechanical properties for different types of grafts.[14 207]

Nonoperative treatment with structured, progressive rehabilitation including intense neuromuscular training is an acceptable treatment option and recommended for patients who want to return to straight-plane activities.[200 201] In cases of persistent functional instability or episodes of giving way, delayed anatomic ACL-R is indicated for this group of patients.[201]

After ACL rupture, individuals experience similar functional, radiographic, and patient-reported outcomes, irrespective of management with ACL-R or rehabilitation alone.[30 208-211] This was also the case in the long-term course, at one, two, five, ten and even 15 years of follow-up after an ACL injury.[190] Similar results in women and men were found for clinical assessments such as Anterior drawer, Pivot-Shift and Lachman test, hop tests, quadriceps or hamstring strength testing, International Knee Documentation Committee (IKDC) knee examination score and loss of ROM.[19] No sex-specific differences were found regarding the development of anterior knee pain, posttraumatic osteoarthritis after ACL-R, graft rupture and graft failure rate.[19] However, statistically significant lower subjective and functional outcomes such as laxity, revision rate, Lysholm score, Tegner Activity Score (TAS) and incidence of not returning to sports were found in females compared to males.[19]

Definition and framework of return to sport

RTS can be seen as a continuum containing the three elements of return to participation, return to sport and return to performance, considering the type of sports/activity and the level at which the injured patient/athlete wants to return to.[34] This process includes interprofessional teamwork and shared-decision making between all stakeholders.[212] Contextual factors which influence the patient's expectations and risk tolerance for RTS are important and need to be considered.[34] This could be the type of ACL injury (e.g., acute versus chronic, partial versus complete rupture), type of treatment (e.g., surgical versus conservative, type of graft if

reconstructed), the athlete's/patient's age (or stage of career), type of sport (e.g., individual or team, contact or non-contact), physical demands of the sport (e.g., cutting, pivoting, landing), level of sport (e.g., leisure versus amateur versus (semi-)professional), upcoming participation opportunities (e.g., final game, preseason preparation), as well as social and financial costs.[34]

Guidelines for rehabilitation and return to sport

The ICF, proposed by the World Health Organization (WHO), is based on the biopsychosocial model and emphasizes an individual-centered approach and inclusion of all domains of human functioning, participation and health.[191] This applies for the management of treatment but also for rehabilitation.[213] However, current clinical practice guidelines do not satisfactorily address the biopsychosocial model and therefore, not all domains of the ICF have been incorporated yet into practical recommendations for RTS after ACL injury.[214]

Irrespective of treatment option, four main objectives of management for a patient with an ACL rupture are defined: to restore knee function, to address psychological barriers to return to activity and sports participation, to prevent further knee injury and reduce the risk of posttraumatic knee osteoarthritis, and to optimize long-term, knee-related quality of life.[30 32] More specific, the goals to be achieved during ACL rehabilitation are preventing deficits in knee extension, restoring strength, regaining full ROM, and preserving stability of the knee joint.[215]
Over the last decade, a shift from conservative, standardized time-based protocols to more accelerated, individualized criterion-based protocols has been observed.[215] These accepted protocols vary in length, but postoperative rehabilitation programs should last for 9–12 months to reduce the risk for subsequent injury.[30 31] The treatment modalities are based on patient-specific findings and preferences leading to a person- or athlete-centered approach.[192 216] It is commonly accepted that early activity, weight-bearing and accelerated rehabilitation are critical for achieving the rehabilitation goals, however, discussion is ongoing to what extent accelerated rehab would be beneficial or too aggressive, eventually even harmful.[215] Based on a systematic review and expert consensus statement, rehabilitation after ACL surgery should include a prehabilitation phase and three criterion-based postoperative phases based on impairment, sport-specific training and RTS.[31] In addition, rehabilitation after ACL-R should be a gradual, progressive process with the use of objective criteria to advance from one rehabilitation stage to the next.[30 32] To guide progression, it is recommended to use a physical performance battery including strength and hop tests, assessments for changes of direction and reaction-agility, and evaluation of quality of movement with video analysis.[31 34] Moreover, physical components should be accompanied by assessments for psychological readiness for RTS[30 34] such as the ACL-Return to Sport Injury scale (ACL-RSI).[24] This extensive test battery should not only be used to decide upon RTS but also to assess the risk for re-injury.[31] The person-centered approach as described for treatment options and rehabilitation should additionally come into play for an informed decision making to RTS.[217] Table 1 gives an overview of recommendations for rehabilitation and RTS after ACL-R, but also for preoperative rehabilitation. Even though most rehabilitation guidelines refer to patients with ACL-R, they can easily be adapted to conservatively treated patients.

Table 1: Summary of conclusions and recommendations regarding rehabilitation after ACL injury (from van Melick et al., 2016[31], with permission from BMJ Publishing Group Ltd., license number 5497510627587)

Conclusions and recommendations	Level of evidence
Preoperative rehabilitation	
A preoperative extension deficit (lack of full extension) is a major risk factor for an extension deficit after ACLR	2
Recommendation: measure the preoperative ROM	
A preoperative deficit in quadriceps strength of >20% has a significant negative consequence for the self-reported outcome 2 years after ACLR	2
Recommendation: measure quadriceps strength and also HS strength	
Prehabilitation ensures better self-reported knee function up to 2 years after ACLR	3
Recommendation: refer the patient to a physical therapist when necessary	
Postoperative rehabilitation	
It is unclear whether there is a benefit of supervised rehabilitation compared to home-based rehabilitation or no rehabilitation at all. A minimally supervised rehabilitation programme may result in successful rehabilitation in specific groups of patients that are highly motivated and live far from a physical therapist	2
When comparing a 19-week with a 32-week rehabilitation programme, there are no differences in terms of laxity, ROM, self-reported knee function, single-leg hop test for distance or isokinetic concentric quadriceps and HS strength	2
Recommendation: continue rehabilitation for 9–12 months, depending on the final return-to-work or play goals of the patient	
Immediate weight bearing does not affect knee laxity and results in decreased incidence of anterior knee pain	2
Recommendation: immediate weight bearing should only be tolerated if there is a correct gait pattern (if necessary with crutches) and no pain, effusion or increase in temperature when walking or shortly after walking	
Cryotherapy is effective in decreasing pain immediately after application up to 1 week postsurgery after ACLR, but has no effect on postoperative drainage or ROM	1
Recommendation: cryotherapy could eventually be applied in the first postoperative week to reduce pain	
Isometric quadriceps exercises are safe from the first postoperative week	2
Recommendation: start isometric quadriceps exercises in this first week for reactivating the quadriceps muscles when they provoke no pain	
Electrostimulation, in combination with conventional rehabilitation, might be more effective for improving muscle strength for up to 2 months after ACLR than conventional rehabilitation alone. However, its effect on long-term functional performance and self-reported knee function is inconclusive.	
Recommendation: electrostimulation can be useful as an addition to isometric strength training for re-educating voluntary contraction of the quadriceps muscles during the first postoperative weeks	1
CKC and OKC training can be used for regaining quadriceps strength	1
After ACLR, OKC exercises can be performed from week 4 postoperative in a restricted ROM of 90–45°	
Recommendation: When the quadriceps is reactivated, concentric and eccentric exercises should be used to replace the isometric exercises, provided that the knee does not react with effusion or (an increase in) pain. CKC exercises can be performed from week 2 postoperative. For BPTB, OKC exercises can be started from 4 weeks postoperative in a restricted ROM of 90–45° and extra resistance is allowed, for example, at a leg extension machine. For HS, OKC exercises also can be started from 4 weeks postoperative in a restricted ROM of 90–45°, but no extra weight should be added in the first 12 weeks to prevent graft elongation. ROM can be increased to 90–30° in week 5, to 90–20° in week 6, to 90–10° in week 7 and to full ROM in week 8 for both graft types	2
Neuromuscular training should be added to strength training to optimise self-reported outcome measurements	1
Altered neuromuscular function and biomechanics after ACLR could be a risk factor for second ACL injury (graft rerupture or contralateral rupture)	2
Recommendation: neuromuscular training should be added to strength training. Pay attention to a correct quality of movement for prevention of reinjuries	
Psychological factors as self-efficacy, locus of control and fear of reinjury have influence on the rehabilitation process and return to play after ACLR	2
Recommendation: evaluate psychological changes during rehabilitation with an objective instrument	
Criteria for return to play	2
An extensive test battery should be used to determine the return-to-play moment, but there are no tests or test batteries that have been tested for construct or predictive validity for return to play	2
It is not clear which cut-off point of the LSI should be used for strength and hop tests	3
Recommendation: perform an extensive test battery for quantity and quality of movement. This test battery should include at least a strength test battery and a hop test battery and measurement of quality of movement. An LSI of >90% could be used as a cut-off point. For pivoting/contact sports, an LSI of ≥100% is recommended	

ACLR, anterior cruciate ligament reconstruction; BPTB, bone-patellar tendon-bone; CKC, closed kinetic chain; HS, hamstring; LSI, Limb Symmetry Index; OKC, open kinetic chain; ROM, range of motion.

Abbreviations: ACLR = anterior cruciate ligament reconstruction; BPTB = bone-patellar tendon-bone; CKC = closed kinetic chain; HS = hamstring; LSI = Limb Symmetry Index; OKC = open kinetic chain; ROM = range of motion

Tests and criteria to assess readiness for return to sport

Clearance for RTS is mainly based on clinical examinations, patient-reported outcome scores and widely used physical performance test batteries.[32 218 219] There is some evidence for the use of functional performance tests to determine RTS after ACL-R220: Multiple physical performance measures – a battery including strength and hop tests, quality of movement and psychological tests[31] - might be more useful for the determination of RTS than a single performance measure.[34] However, RTS criteria are mainly dominated by time- and impairment-based measures [221] which do not address ICF domains such as participation and health.

Five principal criteria were defined which could contribute to safe RTS after ACL-R: performance/functional tests, strength tests, time after surgery, modifiable/non-modifiable risk factors and psychological factors.[33] Psychological readiness seems to be a major factor for successful and safe RTS decision, although mainly strength criteria, outcomes of performance and functional tests are part of RTS test batteries.[32] However, it is still unclear which outcome measures and cut-off values should be used to bring athletes safely back to RTS with a low risk of a second ACL injury.[31] Despite great advances in detailed practice guidelines published, there is still a lack of validity of RTS criteria after ACL-R[33] and consensus about gold standard for reliable RTS assessments and safe RTS cut-off points is missing.[34-36] In addition, the currently suggested RTS criteria do not seem to adequately assess neuromuscular control of the knee joint to judge upon RTS as no EMG-based measure is included in current test batteries so far. To date, mainly nonspecific tests, such as hop tests have been used to test active joint stability. However, testing paradigms that measure neuromuscular control of knee joint stabilizing muscles by assessing neuromuscular activity with EMG in isolation assess the physiological mechanisms more directly.

Functional performance measures

To measure functional performance after ACL-R or injury, mainly the single-leg hop for distance test (SLHD) or a combination of several hop tests are used.[222 223] Besides the SLHD, the triple hop for distance, timed 6-meter jump, cross-over jump for distance, triple jump, and single-leg vertical jump are the most popular assessments.[224] The SLHD is discriminative for men with ACL rupture and shows good responsivity for rehabilitation after ACL rupture.[224] For all other knee-related performance tests, actual evidence regarding psychometric properties is limited, contradictory or unknown.[224]

Functional performance is often expressed as Lower Limb Symmetry Index (LSI) and indicated as percentage of obtained performance comparing injured side with the contralateral side.[222 223] Evaluating strength and hop tests, a LSI of 90% for return to recreational sports, non-contact or non-pivoting sports, and a LSI of ≥100% for return to competitive, contact and pivoting sports is recommended.[31 225] However, the widely used LSI overestimate current sensorimotor competence, the actual state of the injured knee respectively,[219] as both limbs deteriorate after ACL injury.[221 226] Regarding long-term follow up, the function of the contralateral limb worsens in ACL-R patients even one and five years after reconstruction.[227] In addition, the LSI may overestimate the time point of RTS six months after ACL surgery, leading to an increased risk for secondary injury.[219] Therefore, the LSI should not be used in isolation to evaluate functional performance.[219 227]

Often used clinical assessments for impairment after ACL-R do not appear to be related to measured physical performance[228] and do not necessarily reflect readiness for RTS.[220 229] This could be shown for isokinetic strength measures which "have not been validated as useful predictors of successful RTS" following ACL repair.[230] Moreover, commonly used muscle function tests are not sufficiently demanding or sensitive enough to identify differences between injured and non-injured side.[225] Additionally, no measure for assessing quality of functional performance after ACL-R has been reported so far.[31 223 231] However, one-leg balance, isokinetic knee extension strength and hop performance (one-leg hop and side hop) have been identified as feasible, clinical assessments in a test battery for knee function after ACL rupture.[232]

Self- or patient-reported outcomes

Patient-reported outcome measures (PROMs), such as the IKDC, Knee injury and Osteoarthritis Outcome Score (KOOS), Lysholm score and Tampa score, are associated with knee strength and functional symmetry in individuals who have undergone ACL-R with hamstring tendon autograft.[233] Compared to Lysholm and Tampa scores, KOOS and IKDC scores were more likely to be correlated with performance-based outcomes and might contribute to RTS decision making.[233]

For the cross-sectional studies included in this PhD project, participants filled in the KOOS[234] and the TAS:[235] The KOOS is a knee-specific score[234] and is one of the most frequently used PROM in the literature.[110] It has high test–retest reliability for patients with knee injuries and has been used for ACL patients in several studies.[110 222 236-238] The KOOS contains five subscales evaluating both short- and long-term consequences of knee injuries[234] and is available in several languages and versions (www.koos.nu). The Intraclass Correlation Coefficient (ICC) has been described to range from 0.85–0.93 for the subscale "pain", 0.83–0.95 for "symptoms", 0.75–0.91 for "function in ADL", 0.61-0.89 for "function in sport and recreation", and 0.83–0.95 for "knee-related quality of life".[239] The minimum important change (MIC) of the KOOS is reported to be 8–10 points for all five subscales.[240] The Patient Acceptable Symptom State (PASS) threshold was 88.9 points for the KOOS subscale "pain", 57.1 for "symptoms", 100.0 for "function in ADL", 75.0 for "function in sport and recreation", and 62.5 for the subscale "knee-related quality of life".[236]

The TAS is a patient-administered 10-point scale to rate the actual level of activity ranging from 0 (sick leave or disability pension) to 10 (competitive sport on a professional level).[235] The TAS demonstrated acceptable psychometric properties and showed acceptable responsiveness to be used to assess function in early return after ACL treatment.[235] Test-retest reliability at two years postoperatively and again within four weeks was acceptable with an ICC of 0.8.[235] The minimum detectable change (MDC) was reported to be 1.[235] Additionally, floor and ceiling effects were acceptable, and it was responsive to change preoperatively and six, nine, 12, and 24 months postoperatively.[235]

Rates for return to sport

In general, a high rate of RTS overall (81-82%) and a lower rate (44-55%) for athletes after ACL-R in competitive sports can be found.[16 241] The high variability in RTS rates after ACL-R may be due to variable definitions of RTS from a high threshold (return to competition) to a low threshold (clearance by surgeon for RTS).[242] Approximately 90% of patients after ACL-R achieve successful surgical outcomes (impairment-based measures of knee function) and 85% show successful outcome in terms of activity-based measures.[16] Of these patients, 81% return to some form of sports participation, 65% return to their preinjury level of sport and 55% return to competition level after ACL-R.[241] Other systematic reviews found a range of RTS rates between 63 and 97% for elite athletes after ACL-R.[243-245] Most elite athletes RTS on average within one year[244] – this population seems to return earlier than non-elite athletes.[16] However, it remains unclear whether this approach is safe.[244]

Favorable factors for RTS at preinjury level are symmetrical hopping performance, younger age, male gender, playing elite sport, having a positive psychological response, greater psychological readiness to RTS, lower fear of re-injury, a more positive subjective assessment of knee function and using BPTB autograft.[241 246] Hamstring tendon (HT) autograft for surgical reconstruction was identified as favorable factor for returning to competitive sport.[241] The most important reasons for not achieving RTS are high ratings for fear of re-injury, functional problems of the operated knee during sports and low ratings for their knee-related quality of life.[152 225] Returning or not to preinjury level of sports after ACL-R is complex and influenced by multiple factors.[246] Screening for psychological impairments (e.g., kinesiophobia) early after ACL injury or reconstruction could help to identify patients who would be at risk for not returning to sports at preinjury level.[246]

Re-injury risk after return to sport

It is known that returning to high-demanding sports, including jumping, pivoting and hard cutting after ACL-R leads to a more than four-fold increase in re-injury rates over two years.[247] Considering simple decision rules such as RTS not before nine months after reconstruction and achievement of symmetrical quadriceps strength was reported to substantially decrease re-injury rates.[247] However, a literature review did not find an association between regarding current objective criterion-based RTS decisions and risk of a second ACL injury,[226] but these findings were based on only four studies with low quality of evidence.

In general, rates for re-injury and contralateral ACL injury are reported to be higher than the risk to sustain an ACL injury for the first time, which may be related to insufficient, time-based RTS guidelines.[242] Those time-based criteria for RTS do not allow for proper healing or resolution of post-operative impairments and elimination of risk factors associated with both primary and secondary ACL injuries.[242] Athletes who return to their preinjury level have a risk of more than 20% to sustain a second ACL injury.[23 25] Regarding risk for a second ACL injury, 20 - 40% of adult athletes sustain a re-injury within two years following ACL-R despite successful rehabilitation, with young male athletes at highest risk.[24] Neuromuscular impairments have been shown to be predictive of secondary ACL injuries in young athletes.[28] Within the first five years following ACL-R, 4–12% of the patients suffer from a re-rupture of the ACL graft in the ipsilateral knee.[5 243 248] After RTS, mid- to long-term follow-up (minimum 5 years) failure rates of the graft up to 19% and a new rupture of the contralateral ACL in up to 24% of the cases were reported.[20-22] The risk for an ACL rupture in the contralateral knee was double as high (11.8%) five years or longer after an ACL-R compared to the risk for a rupture of the graft.[248] Those high rates for secondary injury, graft failure and rupture of the contralateral ACL are devastating, inacceptable, and underpin the need for further research in this field.

In summary, some RTS criteria can predict the likelihood to RTS activities but fail or may be suboptimal to identify deficits for the risk of ACL re-injury.[226 249] This is also because long-term studies are sparse. It is assumed that neuromuscular abilities, that cannot be assessed in those functional tests, may play a decisive role in ACL injury prevention.[29]

The high rates of re-injury and secondary ACL rupture,[20-23 25 243 248 250] low rates of returning to desired sport or competition level,[241] a lack of validity of RTS criteria after ACL-R[33] and missing consensus about safe RTS cut-off points[34-36] are inacceptable and indicate that more research regarding neuromuscular control and its role in dynamic knee stability for RTS is needed.[35 36 251]

1.4 Neuromuscular control

Sensory receptors and mechanoreceptors in the knee joint, especially in the ACL, are described in Chapter 1.1 in the respective paragraph “Innervation of the ACL and its role in proprioception”.

Reflexes acting on and around the knee

Already in 1900, Payr proposed a “ligamento-muscular protective reflex” and stated that receptors in the ACL would trigger contraction in the hamstrings when large forces would displace the tibia anteriorly beyond the physiological strain limits of the ACL.[252] Additionally, it could be shown that this reflex mechanism elicited activity in the semimembranosus, sartorius and VM muscle when forces on the MCL were applied.[253] The existence of the ligamento-muscular reflex arc for the ACL and the MCL was independently confirmed in animals,[254-256] and humans.[253 257] Investigating the role of muscles in regulating joint stability, this reflex arc was present in the ACL of cats as well, triggered at high-level loads which might be harmful for the ACL.[256] In humans, evidence of a ligamento-muscular reflex from sensory nerves of the ACL was published by several researchers.[53 102 258] The direct neuromuscular link between the sensory nerves of the ACL and all surrounding muscles of the knee in humans could be elicited by direct electrical stimulation of the ACL with fine wires.[102] Previously, it was stated that the ligamento-muscular protective reflex was triggered by the mechano-receptors of ligaments and not by other structures.[257] However, more recent studies suggest that the reflex response in vivo is triggered only to a small extent by elongation of the ACL and mediated by the direct ACL-hamstring reflex pathway.[259 260]

The ligament-spindle reflex is a powerful mechanism and extremely important to maintain knee stability.[53] An elongated spindle - a muscle’s stretch receptor - triggers a powerful action potential discharge which is monosynaptically transmitted to the motor units of the respective muscle.[53] As a result, the muscle contracts and resists elongation.[53] For example, with this powerful mechanism, the hamstrings contract and apply a posteriorly directed force to the proximal tibia, and thus decrease strain on the ACL in situations when forces on ligaments exceed normal, physiologically sustainable level.[256 261] Direct evidence for the ACL-hamstrings-reflex arc in humans was found.[101]

During tibial translation in posterior-anterior direction (relatively to the femur), the ACL comes under tension. In healthy subjects with an intact ACL, the hamstring muscles (BF, semimembranosus, ST muscle) act synergistically to this translational movement (Fig. 10).[135] This synergistic contraction occurs reflexively during appropriately rapid tibial translation, e.g., by a rope-pulley system triggering sudden tibia perturbations which induce a reflex response of the hamstring muscles.[135] After a sudden, anterior tibial translation, the magnitude of protective reflex activation of the hamstrings results in increased active joint stability of the knee; this mechanism protects against injury.[262] This indicates that the extent of the dynamic neuromuscular joint control of the knee stabilizing muscles can be measured closely to the physiological injury mechanism by surface (EMG) during standardized tibia perturbations.[135 263]

It has been shown that non-contact ACL ruptures happen 17-60 milliseconds (ms) after initial contact,[8 262 265] leaving a very short time frame for mechanosensory feedback (e.g., reflex response). With a reflex latency of 70 ms, at least 110 ms (reflex time plus electro-mechanical delay) must elapse before the muscles are able to generate sufficient activity after the ACL has been loaded. Therefore, this excitation reflex cannot serve as an automatic

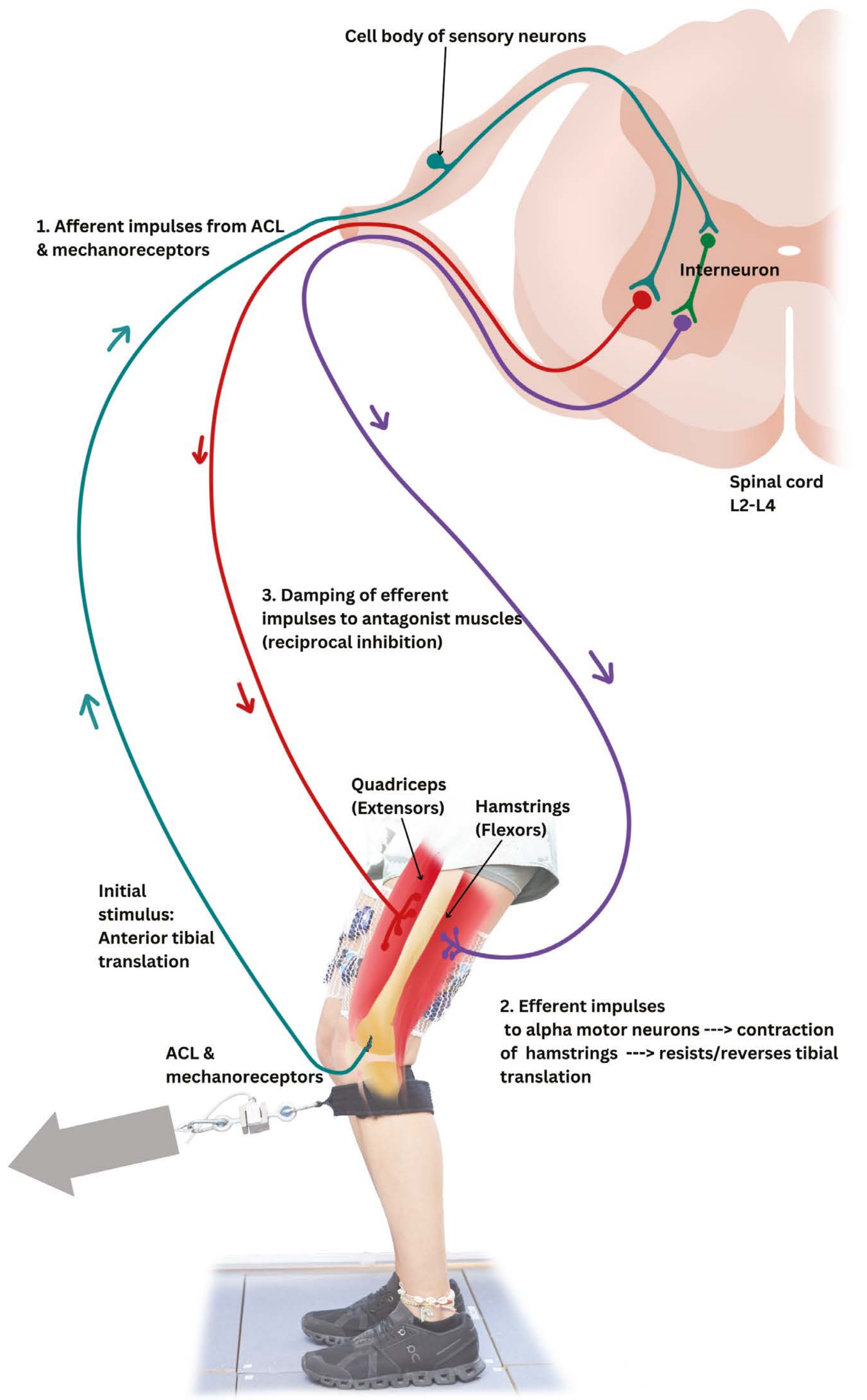

Figure 10: Anterior tibial translation as initial stimulus leads to afferent and efferent pathways (own drawing, adapted from Proffen et al., 2013[264])

Abbreviations: ACL = anterior cruciate ligament; L = lumbar vertebrae protective mechanism for the ACL.[266 267] Pre-activity and reactive neuromuscular responses regulate muscle and joint stiffness, which is influencing dynamic joint stability, consequently influencing ACL injury risk.[13] Thus, adequate pre-activation as well as neuromuscular reflexes may play a role to enhance protective knee stiffness.[262 265] Therefore, it is important to monitor neuromuscular control during exactly this time window from preactivity to perturbation onset and reflexive time windows after joint (stability) perturbation. Muscle activation patterns within this time window give insight into sensorimotor control mechanisms establishing knee joint stability.[135 263 268]

In patients with an ACL deficiency, the latency of hamstrings muscular response after applying a posterior shear force onto the tibia in humans (standing with 30° knee flexion) was nearly doubled in the ACL-deficient leg (mean 90.4 ms) compared to the contralateral side (49.1 ms).[102] As the latency of the reflex might be too long to be protective for the ACL under all stressful conditions, the reflex might primarily play an important role in functional stability of the knee.[269] In addition, the reflex seems to be excitatory during rest and inhibitory during muscular activity, and might be seen as a powerful spinal reflex with fast speed of reflex response due to the short neural pathway.[53] However, despite fast and powerful answers of this protection reflex under normal, daily conditions, tissue damage can occur in situations with overwhelming strength stimuli at high rates.[53]

Neuromuscular control during physical activities

In healthy subjects, it has been shown that an anterior-posterior tibial translation occurs during ambulation.[270] Stairway walking (ascent/descent) as an activity of daily live requires preactivity (joint stiffening) before initial contact and eccentric contraction[271] while 346% of the bodyweight loads the knee joint.[272] In physical activities such as side-cutting maneuvers, decreased pre-activity of the ST and BF muscle were observed in healthy female athletes compared to males.[273] During a single-legged landing task, it has been reported that pre-activity of the rectus femoris muscle predicts anterior tibial shear forces in healthy females, whereas lateral hamstring pre-activity predicts peak stance knee flexion angles.[274] In addition, it has been reported that sex-specific differences influence neuromuscular control during landing tasks.[275]

Regarding ACL rupture, a systematic review and meta-analysis revealed non-significant differences of the VM and VL, such as onset of hamstrings activation prior to landing, between an ACL-injured leg compared to a healthy control leg.[276] This indicates that onset of activation is not the parameter of choice to investigate sensorimotor control in participants with ACL injury.[276] In most studies, knee joint kinematics, kinetics and spatiotemporal gait have been investigated[26 277-281] whereas only few studies have analyzed electromyographic neuromuscular responses. A study by Hall et al. showed significantly increased amplitudes of the ST muscle while decreased rectus femoris amplitudes were found in patients after ACL-R.[26] Regarding chronic ACL ruptures and one-step climbing task, a longer total BF activity was observed in copers, while a delayed peak activity of the VL muscle was reported in non-copers.[279]
Pilot data from our research group regarding neuromuscular control in ADL showed neuromuscular alterations in patients suffering from an ACL rupture:[282-284]

- Altered neuromuscular activations were present one year after ACL-R in the affected limb compared to the contralateral limb and to a healthy matched control limb during stair descent.[282]
- During stair ascent in acutely injured participants with an ACL rupture, reduced neuromuscular activity of the quadriceps was found during preactivation (PRE) and weight-acceptance (WA) compared to healthy controls. Also hamstrings displayed a lower activation in acutely injured patients during push-off (PO). Small differences in the intra-individual comparison showed bilateral consequences following ACL rupture.[283]
- Significant differences in hamstrings' neuromuscular activity between the participants' injured and intact knee was found with higher reflex activity of the ST in participants' deficient knee at baseline, before ACL-R respectively. No differences were found in BF and ST activity in any timeframe comparing baseline with follow-up one year after ACL-R.[284]

Neuromuscular control as criterium for return to sport

A previous study reported that suddenly triggered tibia perturbations by a rope-pulley system induce a reflex response of the hamstring muscles.[135] According to Dhaher and colleagues, this reflex response of the hamstrings has a protective mechanism following sudden tibial translation, leading to adequate stiffness of the knee joint.[262] This result indicates that the extent of the dynamic neuromuscular joint control of the knee stabilizing muscles can be measured closely to the physiological injury mechanism. Nevertheless, nonspecific vertical jump squats, SLHD and side hops in addition to muscle strength tests are often used in daily clinical practice to assess active knee stability or functional performance in general.[32] The clinical examination provides information on passive joint stability and general knee "function".[165] Together with PROMs (e.g., questionnaires such as the KOOS), these assessments are used to determine RTS ability. However, it remains unknown whether the assessed knee joint is eligible for performance testing or even ready for RTS as sensorimotor control of the knee is not directly assessed by measuring reflexes and neuromuscular activation with EMG (Fig. 11).

In addition, a discrepancy between muscle function tests and self-reported outcome measures was found.[225] The commonly used tests of muscle function are not demanding or sensitive enough to differentiate between the ACL-injured and non-injured leg.[225] Consequently, the benefit of those tests for adequate decision making must be questioned as not every athlete returns to pre-injury level of sports.[241] Another gap is the lack of basic knowledge concerning neuromuscular control of the knee for functional stability during ADL, at work or in doing sports. Moreover, the high rates of re-injury and a limited consensus on what physical tests best depict proper knee function indicate that this examination and evaluation practice is insufficient.[29] Obviously, current assessments for RTS do not adequately reflect the level of knee stability needed for a safe RTS. Consequently, more insight into sensorimotor control mechanisms, as well as clear and objective outcomes for active knee stability could then eventually improve the RTS decision making process.[285]

Neuromuscular training is defined as a training to enhance unconscious motor responses by stimulating afferent signals and central mechanisms responsible for dynamic joint control.[286] These exercises are tailored to induce compensatory changes in muscle activation patterns and assist in facilitating dynamic joint stability.[286] Therefore, our definition of neuromuscular control of the knee joint is derived from the above mentioned,[286] and includes volitional and reflexive activity before and during static and dynamic tasks. Adequate neuromuscular control leads to active knee stability during controlled, known ADL but also in situations with sudden (tibial) perturbation. In these cases, sensorimotor competence does not only consist of adequate neuromuscular answers after initial foot-floor contact but also appropriate pre-activation of knee stabilizing muscles before landing. Commonly used physical performance tests do not give insight into those processes as they only assess neuromuscular control indirectly, as surrogates for knee stability. Therefore, direct approaches to measure muscle physiology leading to more appropriate outcome measures for sensorimotor competence are needed.

The methods used to assess and analyze neuromuscular control are described in Chapter 2.5 and in corresponding sections of Chapters 4-6.

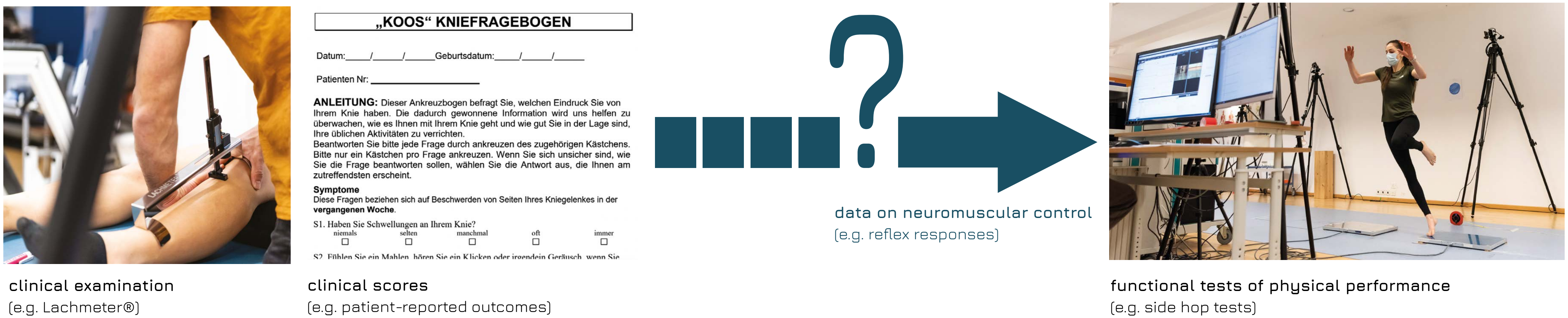

Figure 11: Gap between clinical examination, clinical scores, and functional tests of physical performance. Data on neuromuscular control has the potential to close this gap providing objective data on knee function and control for active knee joint stability (photos: ©Bern Movement Lab)

References

1. Hootman JM, Dick R, Agel J. Epidemiology of collegiate injuries for 15 sports: summary and recommendations for injury prevention initiatives. *J Athl Train* 2007;42(2):311-9. [published Online First: 2007/08/22]

2. Kaeding CC, Leger-St-Jean B, Magnussen RA. Epidemiology and Diagnosis of Anterior Cruciate Ligament Injuries. *Clin Sports Med* 2017;36(1): 1-8. doi: 10.1016/j.csm.2016.08.001 [published Online First: 2016/11/23]

3. Prodromos CC. The Anterior Cruciate Ligament. Reconstruction and Basic Science. 2 ed. Philadelphia: *Elsevier* 2018.

4. Lohmander LS, Englund PM, Dahl LL, et al. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. *Am J Sports Med* 2007;35(10):1756-69. doi: 10.1177/0363546507307396 [published Online First: 2007/09/01]

5. Sanders TL, Maradit Kremers H, Bryan AJ, et al. Incidence of Anterior Cruciate Ligament Tears and Reconstruction: A 21-Year Population-Based Study. *Am J Sports Med* 2016;44(6):1502-7. doi: 10.1177/0363546516629944 [published Online First: 2016/02/28]

6. Boden BP, Sheehan FT. Mechanism of non-contact ACL injury: OREF Clinical Research Award 2021. *J Orthop Res* 2022;40(3):531-40. doi: 10.1002/jor.25257 [published Online First: 2021/12/25]

7. Hewett TE, Myer GD, Ford KR. Anterior cruciate ligament injuries in female athletes: Part 1, mechanisms and risk factors. *Am J Sports Med* 2006a; 34(2):299-311. doi: 10.1177/0363546505284183 [published Online First: 2006/01/21]

8. Krosshaug T, Nakamae A, Boden BP, et al. Mechanisms of anterior cruciate ligament injury in basketball: video analysis of 39 cases. *Am J Sports Med* 2007;35(3):359-67. doi: 10.1177/0363546506293899 [published Online First: 2006/11/10]

9. Pfeifer CE, Beattie PF, Sacko RS, et al. Risk Factors Associated with Non-Contact Anterior Cruciate Ligament Injury: A Systematic Review. *Int J Sports Phys Ther* 2018;13(4):575-87. [published Online First: 2018/08/25]

10. Boden BP, Dean GS, Feagin JA, Jr., et al. Mechanisms of anterior cruciate ligament injury. *Orthopedics* 2000;23(6):573-8. doi: 10.3928/0147-7447-20000601-15 [published Online First: 2000/06/30]

11. Dai B, Mao M, Garrett WE, et al. Biomechanical characteristics of an anterior cruciate ligament injury in javelin throwing. *J Sport Health Sci* 2015;4(4):333-40.

12. Shimokochi Y, Shultz SJ. Mechanisms of non-contact anterior cruciate ligament injury. *J Athl Train* 2008;43(4):396-408. doi: 10.4085/1062-6050-43.4.396 [published Online First: 2008/08/01]

13. Hughes G, Watkins J. A risk-factor model for anterior cruciate ligament injury. *Sports Med* (Auckland, NZ) 2006;36(5):411-28. doi: 10.2165/00007256-200636050-00004 [published Online First: 2006/05/02]

14. Domnick C, Raschke MJ, Herbort M. Biomechanics of the anterior cruciate ligament: Physiology, rupture and reconstruction techniques. *World J Orthop* 2016;7(2):82-93. doi: 10.5312/wjo.v7.i2.82 [published Online First: 2016/03/01]

15. Sonnery-Cottet B, Colombet P. Partial tears of the anterior cruciate ligament. *Orthop Traumatol Surg Res* 2016;102(1 Suppl):S59-67. doi: 10.1016/j.otsr.2015.06.032 [published Online First: 2016/01/23]

16. Ardern CL, Webster KE, Taylor NF, et al. Return to sport following anterior cruciate ligament reconstruction surgery: a systematic review and meta-analysis of the state of play. *Br J Sports Med* 2011;45(7):596-606. doi: 10.1136/bjsm.2010.076364 [published Online First: 2011/03/15]

17. Friel NA, Chu CR. The role of ACL injury in the development of posttraumatic knee osteoarthritis. *Clin Sports Med* 2013;32(1):1-12. doi: 10.1016/j.csm.2012.08.017 [published Online First: 2012/11/28]

18. Lie MM, Risberg MA, Storheim K, et al. What's the rate of knee osteoarthritis 10 years after anterior cruciate ligament injury? An updated systematic review. *Br J Sports Med* 2019;53(18):1162-67. doi: 10.1136/bjsports-2018-099751 [published Online First: 2019/04/03]

19. Tan SH, Lau BP, Khin LW, et al. The Importance of Patient Sex in the Outcomes of Anterior Cruciate Ligament Reconstructions: A Systematic Review and Meta-analysis. *Am J Sports Med* 2016;44(1):242-54. doi: 10.1177/0363546515573008 [published Online First: 2015/03/25]

20. Deehan DJ, Salmon LJ, Webb VJ, et al. Endoscopic reconstruction of the anterior cruciate ligament with an ipsilateral patellar tendon autograft. A prospective longitudinal five-year study. *J Bone Joint Surg Br* 2000;82(7):984-91. doi: 10.1302/0301-620x.82b7.10573 [published Online First: 2000/10/21]

21. Hui C, Salmon LJ, Kok A, et al. Fifteen-year outcome of endoscopic anterior cruciate ligament reconstruction with patellar tendon autograft for „isolated" anterior cruciate ligament tear. *Am J Sports Med* 2011;39(1):89-98. doi: 10.1177/0363546510379975 [published Online First: 2010/10/22]

22. Pinczewski LA, Lyman J, Salmon LJ, et al. A 10-year comparison of anterior cruciate ligament reconstructions with hamstring tendon and patellar tendon autograft: a controlled, prospective trial. *Am J Sports Med* 2007;35(4):564-74. doi: 10.1177/0363546506296042 [published Online First: 2007/01/31]

23. Thomas AC, Villwock M, Wojtys EM, et al. Lower extremity muscle strength after anterior cruciate ligament injury and reconstruction. *J Athl Train* 2013;48(5):610-20.

24. Webster KE, Feller JA. Exploring the High Reinjury Rate in Younger Patients Undergoing Anterior Cruciate Ligament Reconstruction. *Am J Sports Med* 2016;44(11):2827-32. doi: 10.1177/0363546516651845 [published Online First: 2016/07/09]

25. Wiggins AJ, Grandhi RK, Schneider DK, et al. Risk of Secondary Injury in Younger Athletes After Anterior Cruciate Ligament Reconstruction: A Systematic Review and Meta-analysis. *Am J Sports Med* 2016;44(7):1861-76. doi: 10.1177/0363546515621554 [published Online First: 2016/01/17]

26. Hall M, Stevermer CA, Gillette JC. Gait analysis post anterior cruciate ligament reconstruction: knee osteoarthritis perspective. *Gait Posture* 2012;36 (1):56-60. doi: 10.1016/j.gaitpost.2012.01.003 [published Online First: 2012/02/09]

27. Grooms DR, Page SJ, Nichols-Larsen DS, et al. Neuroplasticity Associated With Anterior Cruciate Ligament Reconstruction. *J Orthop Sports Phys Ther* 2017a;47(3):180-89. doi: 10.2519/jospt.2017.7003 [published Online First: 2016/11/08]

28. Paterno MV, Schmitt LC, Ford KR, et al. Biomechanical measures during landing and postural stability predict second anterior cruciate ligament injury after anterior cruciate ligament reconstruction and return to sport. *Am J Sports Med* 2010;38(10):1968-78. doi: 10.1177/0363546510376053 [published Online First: 2010/08/13]

29. Grooms DR, Myer GD. Upgraded hardware horizontal line What about the software? Brain updates for return to play following ACL reconstruction. *Br J Sports Med* 2017b;51(5):418-19. doi: 10.1136/bjsports-2016-096658 [published Online First: 2016/11/01]

30. Filbay SR, Grindem H. Evidence-based recommendations for the management of anterior cruciate ligament (ACL) rupture. *Best Pract Res Clin Rheumatol* 2019;33(1):33-47. doi: 10.1016/j.berh.2019.01.018 [published Online First: 2019/08/23]

31. Van Melick N, Van Cingel RE, Brooijmans F, et al. Evidence-based clinical practice update: practice guidelines for anterior cruciate ligament rehabilitation based on a systematic review and multidisciplinary consensus. *Br J Sports Med* 2016; 50(24):1506-15.

32. Wilk KE, Arrigo CA. Rehabilitation Principles of the Anterior Cruciate Ligament Reconstructed Knee: Twelve Steps for Successful Progression and Return to Play. *Clin Sports Med* 2017;36(1):189-232. doi: 10.1016/j.csm.2016.08.012 [published Online First: 2016/11/23]

33. Kaplan Y, Witvrouw E. When is it safe to return to sport after ACL reconstruction? Reviewing the criteria. *Sports health* 2019;11(4):301-05.

34. Ardern CL, Glasgow P, Schneiders A, et al. 2016 Consensus statement on return to sport from the First World Congress in Sports Physical Therapy, Bern. *Br J Sports Med* 2016;50(14):853-64. doi: 10.1136/bjsports-2016-096278 [published Online First: 2016/05/27]

35. Buckthorpe M. Optimising the Late-Stage Rehabilitation and Return-to-Sport Training and Testing Process After ACL Reconstruction. *Sports Med* (Auckland, NZ) 2019;49(7):1043-58. doi: 10.1007/s40279-019-01102-z [published Online First: 2019/04/21]

36. Dingenen B, Gokeler A. Optimization of the Return-to-Sport Paradigm After Anterior Cruciate Ligament Reconstruction: A Critical Step Back to Move Forward. *Sports Med* (Auckland, NZ) 2017; 47(8):1487-500. doi: 10.1007/s40279-017-0674-6 [published Online First: 2017/01/13]

37. Hassebrock JD, Gulbrandsen MT, Asprey WL, et al. Knee Ligament Anatomy and Biomechanics. *Sports Med Arthrosc Rev* 2020;28(3):80-86. doi: 10.1097/JSA.0000000000000279 [published Online First: 2020/08/03]

38. Kweon C, Lederman ES, Chhabra A. Anatomy and biomechanics of the cruciate ligaments and their surgical implications. . In: Fanelli CG, ed. The Multiple Ligament Injured Knee: A Practical Guide to Management. New York, NY.: *Springer Science & Business Media* 2013:17-27.

39. Flandry F, Hommel G. Normal anatomy and biomechanics of the knee. *Sports Med Arthrosc Rev* 2011;19(2):82-92. doi: 10.1097/JSA.0b013e318210c0aa [published Online First: 2011/05/05]

40. Roessler PP, Schuttler KF, Heyse TJ, et al. The anterolateral ligament (ALL) and its role in rotational extra-articular stability of the knee joint: a review of anatomy and surgical concepts. *Arch Orthop Trauma Surg* 2016;136(3):305-13. doi: 10.1007/s00402-015-2395-3 [published Online First: 2015/12/31]

41. Claes S, Vereecke E, Maes M, et al. Anatomy of the anterolateral ligament of the knee. *J Anat* 2013;223(4):321-8. doi: 10.1111/joa.12087 [published Online First: 2013/08/03]

42. Parsons EM, Gee AO, Spiekerman C, et al. The biomechanical function of the anterolateral ligament of the knee. *Am J Sports Med* 2015;43(3):669-74. doi: 10.1177/0363546514562751 [published Online First: 2015/01/04]

43. Chahla J, Geeslin AG, Cinque ME, et al. Biomechanical Proof for the Existence of the Anterolateral Ligament. *Clin Sports Med* 2018;37(1):33-40. doi: 10.1016/j.csm.2017.07.003 [published Online First: 2017/11/28]

44. Kang KT, Koh YG, Park KM, et al. Effects of the Anterolateral Ligament and Anterior Cruciate Ligament on Knee Joint Mechanics: A Biomechanical Study Using Computational Modeling. *Orthop J Sports Med* 2022;10(4):23259671221084970. doi: 10.1177/23259671221084970 [published Online First: 2022/04/12]

45. Smigielski R, Becker R, Zdanowicz U, et al. Medial meniscus anatomy-from basic science to treatment. *Knee Surg Sports Traumatol Arthrosc* 2015;23(1):8-14. doi: 10.1007/s00167-014-3476-5 [published Online First: 2014/12/30]

46. Krych AJ, Wu IT, Desai VS, et al. High Rate of Missed Lateral Meniscus Posterior Root Tears on Preoperative Magnetic Resonance Imaging. *Orthop J Sports Med* 2018;6(4):2325967118765722. doi: 10.1177/2325967118765722 [published Online First: 2018/04/18]

47. Krych AJ, LaPrade MD, Cook CS, et al. Lateral Meniscal Oblique Radial Tears Are Common With ACL Injury: A Classification System Based on Arthroscopic Tear Patterns in 600 Consecutive Patients. *Orthop J Sports Med* 2020;8(5): 2325967120921737. doi: 10.1177/2325967120921737 [published Online First: 2020/06/04]

48. Hagino T, Ochiai S, Senga S, et al. Meniscal tears associated with anterior cruciate ligament injury. *Arch Orthop Trauma Surg* 2015;135(12):1701-6. doi: 10.1007/s00402-015-2309-4 [published Online First: 2015/08/20]

49. Flaxman TE, Alkjaer T, Simonsen EB, et al. Predicting the Functional Roles of Knee Joint Muscles from Internal Joint Moments. *Med Sci Sports Exerc* 2017;49(3):527-37. doi: 10.1249/MSS.0000000000001125 [published Online First: 2016/10/19]

50. Draganich LF, Vahey JW. An in vitro study of anterior cruciate ligament strain induced by quadriceps and hamstrings forces. *J Orthop Res* 1990;8(1):57-63. doi: 10.1002/jor.1100080107 [published Online First: 1990/01/01]

51. MacWilliams BA, Wilson DR, DesJardins JD, et al. Hamstrings cocontraction reduces internal rotation, anterior translation, and anterior cruciate ligament load in weight-bearing flexion. *J Orthop Res* 1999;17(6):817-22. doi: 10.1002/jor.1100170605 [published Online First: 2000/01/13]

52. Victor J, Labey L, Wong P, et al. The influence of muscle load on tibiofemoral knee kinematics. *J Orthop Res* 2010;28(4):419-28. doi: 10.1002/jor.21019 [published Online First: 2009/11/06]

53. Solomonow M, Krogsgaard M. Sensorimotor control of knee stability. A review. *Scand J Med Sci Sports* 2001;11(2):64-80. doi: 10.1034/j.1600-0838.2001.011002064.x [published Online First: 2001/03/17]

54. Buckthorpe M. Recommendations for Movement Re-training After ACL Reconstruction. *Sports Med* (Auckland, NZ) 2021;51(8):1601-18. doi: 10.1007/s40279-021-01454-5 [published Online First: 2021/04/12]

55. Rhim HC, Lee JH, Han SB, et al. Role of the Triceps Surae Muscles in Patients Undergoing Anterior Cruciate Ligament Reconstruction: A Matched Case-Control Study. *J Clin Med* 2020;9(10) doi: 10.3390/jcm9103215 [published Online First: 2020/10/11]

56. Wilke J, Krause F, Vogt L, et al. What is evidence-based about myofascial chains: a systematic review.. *Arch Phys Med Rehabil* 2016;97:454-61. doi: 0.1016/j. apmr.2015.07.023

57. Myers TM. Anatomy Trains. Myofascial Meridians for Manual Therapists and Movement Professionals. 4th ed: *Elsevier* 2020:360.

58. Adstrum S, Hedley G, Schleip R, et al. Defining the fascial system. *J Bodyw Mov Ther* 2017;21(1):173-77. doi: 10.1016/j.jbmt.2016.11.003 [published Online First: 2017/02/09]

59. Stecco C. Functional atlas of the human fascial system. Oxford: *Elsevier Health Sciences* 2014.

60. Stecco C, Schleip R. A fascia and the fascial system. *J Bodyw Mov Ther* 2016;20(1):139-40. doi: 10.1016/j.jbmt.2015.11.012 [published Online First: 2016/02/20]

61. Gurtner K. Slings Essentials: Resourced-oriented, integrative learning (Slings Myofascial Training®, Volume 2). 2021 ed: independent 2021.

62. Gurtner K, Myers T. Anatomy Trains in Motion: Embrain and embody myofascial meridian anatomy (Slings Myofascial Training®, Volume 1): independent 2019.

63. Odensten M, Gillquist J. Functional anatomy of the anterior cruciate ligament and a rationale for reconstruction. *J Bone Joint Surg Am* 1985;67(2):257-62. [published Online First: 1985/02/01]

64. Petersen W, Tillmann B. Structure and vascularization of the cruciate ligaments of the human knee joint. *Anat Embriol* 1999; 200(3):325-34.

65. Butler DL, Noyes FR, Grood ES. Ligamentous restraints to anterior-posterior drawer in the hu man knee. A biomechanical study. *J Bone Joint Surg Am* 1980;62(2):259-70. [published Online First: 1980/03/01]

66. Markolf KL, Mensch JS, Amstutz HC. Stiffness and laxity of the knee--the contributions of the supporting structures. A quantitative in vitro study. *J Bone Joint Surg Am* 1976;58(5):583-94. [published Online First: 1976/07/01]

67. Takeda Y, Xerogeanes JW, Livesay GA, et al. Biomechanical function of the human anterior cruciate ligament. *Arthroscopy* 1994;10(2):140-7. doi: 10.1016/s0749-8063(05)80081-7 [published Online First: 1994/04/01]

68. Beynnon BD, Johnson RJ, Fleming BC, et al. The effect of functional knee bracing on the anterior cruciate ligament in the weightbearing and non weightbearing knee. *Am J Sports Med* 1997;25(3):353-9. doi: 10.1177/036354659702500314 [published Online First: 1997/05/01]

69. Kapandji AI. Funktionelle Anatomie der Gelenke: Schematisierte und kommentierte Zeichnungen zur menschlichen Biomechanik. 6 ed. Stuttgart, New York: *Thieme* 2016.

70. Matsumoto H, Suda Y, Otani T, et al. Roles of the anterior cruciate ligament and the medial collateral ligament in preventing valgus instability. Journal of orthopaedic science : *J Orthop Sci* 2001; 6(1):28-32. doi: 10.1007/s007760170021 [published Online First: 2001/04/06]

71. Freeman MA, Pinskerova V. The movement of the normal tibio-femoral joint. *J Biomech* 2005;38(2): 197-208. doi: 10.1016/j.jbiomech.2004.02.006 [published Online First: 2004/12/16]

72. Duthon VB, Barea C, Abrassart S, et al. Anatomy of the anterior cruciate ligament. *Knee Surg Sports Traumatol Arthrosc* 2006;14(3):204-13. doi: 10.1007/s00167-005-0679-9 [published Online First: 2005/10/20]

73. Sakane M, Fox RJ, Woo SL, et al. In situ forces in the anterior cruciate ligament and its bundles in response to anterior tibial loads. *J Orthop Res* 1997;15(2):285-93. doi: 10.1002/jor.1100150219 [published Online First: 1997/03/01]

74. Chhabra A, Starman JS, Ferretti M, et al. Anatomic, radiographic, biomechanical, and kinematic evaluation of the anterior cruciate ligament and its two functional bundles. *J Bone Joint Surg Am* 2006;88 Suppl 4:2-10. doi: 10.2106/JBJS.F.00616 [published Online First: 2006/12/05]

75. Forsythe B, Kopf S, Wong AK, et al. The location of femoral and tibial tunnels in anatomic double-bundle anterior cruciate ligament reconstruction analyzed by three-dimensional computed tomography models. *J Bone Joint Surg Am* 2010; 92(6):1418-26. doi: 10.2106/JBJS.I.00654 [published Online First: 2010/06/03]

76. Fu FH, Harner CD, Johnson DL, et al. Biomechanics of knee ligaments: basic concepts and clinical application. *J Bone Joint Surg* 1993;75(11): 1716-27.

77. Girgis FG, Marshall JL, Monajem A. The cruciate ligaments of the knee joint. Anatomical, functional and experimental analysis. *Clin Orthop Relat Res* 1975(106):216-31. doi: 10.1097/00003086-197501000-00033 [published Online First: 1975/01/01]

78. Harner CD, Baek GH, Vogrin TM, et al. Quantitative analysis of human cruciate ligament insertions. *Arthroscopy* 1999;15(7):741-9. doi:10.1016/s0749-8063(99)70006-x [published Online First: 1999/10/19]

79. Takahashi M, Doi M, Abe M, et al. Anatomical study of the femoral and tibial insertions of the anteromedial and posterolateral bundles of human anterior cruciate ligament. *Am J Sports Med* 2006;34(5):787-92. doi: 10.1177/0363546505282625 [published Online First: 2006/02/03]

80. Woo SL, Abramowitch SD, Kilger R, et al. Biomechanics of knee ligaments: injury, healing, and repair. *J Biomech* 2006;39(1):1-20. doi: 10.1016/j.jbiomech.2004.10.025 [published Online First: 2005/11/08]

81. Petersen W, Tillmann B. Anatomie und Funktion des vorderen Kreuzbandes. *Orthopäde* 2002;31: 710-18. doi: 10.1007/s00132-002-0330-0

82. Arnoczky SP. Anatomy of the anterior cruciate ligament. *Clin Orthop Relat Res* 1983(172):19-25. [published Online First: 1983/01/01]

83. Dargel J, Gotter M, Mader K, et al. Biomechanics of the anterior cruciate ligament and implications for surgical reconstruction. *Strategies Trauma Limb Reconstr* 2007;2(1):1-12. doi: 10.1007/s11751-007-0016-6 [published Online First: 2008/04/23]

84. Amis AA, Dawkins GP. Functional anatomy of the anterior cruciate ligament. Fibre bundle actions related to ligament replacements and injuries. *J Bone Joint Surg Br* 1991;73(2):260-7. doi: 10.1302/0301-620X.73B2.2005151 [published Online First: 1991/03/01]

85. Butler DL, Guan Y, Kay MD, et al. Location-dependent variations in the material properties of the anterior cruciate ligament. *J Biomech* 1992;25(5): 511-8. doi: 10.1016/0021-9290(92)90091-e [published Online First: 1992/05/01]

86. Woo SL, Hollis JM, Adams DJ, et al. Tensile properties of the human femur-anterior cruciate ligament-tibia complex. The effects of specimen age and orientation. *Am J Sports Med* 1991;19(3):217-25. doi: 10.1177/036354659101900303 [published Online First: 1991/05/01]

87. Morrison JB. The mechanics of the knee joint in relation to normal walking. *J Biomech* 1970;3(1):51-61. doi:10.1016/0021-9290(70)90050-3 [published Online First: 1970/01/01]

88. Morrison JB. Function of the knee joint in various activities. *Biomed Eng* 1969;4(12):573-80. [published Online First: 1969/12/01]

89. Kondo E, Merican AM, Yasuda K, et al. Biomechanical comparison of anatomic double-bundle, anatomic single-bundle, and nonanatomic single-bundle anterior cruciate ligament reconstructions. *Am J Sports Med* 2011;39(2):279-88. doi: 10.1177/0363546510392350 [published Online First: 2011/01/18]

90. Kondo E, Merican AM, Yasuda K, et al. Biomechanical analysis of knee laxity with isolated anteromedial or posterolateral bundle-deficient anterior cruciate ligament. *Arthroscopy* 2014;30(3): 335-43. doi: 10.1016/j.arthro.2013.12.003 [published Online First: 2014/03/04]

91. Zantop T, Herbort M, Raschke MJ, et al. The role of the anteromedial and posterolateral bundles of the anterior cruciate ligament in anterior tibial translation and internal rotation. *Am J Sports Med* 2007;35(2):223-7. doi: 10.1177/036354650 6294571 [published Online First: 2006/12/13]

92. Haus J, Halata Z. Innervation of the anterior cruciate ligament. *Int Orthop* 1990;14(3):293-6. doi: 10.1007/BF00178762 [published Online First: 1990/01/01]

93. Kennedy JC, Alexander IJ, Hayes KC. Nerve supply of the human knee and its functional importance. *Am J Sports Med* 1982;10(6):329-35. doi: 10.1177/036354658201000601 [published Online First: 1982/11/01]

94. Biedert RM, Stauffer E, Friederich NF. Occurrence of free nerve endings in the soft tissue of the knee joint. A histologic investigation. *Am J Sports Med* 1992;20(4):430-3. doi: 10.1177/036354659202000411 [published Online First: 1992/07/01]

95. Schutte MJ, Dabezies EJ, Zimny ML, et al. Neural anatomy of the human anterior cruciate ligament. *J Bone Joint Surg Am* 1987;69(2):243-7. [published Online First: 1987/02/01]

96. Zimny ML, Schutte M, Dabezies E. Mechanoreceptors in the human anterior cruciate ligament. *Anat Rec* 1986;214(2):204-9. doi: 10.1002/ar.1092140216 [published Online First: 1986/02/01]

97. Relph N, Herrington L, Tyson S. The effects of ACL injury on knee proprioception: a meta-analysis. *Physiotherapy* 2014;100(3):187-95. doi: 10.1016/j.physio.2013.11.002 [published Online First: 2014/04/03]

98. Schultz RA, Miller DC, Kerr CS, et al. Mechanoreceptors in human cruciate ligaments. A histo logical study. *J Bone Joint Surg Am* 1984;66(7):1072-6. [published Online First: 1984/09/01]

99. Cabuk H, Kusku Cabuk F. Mechanoreceptors of the ligaments and tendons around the knee. *Clin Anat* 2016;29(6):789-95. doi: 10.1002/ca.22743 [published Online First: 2016/07/05]

100. Hogervorst T, Brand RA. Mechanoreceptors in joint function. *J Bone Joint Surg Am* 1998;80(9): 1365-78. doi: 10.2106/00004623-199809000-00018 [published Online First: 1998/10/06]

101. Tsuda E, Okamura Y, Otsuka H, et al. Direct evidence of the anterior cruciate ligament-hamstring reflex arc in humans. . *Am J Sports Med* 2001;29(1):83-87.

102. Beard DJ, Kyberd PJ, O'Connor JJ, et al. Reflex hamstring contraction latency in anterior cruciate ligament deficiency. *J Orthop Res* 1994;12(2):219-28. doi: 10.1002/jor.1100120211 [published Online First: 1994/03/01]

103. Spindler KP, Wright RW. Clinical practice. Anterior cruciate ligament tear. *N Engl J Med* 2008;359(20):2135-42. doi: 10.1056/NEJMcp 0804745 [published Online First: 2008/11/14]

104. Prodromos CC, Han Y, Rogowski J, et al. A meta-analysis of the incidence of anterior cruciate ligament tears as a function of gender, sport, and a knee injury-reduction regimen. *Arthroscopy* 2007;23(12):1320-25 e6. doi: 10.1016/j.arthro. 2007.07.003 [published Online First: 2007/ 12/08]

105. Agel J, Arendt EA, Bershadsky B. Anterior cruciate ligament injury in national collegiate athletic association basketball and soccer: a 13-year review. *Am J Sports Med* 2005;33(4):524-30. doi: 10.1177/0363546504269937 [published Online First: 2005/02/22]

106. Moses B, Orchard J, Orchard J. Systematic review: Annual incidence of ACL injury and surgery in various populations. *Res Sports Med* 2012; 20(3-4):157-79. doi: 10.1080/15438627.2012. 680633 [published Online First: 2012/06/30]

107. Bollen S. Epidemiology of knee injuries: diagnosis and triage. *Br J Sports Med* 2000;34(3): 227-8. doi: 10.1136/bjsm.34.3.227-a [published Online First: 2000/06/15]

108. Gans I, Retzky JS, Jones LC, et al. Epidemiology of Recurrent Anterior Cruciate Ligament In juries in National Collegiate Athletic Association Sports: The Injury Surveillance Program, 2004-2014. *Orthop J Sports Med* 2018; 6(6): 2325967118777823. doi: 10.1177/23259671 18777823 [published Online First: 2018/07/07]

109. Gianotti SM, Marshall SW, Hume PA, et al. Incidence of anterior cruciate ligament injury and other knee ligament injuries: a national population-based study. *J Sci Med Sport* 2009; 12(6):622-7. doi: 10.1016/j.jsams.2008.07.005 [published Online First:2008/10/07]

110. Granan LP, Forssblad M, Lind M, et al. The Scandinavian ACL registries 2004-2007: baseline epidemiology. *Acta Orthop* 2009;80(5):563-7. doi: 10.3109/17453670903350107 [published Online First: 2009/11/18]

111. Janssen KW, Orchard JW, Driscoll TR, et al. High incidence and costs for anterior cruciate ligament reconstructions performed in Australia from 2003-2004 to 2007-2008: time for an anterior cruciate ligament register by Scandinavian model? *Scand J Med Sci Sports* 2012;22(4):495-501. doi:10.1111/j.1600-0838.2010.01253.x [published Online First: 2011/01/08]

112. Nielsen AB, Yde J. Epidemiology of acute knee injuries: a prospective hospital investigation. *J Trauma* 1991;31(12):1644-8. doi:10.1097/00005373-199112000-00014 [published Online First: 1991/12/01]

113. Nordenvall R, Bahmanyar S, Adami J, et al. A population-based nationwide study of cruciate ligament injury in Sweden, 2001-2009: incidence, treatment, and sex differences. *Am J Sports Med* 2012;40(8):1808-13. doi: 10.1177/0363546512449306 [published Online First: 2012/06/12]

114. Jacobs CL, Hincapie CA, Cassidy JD. Musculoskeletal injuries and pain in dancers: a systematic review update. *J Dance Med Sci* 2012;16(2):74-84. [published Online First: 2012/06/13]

115. Griffin LY, Albohm MJ, Arendt EA, et al. Understanding and preventing noncontact anterior cruciate ligament injuries: a review of the Hunt Valley II meeting, January 2005. *Am J Sports Med* 2006;34(9):1512-32. doi: 10.1177/0363546506286866 [published Online First: 2006/08/15]

116. Mall NA, Chalmers PN, Moric M, et al. Incidence and trends of anterior cruciate ligament reconstruction in the United States. *Am J Sports Med* 2014;42(10):2363-70. doi:10.1177/0363546514542796 [published Online First: 2014/08/03]

117. Mountcastle SB, Posner M, Kragh JF, Jr., et al. Gender differences in anterior cruciate ligament injury vary with activity: epidemiology of anterior cruciate ligament injuries in a young, athletic population. *Am J Sports Med* 2007;35(10):1635-42. doi: 10.1177/0363546507302917 [published Online First: 2007/05/24]

118. Granan LP, Bahr R, Steindal K, et al. Development of a national cruciate ligament surgery registry: the Norwegian National Knee Ligament Registry. *Am J Sports Med* 2008;36(2):308-15. doi: 10.1177/0363546507308939 [published Online First: 2007/11/09]

119. Lind M, Menhert F, Pedersen AB. The first results from the Danish ACL reconstruction registry: epidemiologic and 2 year follow-up results from 5,818 knee ligament reconstructions. *Knee Surg Sports Traumatol Arthrosc* 2009;17(2):117-24. doi: 10.1007/s00167-008-0654-3 [published Online First: 2008/11/01]

120. Kohn L, Rembeck E, Rauch A. [Anterior cruciate ligament injury in adults : Diagnostics and treatment]. *Orthopade* 2020;49(11):1013-28. doi: 10.1007/s00132-020-03997-3 [published Online First: 2020/10/22]

121. Sobau C, Zimmerer A, Schopf W, et al. Anterior cruciate ligament rupture – when is conservative treatment possible, when is surgery necessary? *OUP* 2017;7(8):374–79. doi: 10.3238/oup.2017.0374–0379

122. Van der Bracht H, Goubau L, Stuyts B, et al. Surgical management of anterior cruciate ligament injuries in Belgium anno 2013. *Acta Orthop Belg* 2015;81(4):738-46. [published Online First: 2016/01/23]

123. Swiss Medical Board. Ruptur des vorderen Kreuzbandes: operative oder konservative Behandlung? , 2009:37. https://www.swiss-medicalboard.ch/fileadmin/public/news/2011_und_aelter/bericht__smb_kreuz-bandriss_lang_2009.pdf

124. Kobayashi H, Kanamura T, Koshida S, et al. Mechanisms of the anterior cruciate ligament injury in sports activities: a twenty-year clinical research of 1,700 athletes. *J Sports Sci Med* 2010;9(4):669-75. [published Online First: 2010/01/01]

125. Walden M, Hagglund M, Werner J, et al. The epidemiology of anterior cruciate ligament injury in football (soccer): a review of the literature from a gender-related perspective. *Knee Surg Sports Traumatol Arthrosc* 2011;19(1):3-10. doi: 10.1007/s00167-010-1172-7 [published Online First: 2010/06/10]

126. Ireland ML. The female ACL: why is it more prone to injury? *Orthop Clin North Am* 2002;33(4):637-51. doi: 10.1016/s0030-5898(02)00028-7 [published Online First: 2003/01/17]

127. Uhorchak JM, Scoville CR, Williams GN, et al. Risk factors associated with noncontact injury of the anterior cruciate ligament: a prospective four-year evaluation of 859 West Point cadets. *Am J Sports Med* 2003;31(6):831-42. doi:10.1177/03635465030310061801 [published Online First: 2003/11/19]

128. Arendt E, Dick R. Knee injury patterns among men and women in collegiate basketball and soccer. NCAA data and review of literature. *Am J Sports Med* 1995;23(6):694-701. doi: 10.1177/036354659502300611 [published Online First: 1995/11/01]

129. Bjordal JM, Arnly F, Hannestad B, et al. Epidemiology of anterior cruciate ligament injuries in soccer. *Am J Sports Med* 1997;25(3):341-5. doi: 10.1177/036354659702500312 [published Online First: 1997/05/01]

130. Piasecki DP, Spindler KP, Warren TA, et al. Intraarticular injuries associated with anterior cruciate ligament tear: findings at ligament reconstruction in high school and recreational athletes. An analysis of sex-based differences. *Am J Sports Med* 2003;31(4):601-5. doi:10.1177/03635465030310042101 [published Online First: 2003/07/16]

131. Prodromos CC, Han Y, Rogowski J, et al. A meta-analysis of the incidence of anterior cruciate ligament tears as a function of gender, sport, and a knee injury-reduction regimen. *Arthroscopy* 2007;23(12):1320-25.e6.doi: 10.1016/j.arthro.2007.07.003

132. Shultz SJ, Schmitz RJ, Benjaminse A, et al. ACL Research Retreat VI: an update on ACL injury risk and prevention. *J Athl Train* 2012;47(5):591-603. doi: 10.4085/1062-6050-

133. Olsen OE, Myklebust G, Engebretsen L, et al. Injury mechanisms for anterior cruciate ligament injuries in team handball: a systematic video analysis. *Am J Sports Med* 2004;32(4):1002-12. doi: 10.1177/0363546503261724 [published Online First: 2004/05/20]

134. Hewett TE, Zazulak BT, Myer GD, et al. A review of electromyographic activation levels, timing differences, and increased anterior cruciate ligament injury incidence in female athletes. *Br J Sports Med* 2005a;39(6):347-50. doi: 10.1136/bjsm.2005.018572 [published Online First: 2005/05/25]

135. Bruhn S, Leukel C, Gollhofer A. Differential effects of stimulus characteristics during knee joint perturbation on hamstring and quadriceps reflex responses. *Hum Mov Sci* 2011;30(6):1079-91. doi: 10.1016/j.humov.2011.07.015 [published Online First: 2011/11/02]

136. Boden BP, Torg JS, Knowles SB, et al. Video analysis of anterior cruciate ligament injury: abnormalities in hip and ankle kinematics. *Am J Sports Med* 2009a;37(2):252-9. doi: 10.1177/0363546508328107 [published Online First: 2009/02/03]

137. Boden BP, Breit I, Sheehan FT. Tibiofemoral alignment: contributing factors to noncontact anterior cruciate ligament injury. *J Bone Joint Surg Am* 2009b;91(10):2381-9. doi: 10.2106/JBJS.H.01721 [published Online First: 2009/10/03]

138. Hewett TE, Myer GD, Ford KR, et al. Biomechanical measures of neuromuscular control and valgus loading of the knee predict anterior cruciate ligament injury risk in female athletes: a prospective study. *Am J Sports Med* 2005b;33(4):492-501. doi: 10.1177/0363546504269591 [published Online First: 2005/02/22]

139. Zebis MK, Andersen LL, Bencke J, et al. Identification of athletes at future risk of anterior cruciate ligament ruptures by neuromuscular screening. *Am J Sports Med* 2009;37(10):1967-73. doi: 10.1177/0363546509335000 [published Online First: 2009/07/04]

140. Del Bel MJ, Flaxman TE, Smale KB, et al. A hierarchy in functional muscle roles at the knee is influenced by sex and anterior cruciate ligament deficiency. *Clin Biomech* (Bristol, Avon) 2018;57:129-36. doi: 10.1016/j.clinbiomech.2018.06.014 [published Online First: 2018/07/10]

141. Huston LJ, Wojtys EM. Neuromuscular performance characteristics in elite female athletes. *Am J Sports Med* 1996;24(4):427-36. doi: 10.1177/036354659602400405 [published Online First: 1996/07/01]

142. Shultz SJ, Perrin DH, Adams MJ, et al. Neuromuscular Response Characteristics in Men and Women After Knee Perturbation in a Single-Leg, Weight-Bearing Stance. *J Athl Train* 2001;36(1):37-43. [published Online First: 2003/08/26]

143. Sigward SM, Powers CM. The influence of gender on knee kinematics, kinetics and muscle activation patterns during side-step cutting. *Clin Biomech* (Bristol, Avon) 2006;21(1):41-8. doi: 10.1016/j.clinbiomech.2005.08.001 [published Online First: 2005/10/08]

144. Urabe Y, Kobayashi R, Sumida S, et al. Electromyographic analysis of the knee during jump landing in male and female athletes. *Knee* 2005;12(2):129-34. doi: 10.1016/j.knee.2004.05.002 [published Online First: 2005/03/08]

145. White KK, Lee SS, Cutuk A, et al. EMG power spectra of intercollegiate athletes and anterior cruciate ligament injury risk in females. *Med Sci Sports Exerc* 2003;35(3):371-6. doi: 10.1249/01.MSS.0000053703.65057.31 [published Online First: 2003/03/06]

146. Chappell JD, Creighton RA, Giuliani C, et al. Kinematics and electromyography of landing preparation in vertical stop-jump: risks for noncontact anterior cruciate ligament injury. *Am J Sports Med* 2007;35(2):235-41. doi: 10.1177/0363546506294077 [published Online First: 2006/11/10]

147. Hanson AM, Padua DA, Troy Blackburn J, et al. Muscle activation during side-step cutting maneuvers in male and female soccer athletes. *J Athl Train* 2008;43(2):133-43. doi: 10.4085/1062-6050-43.2.133 [published Online First: 2008/03/18]

148. Benjaminse A, Gokeler A, Fleisig GS, et al. What is the true evidence for gender-related differences during plant and cut maneuvers? A systematic review. *Knee Surg Sports Traumatol Arthrosc* 2011;19(1):42-54. doi: 10.1007/s00167-010-1233-y [published Online First: 2010/08/25]

149. Hannah R, Folland JP, Smith SL, et al. Explosive hamstrings-to-quadriceps force ratio of males versus females. *Eur J Appl Physiol* 2015;115(4):837-47. doi: 10.1007/s00421-014-3063-y [published Online First: 2014/12/06]

150. Nimphius S, McBride JM, Rice PE, et al. Comparison of Quadriceps and Hamstring Muscle Activity during an Isometric Squat between Strength-Matched Men and Women. *J Sports Sci Med* 2019;18(1):101-08. [published Online First: 2019/02/23]

151. Myklebust G, Maehlum S, Holm I, et al. A prospective cohort study of anterior cruciate ligament injuries in elite Norwegian team handball. *Scand J Med Sci Sports* 1998;8(3):149-53. doi: 10.1111/j.1600-0838.1998.tb00185.x [published Online First: 1998/07/11]

152. Anderson MJ, Browning WM, 3rd, Urband CE, et al. A Systematic Summary of Systematic Reviews on the Topic of the Anterior Cruciate Ligament. *Orthop J Sports Med* 2016;4(3):2325967116634074. doi: 10.1177/2325967116634074 [published Online First: 2016/04/06]

153. Dowling AV, Corazza S, Chaudhari AM, et al. Shoe-surface friction influences movement strategies during a sidestep cutting task: implications for anterior cruciate ligament injury risk. *Am J Sports Med* 2010;38(3):478-85. doi: 10.1177/0363546509348374 [published Online First: 2010/03/03]

154. Drakos MC, Hillstrom H, Voos JE, et al. The effect of the shoe-surface interface in the development of anterior cruciate ligament strain. *J Biomech Eng* 2010;132(1):011003. doi: 10.1115/1.4000118 [published Online First: 2010/06/09]

155. Olsen OE, Myklebust G, Engebretsen L, et al. Relationship between floor type and risk of ACL injury in team handball. *Scand J Med Sci Sports* 2003;13(5):299-304. doi: 10.1034/j.1600-0838.2003.00329.x [published Online First: 2003/09/26]

156. Shelbourne KD, Davis TJ, Klootwyk TE. The relationship between intercondylar notch width of the femur and the incidence of anterior cruciate ligament tears. A prospective study. *Am J Sports Med* 1998;26(3):402-8. doi: 10.1177/03635465980260031001 [published Online First: 1998/06/09]

157. Simon RA, Everhart JS, Nagaraja HN, et al. A case-control study of anterior cruciate ligament volume, tibial plateau slopes and intercondylar notch dimensions in ACL-injured knees. *J Biomech* 2010;43(9):1702-7. doi: 10.1016/j.jbiomech.2010.02.033 [published Online First: 2010/04/14]

158. Stijak L, Herzog RF, Schai P. Is there an influence of the tibial slope of the lateral condyle on the ACL lesion? A case-control study. *Knee Surg Sports Traumatol Arthrosc* 2008;16(2):112-7. doi: 10.1007/s00167-007-0438-1 [published Online First: 2008/02/02]

159. Wojtys EM, Wylie BB, Huston LJ. The effects of muscle fatigue on neuromuscular function and anterior tibial translation in healthy knees. *Am J Sports Med* 1996;24(5):615-21. doi: 10.1177/036354659602400509 [published Online First: 1996/09/01]

160. Zazulak BT, Paterno M, Myer GD, et al. The effects of the menstrual cycle on anterior knee laxity: a systematic review. *Sports Med* (Auckland, NZ) 2006;36(10):847-62. doi: 10.2165/00007256-200636100-00004 [published Online First: 2006/09/29]

161. Malinzak RA, Colby SM, Kirkendall DT, et al. A comparison of knee joint motion patterns between men and women in selected athletic tasks. *Clin Biomech* (Bristol, Avon) 2001;16(5):438-45. doi: 10.1016/s0268-0033(01)00019-5 [published Online First: 2001/06/08]

162. Dai B, Herman D, Liu H, et al. Prevention of ACL Injury, Part I: Injury Characteristics, Risk Factors, and Loading Mechanism. *Res Sports Med* 2012;20(3-4):180-97. doi: 10.1080/15438627.2012.680990

163. Quatman CE, Quatman-Yates CC, Hewett TE. A ‚plane' explanation of anterior cruciate ligament injury mechanisms: a systematic review. *Sports Med* (Auckland, NZ) 2010;40(9):729-46. doi: 10.2165/11534950-000000000-00000 [published Online First: 2010/08/24]

164. Serpell BG, Scarvell JM, Ball NB, et al. Mechanisms and risk factors for noncontact ACL injury in age mature athletes who engage in field or court sports: a summary of the literature since 1980. *J Strength Cond Res* 2012;26(11):3160-76. doi: 10.1519/JSC.0b013e318243fb5a [published Online First: 2011/12/14]

165. Petersen W, Stöhr A, Ellermann A, et al. Wiederkehr zum Sport nach VKB-Rekonstruktion. Empfehlungen der DKG-Expertengruppe *OUP* 2016 2016;5(3):166-76.

166. Kirkendall DT, Garrett WE, Jr. The anterior cruciate ligament enigma. Injury mechanisms and prevention. *Clin Orthop Relat Res* 2000(372):64-8. doi: 10.1097/00003086-200003000-00008 [published Online First: 2000/03/30]

167. Meyer EG, Haut RC. Anterior cruciate ligament injury induced by internal tibial torsion or tibio femoral compression. *J Biomech* 2008;41(16):3377-83. doi: 10.1016/j.jbiomech.2008.09.023 [published Online First: 2008/11/15]

168. Santamaria LJ, Webster KE. The effect of fatigue on lower-limb biomechanics during single--limb landings: a systematic review. *J Orthop Sports Phys Ther* 2010;40(8):464-73. doi: 10.2519/jospt.2010.3295 [published Online First: 2010/08/17]

169. Anderson AF, Dome DC, Gautam S, et al. Correlation of anthropometric measurements, strength, anterior cruciate ligament size, and intercondylar notch characteristics to sex differences in anterior cruciate ligament tear rates. *Am J Sports Med* 2001;29(1):58-66. doi: 10.1177/03635465010290011501 [published Online First: 2001/02/24]

170. Hewett TE, Zazulak BT, Myer GD. Effects of the menstrual cycle on anterior cruciate ligament injury risk: a systematic review. *Am J Sports Med* 2007;35(4):659-68. doi: 10.1177/0363546506295699 [published Online First: 2007/02/13]

171. Pfab B. Zur Blutgefäßversorgung der Menisci und Kreuzbänder. *Deutsche Zeitschrift für Chirurgie* 1927;205:258-64.

172. Voskanian N. ACL Injury prevention in female athletes: review of the literature and practical considerations in implementing an ACL prevention program. *Curr Rev Musculoskelet Med* 2013;6(2):158-63. doi: 10.1007/s12178-013-9158-y [published Online First: 2013/02/16]

173. Pappas E, Carpes FP. Lower extremity kinematic asymmetry in male and female athletes performing jump-landing tasks. *J Sci Med Sport* 2012;15(1):87-92. doi: 10.1016/j.jsams.2011.07.008 [published Online First: 2011/09/20]

174. Pollard CD, Sigward SM, Powers CM. Limited hip and knee flexion during landing is associated with increased frontal plane knee motion and moments. *Clin Biomech* (Bristol, Avon) 2010;25(2):142-6. doi: 10.1016/j.clinbiomech.2009.10.005 [published Online First: 2009/11/17]

175. Nagano Y, Ida H, Akai M, et al. Gender differences in knee kinematics and muscle activity during single limb drop landing. *Knee* 2007;14(3):218-23. doi: 10.1016/j.knee.2006.11.008 [published Online First: 2007/01/12]

176. Pollard CD, Sigward SM, Powers CM. Mechanisms of ACL injury: Current perspectives. *J Biomech* 2007a;40(2):S254.

177. Pollard CD, Sigward SM, Powers CM. Gender differences in hip joint kinematics and kinetics during side-step cutting maneuver. *Clin J Sport Med* 2007b;17(1):38-42. doi: 10.1097/JSM.0b013e3180305de8 [published Online First: 2007/02/17]

178. Myer GD, Ford KR, Hewett TE. The effects of gender on quadriceps muscle activation strategies during a maneuver that mimics a high ACL injury risk position. *J Electromyogr Kinesiol* 2005;15(2):181-9. doi: 10.1016/j.jelekin.2004.08.006 [published Online First: 2005/01/25]

179. Padua DA, Carcia CR, Arnold BL, et al. Gender differences in leg stiffness and stiffness recruitment strategy during two-legged hopping. *J Mot Behav* 2005;37(2):111-25. doi: 10.3200/JMBR.37.2.111-126 [published Online First: 2005/02/26]

180. Belanger L, Burt D, Callaghan J, et al. Anterior cruciate ligament laxity related to the menstrual cycle: an updated systematic review of the literature. *J Can Chiropr Assoc* 2013;57(1):76-86. [published Online First: 2013/03/14]

181. Posthumus M, Collins M, September AV, et al. The intrinsic risk factors for ACL ruptures: an evidence-based review. *Phys Sportsmed* 2011;39(1):62-73. doi: 10.3810/psm.2011.02.1863 [published Online First: 2011/03/08]

182. Steiner M, Baur H, Blasimann A. Sex-specific differences in neuromuscular activation of the knee stabilizing muscles in adults - a systematic review. *Arch Physiother* 2023;13(1):4. doi: 10.1186/s40945-022-00158-x [published Online First: 2023/02/16]

183. Ganko A, Engebretsen L, Ozer H. The rolimeter: a new arthrometer compared with the KT-1000. *Knee Surg Sports Traumatol Arthrosc* 2000;8(1):36-9. doi: 10.1007/s001670050008 [published Online First: 2000/02/09]

184. Benjaminse A, Gokeler A, van der Schans CP. Clinical diagnosis of an anterior cruciate ligament rupture: a meta-analysis. *J Orthop Sports Phys Ther* 2006;36(5):267-88. doi:10.2519/jospt.2006.2011 [published Online First: 2006/05/24]

185. Frobell RB, Roos EM, Roos HP, et al. A randomized trial of treatment for acute anterior cruciate ligament tears. *N Engl J Med* 2010;363(4):331-42. doi: 10.1056/NEJMoa0907797 [published Online First: 2010/07/28]

186. Frobell RB, Roos HP, Roos EM, et al. Treatment for acute anterior cruciate ligament tear: five year outcome of randomised trial. *BMJ* 2013;346:f232. doi: 10.1136/bmj.f232 [published Online First: 2013/01/26]

187. Meuffels DE, Favejee MM, Vissers MM, et al. Ten year follow-up study comparing conservative versus operative treatment of anterior cruciate ligament ruptures. A matched-pair analysis of high level athletes. *Br J Sports Med* 2009;43(5):347-51. doi: 10.1136/bjsm.2008.049403 [published Online First: 2008/07/08]

188. Meunier A, Odensten M, Good L. Long-term results after primary repair or non-surgical treatment of anterior cruciate ligament rupture: a randomized study with a 15-year follow-up. *Scand J Med Sci Sports* 2007;17(3):230-7. doi: 10.1111/j.1600-0838.2006.00547.x [published Online First: 2007/05/16]

189. Moksnes H, Risberg MA. Performance-based functional evaluation of non-operative and operative treatment after anterior cruciate ligament injury. *Scand J Med Sci Sports* 2009; 19(3):345-55. doi: 10.1111/j.1600-0838.2008.00816.x [published Online First: 2008/05/31]

190. Paterno MV, Rauh MJ, Schmitt LC, et al. Incidence of contralateral and ipsilateral anterior cruciate ligament (ACL) injury after primary ACL reconstruction and return to sport. *Clin J Sport Med* 2012;22(2):116-21. doi: 10.1097/JSM.0b013e318246ef9e [published Online First: 2012/02/22]

191. World Health Organization. Classification of Functioning, Disability and Health: ICF. 2001. https://www.who.int/standards/classifications/international-classification-of-functioning-disability-and-health

192. Jesus TS, Bright FA, Pinho CS, et al. Scoping review of the person-centered literature in adult physical rehabilitation. *Disabil Rehabil* 2021; 43(11):1626-36. doi: 10.1080/09638288.2019.1668483 [published Online First: 2019/09/26]

193. Jesus TS, Papadimitriou C, Bright FA, et al. Person-Centered Rehabilitation Model: Framing the Concept and Practice of Person-Centered Adult Physical Rehabilitation Based on a Scoping Review and Thematic Analysis of the Literature. *Arch Phys Med Rehabil* 2022;103(1):106-20. doi: 10.1016/j.apmr.2021.05.005 [published Online First: 2021/07/07]

194. Kaplan Y. Identifying individuals with an anterior cruciate ligament-deficient knee as copers and noncopers: a narrative literature review. *J Orthop Sports Phys Ther 2011;41(10):*758-66. doi: 10.2519/jospt.2011.3384 [published Online First: 2011/10/08]

195. Petersen W, Haner M, Guenther D, et al. Management after acute injury of the anterior cruciate ligament (ACL), part 2: management of the ACL-injured patient. *Knee Surg Sports Traumatol Arthrosc* 2022b doi: 10.1007/s00167-022-07260-4 [published Online First: 2022/12/06]

196. Eggli S, Kohlhof H, Zumstein M, et al. Dynamic intraligamentary stabilization: novel technique for preserving the ruptured ACL. *Knee Surg Sports Traumatol Arthrosc* 2015;23(4):1215-21. doi: 10.1007/s00167-014-2949-x [published Online First: 2014/03/22]

197. Kohl S, Evangelopoulos DS, Ahmad SS, et al. A novel technique, dynamic intraligamentary stabilization creates optimal conditions for primary ACL healing: a preliminary biomechanical study. *Knee* 2014;21(2):477-80. doi: 10.1016/j.knee.2013.11.003 [published Online First: 2014/01/11]

198. Kohl S, Stock A, Ahmad SS, et al. Dynamic intraligamentary stabilization and primary repair: a new concept for the treatment of knee dislocation. *Injury* 2015;46(4):724-8. doi: 10.1016/j.injury.2014.10.012 [published Online First: 2014/12/03]

199. Risberg MA, Holm I, Myklebust G, et al. Neuromuscular training versus strength training during first 6 months after anterior cruciate ligament reconstruction: a randomized clinical trial. *Phys Ther* 2007;87(6):737-50. doi: 10.2522/ptj.20060041 [published Online First: 2007/04/20]

200. Monk AP, Davies LJ, Hopewell S, et al. Surgical versus conservative interventions for treating anterior cruciate ligament injuries. *Cochrane Database Syst Rev* 2016;4:CD011166. doi: 10.1002/14651858.CD011166.pub2 [published Online First: 2016/04/04]

201. Diermeier T, Rothrauff BB, Engebretsen L, et al. Treatment After Anterior Cruciate Ligament Injury: Panther Symposium ACL Treatment Consensus Group. *Orthop J Sports Med* 2020;8(6): 2325967120931097. doi: 10.1177/2325967120931097 [published Online First: 2020/07/09]

202. Petersen W, Guenther D, Imhoff AB, et al. Management after acute rupture of the anterior cruciate ligament (ACL). Part 1: ACL reconstruction has a protective effect on secondary meniscus and cartilage lesions. *Knee Surg Sports Traumatol Arthrosc* 2022a doi: 10.1007/s00167-022-06960-1 [published Online First: 2022/04/22]

203. Samuelsen BT, Webster KE, Johnson NR, et al. Hamstring Autograft versus Patellar Tendon Autograft for ACL Reconstruction: Is There a Difference in Graft Failure Rate? A Meta-analysis of 47,613 Patients. *Clin Orthop Relat Res* 2017; 475(10):2459-68. doi: 10.1007/s11999-017-5278-9 [published Online First: 2017/02/17]

204. Barenius B, Ponzer S, Shalabi A, et al. Increased risk of osteoarthritis after anterior cruciate ligament reconstruction: a 14-year follow-up study of a randomized controlled trial. *Am J Sports Med* 2014;42(5):1049-57. doi: 10.1177/0363546514526139 [published Online First: 2014/03/20]

205. Sajovic M, Strahovnik A, Dernovsek MZ, et al. Quality of life and clinical outcome comparison of semitendinosus and gracilis tendon versus patellar tendon autografts for anterior cruciate ligament reconstruction: an 11-year follow-up of a randomized controlled trial. *Am J Sports Med* 2011; 39(10):2161-9. doi: 10.1177/0363546511411702 [published Online First: 2011/06/30]

206. Slone HS, Romine SE, Premkumar A, et al. Quadriceps tendon autograft for anterior cruciate ligament reconstruction: a comprehensive review of current literature and systematic review of clinical results. *Arthroscopy* 2015;31(3):541-54. doi: 10.1016/j.arthro.2014.11.010 [published Online First: 2014/12/30]

207. Strauss MJ, Miles JW, Kennedy ML, et al. Full thickness quadriceps tendon grafts with bone had similar material properties to bone-patellar tendon-bone and a four-strand semitendinosus grafts: a biomechanical study. *Knee Surg Sports Traumatol Arthrosc* 2022;30(5):1786-94. doi: 10.1007/s00167-021-06738-x [published Online First: 2021/10/01]

208. Chalmers PN, Mall NA, Moric M, et al. Does ACL reconstruction alter natural history?: A systematic literature review of long-term outcomes. *J Bone Joint Surg Am* 2014;96(4):292-300. doi: 10.2106/JBJS.L.01713 [published Online First: 2014/02/21]

209. Filbay SR, Culvenor AG, Ackerman IN, et al. Quality of life in anterior cruciate ligament-deficient individuals: a systematic review and meta-analysis. *Br J Sports Med* 2015;49(16):1033-41. doi: 10.1136/bjsports-2015-094864 [published Online First: 2015/08/01]

210. Muaidi QI, Nicholson LL, Refshauge KM, et al. Prognosis of conservatively managed anterior cruciate ligament injury: a systematic review. *Sports Med* (Auckland, NZ) 2007;37(8):703-16. doi: 10.2165/00007256-200737080-00004 [published Online First: 2007/07/25]

211. Smith TO, Postle K, Penny F, et al. Is reconstruction the best management strategy for anterior cruciate ligament rupture? A systematic review and meta-analysis comparing anterior cruciate ligament reconstruction versus non-operative treatment. *Knee* 2014;21(2):462-70. doi: 10.1016/j.knee.2013.10.009 [published Online First: 2013/11/19]

212. Shrier I, Safai P, Charland L. Return to play following injury: whose decision should it be? *Br J Sports Med* 2014;48(5):394-401. doi: 10.1136/bjsports-2013-092492 [published Online First: 2013/09/07]

213. Rauch A, Cieza A, Stucki G. How to apply the International Classification of Functioning, Disability and Health (ICF) for rehabilitation management in clinical practice. *Eur J Phys Rehabil Med* 2008;44(3):329-42. [published Online First: 2008/09/03]

214. de Queiroz JHM, Murakawa YAB, de Castro SS, et al. Biopsychosocial Model Domains in Clinical Practice Guidelines for Return to Sport After ACL Injury: Systematic Review Using the AGREE II Checklist. *Sports Health* 2023; 15(2):165-75. doi: 10.1177/19417381221094582 [published Online First: 2022/05/19]

215. Jenkins SM, Guzman A, Gardner BB, et al. Rehabilitation After Anterior Cruciate Ligament Injury: Review of Current Literature and Recommendations. *Curr Rev Musculoskelet Med* 2022;15(3):170-79. doi: 10.1007/s12178-022-09752-9 [published Online First: 2022/04/07]

216. Negrini S, Selb M, Kiekens C, et al. Rehabilitation definition for research purposes. A global stake holders' initiative by Cochrane Rehabilitation. *Neurorehab Neural Repair* 2022;36(7):405-14.

217. Rahardja R, Zhu M, Love H, et al. Effect of Graft Choice on Revision and Contralateral Anterior Cruciate Ligament Reconstruction: Results From the New Zealand ACL Registry. *Am J Sports Med* 2020;48(1):63-69. doi: 10.1177/0363546519885148 [published Online First: 2019/11/16]

218. Meredith SJ, Rauer T, Chmielewski TL, et al. Return to Sport After Anterior Cruciate Ligament Injury: Panther Symposium ACL Injury Return to Sport Consensus Group. *Orthop J Sports Med* 2020;8(6):2325967120930829. doi: 10.1177/2325967120930829 [published Online First: 2020/07/11]

219. Wellsandt E, Failla MJ, Snyder-Mackler L. Limb Symmetry Indexes Can Overestimate Knee Function After Anterior Cruciate Ligament Injury. *J Orthop Sports Phys Ther* 2017;47(5):334-38. doi: 10.2519/jospt.2017.7285 [published Online First: 2017/03/31]

220. Narducci E, Waltz A, Gorski K, et al. The clinical utility of functional performance tests within one-year post-acl reconstruction: a systematic review. *Int J Sports Phys Ther* 2011;6(4):333-42. [published Online First: 2011/12/14]

221. Burgi CR, Peters S, Ardern CL, et al. Which criteria are used to clear patients to return to sport after primary ACL reconstruction? A scoping review. *Br J Sports Med* 2019;53(18):1154-61. doi: 10.1136/bjsports-2018-099982 [published Online First: 2019/02/04]

222. Almangoush A, Herrington L. Functional Performance Testing and Patient Reported Outcomes following ACL Reconstruction: A Systematic Scoping Review. *Int Sch Res Notices* 2014;2014:613034. doi: 10.1155/2014/613034 [published Online First: 2014/01/01]

223. Engelen-van Melick N, van Cingel RE, Tijssen MP, et al. Assessment of functional performance after anterior cruciate ligament reconstruction: a systematic review of measurement procedures. *Knee Surg Sports Traumatol Arthrosc* 2013;21(4):869-79. doi: 10.1007/s00167-012-2030-6 [published Online First: 2012/05/15]

224. Hegedus EJ, McDonough S, Bleakley C, et al. Clinician-friendly lower extremity physical performance measures in athletes: a systematic review of measurement properties and correlation with injury, part 1. The tests for knee function including the hop tests. *Br J Sports Med* 2015;49(10):642-48.

225. Thomee R, Kaplan Y, Kvist J, et al. Muscle strength and hop performance criteria prior to return to sports after ACL reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2011;19(11):1798-805. doi: 10.1007/s00167-011-1669-8 [published Online First: 2011/09/21]

226. Losciale JM, Zdeb RM, Ledbetter L, et al. The Association Between Passing Return-to-Sport Criteria and Second Anterior Cruciate Ligament Injury Risk: A Systematic Review With Meta-analysis. *J Orthop Sports Phys Ther* 2019;49(2):43-54. doi: 10.2519/jospt.2019.8190 [published Online First: 2018/12/07]

227. Patterson BE, Crossley KM, Perraton LG, et al. Limb symmetry index on a functional test battery improves between one and five years after anterior cruciate ligament reconstruction, primarily due to worsening contralateral limb function. *Phys Ther Sport* 2020;44:67-74. doi: 10.1016/j.ptsp.2020.04.031 [published Online First: 2020/05/25]

228. Mayer SW, Queen RM, Taylor D, et al. Functional Testing Differences in Anterior Cruciate Ligament Reconstruction Patients Released Versus Not Released to Return to Sport. *Am J Sports Med* 2015;43(7): 1648-55. doi: 10.1177/0363546515578249 [published Online First: 2015/04/15]

229. McGrath TM, Waddington G, Scarvell JM, et al. The effect of limb dominance on lower limb functional performance--a systematic review. *J Sports Sci* 2016;34(4):289-302. doi: 10.1080/02640414.2015.1050601 [published Online First: 2015/06/10]

230. Undheim MB, Cosgrave C, King E, et al. Isokinetic muscle strength and readiness to return to sport following anterior cruciate ligament reconstruction: is there an association? A systematic review and a protocol recommendation. *Br J Sports Med* 2015;49(20):1305-10. doi: 10.1136/bjsports-2014-093962 [published Online First: 2015/06/25]

231. Davies GJ, McCarty E, Provencher M, et al. ACL return to sport guidelines and criteria. *Curr Rev Musculoskelet Med* 2017;10:307-14.

232. Schelin L, Tengman E, Ryden P, et al. A statistically compiled test battery for feasible evaluation of knee function after rupture of the Anterior Cruciate Ligament - derived from long-term follow-up data. *PLoS One* 2017;12(5): e0176247. doi: 10.1371/journal.pone.0176247 [published Online First: 2017/05/02]

233. Harput G, Ozer H, Baltaci G, et al. Self-reported outcomes are associated with knee strength and functional symmetry in individuals who have undergone anterior cruciate ligament reconstruction with hamstring tendon autograft. *Knee* 2018;25(5):757-64.doi:10.1016/j.knee.2018.06.007 [published Online First: 2018/07/26]

234. Roos EM, Roos HP, Lohmander LS, et al. Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. *J Orthop Sports Phys Ther* 1998; 28(2):88-96. doi: 10.2519/jospt.1998.28.2.88 [published Online First: 1998/08/12]

235. Briggs KK, Lysholm J, Tegner Y, et al. The reliability, validity, and responsiveness of the Lysholm score and Tegner activity scale for anterior cruciate ligament injuries of the knee: 25 years later. *Am J Sports Med* 2009;37(5):890-7. doi: 10.1177/0363546508330143 [published Online First: 2009/03/06]

236. Muller B, Yabroudi MA, Lynch A, et al. Defining Thresholds for the Patient Acceptable Symptom State for the IKDC Subjective Knee Form and KOOS for Patients Who Underwent ACL Reconstruction. *Am J Sports Med* 2016;44(11): 2820-26. doi: 10.1177/0363546516652888 [published Online First: 2016/07/31]

237. Roos EM, Boyle E, Frobell RB, et al. It is good to feel better, but better to feel good: whether a patient finds treatment ‚successful' or not depends on the questions researchers ask. *Br J Sports Med* 2019;53(23):1474-78. doi: 10.1136/bjsports-2018-100260 [published Online First: 2019/05/11]

238. Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes* 2003;1:64. doi:10.1186/1477-7525-1-64 [published Online First: 2003/11/14]

239. Alviar MJ, Olver J, Brand C, et al. Do patient-reported outcome measures used in assessing outcomes in rehabilitation after hip and knee arthro-plasty capture issues relevant to patients? Results of a systematic review and ICF linking process. *J Rehab Med* 2011;43(5):374-81.

240. King MT. A point of minimal important difference (MID): a critique of terminology and methods. *Expert Rev Pharmacoecon Outcomes Res* 2011;11(2):171-84. doi: 10.1586/erp.11.9 [published Online First: 2011/04/12]

241. Ardern CL, Taylor NF, Feller JA, et al. Fifty-five per cent return to competitive sport following anterior cruciate ligament reconstruction surgery: an updated systematic review and meta-analysis including aspects of physical functioning and contextual factors. *Br J Sports Med* 2014;48(21):1543-52. doi: 10.1136/bjsports-2013-093398 [published Online First: 2014/08/27]

242. Joreitz R, Lynch A, Rabuck S, et al. Patient-specific and surgery-specific factors that affect return to sport after ACL reconstruction. *Int J Sports Phys Ther* 2016;11(2):264.

243. Lai CC, Feller JA, Webster KE. Fifteen-year audit of anterior cruciate ligament reconstructions in the Australian Football League from 1999 to 2013: return to play and subsequent ACL injury. *Am J Sports Med* 2018a; 46(14):3353-60.

244. Lai CCH, Ardern CL, Feller JA, et al. Eighty-three per cent of elite athletes return to preinjury sport after anterior cruciate ligament reconstruction: a systematic review with meta-analysis of return to sport rates, graft rupture rates and performance outcomes. *Br J Sports Med* 2018; 52(2):128-38. doi: 10.1136/bjsports-2016-096836 [published Online First: 2017/02/23]

245. Mohtadi NG, Chan DS. Return to sport-specific performance after primary anterior cruciate ligament reconstruction: a systematic review. *Am J Sports Med* 2018;46 (13):3307-16.

246. Ardern CL. Anterior cruciate ligament reconstruction—not exactly a one-way ticket back to the preinjury level: a review of contextual factors affecting return to sport after surgery. *Sports Health* 2015;7(3):224-30.

247. Grindem H, Snyder-Mackler L, Moksnes H, et al. Simple decision rules can reduce reinjury risk by 84% after ACL reconstruction: the Delaware-Oslo ACL cohort study. *Br J Sports Med* 2016; 50(13):804-8. doi: 10.1136/bjsports-2016-096031 [published Online First: 2016/05/11]

248. Wright RW, Magnussen RA, Dunn WR, et al. Ipsilateral graft and contralateral ACL rupture at five years or more following ACL reconstruction: a systematic review. *J Bone Joint Surg Am* 2011;93(12): 1159-65. doi: 10.2106/JBJS.J.00898 [published Online First: 2011/07/22]

249. Welling W, Benjaminse A, Lemmink K, et al. Passing return to sports tests after ACL reconstruction is associated with greater likelihood for return to sport but fail to identify second injury risk. *Knee* 2020;27(3):949-57. doi: 10.1016/j.knee.2020.03.007 [published Online First: 2020/04/06]

250. Kay J, Memon M, Marx RG, et al. Over 90% of children and adolescents return to sport after anterior cruciate ligament reconstruction: a systematic review and meta-analysis. *Knee Surg Sports Traumatol Arthrosc* 2018;26:1019-36.

251. Gokeler A, Dingenen B, Hewett TE. Rehabilitation and Return to Sport Testing After Anterior Cruciate Ligament Reconstruction: Where Are We in 2022? *Arthrosc Sports Med Rehabil* 2022;4(1):e77-e82. doi: 10.1016/j.asmr.2021.10.025 [published Online First: 2022/02/11]

252. Payr E. Der heutige Stand der Gelenkchirugie. *Arch Klin Chir* 1900;148::404–51.

253. Palmer Y. Pathophysiology of the medial ligament of the knee joint. *Acta Chir Scand* 1958;115:312-18..

254. Raunest J, Sager M, Burgener E. Proprioceptive mechanisms in the cruciate ligaments: an electro-myographic study on reflex activity in the thigh muscles. *J Trauma* 1996;41(3):488-93. doi: 10.1097/00005373-199609000-00017 [published Online First: 1996/09/01]

255. Skoglund S. Anatomical and physiological studies of knee joint innervation in the cat. *Acta Physiol Scand Suppl* 1956;36(124):1-101. [published Online First: 1956/01/01]

256. Solomonow M, Baratta R, Zhou B, et al. The synergistic action of the anterior cruciate ligament and thigh muscles in maintaining joint stability. *Am J Sports Med* 1987; 15(3):207-13.

257. Stener B, Petersen I. Electromyographic investigation of reflex effects upon effects upon stretching the partially ruptured medial collateral ligament of the knee joint. *Acta Chir Scand* 1962;124:396-411.

258. Grüber J, Wolter D, Lierse W. Der vordere Kreuzbandreflex (LCA-Reflex). *Unfallchirurg* 1986;89(12):551-54.

259. Friemert B, Faist M, Spengler C, et al. Intraoperative direct mechanical stimulation of the anterior cruciate ligament elicits short- and medium-latency hamstring reflexes. *J Neurophysiol* 2005;94(6):3996-4001. doi: 10.1152/jn.00410.2005 [published Online First: 2005/09/02]

260. Friemert B, Bumann-Melnyk M, Faist M, et al. Differentiation of hamstring short latency versus medium latency responses after tibia translation. *Exp Brain Res* 2005;160(1):1-9. doi: 10.1007/s00221-004-1980-4 [published Online First: 2004/08/24]

261. Johansson H, Sjolander P, Sojka P, et al. Reflex actions on the γ-muscle-spindle systems of muscles acting at the knee joint elicited by stretch of the posterior cruciate ligament. *Neuro-orthopedics* 1989;8(1):9-21.

262. Dhaher YY, Tsoumanis AD, Houle TT, et al. Neuromuscular reflexes contribute to knee stiffness during valgus loading. *J Neurophysiol* 2005;93(5):2698-709. doi: 10.1152/jn.00921.2004 [published Online First: 2004/12/24]

263. Behrens M, Mau-Moeller A, Wassermann F, et al. Effect of fatigue on hamstring reflex responses and posterior-anterior tibial translation in men and women. *PLoS One* 2013;8(2):e56988. doi: 10.1371/journal.pone.0056988 [published Online First: 2013/04/11]

264. Proffen BL, Murray MM. Reinnervation and Revascularization in Engineered ACL Healing.. In: Murray M, Vavken P, Fleming B, eds. The ACL Handbook New York, NY. : *Springer* 2013.

265. Bates NA, Schilaty ND, Ueno R, et al. Timing of Strain Response of the ACL and MCL Relative to Impulse Delivery During Simulated Landings Leading up to ACL Failure. *J Appl Biomech* 2020:1-8. doi: 10.1123/jab.2019-0308 [published Online First: 2020/04/23]

266. Konishi Y, Fukubayashi T, Takeshita D. Possible mechanism of quadriceps femoris weakness in patients with ruptured anterior cruciate ligament. *Med Sci Sports Exerc* 2002;34(9):1414-8. doi: 10.1097/00005768-200209000-00003 [published Online First: 2002/09/10]

267. Konishi Y, Suzuki Y, Hirose N, et al. Effects of lidocaine into knee on QF strength and EMG in patients with ACL lesion. *Med Sci Sports Exerc* 2003;35(11):1805-8. doi: 10.1249/01.MSS.0000093753.55866.2F [published Online First: 2003/11/06]

268. Behrens M, Mau-Moeller A, Wassermann F, et al. Repetitive jumping and sprinting until exhaustion alters hamstring reflex responses and tibial translation in males and females. *J Orthop Res* 2015;33(11):1687-92. doi: 10.1002/jor.22935 [published Online First: 2015/05/06]

269. Dyhre-Poulsen P, Krogsgaard MR. Muscular reflexes elicited by electrical stimulation of the anterior cruciate ligament in humans. *J Appl Physiol* (1985) 2000;89(6):2191-5. doi: 10.1152/jappl.2000.89.6.2191 [published Online First: 2000/11/25]

270. Vergis A, Gillquist J. Sagittal Plane Translation of the Knee During Stair Walking. *Am J Sports Med* 1998;26(6):841-46. doi: 10.1177/03635465980260061801

271. McFadyen BJ, Winter DA. An integrated bio mechanical analysis of normal stair ascent and descent. *J Biomech* 1988;21(9):733-44. doi: 10.1016/0021-9290(88)90282-5 [published Online First: 1988/01/01]

272. Kutzner I, Heinlein B, Graichen F, et al. Loading of the knee joint during activities of daily living measured in vivo in five subjects. *J Biomech* 2010;43(11):2164-73. doi: 10.1016/j.jbiomech.2010.03.046 [published Online First: 2010/06/12]

273. Bencke J, Zebis MK. The influence of gender on neuromuscular pre-activity during side-cutting. *J Electromyogr Kinesiol* 2011;21(2):371-5. doi: 10.1016/j.jelekin.2010.10.008 [published Online First: 2010/11/30]

274. Brown TN, McLean SG, Palmieri-Smith RM. Associations between lower limb muscle activation strategies and resultant multi-planar knee kinetics during single leg landings. *J Sci Med Sport* 2014;17(4):408-13. doi: 10.1016/j.jsams.2013.05.010 [published Online First: 2013/07/16]

275. Gehring D, Melnyk M, Gollhofer A. Gender and fatigue have influence on knee joint control strategies during landing. *Clin Biomech* (Bristol, Avon) 2009;24(1):82-7. doi: 10.1016/j.clinbiomech.2008.07.005 [published Online First: 2008/11/04]

276. Theisen D, Rada I, Brau A, et al. Muscle Activity Onset Prior to Landing in Patients after Anterior Cruciate Ligament Injury: A Systematic Review and Meta-Analysis. *PLoS One* 2016;11(5):e0155277. doi: 10.1371/journal.pone.0155277 [published Online First: 2016/05/12]

277. Gao B, Cordova ML, Zheng NN. Three-dimensional joint kinematics of ACL-deficient and ACL-reconstructed knees during stair ascent and descent. *Hum Mov Sci* 2012;31(1):222-35. doi: 10.1016/j.humov.2011.04.009 [published Online First: 2011/07/30]

278. Lepley AS, Gribble PA, Thomas AC, et al. Longitudinal Evaluation of Stair Walking Biomechanics in Patients with ACL Injury. *Med Sci Sports Exerc* 2016;48(1):7-15. doi: 10.1249/MSS.0000000000000741 [published Online First: 2015/08/01]

279. Rudolph KS, Snyder-Mackler L. Effect of dynamic stability on a step task in ACL deficient individuals. *J Electromyogr Kinesiol* 2004;14(5):565-75.

280. Sole G, Pataky T, Tengman E, et al. Analysis of three-dimensional knee kinematics during stair descent two decades post-ACL rupture - Data revisited using statistical parametric mapping. *J Electromyogr Kinesiol* 2017;32:44-50. doi: 10.1016/j.jelekin.2016.12.005 [published Online First: 2017/01/01]

281. Sole G, Tengman E, Grip H, et al. Knee kinematics during stair descent 20 years following anterior cruciate ligament rupture with and without reconstruction. *Clin Biomech* (Bristol, Avon) 2016;32:180-6. doi: 10.1016/j.clinbiomech.2015.11.013 [published Online First: 2015/12/23]

282. Busch A, Blasimann A, Henle P, et al. Neuromuscular activity during stair descent in ACL reconstructed patients: A pilot study. *Knee* 2019;26(2):310-16. doi: 10.1016/j.knee.2018.12.011 [published Online First: 2019/02/09]

283. Busch A, Henle P, Boesch L, et al. Neuromuscular control in patients with acute ACL injury during stair ascent – A pilot study. *Sports Orthop Traumatol* 2019;35(2):158-65. doi: 10.1016/j.orthtr.2019.04.002

284. Schmidt A, Blasimann A, Boesch L, et al. Comparison of neuromuscular hamstring activity of people with acute anterior cruciate ligament rupture and at one-year follow-up - a pilot study. *Swiss Sports & Exerc Med* 2018;66(4):44.

285. Yabroudi MA, Irrgang JJ. Rehabilitation and return to play after anatomic anterior cruciate ligament reconstruction. *Clin Sports Med* 2013;32(1):165-75.

286. Risberg MA, Mork M, Jenssen HK, et al. Design and implementation of a neuromuscular training program following anterior cruciate ligament re construction. *J Orthop Sports Phys Ther* 2001;31(11):620-31. doi: 10.2519/jospt.2001.31.11.620 [published Online First: 2001/11/27]

CHAPTER 2

AIMS AND OUTLINE

Abstract

This PhD project included four studies regarding neuromuscular control and objective criteria for patients after an ACL rupture:

- Study 1 was a systematic literature review and reported which EMG-related outcomes were used to assess neuromuscular control of the knee joint after an ACL injury to determine readiness to RTS.
- Study 2 was a cross-sectional study including patients with an acute ACL rupture and investigated differences in neuromuscular control for knee stability compared to healthy controls.
- Study 3a, a cross-sectional study, evaluated whether sex and treatment effects on neuromuscular control were present in people one year after ACL rupture in comparison to healthy controls.
- Study 3b, cross-sectionally designed, investigated whether inter- or intrasubject leg differences in neuromuscular control were present in people one year after ACL rupture in comparison to healthy controls.

In addition, this chapter provides the objectives, research questions, hypotheses, timeline of the research projects, information concerning methods for neuromuscular control and funding.

Knowledge of the difference in active joint stability between subjects with an intact ACL and people with an ACL deficiency or after ACL-R would provide additional new information on the role of the ACL and its involvement in active joint stability. If the ACL can no longer transmit important afferent information to spinal and supraspinal levels when ruptured, the hypothesis implies that reflex-induced muscle responses will be less adequate compared to the situation with an intact ACL. In addition, knowledge of the possible different reflex responses in patient cohorts (healthy vs. injured and surgically treated vs. rehabilitation alone, conservative treatment respectively) might reveal functional deficits that in turn can be addressed immediately to adjust clinical decision making towards rehabilitation schemes and RTS.

2.1 Objectives

The overall aim of this PhD project was to assess and analyze neuromuscular control of the knee stabilizing muscles in patients suffering from an ACL rupture.

More in detail, the following objectives were part of the projects belonging to this PhD:

- In Study 1, we aimed to provide an overview of EMG-related assessments for neuromuscular control in patients with an ACL rupture at the time for RTS by doing a systematic literature review (Chapter 3).[1] Additionally, a master student, supervised by A. Blasimann, reviewed the evidence regarding sex-specific differences in neuromuscular control when assessed with surface EMG.[2]

- In Study 2, with a cross-sectional design, we wanted to assess neuromuscular control of both lower limbs in patients with an acute ACL rupture and compare the results to healthy controls (Chapter 4).[3]
- In Study 3 we aimed at investigating differences regarding subgroups of ACL patients one year after the injury in comparison to a healthy control group. The first analysis (Study 3a) concerned influence of sex and treatment options – surgical reconstruction and non-surgical, conservative treatment (Chapter 5).[4]
  The second analysis (Study 3b) investigated differences regarding neuromuscular control in the involved and non-involved limb of patients compared to healthy controls (Chapter 6).[5]

2.2 Research questions

This PhD project was divided beforehand into three research projects with four research questions:

- Study 1:
  Which EMG-related outcomes are used to assess neuromuscular control of the knee joint after an ACL injury to determine readiness to RTS? (Chapter 3)[1]
- Study 2:
  Are there differences in neuromuscular control for knee stability in intra- and intersubject comparisons of patients in the acute phase after an ACL rupture and healthy controls? (Chapter 4)[3]
- Study 3a and b:
  Are there any sex and treatment effects on neuromuscular control for knee stability in people 1-year after ACL-R or after conservative treatment in comparison to healthy controls? (Study 3a) (Chapter 5)[4]
  Are there any intra- or intrasubject leg differences in neuromuscular control for knee stability in people 1-year after ACL-R or after conservative treatment in comparison to healthy controls? (Study 3b) (Chapter 6)[5]

2.3 Hypotheses

It is hypothesized that different afferent information is leading to changes in the neuromuscular response, e.g., of the hamstrings. These altered neuromuscular responses might lead to a differentiation between cohorts. The respective outcomes can then be used immediately in further studies or directly in clinical practice as a diagnostic tool: to reveal deficits and to monitor changes, both in neuromuscular control and active joint stability of the knee. This has direct impact on clinical decision making as quantitative data support decision-making for RTS. In addition, current stability status of the knee joint helps to identify injury risk and leads to optimal prevention. Moreover, rehabilitation can be monitored with an appropriate diagnostic tool. Furthermore, impact on further scientific applications such as assessing longitudinal effects of rehabilitation schemes, monitoring longitudinal effects of prevention strategies with quantitative data, identifying functional outcome of surgical procedures with quantitative data, and testing possible differences between surgical approaches can be assumed.

This PhD project is intended to be a first step in the diagnosis of neuromuscular control of the knee in ACL patients to be able to assess surgical measures as well as rehabilitation schemes and their effects in the future. It is hypothesized that, because of altered afferent information, the neuromuscular EMG activity of the quadriceps and hamstrings differs between ACL-intact (healthy) subjects, surgically treated or conservatively treated patients with an ACL rupture. Subjects with former ACL injury may have developed different neuromuscular strategies than subjects who have never ruptured their ACL.[6]

Consequently, we set the following a priori hypotheses:

- As neuromuscular control is not directly assessed in current published rehabilitation guidelines for ACL injury or reconstruction, we hypothesize that there is only limited or no evidence of proposed EMG outcomes to assess neuromuscular control for RTS in these patients. (Chapter 3)[1]
- Patients with an acute ACL deficiency (acute ACL rupture) would show altered neuromuscular control in the injured leg compared to the contralateral, non-involved leg, and differ from healthy matched control subjects. More specifically, patients with an acute ACL rupture would have lower reflex-induced neuromuscular activation than healthy individuals with an intact ACL, due to altered afferent information. This can then be interpreted functionally: Active joint stability is lower in individuals with an ACL deficiency. (Chapter 4)[3]
- Patients with a chronic ACL deficiency who were treated non-surgically and assessed one year after an ACL rupture, would show altered neuromuscular control compared to healthy individuals with an intact ACL. Patients with an ACL-R who were assessed one year after surgery would show altered neuromuscular control compared to healthy individuals with an intact ACL. Both patient groups would differ from each other, and show altered neuromuscular control related to treatment. In addition, we hypothesized that sex differences would be present regarding neuromuscular control. Furthermore, the involved limb of patients would show altered neuromuscular control compared to the non-involved, contralateral side. (Chapter 5 & 6)[4 5]

2.4 Overview of included studies

The timeline of this thesis is illustrated below in Figure 19.

Study 1 of this PhD project was a systematic literature review about EMG-related assessments for neuromuscular control.[1] The project was registered in the international prospective register of systematic reviews (PROSPERO) beforehand and got the number CRD42019122188. In addition, a master thesis investigated sex-related differences in neuromuscular control by doing a systematic literature review, which was registered in PROSPERO under the number CRD42020189504.[2] (Chapter 3)

For Study 2, patients with an acute ACL rupture were included in the "Sensorimotor Knee 1" project. In this research project, 15 patients and 29 healthy subjects had been recruited between February 2016 and February 2020. Data from this pilot study had been published previously.[7 8] In the "Sensorimotor Knee 2" project, the patients were measured again one year after the first measurement (2017 – 2021). However, only 13 patients agreed to participate in the follow-up measurements. Pilot data from the longitudinal study were published as conference abstract.[9] Measurements and data analysis from the acutely injured ACL patients were part of Study 2.[3] (Chapter 4)

For Study 3a investigating sex and treatment effects (Chapter 5) and 3b assessing leg differences (Chapter 6), 26 patients after ACL rupture and 38 patients with ACL-R were measured one year a fter reconstruction, injury respectively, for the research project "Development of valid diagnostics to evaluate sensorimotor competence in patients with anterior cruciate ligament (ACL) injury" between April 2018 and August 2021. In addition, the existing data base from the "Sensorimotor Knee 1 & 2" was completed with 13 additional healthy control subjects who were eligible based on matching criteria. (Chapter 5 & 6)[4,5]

Patients with an acute ACL rupture were recruited by PD Dr. med. Philipp Henle, orthopedic surgeon at the Sonnenhof Orthopedic Center in Bern, Switzerland. Patients who were measured one year after rupture or reconstruction, were recruited by Philipp Henle as well, other orthopedic surgeons in the canton of Bern, physiotherapists of the Hospital Emmental in Burgdorf and Langnau, private physiotherapy practices, local sports and fitness clubs, and private networks. All healthy volunteers were recruited among local sports and fitness clubs, private networks, staff and students at the BFH.

All studies including participants complied with the Declaration of Helsinki and were approved by the Ethics Committee of the Canton of Bern, Switzerland (Study 2: KEK number 213/15; Study 3a/b: KEK number 2017-02282). Written informed consent was obtained from all participants. All clinical assessments including MRI for patients included for Study 2 were performed at the Sonnenhof Orthopedic Center in Bern, Switzerland. Most of the clinical assessments for Study 3a/b and MRI, if needed, were also performed at the Sonnenhof Orthopedic Center. Some patients were recruited through private physiotherapy practices and orthopedic surgeons and therefore, were assessed in other Swiss Hospitals. All measurements were done at the Bern Movement Lab, laboratory at the BFH, School of Health Professions, Division of Physiotherapy Research in Bern, Switzerland.

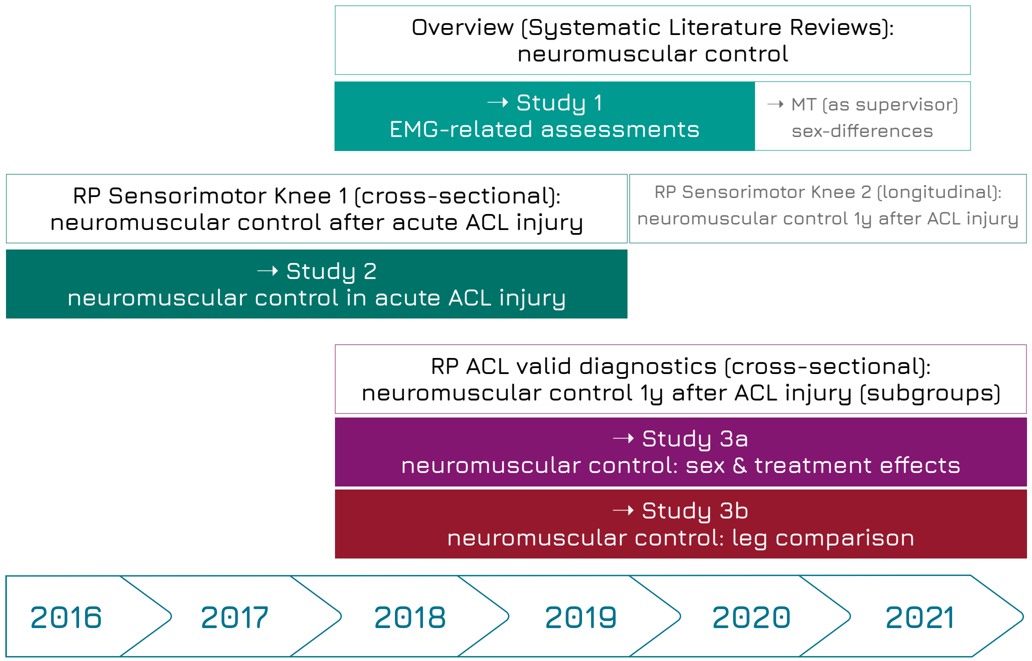

Figure 19: Timeline of PhD project and affiliated studies as overview of research projects (RP) of the BFH (Physiotherapy Research) during the PhD. The colors of the projects correspond to the chapter colors of this thesis

Abbreviations: ACL = anterior cruciate ligament; BFH = Bern University of Applied Sciences; EMG = electromyography; MT = master's thesis[2] leading to a publication; RP = research project; y = year.

In addition to the four studies, there were several additional studies related to the PhD thesis and resulting in a publication or manuscript (as second or last author):

- Busch, A., Blasimann, A., Henle, P., & Baur, H. (2019). Neuromuscular activity during stair descent in ACL reconstructed patients: A pilot study. *Knee*, 26(2), 310-316.[7]
- Busch, A., Henle, P., Boesch, L., Blasimann, A., & Baur, H. (2019). Neuromuscular control in patients with acute ACL injury during stair ascent–A pilot study. *Sports Orthop Traumatol*, 35(2), 158-165.[8]
- Busch, A., Blasimann, A., Mayer, F., & Baur,H. (2021). Alterations in sensorimotor function after ACL reconstruction during active joint position sense testing. A systematic review. *PLoS One* 16(6), e0253503.[10]
- Steiner, M., Baur, H., Blasimann, A. (2023). Sex-specific differences in neuromuscular activation of the knee stabilizing muscles in adults- a systematic review. *Arch Physiother*, 13(1), 1-15.[2]
- Gentsch, A., Blasimann, A., Busch, A., Henle, P., Alfuth, M., Baur, H. (202x). Neuromuscular activity during volitional tasks differs from reflex responses. *Manuscript submitted*
- Abaecherli, K., Blasimann, A., Busch, A., Henle, P., Baur, H. (202x). Neuromuscular activity during stair descent in conservatively and surgically treated ACL-injured participants - a cross-sectional study. *Manuscript submitted*
- Koecker, S., Blasimann, A., Busch, A., Boesch, L., Henle, P., Bruhn, S., Baur, H. (202x). Hamstrings stretch reflex activity in healthy, ACL reconstructed and conservatively treated ACL participants. A cross sectional study. *Manuscript submitted*

2.5 Methods to assess neuromuscular control

As mentioned in Chapter 1.4. our definition of neuromuscular control of the knee joint includes volitional and reflexive activity before and during static and dynamic tasks. Therefore, sensorimotor competence does not only consist of adequate neuromuscular answers after initial foot-floor contact but also appropriate pre-activation of knee stabilizing muscles before landing. As commonly used physical performance tests assess neuromuscular control indirectly, as surrogates for knee stability, we chose direct approaches to get insight into muscle physiology. Surface EMG was used in this PhD thesis to measure neuromuscular activity which was analyzed in the time and amplitude domain:[11] The EMG signal served as an indicator for the initiation of muscle activation (timing) and provided information about force contribution of a single muscle or a muscle group (amplitude).[11]

To evaluate neuromuscular activity of knee-stabilizing muscles in ACL patients and healthy controls, two different situations – stairway walking and artificial tibial perturbation – had been chosen for this PhD project. These two situations have been selected because they represent important, functionally relevant, and demanding situations:

- stairway walking (ascent & descent) as a demanding, volitional activity eliciting muscle preactivity. This activity of daily living requires sufficient preactivity to guarantee active joint stability. The stairway situation enables the analysis of muscle preactivation prior to touch-down. The amount of preactivity of quadriceps and hamstrings indicate the level of joint stiffness before load is applied to the respective extremity.

- artificially induced tibial perturbation as reflex activity and simulation of injury mechanism. This perturbation is applied in posterior-anterior direction relatively to the femur to elicit reflex responses and is later named anterior tibial translation. With this measurement, we simulate the injury mechanism. Monitoring neuromuscular control during the corresponding time window from pre-activity to perturbation onset and time windows for reflex responses after perturbation give insight into sensorimotor control mechanisms to guarantee knee joint stability.[12-14]

Preparation of participants for measurements

The skin was prepared by shaving, smoothing, and cleaning with alcohol. Afterwards, the self-adhesive electrodes (Blue Sensor Type P-00-S; Ambu; inter-electrode distance, 20 mm) were applied to the skin over the muscle belly of the respective main knee stabilizing thigh muscles VM, VL, BF and ST on both limbs, according to the recommendations of SENIAM (Surface Electromyography for the Non-Invasive Assessment of Muscles) (Fig. 12).[15] The reference electrode was always placed on the right patella.

Figure 12: Application of self-adhesive electrodes to the prepared skin for vastus lateralis muscle (©Bern Movement Lab)

Afterwards, the interelectrode impedance was measured (impedance meter D175; Digitimer Ltd., Hertfordshire, United Kingdom) and accepted at <2 kOhm. Then, the cables were attached to the electrodes (Fig. 13), and everything hold together with an elastic, mesh-like tubular bandage around the thigh. For the measurements, all participants wore the same brand and model of gym shoes (Adidas™ duramo 6, ladies and men's model, different sizes) to eliminate effects of different cushioning.

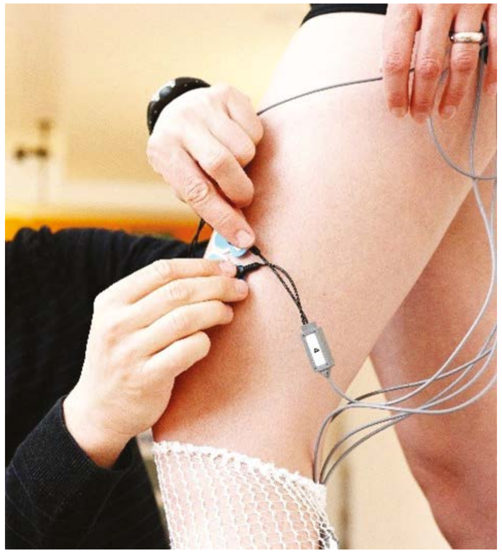

Figure 13: Connecting cables with electrodes and fixation of cables and preamplifier with elastic, mesh-like tubular bandage (©Bern Movement Lab)

The measurements started with a warm-up on an instrumented treadmill (h/p/cosmos; sports & medical GmbH, Nussdorf, Germany) for 10 minutes at 5 km/h (1.39 m/s) to assess maximum voluntary contraction (MVC) of each muscle during gait. This procedure served to normalize the EMG values in the evaluation process and allowed comparison between individuals afterwards.[16-19] After this warm-up, each participant completed the two experimental situations in the same order: stair descent (Fig. 14) first, followed by artificial tibial translation (Fig. 15).

Stair descent

The subjects walked downhill ten times on a staircase instrumented with force plates (Type 9286BA, Kistler®, Winterthur, Switzerland), embedded at the third and fourth step (Fig. 14). Neuromuscular activity was measured and related to the initial ground contact detected by the force plate. Previously published preliminary studies from our research group had shown the feasibility and reliability of this method, and the discriminatory power between different cohorts.[20 21] With this task, which is relevant to everyday life, sensorimotor competence can be assessed in applied situations.

Figure 14: Stair descent on instrumented stairway with force plates embedded to third and fourth step (symbolic image as another device for EMG measurements was used in PhD project) (©Bern Movement Lab)

Artificial anterior tibial translation

The research group of Prof. Dr. Sven Bruhn (University of Rostock, Institute of Sports Science) already established a measurement method in which standardized perturbations at the tibia can be induced.[12 14] The same methodological setup was duplicated at Bern Movement Lab of BFH by our research group (Fig. 15) in cooperation with Prof. Dr. Sven Bruhn. Beforehand, the impulse characteristics were validated,[14] and the influence of fatigue on the reflex response of the muscles securing the knee joint was assessed.[12] Reliability of reflex measurements for the hamstrings was analyzed at the Bern Movement Lab: Measurements of the BF showed ICCs between 0.88 and 0.96 for the defined time intervals (-50 – 0 ms, 20 – 40 ms, 40 – 60 ms, 60 – 95 ms) with bias and limits of agreement ranging between 2 ± 10% and 8 ± 41%.20 ICCs of the ST were between 0.87 and 0.95 with bias and limits of agreement between 3 ± 6% and 11 ± 42%.[22] Test-retest measurements with 14 participants (equal distribution of sex) showed ICCs between 0.87 and 0.96 for intrasession reliability and a test-retest variability of < 5%.[22] ICCs between 0.58 and 0.87 for intersession reliability and a test-retest reliability < 10% were found.[22] This pilot study provided important information on the feasibility of the measurements and the handling of the artificially induced, anterior tibial translations.[22] Additionally, several investigations were done at the Bern Movement Lab with the set-up as described below.[7-9]

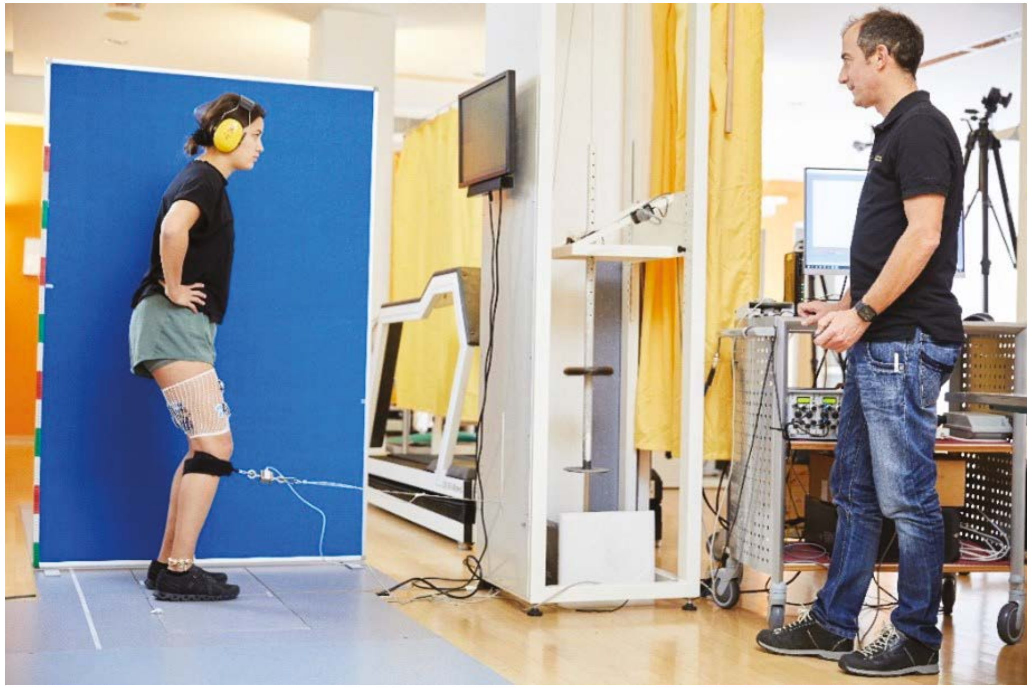

Figure 15: Set-up for reflex measurements at Bern Movement Lab with participant and assessor (©Bern Movement Lab)

The participants were positioned in a relaxed stance with slightly flexed ankle, hip and knee joints (30° flexion) on two force plates (Type 9286BA, Kistler®, Winterthur, CH) (Fig. 15 & 16). The hands were at the hips. Using the force plates, a symmetrical weight distribution on both legs was be checked real-time by both the participant and the assessor. After positioning, subjects completed 2x15 stretch reflex applications per limb with recordings of neuromuscular activity.[12 14] A pause of at least 30 s was provided between each application to check or correct the subject's standardized position. After 15 trials, a break of 2-3 min was provided to relax or walk around. For 15 measurements, neuromuscular fatigue can be neglected.

Figure 16: Check for 30° knee flexion during reflex measurements (©Bern Movement Lab)

Analysis of EMG data and main outcomes

Post-processing of the EMG signals is described in detail in Chapter 4, 5 and 6 in the methods section. The root mean square (RMS) values of stair descent and reflex measurements were normalized to the MVC values recorded during treadmill walking for interindividual comparability. The mean values of the respective gait phases and time windows for reflex responses were then expressed as a percentage to the MVC (%MVC, MVC = 1.0) as it had been applied to related questions before.[16-19]

Outcomes from EMG measurements of stair descent equaled the normalized RMS values during the three defined gait phases such as preactivation (PRE) before touchdown (initial contact foot on step), weight-acceptance (WA) and push-off (PO) (Fig. 17).

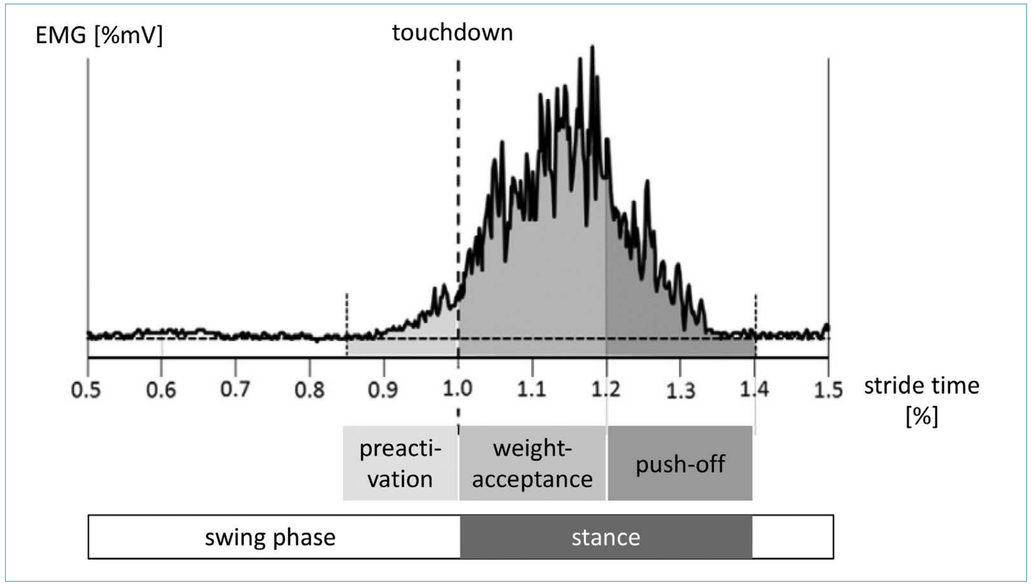

Figure 17: Example of muscle activity for stair descent in three phases of gait corresponding to preactivation, weight-acceptance and push-off phase (adapted from Baur et al., 2011,[19] with permission, license N°5511380859176).
Abbreviation: EMG = electromyography; mV = millivolt

To quantify reflex responses for anterior tibial translation, four defined time intervals corresponding to preactivation after onset of tibial translation (PRE-50; -50 - 0 ms), short-latency reflex response (SLR, 20 – 40 ms), medium-latency reflex response (MLR, 40 – 60 ms), and long-latency reflex responses (LLR, 60 – 95 ms) were used (Fig. 18).[12 14]

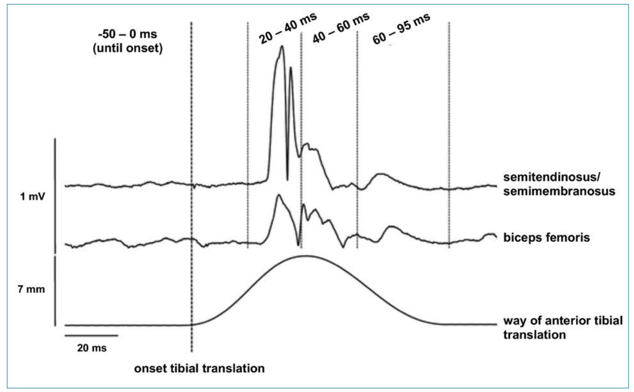

Figure 18: Example of muscle activity in four defined time intervals corresponding to preactivation after onset of tibial translation, short-, medium-, and long-latency reflex responses (adapted from Behrens et al., 2013;[12] Creative Commons Attribution License)
Abbreviations: mm = millimeter; ms = millisecond; mv = millivolt

Table 2 presents the primary and secondary outcomes related to EMG for stair descent and anterior tibial translation measurements.

Table 2: Primary and secondary outcomes: Analysis of EMG signals in time intervals following anterior tibial translation and initial foot-ground contact[12-14 17]

Primary outcomes	Unit
Time intervals after anterior tibial translation	
• -50-0 ms background activity/pre-activation (PRE_50) • 20-40 ms short latency response (SLR) • 40-60 ms medium latency response (MLR) • 60-95 ms long latency response (LLR)	Normalized RMS values [µV µV^{-1}] (%MVC)
Secondary outcomes	**Unit**
Time intervals of gait phases for stair descent	
• Pre-activation (PRE) • Weight-acceptance (WA) • Push-off (PO)	Normalized RMS values [µV µV^{-1}] (%MVC)

Abbreviations: ms = milliseconds; MVC = maximum voluntary contraction; RMS = root mean square; µV = microvolt

2.6 Funding

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References

1. Blasimann A, Koenig I, Baert I, et al. Which assessments are used to analyze neuromuscular control by electromyography after an anterior cruciate ligament injury to determine readiness to return to sports? A systematic review. *BMC Sports Sci Med Rehabil* 2021;13(1):142. doi: 10.1186/s13102-021-00370-5 [published Online First: 2021/11/10]

2. Steiner M, Baur H, Blasimann A. Sex-specific differences in neuromuscular activation of the knee stabilizing muscles in adults - a systematic review. *Arch Physiother* 2023;13(1):4. doi: 10.1186/s40945-022-00158-x [published Online First: 2023/02/16]

3. Blasimann A, Busch A, Henle P, et al. Acute anterior cruciate ligament injury: neuromuscular control during stair descent and artificial tibia translation. *Orthop J Sports Med* 2022 doi: https://doi.org/10.1177/23259671221123299

4. Blasimann A, Busch A, Henle P, et al. Neuromuscular control in males and females 1 year after an anterior cruciate ligament rupture or reconstruction during stair descent and artificial tibial translation. *Sci Rep* 2023;13(1):15316. doi: 10.1038/s41598-023-42491-6 [published Online First: 2023/09/16]

5. Blasimann A, Busch A, Henle P, et al. Bilateral neuromuscular control one year after anterior cruciate ligament reconstruction or conservative treatment. *Sports Orthop Traumatol* 2023;39(2):208-09.

6. Grooms DR, Page SJ, Nichols-Larsen DS, et al. Neuroplasticity Associated With Anterior Cruciate Ligament Reconstruction. *J Orthop Sports Phys Ther* 2017a;47(3):180-89. doi: 10.2519/jospt.2017.7003 [published Online First: 2016/11/08]

7. Busch A, Blasimann A, Henle P, et al. Neuromuscular activity during stair descent in ACL reconstructed patients: A pilot study. *Knee* 2019;26(2):310-16. doi: 10.1016/j.knee.2018.12.011 [published Online First: 2019/02/09]

8. Busch A, Henle P, Boesch L, et al. Neuromuscular control in patients with acute ACL injury during stair ascent – A pilot study. *Orthop Traumatol* 2019;35(2):158-65. doi: 10.1016/j.orthtr.2019.04.002

9. Schmidt A, Blasimann A, Boesch L, et al. Comparison of neuromuscular hamstring activity of people with acute anterior cruciate ligament rupture and at one-year follow-up - a pilot study. *Swiss Sports & Exerc Med* 2018;66(4):44.

10. Busch A, Blasimann A, Mayer F, et al. Alterations in sensorimotor function after ACL reconstruction during active joint position sense testing. A systematic review. *PLoS One* 2021;16(6):e0253503. doi: 10.1371/journal.pone.0253503 [published Online First: 2021/06/26]

11. De Luca CJ. The use of surface electromyography in biomechanics. *J Appl Biomech* 1997;13(2):135-63.

12. Behrens M, Mau-Moeller A, Wassermann F, et al. Effect of fatigue on hamstring reflex responses and posterior-anterior tibial translation in men and women. *PLoS One* 2013;8(2):e56988. doi: 10.1371/journal.pone.0056988 [published Online First: 2013/04/11]

13. Behrens M, Mau-Moeller A, Wassermann F, et al. Repetitive jumping and sprinting until exhaustion alters hamstring reflex responses and tibial translation in males and females. *J Orthop Res* 2015;33(11):1687-92. doi: 10.1002/jor.22935 [published Online First: 2015/05/06]

14. Bruhn S, Leukel C, Gollhofer A. Differential effects of stimulus characteristics during knee joint perturbation on hamstring and quadriceps reflex responses. *Hum Mov Sci* 2011;30(6):1079-91. doi: 10.1016/j.humov. 2011.07.015 [published Online First: 2011/11/02]

15. Hermens HJ, Freriks B, Disselhorst-Klug C, et al. Development of recommendations for SEMG sensors and sensor placement procedures. *J Electromyogr Kinesiol* 2000;10(5):361-74. doi: 10. 1016/s1050-6411(00)00027-4 [published Online First:2000/10/06]

16. Baur H, Hirschmuller A, Cassel M, et al. Gender-specific neuromuscular activity of the M. peroneus longus in healthy runners - A descriptive laboratory study. *Clin Biomech* (Bristol, Avon) 2010;25(9): 938-43. doi: 10.1016/j.clinbiomech.2010.06.009 [published Online First: 2010/07/27]

17. Baur H, Hirschmuller A, Muller S, et al. Is EMG of the lower leg dependent on weekly running mileage? *Int J Sports Med* 2012;33(1):53-7. doi: 10.1055/s-0031-1286250 [published Online First: 2011/11/19]

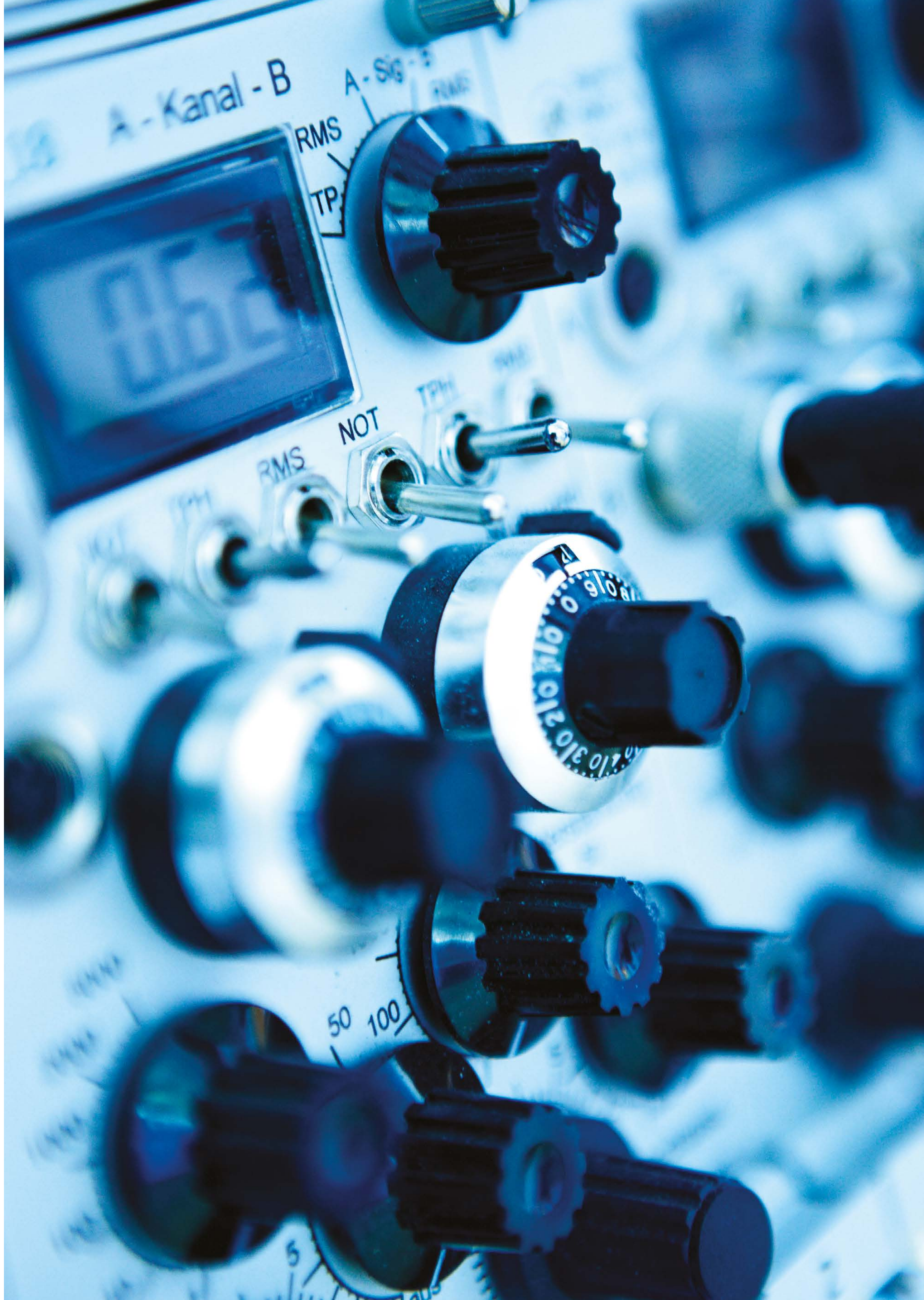
18. Baur H, Hirschmuller A, Muller S, et al. Neuromuscular activity of the peroneal muscle after foot orthoses therapy in runners. *Med Sci Sports Exerc* 2011;43(8):1500-6. doi: 10.1249/MSS.0b013e31820c64ae [published Online First: 2011/01/15]

19. Baur H, Muller S, Hirschmuller A, et al. Comparison in lower leg neuromuscular activity between runners with unilateral mid-portion Achilles tendinopathy and healthy individuals. *J Electromyogr Kinesiol* 2011;21(3):499-505. doi: 10.1016/j.jelekin. 2010.11.010 [published Online First: 2011/01/11]

20. Leitner M, Schmid S, Hilfiker R, et al. Test-retest reliability of vertical ground reaction forces during stair climbing in the elderly population. *Gait Posture* 2011;34(3):421-5. doi: 10.1016/j. gaitpost.2011.06.014 [published Online First: 2011/07/19]

21. Luder G, Schmid S, Stettler M, et al. Stair climbing - an insight and comparison between women with and without joint hypermobility: a descriptive study. *J Electromyogr Kinesiol* 2015;25(1): 161-7. doi: 10.1016/j.jelekin.2014.07.005 [published Online First: 2014/08/30]

22. Baur H, Hanke T, Bamert U, et al. Reliability of hamstring reflex responses after tibia perturbation. *Physiotherapy* 2015;101:e130.



CHAPTER 3

STUDY 1

Assessments for neuromuscular control

Which assessments are used to analyze neuromuscular control by electromyography after an anterior cruciate ligament injury to determine readiness to return to sports? A systematic review

Angela Blasimann[1,2,*], Irene Koenig[1], Isabel Baert[2], Heiner Baur[1], and Dirk Vissers[2]

BMC Sports Sci Med Rehabil 2021 Nov 8;13(1):142.
doi: 10.1186/s13102-021-00370-5.

Abstract

Background: Adequate neuromuscular control of the knee could be one element to prevent secondary injuries after an anterior cruciate ligament (ACL) injury. To assess neuromuscular control in terms of time, amplitude and activity, electromyography (EMG) is used. However, it is unclear which assessments using EMG could be used for a safe return to sports (RTS). Therefore, we aimed to summarize EMG-related assessments for neuromuscular control of the knee in adult patients after an ACL injury to decide upon readiness for RTS.

Methods: This systematic review followed guidelines of Preferred Reporting of Items for Systematic Reviews and Meta-Analyses (PRISMA) and Cochrane recommendations. MEDLINE/PubMed, EMBASE, CINAHL, Cochrane Library, Physiotherapy Evidence Database (PEDro), SPORTDiscus and the Web of Science were searched from inception to March 2019 and updated in November 2020. Studies identifying electromyographic assessments for neuromuscular control during dynamic tasks in adult, physically active patients with an anterior cruciate ligament injury were eligible and qualitatively synthesized. Two independent reviewers used a modified Downs and Black checklist to assess risk of bias of included studies.

Results: From initially 1388 hits, 38 mainly cross-sectional, case-controlled studies were included for qualitative analysis. Most studies provided EMG outcomes of thigh muscles during jumping, running or squatting. Outcomes measures described neuromuscular control of the knee in domains of time, amplitude or activity. Risk of bias was medium to high due to an unclear description of participants and prior interventions, confounding factors and incompletely reported results.

Conclusions: Despite a wide range of EMG outcome measures for neuromuscular control, none was used to decide upon return to sports in these patients. Additional studies are needed to define readiness towards RTS by assessing neuromuscular control in adult ACL patients with EMG. Further research should aim at finding reliable and valid, EMG-related variables to be used as diagnostic tool for neuromuscular control. Moreover, future studies should aim at more homogenous groups including adequately matched healthy subjects, evaluate gender separately and use sport-specific tasks.

Registration: The protocol for this systematic review was indexed beforehand in the International Prospective Register of Systematic Reviews (PROSPERO) and registered as CRD42019122188.

Keywords: Knee, Anterior cruciate ligament injuries, ACL, Electromyography, EMG, Rehabilitation, Patient outcome assessment, Neuromuscular control, Return to sports, RTS

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Background

Anterior cruciate ligament (ACL) injuries happen quite frequently and concern athletes (0.15 injuries per 1000 athletic exposures (AEs)) but also the active part of the general population.[1, 2] Most ACL injuries are due to a non-contact, multiplane mechanism[3] and may lead to instability, secondary meniscal injury or even knee osteoarthritis in the long run.[4] Consequently, this injury means several months or even years of physical impairment with wide consequences for the patients concerning return to work, return to activity or return to sport (RTS). RTS rates between 63 and 97% are reported for patients after ACLR.[5,6.] Most elite athletes return to sports earlier than non-elite athletes,[5] on average within 12 months [6]. However, it remains unclear whether this approach is safe,[6] omitting further injury, respectively. Athletes after ACLR returning to high-demanding sports (including jumping, pivoting and hard cutting) show a more than fourfold increase in reinjury rates over two years.[7] More than 5% of athletes with an ACLR sustain a re-rupture of the graft [6, 8] in the ipsilateral knee after RTS. The risk for an ACL tear in the contralateral knee is as double as high (11.8%) even five years or longer after an ACLR.[8.] Overall, the recurrence rates even after successful ACLR and subsequent rehabilitation are high (29.5% or 1.82/1000 AEs), with a tear of the ACL graft (9.0%), an ACL injury of the opposite leg (20.5%), muscle injuries on the ipsilateral side or even bilateral consequences.[9, 10]

It is known that ipsilateral deficits in clinical knee function and knee laxity persist even years after ACLR.[11,12] ACL patients show altered kinematics and kinetics[13] and different neuromuscular strategies during walking,[14] not only in the injured limb but also in the non-affected side.[13, 15.] These changes are referred to neuromuscular adaptations due to altered sensori-motor control[16] and are caused by altered afferent inputs to the central nervous system due to the loss of the mechanoreceptors of the native (original) ACL.[17] Current literature regarding in ACL patients emphasises the importance of understanding consequences of ACL injury regarding neuromuscular control and kinematics.[18–20.] To describe neuromuscular control in terms of simultaneously activated agonist/antagonist muscle pairs, generalized knee muscle co-contraction parameters are used.[21, 22]

In daily clinical practice, physical performance tests batteries including jumps and tests of muscle function[23] are often used to assess neuromuscular control for RTS. However, there is only limited evidence that passing RTS test batteries—interpreted as having achieved adequate levels of mobility, stability, strength, balance, and neuromuscular control for RTS—reduces the risk for a second ACL injury.[24] Moreover, it remains unclear which measures should be used to bring athletes safely back to RTS with a low risk of re-injury.[25] In conclusion, the currently suggested RTS criteria do not seem to be adequate to assess neuromuscular control of the knee joint to judge upon a safe RTS or even competition. Therefore, meaningful, reliable, valid and accurate diagnostic tools for patients with an ACL injury (either treated surgically or conservatively) are needed and may aid clinical decision-making towards a safe RTS following ACLR. Objective measurements of neuromuscular control should include electromyography (EMG) of involved muscles to judge upon quantity, quality and timing of voluntary activation and reflex activity.[13, 20, 26.] However, up to date it is unclear which EMG-related measurements for neuromuscular control are used in patients with an ACL injury to decide upon a safe RTS.

Objectives

The first objective of this systematic review was therefore to summarize the scientific literature regarding EMG- related assessments for neuro-muscular control in adult, physically active patients with an ACL injury (either treated surgically or conservatively) during functional tasks. The second aim was to analyze whether these assessments for neuromuscular control were used to decide upon readiness for RTS in these patients.

Methods

This systematic review was planned, conducted and analyzed according to the guidelines of Preferred Reporting of Items for Systematic Reviews and Meta-Analyses (PRISMA)[27] and followed the recommendations of Cochrane group.[28]

The protocol for this systematic review was indexed beforehand in the International Prospective Register of Systematic Reviews (PROSPERO) and got the registra-tion number CRD42019122188.

Eligibility criteria

To define the relevant key words for the literature search, the Participants-Intervention-Control-Out-come-Study design (PICOS) scheme was used as follows *(Table 1)*.

Studies were considered eligible for this systematic review if they met the following inclusion criteria: Study participants—either females, males or both—had to be 18 years or older, suffer from an ACL injury —either treated conservatively or surgically—with a time since injury/surgery of six months at least, be athletes or physically active people who participate in sports activities on a regular basis (as defined by each study, e.g. Tegner Activity Score (TAS) ≥ 3) to get data to decide upon RTS. Moreover, included studies had to have used active or functional tasks such as walking, stair climbing or jumps, applied assessments for neuromuscular control of lower limb muscles using EMG, be original articles published in peer-reviewed, scientific journals in English, German, French, Italian or Dutch, and available as full texts. Exclusion criteria were model-driven approaches, animals or cadavers, comparisons of surgical techniques, passive or non-functional tasks (such as isokinetic measurements for strength and isometric muscle activity), editorials, conference abstracts, book chapters, theses, systematic reviews and meta-analyses.

Data sources

The search was effectuated from inception until March 2019 and updated in November 27th, 2020 in the electronic databases MEDLINE/PubMed, EMBASE, CINAHL, Cochrane Library, Physiotherapy Evidence Database (PEDro), SPORTDiscus and in the Web of Science. To ensure new articles matching the search terms, e-mail alerts were established from each of the databases if possible.[29] Furthermore, a hand search was done using the reference lists of included articles to identify additional and potentially eligible articles that had been missed in the electronic database searches. The hits from these two additional sources were also screened for eligibility applying the same criteria as for the articles from the database search.

Search strategy

In all sources, the advanced search mode was used if available. A search matrix combining relevant keywords (if possible MeSH-terms) with the Boolean operators AND and OR was used and customized for searches in all databases if necessary (see Additional file "Search string for MEDLINE/PubMed" 1): "anterior cruciate liga- ment/anterior cranial cruciate ligament/ACL"; "anterior cruciate ligament injuries/strains and sprains/rupture/tear/injury/deficiency"; "anterior ligament reconstruction/anterior cruciate ligament/surgery/reconstructive surgical procedures/orthopedic procedure/ orthopedic procedure/tendon graft/tendon transfer/conservative treatment/non-surgical/rehabilitation/physical therapy modalities / physiotherapy / kinesiotherapy/exercise/instruction/resistance training/neuromuscular training/postoperative care";"neuromuscular control/neuromuscular activity/sensorimotor control/muscle activity/active stability"; "electromyography/EMG/electromyogram/amplitude/timing/mean activity/peak activity/duration of activity/onset/offset/on–off-pattern/ pre-activity/latency/reflex response". In the updated search, articles were filtered by date of publication, with the aim of including only those published between March 2019 and November 2020.

Study selection

All hits obtained by the database searches were down-loaded to the Rayyan reference management platform [30] and inserted into EndNote (Clarivate Analytics, Philadelphia, USA). Prior to screening, duplicates were removed. Two authors (AB and IK) independently screened title and abstract of the records, one by using the software EndNote (Clarivate Analytics, Philadelphia, USA) and the other with the help of the free software "rayyan" [30]. After screening, full texts of relevant hits were read by the two authors (IK, AB) to decide upon in- or exclusion. If their decisions did not match, discussion took place until consensus was achieved. If consensus would not have been reached, a third author (IB or HB) would have finally decided upon in- or exclusion of the record in question; however, this was not necessary.

Table 1 Overview of PICOS criteria for key word definitions

Parameter	Criteria
Participants (P)	Adult people (age of 18–65 years) who sustained an ACL injury, either treated conservatively or surgically (repaired with an autograft)
Intervention (I)	Assessment of neuromuscular control, active knee stability, sensorimotor control, active stability of the lower limb or similar during dynamic activities
Control (C)	Uninjured limb/contralateral side or contralateral lower limb of the ACL-injured participant, or a healthy control group
Outcomes (O)	Any EMG-related outcome describing neuromuscular activity/control in domains of time, amplitude etc.; parameters describing EMG activity of lower limb muscles; related to EMG variables, such as amplitude, timing, mean or peak activity, duration of activity, onset and offset/on–off-pattern respectively, pre-activity, latency, reflex response [14, 20]
Study design (S)	Any laboratory or interventional study, cross-sectional or longitudinal such as randomized controlled trials, clinically controlled trials without randomization, laboratory/experimental controlled trials etc

Data collection process and data extraction

After final decision of all studies, data extraction for each eligible study was performed by the first author (AB) with a predefined Microsoft® Excel (Microsoft Corporation, Redmond WA, USA) spreadsheet as piloted form. The first author (AB) extracted necessary information from each article describing the study design, groups measured and their characteristics, the tasks to be fulfilled by all participants, and all EMG-related assessments or methods used to evaluate neuromuscular control. Furthermore, the chosen assessment for neuromuscular control were judged whether they were used to clear the participants for RTS. The second author (IK) checked the extracted data at random. As all included studies provided enough information to be qualitatively analyzed, it was not necessary to contact corresponding authors for obtaining or confirming data.

Assessment of risk of bias in included studies

The risk of bias of all the included articles was independently assessed by two raters (AB, IK) by using the Downs and Black checklist [31] in a modified form.[29, 32] The following categories were evaluated: (1) reporting bias: objectives/hypothesis, main outcomes, patients' characteristics, interventions, principal confounders, main findings, estimates of random variability, actual probability values; (2) external validity bias: study subjects/staff/places/facilities representative; (3) internal validity bias: blinding subjects/assessors, data dredging present, different lengths of follow-up/same time period between intervention and outcome for cases and controls, statistical tests/main outcome measures appropriate; (4) selection bias: patients and controls from same population and over same period of time, randomization, allocation concealed, adjustments for confounding, loss to follow-up; and (5) power analysis (see Additional file "Methodological quality assessment" 2). Each question of the categories was scored with 1 or 2 points if the criterium was fulfilled (answer "yes"), zero points if the answer was "no", "not fulfilled" and an "X" if the criterium was not applicable, e.g. randomization for a case–control or cross-sectional study, "IC" for intrasubject comparison, respectively.

For this systematic review, studies with a total score of 17 or above out of 25 (more than 2/3 of the maximum total score) were considered as being of high methodological quality, showing a "low" risk of bias respectively.[29] Studies which reached 13 to 16 points (more than 50% of the maximum total score) were rated as being of "medium" quality, and total scores below 13 were rated as being of low methodological quality, "high" risk of bias respectively. As the aim of this systematic review was to summarize the applied measures for neuromuscular control, the methodological quality of the included studies was of secondary interest. Therefore, no study was excluded due to a low total score in the risk of bias assessment.

Results

Study selection

Hits from the first and the updated database search including e-mail alerts and hand search were screened for duplicates. After applying in- and exclusion criteria according to PRISMA flowchart,[27] a total of 38 articles involving 1236 subjects—809 participants with ACLR or ACL deficiency and 427 healthy controls—could be used for qualitative analysis. Reasons for exclusion were participants younger than 18 years, not able to achieve RTS, time since injury or surgery less than six months, static or non-functional task, study design (e.g. systematic review, study protocol), unclear or inadequate outcome, healthy participants or without ACL injury. Included studies had mainly a cross-sectional, case-controlled study design. Details about every step of the search are illustrated in the following flowchart (Fig. 1).

Risk of bias assessment

Risk of bias of half (19 studies, 50.0%) of the included studies was medium,[13, 33–50] six (15.8%) showed high methodological quality [51–56] and 13 studies (34.2%) were of low quality [57–69] *(Table 2)*. The main reasons for a medium to low methodological quality were due to an unclear description of participants and prior interventions, confounding factors, and incompletely reported results. Table 2 provides details about the risk of bias assessment for each included study.

Characteristics of included studies *Study design*

All included studies were case–control studies, except two which where case series[56] or a single-case study.[69] Two reported a retrospective or secondary data analysis[52, 55] or provided a subgroup analysis from a larger trial[45, 47–49, 65–67] *(Table 2)*. Thirty-five studies compared the ACL participants with at least one control group (other ACL treatment, e.g. surgical versus conservative, or healthy controls), the remaining three studies made a comparison between the injured and the non-injured leg of the participants[42, 44] or compared the pre-injury status with follow-up data from pre- and post-surgery.[69]

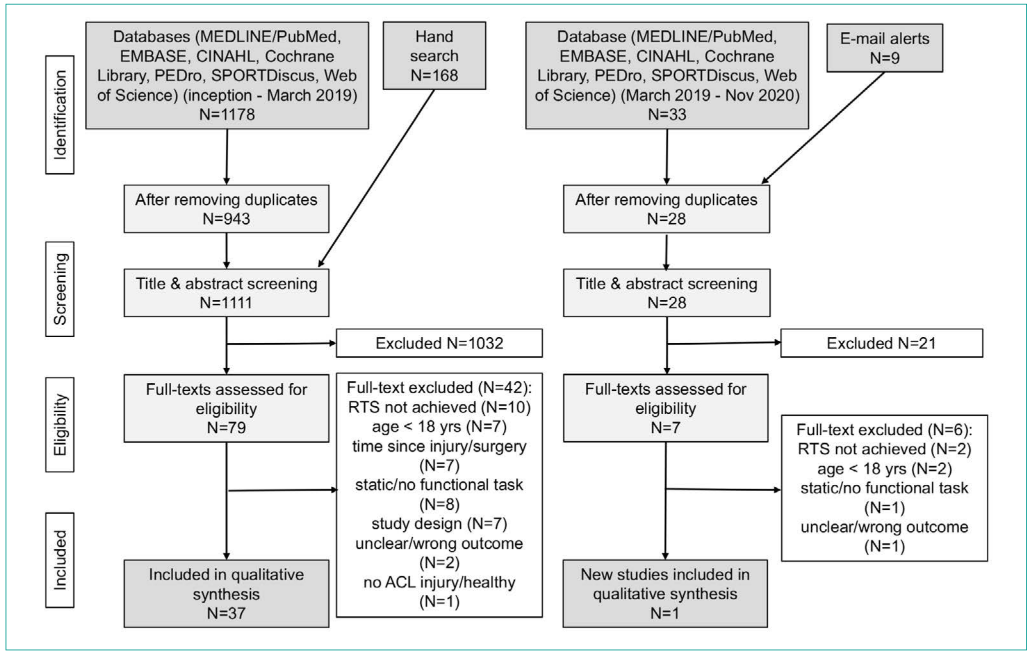
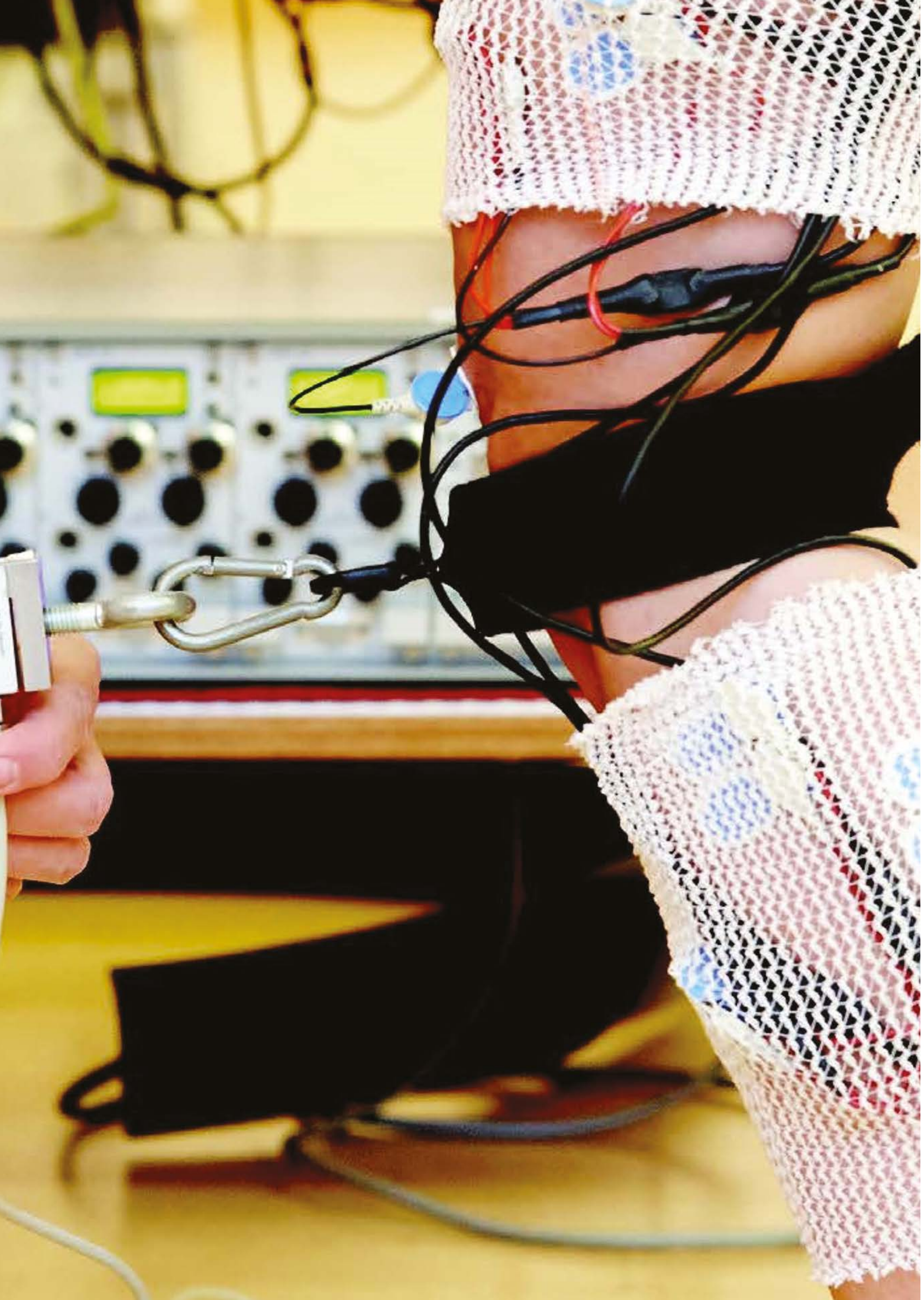


Fig. 1 Flowchart of literature search according to guidelines of PRISMA[27]. PEDro = Physiotherapy evidence database; PRISMA = Preferred Reporting of Items for Systematic reviews and Meta-Analyses



Participants

The number of included, adult participants with ACL injury varied from N = 1 [69] to a maximum of N = 70 [62] with a wide range of described physical activity from "normal",[58] "regular",[64] "active in at least one sport",[61] TAS ≥ 3,[50] minimal 2 h/week[33, 34] to athletes at level I sports including jumping, pivoting and hard cutting,[42, 57, 59] elite soccer players[35, 38, 67, 69] or elite skiers.[50] Some authors restricted study participation to either males[33, 34, 36, 39, 44–46, 50, 58,60, 67] or females,[50, 51, 64–66, 68, 69] others measured females and males.[13, 35, 37, 40, 41, 47–49, 52, 54–57, 59, 61, 62] Three studies did not provide any data about the gender of their participants.[42, 53, 63] More patient characteristics of included studies can be found in Table 3.

Details regarding methodological aspects of all included studies are presented in Table 4 below.

Interventions

The number of muscles assessed ranged from one[37, 45, 61] to ten.[59] Mainly muscle activity of four muscles of the thigh, vastus lateralis, vastus medialis, biceps femoris and semitendinosus, had been assessed. However, there were also studies measuring the adductor longus,[39, 62] gluteus medius,[39, 65, 66] gluteus maximus,[41, 52, 54–56, 59, 65, 66] and calf muscles such as soleus, medial and lateral gastrocnemius.[47–49, 54–56, 59, 60, 63]

The tasks used were very diverse: there were activities of daily life such as walking on even ground and downhill,[33, 47, 53, 57, 58, 62, 63, 68] and stair climbing.[13, 49] Other activities went more towards sports such as running[44, 45, 60, 67, 68] and jumping[36, 37, 39–42, 48, 50–52, 54–56, 59, 61, 65, 66, 68] where mainly the single-leg hop for distance, drop jumps and countermovement jumps were used. Some authors chose typical rehabilitation exercises such as forward lunges,[34] Nordic hamstrings or hamstring curls[35] and squats.[64] At the other end of the scale, more complex, highly demanding, sport-specific tasks such as an instep soccer kick[38] or a side-cutting maneuver[69] were reported. Only few research groups used perturbation platforms to simulate injury mechanisms during walking[53] or squatting,[46, 64] or applied devices to stress the ACL in the posterior-anterior direction.[50] In addition, two studies even investigated the influence of fatigue on neuromuscular control.[41, 52]

Table 2 Risk of bias assessment with modified Downs and Black checklist [29, 31, 32]

Authors and year	Design	Reporting								External validity			Internal validity												Power	Score	RoB
		1	2	3	4	5	6	7	10	11	12	13	14	15	16	17	18	20	21	22	23	24	25	26	27	Total	Rating
Busch et al. (2019) [13]	CCS	1	1	1	1	2	1	1	1	X	0	1	X	X	1	X	1	1	X	X	X	X	1	X	0	14	Medium
Alkjaer et al. (2003) [33]	CCS	1	1	1	1	2	1	1	1	X	0	1	X	X	1	X	1	1	X	X	X	X	1	X	0	14	Medium
Alkjaer et al. (2002) [34]	CCS	1	1	1	1	2	1	1	1	X	0	1	X	X	1	X	1	1	X	X	X	X	1	1	0	15	Medium
Arnason et al. (2014) [35]	CCS	1	1	1	1	2	1	1	1	X	0	1	X	X	1	X	1	1	1	X	X	X	1	X	0	15	Medium
Bryant et al. (2009) [36]	CCS	1	1	1	1	2	1	1	1	X	0	1	X	X	1	1	1	1	1	X	X	X	1	X	0	16	Medium
Burland et al. (2020) [37]	CSS	1	1	1	1	2	1	1	0	X	X	1	X	X	1	X	1	1	1	X	X	X	1	X	1	15	Medium
Cordeiro et al. (2015) [38]	CCS	1	1	1	1	2	1	1	1	X	0	0	X	X	1	X	1	1	1	X	X	X	X	X	1	14	Medium
Dashti Rostami et al. (2019) [39]	CCS	1	1	1	1	2	1	1	1	X	0	1	X	X	1	1	1	1	X	X	X	X	1	X	0	15	Medium
Jordan et al. (2016) [40]	CCS	1	1	1	1	2	1	1	1	X	0	0	X	X	1	X	1	1	1	X	X	X	X	X	1	14	Medium
Lessi et al. (2017) [41]	CCS	1	1	1	1	2	1	1	0	X	0	1	X	X	1	X	1	1	X	X	X	X	1	X	1	14	Medium
Oliver et al. (2018) [42]	P, CCS	1	1	1	1	1	1	1	1	X	0	1	X	X	1	1	1	1	IC	1	X	X	IC	X	0	14	Medium
Ortiz et al. (2014) [43]	CCS	1	1	1	1	2	1	1	1	X	0	1	X	X	1	X	1	1	1	X	X	X	0	1	0	15	Medium
Patras et al. (2009) [44]	CCS	1	1	1	1	2	1	1	1	X	0	0	X	X	1	0	1	1	IC	X	X	X	IC	X	0	12	Medium
Patras et al. (2010) [45]	CCS	1	1	1	1	2	1	1	1	0	0	0	X	X	1	X	1	1	X	X	X	X	1	X	0	13	Medium
Pincheira et al. (2018) [46]	CCS	1	1	1	1	2	1	1	0	0	0	0	X	X	1	X	1	1	1	X	X	X	X	X	1	13	Medium
Rudolph et al. (2001) [47]	CCS	1	1	1	1	1	1	1	1	1	1	1	X	X	1	X	1	1	1	X	X	X	X	X	0	15	Medium
Rudolph et al. (2000) [48]	CCS	1	1	1	1	1	1	1	1	1	1	1	X	X	1	X	1	1	1	X	X	X	X	X	0	15	Medium
Rudolph and Snyder-Mackler (2004) [49]	CCS	1	1	1	1	1	1	0	1	1	1	0	X	X	1	X	1	1	1	X	X	X	X	X	0	13	Medium
Swanik et al. (2004) [50]	CCS	1	1	1	1	2	1	1	1	X	0	0	X	X	1	X	1	1	0	X	X	X	X	X	1	13	Medium
Briem et al. (2016) [51]	CCS	1	1	1	1	2	1	1	1	1	0	1	X	X	1	X	1	1	1	1	X	X	1	X	1	18	Low
Lessi et al. (2018) [52]	R, CCS	1	1	1	1	2	1	1	1	X	0	1	X	X	1	1	1	1	1	0	X	X	1	X	1	17	Low
Lustosa et al. (2011) [53]	CCS	1	1	1	1	1	1	1	1	1	1	0	X	X	1	1	1	1	1	1	X	X	1	X	0	17	Low
Nyland et al. (2010) [54]	CCS	1	1	1	1	2	1	1	1	1	1	1	X	X	1	1	1	1	0	1	X	X	0	X	0	17	Low
Nyland et al. (2013) [55]	R, CCS	1	1	1	1	2	1	1	1	1	0	1	X	X	1	1	1	1	1	1	X	X	1	X	0	18	Low
Nyland et al. (2014) [56]	CS	1	1	1	1	2	1	1	1	1	0	1	X	X	1	1	1	1	X	1	X	X	1	X	0	17	Low
Boerboom et al. (2001) [57]	CCS	1	1	1	1	2	1	0	0	X	X	1	X	X	1	0	1	0	0	X	X	X	1	X	0	11	High
Bulgheroni et al. (1997) [58]	CCS	1	1	0	1	1	1	0	0	X	X	1	X	X	1	0	1	1	0	0	X	X	X	X	0	9	High
Gokeler et al. (2010) [59]	CCS	1	1	1	1	1	1	1	1	X	0	1	X	X	1	X	1	1	X	X	X	X	X	X	0	12	High
Hansen et al. (2017) [60]	CCS	1	1	1	1	2	1	1	1	X	0	0	X	X	1	X	1	1	X	X	X	X	X	X	0	12	High
Klyne et al. (2012) [61]	CCS	1	1	0	1	1	1	1	1	1	0	1	X	X	1	X	1	1	X	X	X	X	X	X	0	12	High
Knoll et al. (2004) [62]	CCS	1	1	1	1	2	0	0	1	X	X	0	X	X	1	X	1	1	0	X	X	X	X	X	0	10	High
Kuster et al. (1995) [63]	CCS	1	1	1	1	2	1	1	0	X	X	1	X	X	1	X	1	1	0	X	X	X	X	X	0	12	High
Madhavan and Shields (2011) [64]	CCS	1	1	1	1	2	0	0	0	0	0	0	X	X	1	X	1	1	X	X	X	X	X	X	0	9	High

Table 2 (continued)

Authors and year	Design	Reporting								External validity			Internal validity												Power	Score	RoB
		1	2	3	4	5	6	7	10	11	12	13	14	15	16	17	18	20	21	22	23	24	25	26	27	Total	Rating
Ortiz et al. (2008) [65]	CCS	1	1	1	1	2	0	0	1	X	0	1	X	X	1	X	1	1	X	X	X	X	0	X	0	11	High
Ortiz et al. (2011) [66]	CCS	1	1	1	1	2	0	0	0	X	0	1	X	X	1	X	1	1	X	X	X	X	0	X	0	10	High
Patras et al. (2012) [67]	CCS	1	1	0	1	2	0	1	0	X	0	0	X	X	0	X	1	1	X	X	X	X	X	X	0	8	High
Swanik et al. (1999) [68]	CCS	1	1	1	1	2	0	1	0	X	0	0	X	X	1	X	1	1	0	X	X	X	X	X	0	10	High
Zebis et al. (2017) [69]	CS	1	1	1	1	2	1	0	0	X	0	1	X	X	1	X	1	1	X	X	X	X	X	X	0	11	High

CCS = Case–control study, CS = case study, IC = intrasubject comparison (injured leg versus healthy leg), P = prospective, R = retrospective (secondary analysis), RoB = risk of bias, X = not applicable or unclear

Table 3 Participants' characteristics of included studies

Authors and year	Number of participants (age, sex, group-specific inclusion criteria)	Diagnosis and treatment (only ACL)	Level of activity or sports (RTA, RTS, RTP)	Intervention Group	Control Group 1 (ACL patients)	Control Group 2 (healthy people)	Significant difference between groups?
Busch et al. (2019) [13]	N = 20; N = 10 ACLR (age: 26 ± 10 yrs; height: 175 ± 6 cm; mass: 75 ± 14 kg) and N = 10 healthy matched controls (age: 31 ± 7 yrs; height: 175 ± 7 cm; mass: 68 ± 10 kg)	N = 10 ACLR (13.2 ± 2 months since repair), quadriceps tendon graft by same surgeon, some with additional injuries which needed surgery	TAS min. 4	N = 10 ACLR participants; age 26 ± 10 yrs, height: 175 ± 7 cm, weight: 75 ± 14 kg, 3 females and 7 males, TAS 7 ± 2	n.a.	N = 10 healthy participants without prior injury of the knee, age 31 ± 7 yrs, height 175 ± 8 cm, weight 68 ± 10 kg, 3 females and 7 males, TAS 6 ± 1; matched according to age, height, weight, gender, (sports) activity level and leg dominance	No
Alkjaer et al. (2003) [33]	N = 29; N = 19, all male, complete chronic (post-injury time 6 months or more) ACLD and N = 10 healthy males as controls for EMG	Complete chronic ACLD, min. 6 months of rehab program after injury, ACL injury clinically diagnosed by experienced orthopedic surgeons with Lachman, Anterior Drawer and Pivot-Shift Tests; TLS scores applied to separate ACLD-participants in copers and non-copers	Min. 2 h/wk of physical activity	N = 9; male copers; (mass: 76.7 (14.3) kg, height: 1.81 (0.06) m, age: 28.3 (6.1) yrs); mean TLS scores: 87.1 (5.8) and 6.1 (0.6) respectively; mean time after injury: 39.1 (42.3) (range 6.0–120.0) months	N = 10; male non-copers; mass: 80.4 kg (SD 6.7); height: 1.79 m (SD 0.05), age: 31.7 yrs (SD 5.9); mean TLS scores: 74.0 (SD 7.1) and 3.8 (SD 0.6), respectively; mean time after injury: 55.0 months (SD 42.7) (range 6.0–144.0)	N = 10; male healthy; mass: 77.5 kg (SD 7.9), height: 1.82 m (SD 0.05), age: 31.0 yrs (SD 2.8)	No
Alkjaer et al. (2002) [34]	N = 23 all male; N = 17 males with complete ACLD, N = 6 healthy controls	Complete ACLD, min. 6 months of rehab program after injury; TLS scores applied to separate ACLD-participants in copers and non-copers	Min. 2 h/wk	N = 8; male copers; weight: 76.6 kg (SD 14.8); height: 1.81 m (SD 0.06), age: 26.0 yrs (SD 4.0); mean TLS scores: 85.5 (SD 5.3) and 6.25 (SD 0.5), respectively, mean time after injury: 34.0 months (SD 39.2) (range 6.0–120.0)	N = 9; male non-copers; weight: 80.6 kg (SD 7.1); height: 1.79 m (SD 0.06), age: 31.2 yrs (SD 6.0); mean TLS scores: 74.0 (SD 7.1) and 3.8 (SD 0.6), respectively; mean time after injury: 51.8 months (SD 44.0) (range 6.0–144.0)	N = 6; male healthy; weight: 73.8 kg (SD 7.9), height: 1.81 m (SD 0.05), age: 31.0 yrs (SD 1)	No

Table 3 (continued)

Authors and year	Number of participants (age, sex, group-specific inclusion criteria)	Diagnosis and treatment (only ACL)	Level of activity or sports (RTA, RTS, RTP)	Intervention Group	Control Group 1 (ACL patients)	Control Group 2 (healthy people)	Significant difference between groups?
Arnason et al. (2014) [35]	N = 36; N = 18, female and male soccer players with ACLR (post-injury time 1–6 yrs) and N = 18 healthy female and male soccer players from the same team (men's and women's top league in Iceland), matched for gender, height, body mass and "involved" side designation, as controls	ACLR: successful return to full participation in soccer; no muscle strain injury in knee flexors in past 3 months, no orthopedic condition excluding from soccer	Full participation in soccer (Icelandic top leagues)	N = 18 ACLR participants in total; N = 8 males, N = 10 females; all participants mean mass: 69.2 (11.8) kg, height: 1.73 (0.09) m, age: 23.7 (3.6) yrs; mean BMI: 23.0 (2.4) kg/m^2; left/right dominance 2/16; involved/uninvolved is the dominant leg 8/10; time since injury 1–6 yrs	n.a.	N = 18 healthy participants; N = 8 males, N = 10 females; all participants mean mass: 68.6 (11.2) kg, height: 1.73 (0.08) m,age: 20.5 (3.7) yrs; mean BMI: 22.7 (2.0) kg/m2	No
Bryant et al. (2009) [36]	N = 59; N = 10 males with ACLD (18–35 yrs); N = 27 matched males with ACLR (14 with patella tendon graft, 13 with combined ST and gracilis graft); N = 22 matched controls	Cincinnati Knee Rating System (0–100 points); ACLD: full ROM, neg. Lachman, neg. Pivot-Shift; confirmed isolated ACL rupture (arthroscopic) min. 1 yr before testing; same orthopedic surgeon for all ACLR	n.m., but hopping required	N = 10 male with ACLD (18–35 yrs)	N = 27 matched males with ACLR (14 with patella tendon graft, 13 with combined ST and gracilis graft)	N = 22 matched (age, activity level, anthropometrics), healthy controls no history of trauma or disease in either knee and no evidence of abnormality on clinical examination	No
Burland et al. (2020) [37]	N = 36; N = 16 females ACLR, N = 10 males ACLR, N = 8 healthy controls (N = 4 females, N = 4 males)	Unilateral ACLR, 21 subjects with BPTB graft, 5 with hamstrings graft; enrolled in physician-directed rehabilitation program, able to do single limb forward hop	n.m. as criteria for in-/exclusion; minimum TAS of 5 preinjury/after surgery	N = 26 with ACLR, age: 20.2 ± 2.7 yrs, mean time since injury: 2.2 ± 2.7 yrs, TAS preinjury: median 8.0 (range 5.0–10.0), after surgery 7.0 (range 5.0–9.0) points, cleared for unrestricted RTS	n.a.	N = 8 healthy controls, age: 23.3 ± 1.8 yrs, TAS: median 9.0 (range 5.0–10.0) points	No, except age
Cordeiro et al. (2015) [38]	N = 17 males; N = 8 with ACLR and N = 9 healthy controls	ACLR: min. 6 months post-surgery on dominant leg, bone-tendon-bone arthroscopy, no problems at end of physiotherapy phase	Soccer, professional level	N = 8 professional male soccer players (age: 24.6 ± 3.5 yrs, height: 1.83 ± 0.06 m, mass: 77.3 ± 7 kg) with ACLR min. 6 months since surgery	n.a.	N = 9 healthy controls; professional male soccer players (age: 24.0 ± 3.5 yrs, height: 1.76 ± 0.05 m, mass: 72.9 ± 3.5 kg), no knee or leg injuries or previous ACL surgeries	No

Table 3 (continued)

Authors and year	Number of participants (age, sex, group-specific inclusion criteria)	Diagnosis and treatment (only ACL)	Level of activity or sports (RTA, RTS, RTP)	Intervention Group	Control Group 1 (ACL patients)	Control Group 2 (healthy people)	Significant difference between groups?
Dashti Rostami et al. (2019) [39]	N = 36; N = 12 ACLD, N = 12 ACLR; N = 12 healthy controls; all male athletes	For patients: primary unilateral ACL injury	Athletes, regular sports participation, ACLD = copers	N = 12 males, 18 to 36 months post-ACLR	N = 12 males, 18 to 36 months after ACL rupture (= ACLD, copers); grade 2 or 3 rupture including the following definition of copers: athletes with ACLD for at least 18 months, no symptoms of knee instability during regular sports participation	N = 12 healthy males, matched controls; no knee injury, no knee pain	No
Jordan et al. (2016) [40]	N = 22; N = 11 ACLR, N = 11 control; elite skiing athletes from Canada's national alpine skiing and skier cross team	ACLR: primary ACL injury, at least 12 months post-surgery, actively competing athletes at the Federation International de Ski World Cup level with full medical clearance to compete	Elite ski racers, TAS 10, competing at international level	N = 11 actively competing ACLR skiers (females, n = 5: age: 23.6 ± 1.8 yrs, mass: 61.0 ± 5.3 kg; males, n = 6: age: 26.5 ± 5.8 yrs, mass: 84.4 ± 9.0 kg; 7 subjects with ST autograft, 1 with BPTB autograft, 3 with cadaver allograft	n.a.	N = 11 matched controls with no history of ACL injury (females, n = 5: age: 21.8 ± 3.2 yrs, mass: 63.7 ± 4.6 kg; males, n = 6: age: 23.3 ± 3.3 yr, mass: 84.7 ± 5.1 kg; active competitors at the international level defined as participation in the Federation International de Ski World Cup circuit	n.m.
Lessi et al. (2017) [41]	N = 40; N = 20 with ACLR, N = 20 healthy controls	ACLR: non-contact ACL injury, unilateral reconstruction of the ACL with no prior history of a contralateral ACL injury, no recent history of an ankle, hip, spine, or contralateral knee injury in the past 12 months; rehabilitation completed, cleared to RTS by both their physician and physical therapist	Recreational sports, meaning aerobic or athletic activity at least 3x/wk	N = 20 with ACLR, 13 males, 7 females, at least 12 months post-surgery, 13 with hamstring ipsilateral autografts, 7 with BPTB ipsilateral autograft	n.a.	N = 20 healthy controls, 13 males, 7 females, no history of any dysfunction or previous joint trauma, no prior history of ACL injury or injury of lower extremity in last 12 months; were matched by age, sex, weight, and current sporting activity type	No

Table 3 (continued)

Authors and year	Number of participants (age, sex, group-specific inclusion criteria)	Diagnosis and treatment (only ACL)	Level of activity or sports (RTA, RTS, RTP)	Intervention Group	Control Group 1 (ACL patients)	Control Group 2 (healthy people)	Significant difference between groups?
Oliver et al. (2018) [42]	N = 25 ACLD, mean age: 22 ± 4.61 yrs, mean mass: 71.18 ± 10.57 kg, mean height: 177.55 ± 9.69 cm; N = 18 males (72%); N = 2 lost to follow-up due to personal issues, all remaining 23 patients concluded the study (pre-surgery, 4 and 6 months post-surgery for questionnaires, at 6 months for jumps)	Complete ACL tear was based on clinical symptoms, on positive Lachman and pivot shift tests, and was confirmed by magnetic resonance imaging; reconstruction 2–3 months after the injury by same surgeon using BTB-technique	More than 200 h of sports activity per year, including jumping, pivoting and twisting actions	Injured knee	Non-injured knee	n.a.	n.a.
Ortiz et al. (2014) [43]	N = 31 females; N = 15 ACLR, N = 16 healthy females	ACLR: same orthopedic surgeon, same rehabilitation protocol, N = 13 were injured while participating in competitive volleyball at the collegiate or professional level; at least 12 months post-surgery, full RTS allowed (without restrictions) to pre-injury level	Sports-specific physical activities as described by the Activity Rating Scale, scores from 12 to 16, consistent with activities such as running, cutting, decelerating, and pivoting more than 2x/wk = high level of participation	N = 15 ACLR with SG graft, age range: 21–35 yrs (height: 167.71 ± 9.0 cm, body mass: 67.68 ± 11.66 kg), time since surgery was between 12 months and 5 yrs, fullRTS allowed (pre-injury level); N = 1 drop-out due to inability to perform tasks	n.a.	N = 16 healthy females, participating in volleyball, basketball, and soccer at the collegiate or intramural sports level, age range: 21–35 yrs, height: 160.50 ± 5.17 cm, body mass: 59.35 ± 10.37 kg	No for age and activity, height and weight
Patras et al. (2009) [44]	N = 9 males with ACLR	ACLR: unilateral ACL tear confirmed by MRI and arthroscopy, BPTB graft within 6 months after injury, same rehabilitation protocol, RTS permitted 6 months post-surgery	Athletes, amateur soccer players, at least TAS 7	N = 9 males with ACLR, mean age: 27.7 ± 3.5 yrs, mean weight: 79.5 ± 7.3 kg, mean height: 178 ± 5.9 cm, mean time since surgery: 19.2 ± 5.7 months, median Lysholm score: 95 (range 94–96), TAS: 8 (range 7–9), resumed their sports activities	n.a.	n.a., non-injured side respectively	n.a.

Table 3 (continued)

Authors and year	Number of participants (age, sex, group-specific inclusion criteria)	Diagnosis and treatment (only ACL)	Level of activity or sports (RTA, RTS, RTP)	Intervention Group	Control Group 1 (ACL patients)	Control Group 2 (healthy people)	Significant difference between groups?
Patras et al. (2010) [45]	N = 28 males; N = 14 ACLR, N = 14 healthy controls	ACLR: unilateral ACL tear confirmed by MRI and arthroscopy, BPTB graft, performed within 6 months after injury, same surgeon, same rehabilitation, RTS permitted after 6 months post-surgery	Amateur soccer players	N = 14 males with ACLR, mean age: 24.8 ± 5.3 yrs; mean height: 177 ± 5.3 cm, mean weight 77.3 ± 7.5 kg, time since surgery: mean 18.5 ± 4.3 months, pre-injury level of sports participation, median Lysholm score 95 (range 94–100) and TAS 8 (range 7–9)	n.a.	N = 14 healthy males, mean age: 21.7 ± 4.4 yrs; mean height: 180 ± 9.0 cm, mean weight 72.2 ± 8.3 kg, never suffered of any kind of orthopedic or neurological condition; left leg = control leg	n.m.
Pincheira et al. (2018) [46]	N = 50 male soccer players; N = 25 with unilateral ACLR, N = 25 uninjured controls	ACLR: unilateral ACLR with ST-gracilis graft, same surgical team, at least 6 months post surgery; non-contact mechanism during soccer match on the dominant limb	Amateur soccer players, playing at least 2x/wk	N = 25 males with ACLR, age: 28.36 ± 7.87 yrs; weight: 77.56 ± 6.35 kg, height: 169 ± 7 cm, time after surgery: 9 ± 3 months, time between ACL injury and surgery: 3.4 ± 1 months; at time of measurements cleared for full RTS	n.a.	N = 25 healthy males, age: 24.16 ± 2.67 yrs; weight 78.16 ± 5.46 kg, height 172 ± 5 cm; without injury or surgery on lower limb	No
Rudolph et al. (2001) [47]	One component of a larger study; N = 31; N = 10 healthy controls, N = 11 ACLD copers, N = 10 ACLD non-copers	ACLD: full range of motion in both knees, no visible or palpable knee effusion, no symptoms of locking, an uninvolved, healthy knee	Athletes, regular activity in level I sports (involving jumping, pivoting, and hard cutting) and level II sports (involving lateral motions) before injury	N = 11 ACLD copers (2 females, 9 males), age range: 22–43 yrs, mean 30.7 yrs, high-level athletes with ACLD for at least 1 year (confirmed by MRI), any knee instability during regular participation in level I and II sports, no more than one episode of giving way, even during sports, since injury	N = 10 non-copers ACLD (4 females, 6 males), age range: 16–43 yrs, mean 28.1 yrs; more than one episode of giving way since injury, instability during ADL, not returned to sports	N = 10 uninjured individuals, matched by age and activity level to the coper subjects (2 females, 8 men), age range: 23–41 yrs, mean 32.2 yrs)	No (age and joint laxity)

Table 3 (continued)

Authors and year	Number of participants (age, sex, group-specific inclusion criteria)	Diagnosis and treatment (only ACL)	Level of activity or sports (RTA, RTS, RTP)	Intervention Group	Control Group 1 (ACL patients)	Control Group 2 (healthy people)	Significant difference between groups?
Rudolph et al. (2000) [48]	One component of a larger study; N = 31; N = 10 healthy controls, N = 11 ACLD copers, N = 10 ACLD non-copers	ACLD: full range of motion in both knees, no visible or palpable knee effusion, no symptoms of locking, an uninvolved, healthy knee	athletes, regular activity in level I sports (involving jumping, pivoting, and hard cutting) and level II sports (involving lateral motions) before injury	N = 11 ACLD copers (2 females, 9 males), age range: 22–43 yrs, mean 30.7 yrs, high-level athletes with ACLD for at least 1 year (confirmed by MRI, any knee instability during regular participation in level I and II sports, no more than one episode of giving way, even during sports, since injury	N = 10 non-copers ACLD (4 females, 6 males), age range: 16–43 yrs, mean 28.1; more than one episode of giving way since injury, instability during ADL, not returned to sports	N = 10 uninjured individuals, matched by age and activity level to the coper subjects (2 females, 8 men), age range: 23–41 yrs, mean 32.2 yrs)	n.m.
Rudolph and Snyder-Mackler (2004) [49]	One component of a larger study; N = 31; N = 10 healthy controls, N = 11 ACLD copers, N = 10 ACLD non-copers	ACLD: full range of motion in both knees, no visible or palpable knee effusion, no symptoms of locking, an uninvolved, healthy knee	Athletes, regular activity in level I sports (involving jumping, pivoting, and hard cutting) and level II sports (involving lateral motions) before injury	N = 11 ACLD copers (2 females, 9 males), age range: 22–43 yrs, mean 30.7 yrs, high-level athletes with ACLD for at least 1 year (confirmed by MRI, any knee instability during regular participation in level I and II sports, no more than one episode of giving way, even during sports, since injury	N = 10 non-copers ACLD (4 females, 6 males), age range: 16–43 yrs, mean 28.1 yrs; more than one episode of giving way since injury, instability during ADL, not returned to sports	N = 10 uninjured individuals, matched by sex, age and activity level to the coper subjects (2 females, 8 men), age range: 23–41 yrs, mean 32.2 yrs)	No (age and leg length)
Swanik et al. (2004) [50]	N = 29; N = 12 female ACLD, N = 17 female controls	Complete unilateral ACL tear, at least 1 year after injury, mechanical instability (positive Lachman and Pivot-Shift tests), rehabilitation program completed, no ACL surgery	Minimum TAS of 3	N = 12 females with ACLD, age: 25.2 ± 7.3 yrs, mean time since injury 33.6 ± 5.2 months, TAS 5.4 ± 1.83 points	n.a.	N = 17 healthy females, age: 22.7 ± 4.0 yrs, TAS 5.41 ± 1.5 points	n.m.

Table 3 (continued)

Authors and year	Number of participants (age, sex, group-specific inclusion criteria)	Diagnosis and treatment (only ACL)	Level of activity or sports (RTA, RTS, RTP)	Intervention Group	Control Group 1 (ACL patients)	Control Group 2 (healthy people)	Significant difference between groups?
Briem et al. (2016) [51]	N = 36; N = 18, female players with ACLR (post-injury time 1–6 yrs) and N = 18 healthy female players from the same team (from Icelandic women's top league in handball, football, basketball), matched for gender, height, body mass and "involved" side designation, as controls	No information about diagnosis or treatment; exclusion criteria: current musculoskeletal injury, lower limb muscle strain within 3 previous months, not being able to do single-limb hops	ACLR: successful return to competition with their teams; healthy: full participation in soccer (Icelandic top leagues)	N = 18 females, ACLR, recruited via advertisement from teams competing in the top leagues in three team sports handball (n = 5), basketball (n = 4), and football (n = 9)]. In 12 instances, the surgical limb was the individual's dominant one. Characteristics: mean mass: 67.2 (7.8) kg, height: 1.714 (0.05) m, age: 22.7 (3.5) yrs; mean BMI 22.8 (2.4) kg/m2; involved/uninvolved is the dominant leg 12/18; time since injury 1–6 yrs	n.a.	N = 18 healthy females recruited from the same teams, matched for age, height, weight. Characteristics mean mass: 66.3 (7.1) kg, height: 1.708 (0.05) m, age: 21.5 (2.7) yrs; mean BMI 22.7 (2.2) kg/m2	No
Lessi et al. (2018) [52]	N = 14 ACLR (7 males, 7 females) from study of Lessi et al. (2017) [41]	Non-contact ACL injury; unilateral ACLR with autologous ipsilateral graft at least 12 months before recruitment; undergone a rehabilitation program; returned to sports participation; no contralateral ACL injury	Recreational sports	N = 7 males ACLR, age: 23.90 ± 2.80 yrs, height: 1.80 ± 0.1 m, mass: 83.3 ± 7.8 kg, 3 with BPTB graft, 4 with flexor tendons grafts	N = 7 females ACLR, age: 24.7 ± 5.3 yrs, height: 1.63 ± 0.1 m, mass: 65.9 ± 9.0 kg, 2 with BPTB graft, 5 with flexor tendons grafts	n.a.	No, except men were taller than women (P < 0.001) and performed a higher number of sets of the protocol before becoming fatigued their reconstructed limb (P = 0.006)
Lustosa et al. (2011) [53]	N = 25 ACLR; N = 15 with Cincinnati Knee Rating System (CKRS) > 90 points (full RTS), N = 10 with CKRS < 85 points (limited RTS)	At least 2 yrs post-surgery, same rehabilitation program which allowed full RTS activities 7 months post-surgery	Full RTS allowed, not further specified	N = 10 ACLR with CKRS 77.30 ± 6.14 points, age: 33.4 ± 7.53 yrs, time between injury and surgery 52.20 ± 31.33 months, 3 with associated meniscal injuries, 7 without	N = 15 ACLR with CKRS 96.87 ± 2.75 points, age: 34.5 ± 8.85 yrs, time between injury and surgery 67.3 ± 28.5 months, 3 with associated meniscal injuries, 12 without	n.a.	No

Table 3 (continued)

Authors and year	Number of participants (age, sex, group-specific inclusion criteria)	Diagnosis and treatment (only ACL)	Level of activity or sports (RTA, RTS, RTP)	Intervention Group	Control Group 1 (ACL patients)	Control Group 2 (healthy people)	Significant difference between groups?
Nyland et al. (2010) [54]	N = 70 ACLR; N = 35 males; N = 35 females, 5.3 ± 3 yrs post-surgery	Minimum of 2 yrs since unilateral primary ACL reconstruction with allografts performed by same surgeon, standard rehabilitation program with sufficient adherence	Met or exceeded standard accepted RTS activity goals of a minimum 85% bilateral equivalence with single-leg hop–for–distance testing and 60°/s isokinetic peak knee extensor and flexor torque testing	N = 35 males with ACLR, age n.m., height: 180.3 ± 6.9 cm, weight: 88.9 ± 13.3 kg, time after surgery 5.6 ± 3.2 yrs	N = 35 females with ACLR, age n.m., height: 166.6 ± 7.1 cm, weight: 68.2 ± 18.9 kg, time after surgery 5.1 ± 2.6 yrs	n.a.	n.m.
Nyland et al. (2013) [55]	N = 70 ACLR; 35 male and 35 females, 5.3 ± 3 yrs after surgery; secondary analysis of Nyland et al., 2010 [54]	Minimum of 2 yrs since unilateral primary ACL reconstruction with allografts performed by same surgeon, standard rehabilitation program with sufficient adherence	Met or exceeded standard accepted RTS activity goals of a minimum 85% bilateral equivalence with single-leg hop–for–distance testing and 60°/s isokinetic peak knee extensor and flexor torque testing	N = 24 ACLR well-trained/frequently sporting, 50% males, age at surgery 29.8 ± 11.4 yrs, height: 172.5 ± 8.6 cm, weight: 77.1 ± 18.2 kg, time post-surgery 5.7 ± 2.8 yrs, IKDC 87.3 ± 11.5	N = 26 ACLR only sporting sometimes, 50% males, age at surgery 33.1 ± 13.5 yrs, height: 171.7 ± 9.7 cm, weight: 79.4 ± 23.2 kg, time post-surgery 5.4 ± 3.1 yrs, IKDC 87.3 ± 11.5	No healthy control group, but N = 20 ACLR highly competitive subjects, 50% males, age at surgery 26.5 ± 9.4 yrs, height: 176.5 ± 9.4 cm, weight: 76.8 ± 13.9 kg, time post-surgery 4.6 ± 3.0 yrs, IKDC 91.0 ± 9.4	No
Nyland et al. (2014) [56]	N = 65 ACLR; 32 male and 33 females, 5.2 ± 2.9 yrs after surgery; subject group assignments were made based on how they responded to the following question: "Compared to prior to your knee injury how capable are you now in performing sports activities", very capable (group 1 see field for healthy controls), capable (group 2), or not capable (group 3)	Minimum of 2 yrs since unilateral primary ACL reconstruction with allografts performed by same surgeon, standard rehabilitation program with sufficient adherence	Met or exceeded standard accepted RTS activity goals of a minimum 85% bilateral equivalence with single-leg hop–for–distance testing and 60°/s isokinetic peak knee extensor and flexor torque testing	N = 23 "capable = group 2", 52.2% males, age at surgery 29.3 [95% CI: 24.1, 34.4] yrs, height: 172.8 [168.4, 177.3] cm, weight: 76.8 [68.3, 85.2] kg, time post-surgery 5.4 [4.2, 6.6] yrs, IKDC 87.2 [82.1, 92.4]	N = 22 "not capable = group 3", 45.5% males, age at surgery 33.6 [95% CI: 26.4, 39.1) yrs, height: 172.1 [167.1, 177.1] cm, weight: 79.7 [68.0, 91.3] kg, time post-surgery 5.2 [3.8, 6.5] yrs, IKDC 78.6 [71.7, 85.5]	No healthy control group, but N = 20 "very capable = group 1", 50% males, age at surgery 26.5 [95% CI: 21.9, 31.8] yrs, height: 176.5 [170.4, 180.1] cm, weight: 76.8 [67.4, 80.3] kg, time post-surgery 4.6 [2.8, 6.2] yrs, IKDC 91.0 [84.1, 94.6]	No

Table 3 (continued)

Authors and year	Number of participants (age, sex, group-specific inclusion criteria)	Diagnosis and treatment (only ACL)	Level of activity or sports (RTA, RTS, RTP)	Intervention Group	Control Group 1 (ACL patients)	Control Group 2 (healthy people)	Significant difference between groups?
Boerboom et al. (2001) [57]	N = 20; N = 10 ACLD (5 copers, 5 non-copers), N = 10 controls	ACLD: ACL rupture confirmed by physical examination and arthroscopy, conservative treatment	Before injury: all ACLD participants at level I (of the IKDC score), after injury: level I (all copers), level II and III (non-copers)	N = 5 copers (all males) with ACLD, median age: 32 yrs, range 21–46 yrs, median time between primary injury and gait analysis 39 months (13–67), acting at same level of sports and dailyactivities (level I) as before the injury	N = 5 non-copers (3 males, 2 females) with ACLD, with functional instability, median age: 27 yrs, range 23–35 yrs, median time between injury and gait analysis 22 months (16–87), acting at lower level (4 at level III, 1 at level II)	N = 10 healthy males, without a history of knee injury, median age was 22 yrs (range 18–24 yrs)	No in patient groups (age, time between injury and gait analysis); in comparison with healthy controls: n.m
Bulgheroni et al. (1997) [58]	N = 30 all males; N = 15 with ACLR, N = 10 with ACLD, N = 5 healthy controls	ACLR: BPTB graft	Normal activity	N = 15 males with ACLR, age 25 ± 3 yrs, time after reconstruction: 17 ± 5 months, normal activity	N = 10 males with ACLD, age 27 ± 6 yrs, mean time after injury: 20.4 months after injury (range 8–48 months), knee instability	N = 5 males, healthy controls, age 28 ± 3 yrs, no history of musculoskeletal pathology	n.m.
Gokeler et al. (2010) [59]	N = 20; N = 9 ACLR patients, N = 11 healthy controls	ACLR: 6 months after surgery, isolated ACL lesion, no major meniscal or cartilage lesion, normal limb alignment, no relevant previous surgery at any other joint of the limbs, same rehab program at same institution, unrestricted RTS allowed after 9 months post-surgery	Level I-II athletes	N = 9 ACLR patients (6 males, 3 females), mean age: 28.4 ± 9.7 yrs, 27 ± 1.5 wk postoperatively (BPTB technique, same surgeon)	n.a.	N = 11 healthy subjects (8 males, 3 females), level I-II athletes,	n.m.

Table 3 (continued)

Authors and year	Number of participants (age, sex, group-specific inclusion criteria)	Diagnosis and treatment (only ACL)	Level of activity or sports (RTA, RTS, RTP)	Intervention Group	Control Group 1 (ACL patients)	Control Group 2 (healthy people)	Significant difference between groups?
Hansen et al. (2017) [60]	N = 37; N = 18 male patients, N = 19 healthy participants	ACLR: discharged from rehabilitation facility	Ready to return to on-fields sports specific activity	N = 18 male ACLR at the end of their rehabilitation and allowed to running, 7 ± 2 months post-surgery; N = 8 with a BPTB graft, age: 27 ± 7.69 yrs, weight: 80.40 ± 9.44 kg, height: 178.49 ± 7.29 cm; N = 10 with a hamstring graft, age: 26 ± 3.84 yrs, weight: 74.16 ± 7.19 kg, height: 176.89 ± 5.6 cm	n.a.	N = 19 injury-free male controls, age: 35.4 ± 7.8 yrs, weight: 77.6 ± 8.4 kg, height: 179.1 ± 5.6 cm	n.m.
Klyne et al. (2012) [61]	N = 26; N = 15 ACLD, N = 11 healthy controls	ACLD: chronic, unilateral ACL rupture demonstrated with a positive pivot shift and confirmed by orthopedic surgeon, plus a history of subjective stability and a right skill preference in the lower limb, without previous ACL surgery	Active in at least one sport	N = 15 ACLD, 10 males and 5 females, age: 28 ± 7 yrs, average time since injury 34 months (± 17 months), sustained injury while playing sport	n.a.	N = 11 healthy controls, 9 males, 2 females (age: 29 ± 8 yrs), active in at least one sport, no other musculoskeletal problems, right skill preferred in their lower limb, matched for age and activity level	n.m.

Table 3 (continued)

Authors and year	Number of participants (age, sex, group-specific inclusion criteria)	Diagnosis and treatment (only ACL)	Level of activity or sports (RTA, RTS, RTP)	Intervention Group	Control Group 1 (ACL patients)	Control Group 2 (healthy people)	Significant difference between groups?
Knoll et al. (2004) [62]	N = 76; N = 25 ACLR (pre- and postsurgery), N = 51 healthy controls	No previous injury, no meniscal damage, BPTB graft, rehabilitation program	Non-professional athletes pursuing some sports 2-3x/wk	N = 25 with ACLD (before surgery, later ACLR), 18 males, 7 females; first subgroup: 9 male with acute ACLD (mean age: 29.86 ± 6.52 yrs, mean height: 1.77 ± 0.8 m, mean mass: 81.40 kg ± 9.06 kg); second subgroup: 9 males with chronic ACLD (mean age: 39.70 ± 2.1 yrs, mean height: 1.70 ± 0.21 m, mean mass: 88.1 ± 20.2 kg) and 7 females with chronic ACLD (mean age: 30.31 ± 9.48 yrs, mean height: 1.64 ± 0.32 m, mean mass: 62.0 ± 8.4 kg). The chronic ACLD group was examined an average of 28.2 months after injury (ranging from 24 to 52 months), but before surgery	Same population of ACLD, but after surgery ACLR, measured at wk 6, and 4, 8, and 12 months post-surgery	N = 51 healthy controls, 31 males, 20 females, mean age: 31.70 ± 4.1 yrs, mean height: 1.71 ± 0.12 m, mean mass 72.1 ± 25.2 kg, no pathology that would affect gait, unfamiliar with treadmill walking	n.m.
Kuster et al. (1995) [63]	N = 33; N = 21 with ACLD, N = 12 healthy controls	ACLD: arthroscopically confirmed complete ACL ruptures at least 1 year previously	ACLD: TAS range 6–10 (mean 8.2) before injury and range 3–9 (mean 5.3) after injury; controls: TAS range 4–8 (mean 6.1)	N = 19 with 21 ACLD, mean age: 28.2 yrs (range 19–42 yrs), mean height: 174.1 cm (156–187.6 cm), mean weight: 77.9 kg (50–112 kg), mean time since injury 45 months (range of 12–108 months), mean Lysholm score 82 (range 55–100)	n.a.	N = 12 healthy controls, similar in height and weight, mean height: 171.2 cm; weight 70.8 kg, no lower limb injury	Unclear (similar for height and weight)

Table 3 (continued)

Authors and year	Number of participants (age, sex, group-specific inclusion criteria)	Diagnosis and treatment (only ACL)	Level of activity or sports (RTA, RTS, RTP)	Intervention Group	Control Group 1 (ACL patients)	Control Group 2 (healthy people)	Significant difference between groups?
Madhavan and Shields (2011) [64]	N = 24 females; N = 12 with ACLR, N = 12 healthy controls	Complete reconstruction of the ACL with BPTB or HS autograft, ability to climb stairs without difficulty, full joint ROM, SR-36, KOOS, IKDC	Regular physical activity, TAS	N = 12 females ACLR, age: 22.4 ± 2.4 yrs, mean time from surgery 3.7 ± 1.8 yrs, weight: 144.1 ± 19 kg, height: 164.5 ± 5.28 cm, TAS (current) 7.1 ± 2.4	n.a.	N = 12 healthy females, no previous history of knee pathology, age: 24.1 ± 3.2 yrs, weight: 136.5 ± 20.3 kg, height: 163.8 ± 7.3 cm, TAS (current) 6.9 ± 2.1; matched to age	No
Ortiz et al. (2008) [65]	N = 28 females; N = 13 ACLR, N = 15 non-injured controls	Not controlled for graft/surgery or rehabilitation protocol (only similarities); at least 1-year post surgery, no multiple surgeries on the same knee	Recreational fitness activities such as jogging, running, and weightlifting, none of the participants formed part of any intercollegiate, varsity, or competitive sport team	N = 14 physically active young women with ACLR (age: 25.4 ± 3.1 yrs; height:167.5 ± 5.9 cm; body mass: 63.2 ± 6.7 kg; mean time after surgery 7.2 ± 4.2 yrs (1–16 yrs after reconstruction); N = 9 with BPTB graft, N = 3 with gracilis-ST-graft, N = 2 with Achilles tendon graft; N = 1 excluded due to inability to perform tasks	n.a.	N = 15 healthy, noninjured young women from physiotherapy school (age: 24.6 ± 2.6 yrs; height: 164.7 ± 6.5 cm; body mass: 58.4 ± 8.9 kg	n.m.
Ortiz et al. (2011) [66]	N = 28 females; N = 13 ACLR, N = 15 non-injured controls (same group as for Ortiz et al., 2008 [65])	Not controlled for graft/surgery or rehabilitation protocol (only similarities); at least 1-year post surgery, no multiple surgeries on the same knee	Recreational fitness activities such as jogging, running, and weightlifting, none of the participants formed part of any intercollegiate, varsity, or competitive sport team	N = 14 physically active young women with ACLR (age: 25.4 ± 3.1 yrs; height: 167.5 ± 5.9 cm; body mass: 63.2 ± 6.7 kg; mean time after surgery 7.2 ± 4.2 yrs (1 – 16 yrs after reconstruction); N = 9 with BPTB graft, N = 3 with gracilis-ST-graft, N = 2 with Achilles tendon graft; N = 1 excluded due to inability to perform tasks	n.a.	N = 15 healthy, non-injured young women from physiotherapy school (age: 24.6 ± 2.6 yrs; height: 164.7 ± 6.5 cm; body mass: 58.4 ± 8.9 kg	n.m.

Table 3 (continued)

Authors and year	Number of participants (age, sex, group-specific inclusion criteria)	Diagnosis and treatment (only ACL)	Level of activity or sports (RTA, RTS, RTP)	Intervention Group	Control Group 1 (ACL patients)	Control Group 2 (healthy people)	Significant difference between groups?
Patras et al. (2012) [67]	N = 28 males; N = 14 ACLR and N = 14 healthy controls	ACLR: performed sub-acutely within 6 months after the injury from the same surgeon (range 1 to 4 months), unilateral ACL tear confirmed by MRI and arthroscopy; full RTS allowed 6 months post-surgery	Competitive soccer players	N = 14 ACLR with BPTB autograft, age: 24.8 ± 5.3 yrs, weight: 77.3 ± 7.5 kg, height: 177 ± 5.3 cm, mean time since surgery 18.5 ± 4.3 months; TAS 8 (range 7–9), Lysholm score 95 (range 94–100)	n.a.	N = 14 healthy male controls, age: 21.7 ± 4.4 yrs, weight: 72.2 ± 8.3 kg, height: 180 ± 9.0 cm	n.m.
Swanik et al. (1999) [68]	N = 24 females, mean age: 29.4 ± 10.4 yrs; mean height: 168 + 10.7 cm; mean weight: 61.2 ± 6 kg; N = 6 ACLD, N = 12 ACLR, N = 6 controls	Complete unilateral ACL tear, ACLR: BPTB grafts, testing 6–30 months after surgery, rehabilitation program completed, attempt to previous level of activity	Recreational activity at least for healthy controls, TAS of experimental groups 6.8 ± 1.5 points, Lysholm Knee Scoring Scale of experimental groups 92.9 ± 5.4	N = 6 females with ACLD	N = 12 females with ACLR	N = 6 females, healthy controls, recreational activity, no previous history of knee pathology, dominant limb (leg to kick a ball with)	n.m.
Zebis et al. (2017) [69]	N = 1 female, age: 21 yrs	Non-contact ACL injury (video-recorded) in the right knee during match play, ST-gracilis graft, standardized rehabilitation	Elite soccer player	N = 1 female elite soccer player at high level with no previous history of ACL injury	n.a.	Screening of elite soccer players pre-season	n.a.

ACLD = Anterior cruciate ligament deficiency (conservative/non-surgical treatment); ACLR = anterior cruciate ligament reconstruction/repair (surgery); BPTB = bone-patella-tendon-bone technique for ACLR; CI = confidence interval; IKDC = International Knee Documentation Committee; Level I: sports are described as jumping, pivoting and hard cutting sports; Level II sports: also involve lateral motion, but with less jumping or hard cutting than level I; n.a. = not applicable; n.m. = not mentioned; RTA = return to activity (return to participation); RTS = return to sports; RTP = return to performance; SD = standard deviation; ST = semitendinosus muscle; TAS = Tegner Activity Score; TLS = Tegner and Lysholm Score; TSK = Tampa Scale for Kinesiophobia; vs. = versus; wk = week; yrs = years

Table 4 Characteristics of methods of included studies

Authors and year	Tasks: number of repetitions, duration, frequency	Muscles/legs measured	EMG related outcome measure(s), variables	Direct link to RTS?
Busch et al. (2019) [13]	10 × stair descent, warm-up on treadmill with 5 km/h for 10 min to normalize EMG data, (KOOS, Tegner Activity Score, VAS for pain and general well-being)	VM, VL, BF, ST bilaterally	Normalized root mean squares for each muscle, limb and movement phase (preactivation, weight acceptance, push-off) (%subMVC)	No
Alkjaer et al. (2003) [33]	6 trails of walking across 2 force plates at a speed of 4.5 km/h	VL, VM, ST, BF of injured leg of patients and right leg of healthy controls	Mean amplitudes during weight acceptance (%maxEMG); coactivation between VL and BF (method by Rudolph et al. 2001 [45]) (%maxEMG)	(No) → copers and non-copers
Alkjaer et al. (2002) [34]	15 consecutive forward lunges with recordings from hitting a force plate (rest between trials if wanted)	VL, VM, ST, BF of injured leg of patients and right leg of healthy controls	Peak and mean values of EMG amplitudes (microvolts)	(No) → copers and non-copers
Arnason et al. (2014) [35]	3 trials of Nordic hamstring exercise, 3 trials of TRX hamstring curl exercise; order of exercises was randomized, time	MH, LH bilaterally	Peak normalized muscle activation (%MVIC)	(No) → soccer
Bryant et al. (2009) [36]	ACLD and ACLR: involved limb; healthy controls: both limbs; maximal single limb hop for distance on their involved limb from a standing position. 5 trials with 1 min rest in between trials, landing in a fixed position on the takeoff foot	VL, VM, ST, BF	Timing of the onset of muscle activity relative to IC (onset-IC; ms) and timing of the peak of muscle activity relative to IC (ms)	No
Burland et al. (2020) [37]	Single limb forward hop task, distance of their limb length (tip of the greater trochanter to the tip of the lateral malleolus) → unlimited practice trials, 3 successful trials captured consecutively for each limb (trial = successful when participants landed on force platform and balanced on injured limb for a least 1 s); task performed bilaterally, order of limb testing was randomized	VL bilaterally	Peak muscle activity of the VL: EMG signals from heel strike (defined as 10.0 N) to when PKEM was reached were used for statistical analysis. Mean peak muscle activity obtained from this period of interest across the 3 trials was used Dynamic EMG data recorded during task were then normalized to the peak muscle activity recorded across all trials. Muscle activity onset times of VL relative to PKEM (EMG onset = time of PKEM–time of EMG "on") were established using the Teager–Kaiser Energy Operator (EMG onset = median + 3SD)	No
Cordeiro et al. (2015) [38]	3 instep soccer kicks with dominant leg, (KOOS, TSK)	RF, VL, VM, BF, ST	Muscle activation during knee extension phase (% MVC)	(No) → soccer, instep kick

Table 4 (continued)

Authors and year	Tasks: number of repetitions, duration, frequency	Muscles/legs measured	EMG related outcome measure(s), variables	Direct link to RTS?
Dashti Rostami et al. (2019) [39]	Single leg vertical drop landing; 3 proper trials	GM, AL; only the injured limb of ACLR and ACLD individuals and the dominant limb of controls were tested	Preparatory and reactive muscle activity and coactivation from 100 ms prior to initial contact to 250 ms after contact; mean and peak activity (%MVIC); coactivation of GM:AL (method by Rudolph et al. 2001 [45])	No
Jordan et al. (2016) [40]	80 s repeated squat jump test (jump test) on a dual force plate system	VL, VM, BF, ST	Normalized EMG amplitudes at take-off, at the 25-ms interval prelanding, and at postlanding for the ACLR limb (affected limb), contralateral limb, and limbs of the control subjects (control limb), (Asymmetry index, jump height of body center of mass)	(No) → fatigue, downhill skiing
Lessi et al. (2017) [41]	Single leg landing before and after fatigue (fatigue protocol: 10 squats, 2 vertical jumps, 20 steps)	VL, BF, Gmax	EMG average amplitude of activation, expressed as a %peak EMG during landing	No
Oliver et al. (2018) [42]	Single leg jump from a 25-cm tall box, with hands on hips and without gaining momentum; five times with each leg (injured/non-injured)	VM, VL, RF, ST, BF	Mean values per each patient, leg, and muscle were considered in the analysis; muscle latency time over time of each muscle was defined as the time from touchdown to peak amplitude of EMG activity (RMS) in each muscle. RMS was normalized at the maximum activity of the muscles (%MVC)	No
Ortiz et al. (2014) [43]	60-cm double legged and a 40-cm single legged drop jumps to assess bilateral and unilateral landing strategies, respectively	VM, VL, RF, MH, LH measured in the involved leg of women with ACLR and the dominant leg of the control subjects	Rectified normalized electromyographic activityof the quadriceps and hamstrings (amplitude and latency) in %maximum contraction; quadriceps/hamstrings electromyographic co-contraction ratio (values between 0 and 1); time to maximum neuromuscular activation (time-to-peak muscle activation) in seconds for hamstring and quadriceps muscle groups	No

Table 4 (continued)

Authors and year	Tasks: number of repetitions, duration, frequency	Muscles/legs measured	EMG related outcome measure(s), variables	Direct link to RTS?
Patras et al. (2009) [44]	10 min running at moderate intensity (20% below the lactate threshold) and 10 min running at high intensity (40% above the lactate threshold) on separate occasions separated by a time span of 48 h and completed within 10–12 days; moderate intensity = at 20% below the lactate threshold; high intensity = at 40% above the lactate threshold	VL, BF bilaterally	Values from 15 strides averaged to calculate the mean peak amplitude during stance for each recording period	No
Patras et al. (2010) [45]	10 min running at moderate intensity and 10 min running at high intensity on separate occasions separated by a time span of 48 h; moderate intensity = at 80% of the lactate threshold; high intensity = at 40% of the difference betweenVO2max and lactate threshold	VL bilaterally	EMG amplitude during stance, over time respectively in microvolts	No
Pincheira et al. (2018) [46]	2 destabilizing platforms (1 for each limb) generated a controlled perturbation at the ankle of each participant (30° of inversion, 10° plantarflexion simultaneously) in a weight bearing condition; time between the release and the stop (impact) of the mechanism was 200 ± 10 ms	VM, ST	Muscle activation onset times (ms)	No
Rudolph et al. (2001) [47]	5 trials of walking and jogging with 1-3 min rest intervals between trials	LH, VL, SO, medial head of the gastrocnemius muscles of both limbs	Peak EMG activity; onset and termination of muscular activation; duration of muscular activity; co-contraction (integrals calculated)	(No) → copers and non-copers
Rudolph et al. (2000) [48]	Single leg hops	LH, VL, SO, medial head of the gastrocnemius muscles of both limbs	Peak EMG activity over 30 ms from either the dynamic or maximum isometric trials was used to normalize the EMG data (%MVIC); muscle timing variables, muscle intensity: integrating the linear envelope of the EMG curves over a weight acceptance interval (defined as the range from 100 ms prior to initial contact to the point of peak knee flexion. Muscle co-contraction: using normalized EMG data, between the VL and LH, and VL and medial gastrocnemius	(No) → copers and non-copers

Table 4 (continued)

Authors and year	Tasks: number of repetitions, duration, frequency	Muscles/legs measured	EMG related outcome measure(s), variables	Direct link to RTS?
Rudolph and Snyder-Mackler (2004) [49]	Step up and over a 26 cm high step; 10 trials, 5 each with the right and left leg ascending a 26 cm step (higher than a typical step, provide a more challenging condition), EMG collected from landing limb	LH, VL, SO, medial head of the gastrocnemius muscles of both limbs	Peak EMG activity (%max); onset and termination of muscular activation; duration of muscular activity; co-contraction	(No) → copers and non-copers
Swanik et al. (2004) [50]	Landing from a hop: The subject stood on a 20-cm step, balanced momentarily on test limb, and hopped to target placed 30 cm horizontally; knee perturbation (special knee pertubation device, 100 N force on the posterior aspect of the tibia → anterior displacement of the tibia)	VL, VM, MH, LH	Muscle activity before and after landing from a hop (area of integrated EMG recordings), hamstring latency after joint perturbation (reflexive muscle activity in the hamstrings assessed by measuring the onset time after anterior translation of the tibia)	No
Briem et al. (2016) [51]	3 consecutive maximal hops (triple jump, single-limb crossover hop for distance), 2 practice trials, 1 single maximal test trial; same procedure for each limb. ACLR participants started with non-surgical limb, each matched control participant with matched limb	MH, LH	Peak activation of the normalized signal (%MVIC)	No
Lessi et al. (2018) [52]	Single leg drop vertical jump landing before and after fatigue protocol (fatigue protocol: 10 squats, 2 vertical jumps, 20 steps)	VL, GM, Gmax	Mean amplitude of activation during landing (% of the peak RMS obtained during the landing task)	No
Lustosa et al. (2011) [53]	Walking at self-selected speed on a 3 m-walkway with 2 stable platforms and 1 electromechanical balance board that could apply a sudden perturbation (20° tilt in the frontal plane (medial/lateral) → varus stress in the slightly flexed knee, leading to external rotation of the femur (= common etiology of ACL injury))	VL, BF	Co-contraction pre- and postperturbation between groups and limbs (co-contraction levels in the 250 ms before perturbation and in the 250 ms after perturbation periods), %MVIC; muscular co-contraction calculated	(No) → stratification of included patients (full RTS or limited RTS)
Nyland et al. (2010) [54]	Single leg CMJ performance	Gmax, VM, MH, GC	Mean EMG signal amplitudes (%MVIC); EMG activation duration during propulsion and landing phase (ms)	No

Table 4 (continued)

Authors and year	Tasks: number of repetitions, duration, frequency	Muscles/legs measured	EMG related outcome measure(s), variables	Direct link to RTS?
Nyland et al. (2013) [55]	Single leg CMJ performance	Gmax, VM, MH, GC	EMG amplitude comparison during single leg CMJ propulsion (Difference = involved—uninvolved lower extremity) (%MVIC)	No
Nyland et al. (2014) [56]	Single leg hop test for distance	Gmax, VM, MH, GM	Standardized EMG amplitudes during single leg hop for distance propulsion [%MVIC involved lower extremity − %MVICuninvolved lower extremity); standardized EMG amplitudes during single leg hop for distance landing [%MVIC involved lower extremity − %MVIC uninvolved lower extremity]	No
Boerboom et al. (2001) [57]	Walking at normal, slower, and faster than normal speed	VM, VL, BF, ST, GC medialis, GC lateralis; of injured leg (patients)	Deviations of the normative EMG profiles (individual averaged EMG pattern during gait)	(No) → copers and non-copers
Bulgheroni et al. (1997) [58]	At least 5 trials of walking at natural cadence (112 ± 5.1 steps/min), 20-m distance used to reach steady state of walking	VL, RF, BF, ST	Amplitude of EMG activity, EMG normalized to the maximum recorded signal amplitude during a single walking cycle	No
Gokeler et al. (2010) [59]	Single leg hop test for distance (arms behind back, maintained balance for at least 1 s after landing, 3 maximal trials for each limb; (IKDC, Rolimeter device for laxity testing)	Gmax, BF, ST, SM, VM, VL, RF, MG, LG, SO	Mean onset times (= preparatory activity before landing) of the EMG signals of each muscle	No
Hansen et al. (2017) [60]	Running on weight-supporting treadmill ("anti-gravity", Alter G, respectively) at 16 km/h with 6 different body weight conditions from 50% (half weight) to 100% (full weight-bearing) in random order	SM, SL, MG, LG, MH, LH	Soleus, gastrocnemius and hamstring cluster formed, SPM used to analyze entire time-dependent EMG signal, comparison of injured vs. non-injured leg and left vs. right leg; EMG signal normalized to its MVC value during 100% body weight running trials for each participant	No
Klyne et al. (2012) [61]	Controlled single leg hop on each limb (arms behind back, landing position hold for at least 1-2 s), length of the horizontal distance hopped was equal to the measured length of the lower leg; 3 successful trials	MG	Onset and offset of MG activation relative to take-off, during flight and landing, muscle activity (RMS), 7 temporal variables (ms, %activity)	No [59]

Table 4 (continued)

Authors and year	Tasks: number of repetitions, duration, frequency	Muscles/legs measured	EMG related outcome measure(s), variables	Direct link to RTS?
Knoll et al. (2004) [62]	Walking on treadmill at least 10 min at a constant speed of 2 km/h	VL, VM, BF, AL	Linear envelope EMG curve determined by root mean square method and normalized to average of peak EMG signal values of six gait cycles → EMG patterns during % of gait cycle	(No) → pre-operatively and follow-up (6 weeks, 4, 8, 12 months post-surgery)
Kuster et al. (1995) [63]	At least 5 trials of each task to obtain at least 10 cycles of EMG data for ensemble average processing; level walking and downhill walking on dismountable slope (6 m length, -19° gradient)	RF, BF, GC	Peak muscular activity at heel strike, just before heel strike; values normalized to subject's individual peak levels	No
Madhavan and Shields (2011) [64]	Single leg squat maneuver with random/unexpected perturbations at the start of the flexion phase (triggered compensatory reflex activity)	VM obliquus, RF, VL, LH, MH of exercised limb (reconstruced leg of ACLR subjects, pseudorandomly selected limb of healthy controls to counterbalance ACLR limbs)	Normalized long latency responses (= difference between the mean EMG of perturbation trials and the mean EMG of unperturbed trials, divided by the mean EMG of the unperturbed trials) between 50 and 200 ms after the onset of perturbation of quadriceps and hamstrings; peak velocity (cm/s); latency of peak LLR (= time to peak EMG activity between 50–200 ms following the perturbation); mean muscle EMG activity (%MVIC) in the 200 ms prior to perturbation, 50–200 ms after the perturbation, and 200–400 ms post perturbation	No
Ortiz et al. (2008) [65]	5 trials of a single legged 40-cm drop jump: standing initially on both feet on the 40-cm platform and then standing on the jumping leg, and then to drop when ready to do so, maximal-effort vertical jump on landing single legged on the center of the force plate, use of arms allowed for balance; 2 trials of a 20-cm up-down hop task, participant stood facing a 20-cm step and performed 10 consecutive jumps up to and down when ready. The 10 consecutives up and down hops composed 1 trial	GM, GMax, RF, LH, MH; dominant leg in noninjured women and reconstructed leg in ACLR women	Quadriceps/hamstring cocontraction ratios (values between 0 and 1; closer to 1 = excellent co-contraction, closer to 0 = poor co-contraction) and normalized EMG activity of lower extremity muscles (values between 0 and 1; effect sizes respectively)	No

Table 4 (continued)

Authors and year	Tasks: number of repetitions, duration, frequency	Muscles/legs measured	EMG related outcome measure(s), variables	Direct link to RTS?
Ortiz et al. (2011) [66]	Side-to-side hopping task that consisted of hopping single legged 10 times consecutively from side to side across 2 lines marked 30 cm apart on 2 individual force plates. The task was designated as a side hopping when the hop was to the opposite side of the stance leg and as crossover hopping when the hop was toward the side of the stance leg	GM, GMax, RF, LH, MH; dominant leg in noninjured women and reconstructed leg in ACLR women	Quadriceps/hamstring cocontraction ratios (values between 0 and 1; closer to 1 = excellent co-contraction, closer to 0 = poor co-contraction) and normalized EMG activity of lower extremity (values between 0 and 1; effect sizes respectively)	No
Patras et al. (2012) [67]	2 10-min treadmill runs on 2 occasions in the lab, 1 at a moderate (80%VO2max) and 1 at a high intensity (85–88% VO2max), EMG recordings at the 3rd, 5th, 7th, and 10th minute of the runs	VL, BF bilaterally: left leg of controls selected for analysis	Peak EMG amplitude during the stance phase	No
Swanik et al. (1999) [68]	4 functional activities: downhill walking (15°, 0.92 m/s), level running (2.08 m/s), and hopping (self-paced) and landing from a jump (20.3 cm)	VL, VM, MH, LH	IntegratedEMG (microvolts x ms) normalized to mean amplitude of 3–6 consecutive test repetitions → mean area and peak integrated EMG of a 250 ms-period after ground contact = reactive muscle activity; testing order and leg assessed by random	No
Zebis et al. (2017) [69]	Standardized side cutting maneuver, CJM with the hands placed at the hip (akimbo), and maximal jump height was calculated	VL, BF, ST	EMG preactivity	(No) → single case, risk profile retrospective, pre-/post-surgery and post-intervention

AL = adductor longus muscle; BF = biceps femoris muscle; CMJ = countermovement jump(ing); EMG = electromyography; GC = gastrocnemius muscles; GM = gluteus medius muscle; GMax = gluteus maximus muscle; GRF = ground reaction force; Hz = Hertz; LG = gastrocnemius lateral head; LH = lateral hamstring muscle; MG = gastrocnemius medial head; MH = medial hamstring muscle; ms = milliseconds; PKEM = peak knee extension moment; RF = rectus femoris muscle; SL = soleus lateralis muscle; SM = soleus medialis muscle; SO = soleus muscle; SPM = Statistical Parametric Mapping; ST = semitendinosus muscle; VL = vastus lateralis muscle; VM = vastus medialis muscle; vs. = versus; WA = weight acceptance

Outcomes

All included studies used surface EMG as method to assess neuromuscular control and provided EMG-related variables such as peak and mean amplitudes, timing and peak of muscle activity, preparatory and reactive muscle activity, on- and offset of muscular activation, co-activation/co-contraction ratios, or asymmetry index. The outcome variables were expressed as percentage of maximum voluntary (isometric) contraction (%MVIC or %MVC) or reported in microvolts or milliseconds according to the variable chosen in amplitude or time domain.

Decision for Return to Sports (RTS)

None of the included studies used the surface EMG measurements to decide upon readiness for RTS *(Table 4)*. However, the results from about a third of the studies (31.6%, 12 studies) could provide useful information by the choice of the assessed groups such as copers versus non-copers,[33, 34, 47–49, 57] intervention and control group from the same team or level/league,[35, 38, 40] data from pre-injury/ pre-surgery including postsurgical follow up[62, 69] or participants with full RTS versus limited RTS.[53] In addition, two studies even investigated the influence of fatigue on neuromuscular control.[41, 52]

More detailed information regarding EMG methods and procedures such as EMG type, detection, normali- zation, data processing and electrode placement can be found in Additional file "EMG methods and procedures of included studies".

Discussion

The aim of this systematic review was to summarize the scientific literature regarding EMG-related assessments for neuromuscular control in patients with an ACL injury (either treated surgically or conservatively). The second aim was to analyze whether these assessments for neuromuscular control were used to decide upon readiness for RTS in these patients.

There were many factors present which could have an influence on neuromuscular control.

Influence by type of comparison (intra- versus inter-subject)

The use of the contralateral, non-injured leg in intra-subject comparison, without a "real" control group[42, 44] may lead to an overestimation of the physical performance in the ACL reconstructed or –injured leg. After ACLR, functional performance is often expressed with the LSI.[70] As the non-affected limb may also have deteriorated, the LSI may overestimate the right time for a safe RTS, and therefore, the risk for secondary injury may be higher.[23] In acutely injured ACL patients, intra-individual comparison showed bilateral conse- quences during stair ascent and indicates an alteration in the motor program ("pre-programmed activity").[71] In addition, in case of a case-controlled study design, the subjects in the control group should be matched to the ACL participants regarding sex, age, body mass, height, activity level and leg dominance.

Influence by level of activity and fatigue

Some of the included studies used very challenging, sports-specific tasks to assess neuromuscular control, some even assessed neuromuscular control after fatiguing tasks. It is known that most of ACL tears are non- contact injuries happening at the end of a training session or a play.[72] Therefore, the closer the task to the sports and injury-risky situation, the safer the decision towards full RTS or even return to competition will be. However, assessing performance-based tests or movement quality may be more difficult to standardize, require more complex equipment and large amounts of space. But if only impairments will be tested, there will be a lack of information regarding an "athlete's capacity to cope with the physical and mental demands of playing sport".[73] It is therefore recommended to search for a standardized assessment close to the injury mechanism.

Influence by gender

Not all included studies reported findings of mixed groups separately by gender. Some did not even state whether study participants were male or female. This could partly be explained by the date of publication as gender difference in ACL patients has not been in the focus of former ACL research. It is known that female athletes are more likely to sustain an ACL injury than men;[74, 75] the increased risk is probably multifactorial.[76] Several studies indicate that hormonal factors play a role[3, 77] contributing to an increased laxity of ligaments in the first half of the menstrual cycle. However, biomechanical and neuromuscular aspects as indicators are discussed controversially in literature: Gender-specific neuromuscular adaptations and biomechanical landing techniques are considered being the most important ones to explain the increased risk of injury in women.[78, 79] The higher risk for females to suffer from an ACL injury can be explained by motion and loading of the knee joint during performance.[74] Female athletes typically perform movements in sports with a greater knee valgus angle than men. Therefore, the amount of stress on the ACL in these situations is higher caused by a high activation of the quadriceps despite limited knee and hip flexion, greater hip adduction and a large knee adduction moment.[80, 81] The dominance of the quadriceps muscle in women could contribute to increased anterior tibial translation[82, 83] and was found in various activities such as jumps and cutting maneuvers.[84–86] Moreover, females typically land with an internally or externally rotated tibia,[87] leading to an increased knee valgus stress due to greater and more laterally orientated ground reaction forces.[83] In contrast, other researchers did not find any gender-specific differences in the quadriceps-hamstrings ratio,[88] not even in landing and cutting maneuvers.[89] A systematic review summarized biomechanical gender differences and stated that these were based on questionable clinical relevance.[89] In addition, strength-paired women and men showed no significant differences in neuromuscular activity.[90]

Influence by treatment

The included studies reported different treatment options (ACLR with different graft types, conservative treatment). Depending on the classification of the participants in copers and non-copers, the results in neuromuscular control may differ from a population of ACLR participants. Therefore, all researchers who worked with copers and non-copers made intra- and inter-group comparisons without an ACLR group. A Cochrane review revealed low evidence for no difference in young, active adults after two and five years after the injury, assessed with patient-reported outcomes. However, many participants described as "non-copers" with unstable knee with conservative treatments remain symptomatic, and therefore, later opt for ACL surgery.[91] It has been described that persistent co-contraction and joint stiffening in these "non-copers" is likely to be due to an abnormal neuromuscular strategy failing to restore joint stability in these ACL deficient group.[92] Furthermore, the choice of graft would influence the neuromuscular control of measured muscles due to the morbidity of the harvesting site of the graft (e.g. hamstrings).

EMG variables

If the researchers mentioned the procedures for collecting EMG data, they referred to standardized applications and guidelines such as SENIAM (Surface Electromyography for the Non-Invasive Assessment of Muscles).[93] The provided EMG-related variables were in accordance to the ones mentioned in a systematic review searching for knee muscle activity in ACL deficient patients and healthy controls during gait.[14] Current literature suggests greater co-contraction indices, increased joint stiffness and earlier muscle activation onset times as measures of neuromuscular function reflecting the incomplete restoration of normal joint stability.[19, 92] Some of the included studies reported values of muscle onset activity in milliseconds and percentage of gait cycle as a systematic review did by summarizing and quantitatively analyzing muscle onset activity prior to landing in patients after ACL injury.[20] However, no cut-off values out of EMG-related variables were provided to determine an adequate level of neuromuscular control. Moreover, some of the researchers only provided integrated EMG values which would make it difficult to be compared to other studies using the respective units (milliseconds, millivolts) or widely used percentage values (%MVIC, %MVC).

Return to sports (RTS)

Regarding the determination of RTS after ACLR, there is some evidence for the use of functional performance tests, which had also been widely used in the included studies. Multiple functional performance measures—a battery including strength and hop tests, quality of movement and psychological tests[25]—might be more useful for the determination of RTS than a single performance measure. However, it is still unclear, which measures should be used to bring athletes safely back to RTS with a low risk of a second ACL injury.[25] Currently used RTS criteria or assessments, such as time, strength tests, hop tests, patient-reports, clinical examination, thigh circumference, ligamentous stability, range of motion, effusion and performance-based criteria, may be suboptimal at reducing the risk of a second ACL injury.[73, 94] Recovery of neuromuscular function was mentioned to be important because of the existing connection between the variables time since surgery and the risk for re-injury of the knee joint; but adequate assessment procedures to assess neuromuscular function are still a matter of debate.[7] In contrast, authors of an included study stated that "studies like ours that focus on the objective measurement of the change of the muscle latency time over time may allow patients to return to full activity and to sports earlier than the standard time of 6–12 months".[42] However, this statement only based on one outcome measure and contrasts with current criterion- and time- based recommendations for RTS. Therefore, this recom- mendation seems to be rather dangerous.

Limitations

The sample size of all the studies was quite low, however, providing reasonable sample size calculations and depending on the variable investigated, the results were acceptable. Furthermore, the more restrictive the inclusion criteria for the participants, the more homogeneous the intervention and the control groups were, but the more challenging the recruitment process was, leading to smaller groups to be investigated.

The used assessment for the risk of bias, the Downs and Black checklist[31] in a modified form[29, 32] is designed for randomized and non-randomized controlled studies, however, the latter score lower in some items, get lower total scores and therefore a worse overall rating of the methodological quality. Despite this disadvantage, we decided to use the modified checklist as we could assess all studies with different designs included in this systematic review. However, the use of total scores and choice of cut-off values for low, medium and high risk of bias, respectively, were arbitrary and not based on literature.

Conclusions

Implications for clinical practice

This systematic review summarized assessments using EMG variables for neuromuscular control of the knee in patients suffering from an ACL injury (either treated surgically or conservatively). Despite 38 articles providing a wide range of EMG-related assessments, none was used to decide upon readiness towards a safe and successful RTS in patients after an ACL injury. So far, there is no diagnostic measure to assess neuromuscular control and therefore, clinicians should use a multimodal approach including assessments for active and passive knee stability under different sports-related conditions but be aware of not being able to evaluate neuromuscular control in depth without EMG-related assessments. Moreover, the widely used LSI may overestimate the physical performance of an ACL patient as the non-affected limb is likely to have deteriorated, too.

Implications for further research

Additional studies are needed to define readiness towards RTS by assessing neuromuscular control in adult ACL patients with EMG. Further research should aim at finding reliable and valid, EMG-related variables to be used as diagnostic tool for neuromuscular control.

Due to the heterogeneity in participants, interventions and outcomes used, future studies should aim at more homogenous patient groups, evaluate females and males separately, provide adequately matched healthy subjects (gender, height, weight, activity level etc.), control for confounding factors such as type of treatment, and use tasks close to the injury mechanism, as sport specific as possible, respectively. Moreover, it would be interesting to assess not only lower leg but pelvic and core muscles in addition. This would help to give insight in the complex field of ACL injuries and subsequent rehabilitation strategies, and therefore improve knowledge towards a safe RTS in these patients.

Abbreviations

ACL: Anterior cruciate ligament; ACLR: Anterior cruciate ligament reconstruction; EMG: Electromyography; LSI: Limb Symmetry Index; PEDro: Physiotherapy Evidence Database; PICOS: Participants-Intervention-Control-Outcome-Study design; PRISMA: Preferred Reporting of Items for Systematic reviews and Meta-Analyses; PROSPERO: International prospective register of systematic reviews; RTS: Return to sports; SENIAM: Surface Electromyography for the Non-Invasive Assessment of Muscles; TAS: Tegner Activity Score.

Supplementary Information

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Additional file 1 Search string for MEDLINE/PubMed.
Additional file 2 Methodological quality assessment.
Additional file 3 EMG methods and procedures of included studies.

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Authors' contributions

AB participated in the design of the study, contributed to data collection/reduction/analysis and interpretation of results and was the main contributor in writing the manuscript; IK contributed to data collection, reduction and analysis; IB and DV participated in the design of the study; HB participated in the design of the study and was an important contributor in writing the manuscript, contributed to data analysis and interpretation of results. All authors contributed to the manuscript writing, read, and approved the final version of the manuscript and agreed with the order of authors as listed.

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Availability of data and materials

The datasets used and analyzed in the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

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Competing interests

The authors declare that they have no competing interests.

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References

1. Hootman JM, Dick R, Agel J. Epidemiology of collegiate injuries for 15 sports: summary and recommendations for injury prevention initiatives. *J Athl Train.* 2007;42(2):311–9.
2. Kaeding CC, Leger-St-Jean B, Magnussen RA. Epidemiology and diagnosis of anterior cruciate ligament injuries. *Clin Sports Med.* 2017;36(1):1–8.
3. Hewett TE, Zazulak BT, Myer GD. Effects of the menstrual cycle on anterior cruciate ligament injury risk: a systematic review. *Am J Sports Med.* 2007;35(4):659–68.
4. Friel NA, Chu CR. The role of ACL injury in the development of posttrau- matic knee osteoarthritis. *Clin Sports Med.* 2013;32(1):1–12.
5. Ardern CL, Webster KE, Taylor NF, Feller JA. Return to sport following ante- rior cruciate ligament reconstruction surgery: a systematic review and meta-analysis of the state of play. *Br J Sports Med.* 2011;45(7):596–606.
6. Lai CCH, Feller JA, Webster KE. Fifteen-year audit of anterior cruciate ligament reconstructions in the australian football league from 1999 to 2013: return to play and subsequent ACL injury. *Am J Sports Med.*2018; 46(14):3353–60.
7. Grindem H, Snyder-Mackler L, Moksnes H, Engebretsen L, Risberg MA. Simple decision rules can reduce reinjury risk by 84% after ACL reconstruction: the delaware-oslo ACL cohort study. *Br J Sports Med.* 2016;50(13):804–8.
8. Wright RW, Magnussen RA, Dunn WR, Spindler KP. Ipsilateral graft and contralateral ACL rupture at five years or more following ACL reconstruc- tion: a systematic review. *J Bone Joint Surg Am.* 2011;93(12): 1159–65.
9. Paterno MV, Rauh MJ, Schmitt LC, Ford KR, Hewett TE. Incidence of contralateral and ipsilateral anterior cruciate ligament (ACL) injury after primary ACL reconstruction and return to sport. *Clin J Sport Med.* 2012;22(2):116–21.
10. Paterno MV, Rauh MJ, Schmitt LC, Ford KR, Hewett TE. Incidence of sec- ond ACL injuries 2 years after primary ACL reconstruction and return to sport. *Am J Sports Med.* 2014;42(7):1567–73.
11. Akelman MR, Fadale PD, Hulstyn MJ, Shalvoy RM, Garcia A, Chin KE, et al. Effect of matching or over-constraining knee laxity during anterior cruciate ligament reconstruction on knee osteoarthritis and clinical outcomes: a randomized controlled trial with 84-month follow-up. *Am J Sports Med.* 2016;44(7):1660–70.
12. Group MK, Spindler KP, Huston LJ, Chagin KM, Kattan MW, Reinke EK, et al. Ten-year outcomes and risk factors after anterior cruciate ligament reconstruction: a MOON longitudinal prospective cohort study. *Am J Sports Med.* 2018;46(4):815–25.
13. Busch A, Blasimann A, Henle P, Baur H. Neuromuscular activity during stair descent in ACL reconstructed patients: a pilot study. *Knee.* 2019;26(2):310–6.
14. Shanbehzadeh S, Mohseni Bandpei MA, Ehsani F. Knee muscle activity during gait in patients with anterior cruciate ligament injury: a systematic review of electromyographic studies. *Knee Surg Sports Traumatol Arthrosc.* 2017;25(5):1432–42.
15. Mantashloo Z, Letafatkar A, Moradi M. Vertical ground reaction force and knee muscle activation asymmetries in patients with ACL reconstruction compared to healthy individuals. *Knee Surg Sports Traumatol Arthrosc.* 2020; 28(6):2009–14.
16. Grooms DR, Page SJ, Nichols-Larsen DS, Chaudhari AM, White SE, Onate JA. Neuroplasticity associated with anterior cruciate ligament reconstruction. *J Orthop Sports Phys Ther.* 2017;47(3):180–9.
17. Zimny ML, Schutte M, Dabezies E. Mechanoreceptors in the human anterior cruciate ligament. *Anat Rec.* 1986;214(2):204–9.
18. Lanier AS, Knarr BA, Stergiou N, Snyder-Mackler L, Buchanan TS. ACL injury and reconstruction affect control of ground reaction forces pro- duced during a novel task that simulates cutting movements. *J Orthop Res.* 2020;38(8):1746–52.
19. Nawasreh ZH, Marmon AR, Logerstedt D, Snyder-Mackler L. The effect of training on a compliant surface on muscle activation and co-con- traction after anterior cruciate ligament injury. *Int J Sports Phys Ther.* 2019;14(4):3554–63.
20. Theisen D, Rada I, Brau A, Gette P, Seil R. Muscle activity onset prior to landing in patients after anterior cruciate ligament injury: a systematic review and meta-analysis. *PLoS One.* 2016;11(5):e0155277.
21. Ford KR, van den Bogert J, Myer GD, Shapiro R, Hewett TE. The effects of age and skill level on knee musculature co-contraction during functional activities: a systematic review. *Br J Sports Med.* 2008;42(7):561–6.
22. Tsai LC, McLean S, Colletti PM, Powers CM. Greater muscle co-contraction results in increased tibiofemoral compressive forces in females who have undergone anterior cruciate ligament reconstruction. *J Orthop Res.* 2012;30(12):2007–14.

23. Wellsandt E, Failla MJ, Snyder-Mackler L. Limb symmetry indexes can overestimate knee function after anterior cruciate ligament injury. *J Orthop Sports Phys Ther.* 2017;47(5):334–8.

24. Webster KE, Feller JA. A research update on the state of play for return to sport after anterior cruciate ligament reconstruction. *J Orthop Traumatol.* 2019; 20(1):10.

25. van Melick N, van Cingel RE, Brooijmans F, Neeter C, van Tienen T, Hullegie W, et al. Evidence-based clinical practice update: practice guidelines for anterior cruciate ligament rehabilitation based on a systematic review and multidisciplinary consensus. *Br J Sports Med.* 2016; 50(24):1506–15.

26. Bruhn S, Leukel C, Gollhofer A. Differential effects of stimulus character- istics during knee joint perturbation on hamstring and quadriceps reflex responses. *Hum Move Sci.* 2011;30(6):1079–91.

27. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009;6(7):e1000097.

28. Higgins JPT, Green S. Cochrane handbook for systematic reviews of interventions. Chichester: *Wiley*; 2008.

29. Ramsey CA, Lamb P, Kaur M, Baxter GD, Ribeiro DC. How are run- ning shoes assessed? A systematic review of characteristics and measurement tools used to describe running footwear. *J Sports Sci.* 2019;37(14):1617–29.

30. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. *Syst Rev.* 2016;5(1):210.

31. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non- randomised studies of health care interventions. *J Epidemiol Community Health.* 1998;52(6):377–84.

32. Pairot-de-Fontenay B, Willy RW, Elias ARC, Mizner RL, Dube MO, Roy JS. Running biomechanics in individuals with anterior cruciate ligament reconstruction: a systematic review. *Sports Med* (Auckland, NZ). 2019; 49(9):1411–24.

33. Alkjaer T, Simonsen EB, Jorgensen U, Dyhre-Poulsen P. Evaluation of the walking pattern in two types of patients with anterior cruciate ligament deficiency: copers and non-copers. *Eur J Appl Physiol.* 2003; 89(3):301–8.

34. Alkjaer T, Simonsen EB, Peter Magnusson SP, Aagaard H, Dyhre-Poulsen P. Differences in the movement pattern of a forward lunge in two types of anterior cruciate ligament deficient patients: copers and non-copers. *Clin Biomech* (Bristol, Avon). 2002;17(8):586–93.

35. Arnason SM, Birnir B, Guomundsson TE, Guonason G, Briem K. Medial hamstring muscle activation patterns are affected 1–6 years after ACL reconstruction using hamstring autograft. *Knee Surg Sports Traumatol Arthrosc.* 2014;22(5):1024–9.

36. Bryant AL, Newton RU, Steele J. Successful feed-forward strategies following ACL injury and reconstruction. *J Electromyogr Kinesiol.* 2009;19(5):988–97.

37. Burland JP, Lepley AS, Frechette L, Lepley LK. Protracted alterations in muscle activation strategies and knee mechanics in patients after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2020;28(12):3766–72.

38. Cordeiro N, Cortes N, Fernandes O, Diniz A, Pezarat Correia P. Dynamic knee stability and ballistic knee movement after ACL reconstruction: an application on instep soccer kick. Knee Surg Sports Traumatol Arthrosc: *Off J ESSKA.* 2015;23(4):1100–6.

39. Dashti Rostami K, Naderi A, Thomas A. Hip Abductor and adductor muscles activity patterns during landing after anterior cruciate ligament injury. *J Sport Rehabil.* 2019;28:871–6.

40. Jordan MJ, Aagaard P, Herzog W. Asymmetry and thigh muscle coactivity in fatigued anterior cruciate ligament-reconstructed elite skiers. *Med Sci Sports Exer.* 2017;49(1):11–20.

41. Lessi GC, Serrao FV. Effects of fatigue on lower limb, pelvis and trunk kinematics and lower limb muscle activity during single-leg landing after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2017;25(8):2550–8.

42. Oliver G, Portabella F, Hernandez JA. A comparative study of the neuromuscular response during a dynamic activity after anterior cruciate ligament reconstruction. Eur J Orthop Surg Traumatol: *Orthop Traumatol.* 2019; 29:633–8.

43. Ortiz A, Capo-Lugo CE, Venegas-Rios HL. Biomechanical deficiencies in women with semiten dinosus-gracilis anterior cruciate ligament reconstruction during drop jumps. PM & R: *J Injury Funct Rehab.*2014; 6(12):1097–106.

44. Patras K, Ziogas G, Ristanis S, Tsepis E, Stergiou N, Georgoulis AD. High intensity running results in an impaired neuromuscular response in ACL reconstructed individuals. *Knee Surg Sports Traumatol Arthrosc.*2009; 17(8):977–84.

45. Patras K, Ziogas G, Ristanis S, Tsepis E, Stergiou N, Georgoulis AD. ACL reconstructed patients with a BPTB graft present an impaired vastus lateralis neuromuscular response during high intensity running. *J Sci Med Sport.* 2010;13(6):573–7.

46. Pincheira PA, Silvestre R, Armijo-Olivo S, Guzman-Venegas R. Ankle perturbation generates bilateral alteration of knee muscle onset times after unilateral anterior cruciate ligament reconstruction. *PeerJ.* 2018; 6:19.

47. Rudolph KS, Axe MJ, Buchanan TS, Scholz JP, Snyder-Mackler L. Dynamic stability in the anterior cruciate ligament deficient knee. *Knee Surg Sports Traumatol Arthrosc.* 2001;9(2):62–71.

48. Rudolph KS, Axe MJ, Snyder-Mackler L. Dynamic stability after ACL injury: who can hop? Knee Surg Sports Traumatol Arthrosc: *Off J ESSKA.* 2000; 8(5):262–9.

49. Rudolph KS, Snyder-Mackler L. Effect of dynamic stability on a step task in ACL deficient individuals. *J Electromyogr Kinesiol.* 2004;14(5):565–75.

50. Swanik CB, Lephart SM, Swanik KA, Stone DA, Fu FH. Neuromuscular dynamic restraint in women with anterior cruciate ligament injuries. *Clin Orthop Related Res.* 2004;425:189–99.

51. Briem K, Ragnarsdottir AM, Arnason SI, Sveinsson T. Altered medial versus lateral hamstring muscle activity during hop testing in female athletes 1–6 years after anterior cruciate ligament reconstruction. Knee Surg Sports Traumatol Arthrosc: *Off J ESSKA.* 2016; 24(1):12–7.

52. Lessi GC, Silva RS, Serrao FV. Comparison of the effects of fatigue on kin- ematics and muscle activation between men and women after anterior cruciate ligament reconstruction. *Phys Ther Sport.* 2018;31: 29–34.

53. Lustosa LP, Ocarino JM, de Andrade MA, Pertence AE, Bittencourt NF, Fonseca ST. Muscle co-contraction after anterior cruciate ligament reconstruction: influence of functional level. J Electromyogr Kinesiol: *Off J Int Soc Electrophysiol Kinesiol.* 2011;21(6):1050–5.

54. Nyland J, Klein S, Caborn DNM. Lower extremity compensatory neuromuscular and biomechanical adaptations 2 to 11 years after anterior cruciate ligament reconstruction. *Arthrosc-J Arthroscop Relat Surg.* 2010;26(9):1212–25.

55. Nyland J, Mauser N, Caborn DNM. Sports involvement following ACL reconstruction is related to lower extremity neuromuscular adaptations, subjective knee function and health locus of control. *Knee Surg Sports Traumatol Arthrosc.* 2013;21(9):2019–28.

56. Nyland J, Wera J, Klein S, Caborn DN. Lower extremity neuromuscular compensations during instrumented single leg hop testing 2–10 years following ACL reconstruction. *Knee.* 2014;21(6):1191–7.

57. Boerboom AL, Hof AL, Halbertsma JP, van Raaij JJ, Schenk W, Diercks RL, et al. Atypical hamstrings electromyographic activity as a compensatory mechanism in anterior cruciate ligament deficiency. *Knee Surg Sports Traumatol Arthrosc.* 2001;9(4):211–6.

58. Bulgheroni P, Bulgheroni MV, Andrini L, Guffanti P, Giughello A. Gait pat- terns after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 1997;5(1):14–21.

59. Gokeler A, Hof AL, Arnold MP, Dijkstra PU, Postema K, Otten E. Abnormal landing strategies after ACL reconstruction. *Scand J Med Sci Sports.* 2010;20(1): e12–9.

60. Hansen C, Einarson E, Thomson A, Whiteley R, Witvrouw E. Hamstring and calf muscle activation as a function of bodyweight support during treadmill running in ACL reconstructed athletes. *Gait Posture.* 2017;58:154–8.

61. Klyne DM, Keays SL, Bullock-Saxton JE, Newcombe PA. The effect of anterior cruciate ligament rupture on the timing and amplitude of gastrocnemius muscle activation: a study of alterations in EMG measures and their relationship to knee joint stability. J Electromyogr Kinesiol: *Off J Int Soc Electrophysiol Kinesiol.* 2012;2 2(3):446–55.

62. Knoll Z, Kocsis L, Kiss RM. Gait patterns before and after anterior cruci- ate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2004;12(1):7–14.

63. Kuster M, Blatter G, Hauswirth L, Neuer W, Wood GA. The anterior cruciate ligament, an important structure of the knee joint. *Praxis* (Bern 1994). 1995;84(5):134–9.

64. Madhavan S, Shields RK. Neuromuscular responses in individuals with anterior cruciate ligament repair. *Clin Neurophysiol.* 2010;122(5):997–1004.

65. Ortiz A, Olson S, Libby CL, Trudelle-Jackson E, Kwon YH, Etnyre B, et al. Landing mechanics between noninjured women and women with anterior cruciate ligament reconstruction during 2 jump tasks. *Am J Sports Med.* 2008;36(1):149–57.

66. Ortiz A, Olson S, Trudelle-Jackson E, Rosario M, Venegas HL. Landing mechanics during side hopping and crossover hopping maneuvers in noninjured women and women with anterior cruciate ligament reconstruction. *J Injury Funct Rehab.* 2011;3(1):13–20.

67. Patras K, Zampeli F, Ristanis S, Tsepis E, Ziogas G, Stergiou N, et al. Hamstring-dominant strategy of the bone-patellar tendon-bone graft anterior cruciate ligament-reconstructed leg versus quadriceps-domi- nant strategy of the contralateral intact leg during high-intensity exercise in male athletes. *Arthroscopy*. 2012; 28(9):1262–70.

68. Swanik CB, Lephart SM, Giraldo JL, Demont RG, Fu FH. Reactive muscle firing of anterior cruciate ligament-injured females during functional activities. *J Athl Train*. 1999;34(2):121–9.

69. Zebis MK, Andersen CH, Bencke J, Orntoft C, Linnebjerg C, Holmich P, et al. Neuromuscular coordination deficit persists 12 months after ACL reconstruction but can be modulated by 6 weeks of kettlebell training: a case study in women's elite soccer. *Case Rep Orthop*. 2017;2017:4269575.

70. Engelen-van Melick N, van Cingel RE, Tijssen MP, Nijhuis-van der Sanden MW. Assessment of functional performance after anterior cruciate ligament reconstruction: a systematic review of measurement procedures. *Knee Surg Sports Traumatol Arthrosc*. 2013;21(4):869–79.

71. Busch A, Helne P, Boesch L, Blasimann A, Baur H. Neuromuscular control in patients with acute ACL injury during stair ascent—a pilot study. *Sports Orthop Traumatol*. 2019;35(2):158–65.

72. Price RJ, Hawkins RD, Hulse MA, Hodson A. The football association medi- cal research programme: an audit of injuries in academy youth football. *Br J Sports Med*. 2004;38(4):466–71.

73. Burgi CR, Peters S, Ardern CL, Magill JR, Gomez CD, Sylvain J, et al. Which criteria are used to clear patients to return to sport after primary ACL reconstruction? A scoping review. *Br J Sports Med*. 2019;53(18): 1154–61.

74. Hewett TE, Myer GD, Ford KR, Heidt RS Jr, Colosimo AJ, McLean SG, et al. Biomechanical measures of neuromuscular control and valgus loading of the knee predict anterior cruciate ligament injury risk in female athletes: a prospective study. *Am J Sports Med*. 2005; 33(4):492–501.

75. Montalvo AM, Schneider DK, Yut L, Webster KE, Beynnon B, Kocher MS, et al. "What's my risk of sustaining an ACL injury while playing sports?" A systematic review with meta-analysis. *Br J Sports Med*. 2019;53(16):1003–12.

76. Balachandar V, Marciniak JL, Wall O, Balachandar C. Effects of the men- strual cycle on lower-limb biomechanics, neuromuscular control, and anterior cruciate ligament injury risk: a systematic review. *Muscles Ligaments Tendons J*. 2017;7(1):136–46.

77. Belanger L, Burt D, Callaghan J, Clifton S, Gleberzon BJ. Anterior cruciate ligament laxity related to the menstrual cycle: an updated systematic review of the literature. *J Can Chiropr Assoc*. 2013;57(1):76–86.

78. Voskanian N. ACL Injury prevention in female athletes: review of the lit- erature and practical considerations in implementing an ACL prevention program. *Curr Rev Musculoskelet Med*. 2013;6(2):158–63.

79. Wojtys EM, Wylie BB, Huston LJ. The effects of muscle fatigue on neuromuscular function and anterior tibial translation in healthy knees. *Am J Sports Med*. 1996;24(5):615–21.

80. Pappas E, Carpes FP. Lower extremity kinematic asymmetry in male and female athletes performing jump-landing tasks. *J Sci Med Sport*. 2012;15(1):87–92.

81. Pollard CD, Sigward SM, Powers CM. Limited hip and knee flexion during landing is associated with increased frontal plane knee motion and moments. *Clin Biomech* (Bristol, Avon). 2010;25(2):142–6.

82. Hanson AM, Padua DA, Troy Blackburn J, Prentice WE, Hirth CJ. Muscle activation during side-step cutting maneuvers in male and female soccer athletes. *J Athl Train*. 2008;43(2):133–43.

83. Sigward SM, Powers CM. Loading characteristics of females exhibiting excessive valgus moments during cutting. *Clin Biomech* (Bristol, Avon). 2007;22(7):827–33.

84. Malinzak RA, Colby SM, Kirkendall DT, Yu B, Garrett WE. A comparison of knee joint motion patterns between men and women in selected athletic tasks. *Clin Biomech* (Bristol, Avon). 2001;16(5):438–45.

85. Myer GD, Ford KR, Hewett TE. The effects of gender on quadriceps muscle activation strategies during a maneuver that mimics a high ACL injury risk position. J Electromyogr Kinesiol: *Off J Int Soc Electrophysiol Kinesiol*. 2005;15(2):181–9.

86. Padua DA, Carcia CR, Arnold BL, Granata KP. Gender differences in leg stiffness and stiffness recruitment strategy during two-legged hopping. *J Mot Behav*. 2005;37(2):111–25.

87. Nagano Y, Ida H, Akai M, Fukubayashi T. Gender differences in knee kinematics and muscle activity during single limb drop landing. *Knee*. 2007;14(3):218–23.

88. Hannah R, Folland JP, Smith SL, Minshull C. Explosive hamstrings-to-quadriceps force ratio of males versus females. *Eur J Appl Physiol*. 2015;115(4):837–47.

89. Benjaminse A, Gokeler A, Fleisig GS, Sell TC, Otten B. What is the true evidence for gender-related differences during plant and cut maneuvers? A systematic review. *Knee Surg Sports Traumatol Arthrosc*. 2011;19(1):42–54.

90. Nimphius S, McBride JM, Rice PE, Goodman-Capps CL, Capps CR. Comparison of quadriceps and hamstring muscle activity during an isometric squat between strength-matched men and women. *J Sports Sci Med*. 2019;18(1):101–8.

91. Monk AP, Davies LJ, Hopewell S, Harris K, Beard DJ, Price AJ. Surgical versus conservative interventions for treating anterior cruciate ligament injuries. *Cochrane Database Syst Rev*. 2016;4:CD011166.

92. Behnke AL, Parola LR, Karamchedu NP, Badger GJ, Fleming BC, Beveridge JE. Neuromuscular function in anterior cruciate ligament reconstructed patients at long-term follow-up. *Clin Biomech* (Bristol, Avon). 2021;81:105231.

93. Hermens HJ, Freriks B, Disselhorst-Klug C, Rau G. Development of recommendations for SEMG sensors and sensor placement procedures. J Electromyogr Kinesiol: *Off J Int Soc Electrophysiol Kinesiol*.2000; 10(5):361–74.

94. Losciale JM, Zdeb RM, Ledbetter L, Reiman MP, Sell TC. The association between passing return-to-sport criteria and second anterior cruciate ligament injury risk: a systematic review with meta-analysis. *J Orthop Sports Phys Ther*. 2019;49(2):43–54.

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Additional file 1: Search string for MEDLINE/PubMed

((((((((anterior cruciate ligament[MeSH Terms]) OR anterior cruciate ligament[Title/Abstract]) OR anterior cruciate ligaments[Title/Abstract]) OR anterior cranial cruciate ligament[Title/Abstract]) OR anterior cranial cruciate ligaments[Title/Abstract]) OR ACL[Title/Abstract])) AND ((((((((((((((((((anterior cruciate ligament injuries[MeSH Terms]) OR anterior cruciate ligament injuries[Title/Abstract]) OR anterior cruciate ligament injury[Title/Abstract]) OR rupture[Title/Abstract]) OR ruptures[Title/Abstract]) OR strain[Title/Abstract]) OR strains[Title/Abstract]) OR sprain[Title/Abstract]) OR sprains[Title/Abstract]) OR tear[Title/Abstract]) OR tears[Title/Abstract]) OR ((strains and sprains[MeSH Terms]))) OR ((strains[Title/Abstract] AND sprains[Title/Abstract]))) OR injury[Title/Abstract]) OR injuries[Title/Abstract]) OR partial tear[Title/Abstract]) OR partial tears[Title/Abstract]) OR deficiency[Title/Abstract]))) AND ((((((((((((((((anterior ligament reconstruction[MeSH Terms]) OR anterior ligament reconstruction[Title/Abstract]) OR anterior ligament reconstructions[Title/Abstract]) OR anterior cruciate ligament/surgery[Title/Abstract]) OR anterior cruciate ligament/surgery[MeSH Terms]) OR anterior cruciate ligament/surgery[Title/Abstract]) OR reconstructive surgical procedures[MeSH Terms]) OR reconstructive surgical procedures[Title/Abstract]) OR reconstructive surgical procedure[Title/Abstract]) OR reconstruction[Title/Abstract]) OR reconstructions[Title/Abstract]) OR reconstructive[Title/Abstract])))) AND (((((((((neuromuscular control[Title/Abstract]) OR neuromuscular activity[Title/Abstract]) OR sensorimotor control[Title/Abstract]) OR muscle activity[Title/Abstract]) OR muscular activity[Title/Abstract]) OR active stability[Title/Abstract]) OR active joint stability[Title/Abstract]) OR active knee stability[Title/Abstract]) OR active knee joint stability[Title/Abstract]))) AND (((((((((((((((electromyography[MeSH Terms]) OR electromyography[Title/Abstract]) OR surface electromyography[Title/Abstract]) OR electromyogram[Title/Abstract]) OR EMG[Title/Abstract]) OR amplitude[Title/Abstract]) OR timing[Title/Abstract]) OR mean activity[Title/Abstract]) OR peak activity[Title/Abstract]) OR duration of activity[Title/Abstract]) OR onset of activity[Title/Abstract]) OR offset of activity[Title/Abstract]) OR on-off-pattern[Title/Abstract]) OR pre-activity[Title/Abstract]) OR latency[Title/Abstract]) OR reflex response[Title/Abstract])

Additional file 2: Methodological quality assessment from Downs & Black (1998), [31] modified by Ramsey et al. (2019) [29] and Pairot-de-Fontenay et al. (2019) [32] with adaptations

Category	Question number in Downs and Black	Question	Application to this review
Reporting	1.	Is the hypothesis/aim/objective of the study clearly described?	Score of 1 = if hypothesis/aim/objective described. 0 = for NO description.
Reporting	2.	Are the main outcomes to be measured clearly described in the introduction or methods section?	Score of 1 = if main outcome measure(s) described in introduction or methods. 0 = for NO description.
Reporting	3.	Are the characteristics of the patients included in the study clearly described?	Score of "1" for YES "0" for NO defined criteria. ACLR group: Clear inclusion and exclusion criteria; Injured leg: primary ACLR, non-injured leg: history of surgery, knee injury or pathology; Control group: history of surgery, knee injury or pathology.
Reporting	4.	Are the interventions of interest clearly described?	assessment / measurement of lower extremity of ACL injured people or their controls to assess neuromuscular control of the knee/active knee stability/knee joint stability under dynamic conditions Score of "1" if intervention clearly described. "0" for no or insufficient/unclear description. "X" for unable to determine
Reporting	5.	Are the distributions of principal confounders for each group to be compared clearly described?	Age, gender, BMI or body mass & height respectively, activity level/sports activity (Tegner score desirable, but not mandatory) were considered the main confounders. If >1 group of patients: time since injury as additional confounder If 3 or 4 of these were specified: score of "2" If 1 or 2 of these were specified: score "1" If none of these were specified: score "0"
Reporting	6.	Are the main findings of the study clearly described?	Score of "1" if YES, main findings clearly described respectively. Score "0" for NO description.
Reporting	7.	Does the study provide estimates of the random variability in the data for the main outcomes?	SD, SE, CI were considered for measures of variability. Score of "1" if any of these measures of variability given. Score "0" for no description of measures of variability. In non-normally distributed data: inter-quartile range of results should be reported; in normally distributed data: SE, SD or CI should be reported
Reporting	10.	Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where probability value is less than 0.001?	Score of "1" if actual probability values described. Score "0" for no description.
External validity bias	11.	Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	Score of "1" if participants recruited were from the community. Score "X" for unable to determine and "0" if the participants were from a single hospital.
External validity bias	12.	Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	Score of "1" if participants who contacted were from the community and the cohort was finalised from this community-based population based on the inclusion criteria. Score "0" for no description. "X" for unable to determine
External validity bias	13.	Were the staff, places, and facilities where the patients/participants were treated, representative of the treatment/intervention the majority of patients received?	Score of "1" if intervention/task was representative of that in use in the source population → stairs, gait, walking, running, jumping, squats, stop & go manoeuvres etc. Score "0" if e.g. intervention was undertaken in a specialist centre unrepresentative of the locations/hospitals/private practices most of the source population would attend → activities in a movement lab or similar tasks such as treadmill running or walking, legpress, dynamometry etc. "X" for unable to determine
Internal validity bias	14.	Was an attempt made to blind study subjects to the intervention they have received?	Score of "1" if an attempt was made or the study participant was blinded to the intervention. Score "0" if no attempt was made despite the possibility to blind participants. Score "X" if unable to determine, study design was not a RCT respectively.
Internal validity bias	15.	Was an attempt made to blind those measuring main outcomes of the intervention?	Score of "1" if YES, given if blinding done during data processing. Score "0" for NO description. Score "X" if unable to determine, study design was not a RCT respectively.
Internal validity bias	16.	If any of the results of the study were based on "data dredging", was this made clear?	Score of "1" for clearly mentioning the outcome measures planned. Score "0" if data dredging was there. "X" for unable to determine

Internal validity bias	17.	In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?	Score of “1” if YES. Score “0” if NO. Score “X” if unable to determine, in case of a healthy control group respectively.
Internal validity bias	18.	Were the statistical tests used to assess the main outcomes appropriate?	Score of “1” if YES, appropriate statistical tests used. Score “0” for non-appropriate statistical tests and “0” for no description. “X” for unable to determine
Internal validity bias	20.	Were the main outcome measures used accurate (valid and reliable)?	Score of “1” if reference given for reliability or validity of the outcome measures used or use of an established measure/assessment such as EMG. Score “0” for no description, use of a new, not sufficiently tested measure. “X” for unable to determine
Internal validity: selection bias	21.	Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?	It was considered important that groups were matched for age (within a mean of 5 years), BMI or body mass & height respectively, sport level, gender. Score of “1” if age, BMI or body mass & height respectively, sport level and gender matched in both groups. In other words: no statistical group differences. Score “0” if groups were not matched and “0” for no description. Score “X” if unable to determine (cohort studies, case-control studies). Apply “IC” when comparison with the contralateral limb was done.
Internal validity: selection bias	22.	Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	Score “1” if YES. Score “0” if NO. Score “X” if unable to determine, in case of cross-sectional study, time not specified.
Internal validity: selection bias	23.	Were study subjects randomised to intervention groups?	Score “1” if YES. Score “0” if NO. Score “X” if it is another study design than a RCT, e.g. a case-control study or if unable to determine.
Internal validity: selection	24.	Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?	Score “1” if YES. Score “0” if NO. Score “X” if it is another study design than a RCT, e.g. a case-control study or if unable to determine.
bias			
Internal validity: selection bias	25.	Was there adequate adjustment for the confounding in the analysis from which the findings were drawn?	A score of “1” was applied If neuromuscular control/active knee stability was not significantly different between groups, alternatively if this was considered a confounding factor in the statistical analysis. Score of “0” if neuromuscular control/active knee stability was significantly different between groups and not considered as a confounding factor in the statistical analysis. Score of “X” for unable to determine. Apply “IC” when comparison with the contralateral limb was done.
Internal validity: selection bias	26.	Were losses of patients to follow-up taken into account?	Score “1” if YES. Score “0” if NO. Score “X” if unable to determine. Score “X” if e.g. study design without follow-up such as cross-sectional or cohort study
Power	27.	Were appropriate power calculations reported?	A score of “1” was applied when a power or a sample size calculation was provided. If these were not given or there was no explanation whether the number of participants was appropriate a “0” was applied.

Explanations/Abbreviations: ACLR: Anterior cruciate ligament reconstruction; BMI: Body Mass Index; CI: Confidence interval; SD: Standard deviation; SE: Standard error; IC: intrasubject comparison (comparison with contralateral limb)

Additional file 3: EMG methods and procedures of included studies

Authors & Year	Type	Detection	Electrode placement	Sampling	Rectification	Post-Processing	Normalization
Busch et al. (2019) (13)	sEMG	bipolar	according to SENIAM (Hermens et al., 2000 (93))	differential-preamplifier (gain: 500, input impedance: 4000 M, common mode rejection ratio 90 dB at 60 Hz) to a telemetric main amplifier (band-pass filter: 10 Hz to 1 kHz, gain: 5.0, resultant overall gain: 2500) sampling rate: 2000Hz	n.m.	band-pass filter 10–500 Hz (Butterworth, 2nd order)	to the individual, submaximal MVC during walking on treadmill at 5 km/h (1.39 m/s) (%subMVC)
Alkjaer et al. (2003) (33)	sEMG	bipolar	2 cm apart over the most prominent part of the muscle belly	custom-built preamplifiers (input impedance 80 MΩ, gain=50), custom-built amplifiers with a frequency response between 20 Hz and 10 kHz sampling rate: n.m.	full-wave	digitally high- and low-pass filtered (Butterworth 4th order, cut-off frequencies 20 Hz and 500 Hz, respectively), low-pass filtered at 15 Hz	to the maximal EMG amplitude (%maxEMG) recorded during MVIC for each muscle group
Alkjaer et al. (2002) (34)	sEMG	bipolar	n.m.	custom-built preamplifiers (input impedance 80 MΩ, gain=50) with a frequency response between 20 Hz and 10 kHz sampling rate: 1000 Hz	full-wave	digitally high- and low-pass filtered (Butterworth 4th order, cut-off frequencies 20 Hz and 500 Hz, respectively), low-pass filtered at 15 Hz	n.m.
Arnason et al. (2014) (35)	sEMG	bipolar	according to SENIAM (Hermens et al., 2000 (93)) & palpation during muscle contraction	signal bandwidth of 16–500 Hz sampling rate: 1600 Hz	full-wave	high-pass filtered at 25 Hz moving 250 ms window	to the maximum signal collected during 3 MVIC, each lasting 5 s
Bryant et al. (2009) (36)	sEMG	bipolar	over the relevant muscle bellies according to Daanen et al., 1990 & De Luca, 1997	amplifier (gain 10000; common mode rejection >120 dB; input impedance >1012 Ω), following amplification (gain = 10000; common mode rejection >120 dB; input bias current <40 pA; input impedance >1012 Ω) sampling rate: 1000 Hz	full-wave	4th order zero-phase-shift Butterworth filter (Winter, 1990; high-pass fc = 15 Hz; low-pass fc = 250 Hz) for linear envelope, after rectification: 4th order zero-phase-shift Butterworth low-pass filter (fc = 30 Hz).	n.m.
Burland et al. (2020) (37)	sEMG	bipolar	n.m.	n.m.	yes, not further specified	high-pass Butterworth filter using a 12.0 Hz cut-off frequency, after rectification processed using a RMS algorithm with a 50 ms moving window	EMG data from single-limb forward hop normalized to peak muscle activity recorded across all trials
Cordeiro et al. (2015) (38)	sEMG	bipolar	according to SENIAM (Hermens et al., 2000 (93))	amplified with a band-pass (10–500 Hz), common mode rejection ratio (120 dB) and input impedance > 100 MW sampling rate: 1050 Hz	full-wave	digitally filtered (20–500 Hz), after rectification low-pass filter (25 Hz, 7th order Butterworth)	to amplitude expressed as RMS obtained during MVIC
Dashti Rostami et al. (2019) (39)	sEMG	bipolar	according to SENIAM (Hermens et al., 2000 (93))	sampling rate: 2000 Hz	full-wave	band-pass filtered using 4th order, zero-lag Butterworth filter with high- and low-pass cut-off frequencies of 10 and 500 Hz, respectively, after rectification: using RMS-algorithm with 50ms moving window.	dynamic EMG data from landing task normalized to the peak muscle activity recorded during MVIC
Jordan et al. (2016) (40)	sEMG	bipolar	according to SENIAM (Hermens et al., 2000 (93))	Preamplification (overall gain 500), filtered with 1st order high-pass filter (10 Hz) and low-pass filtered (cut-off 500 Hz), common mode rejection ratio >100 dB sampling rate: 1500 Hz	n.m.	high-pass filtered (cut-off frequency = 10 Hz) using Butterworth 4th order zero-lag filter, smoothed using a point-by-point moving 50 ms symmetric RMS filter	RMS for each muscle during jump test normalized to the maximal RMS amplitude obtained from respective muscle during MVIC
Lessi et al. (2017) (41)	sEMG	bipolar	according to SENIAM (Hermens et al., 2000 (93))	preamplification (operating range 40 m, transmission frequency 2.4 GHz, common mode rejection ratio >80 dB; bandwidth of 450 Hz at >80 dB/s) sampling rate: 2400 Hz	full-wave	band-pass filtered at 20–400 Hz, smoothed by symmetrical moving RMS filter (20 ms time constant)	to peak RMS amplitude recorded during landing, representing 100% activity (%peak EMG during landing)
Oliver et al. (2018) (42)	sEMG	bipolar	according to SENIAM (Hermens et al., 2000 (93))	amplification and band-pass-filter in working frequency of 1000 Hz	n.m.	n.m.	by setting RMS amplitude at a percentage related to the MVC (%MVC)
Ortiz et al. (2014) (43)	sEMG	bipolar	according to Cram et al., 1998	signal bandwidth: 20-450 Hz [3 dB]; impedance: >100 KU; noise: <1.2 mV amplified (gain = 1000) sampling rate: 1000 Hz	n.m.	band-pass filter (20-450 Hz)	by dividing the mean signal during each specific task trial by the maximum signal generated during the middle 3 seconds of the 5-second tuck jumps performed during warm-up
Patras et al. (2009) (44)	sEMG	bipolar	according to SENIAM (Hermens et al., 2000 (93)) and Merletti & Hermens, 2004	signal bandwidth: 10–500 Hz sampling rate: 1500 Hz	full-wave	high-pass filtered with an 8th order Butterworth filter, smoothed with a 100 ms RMS algorithm	n.m.

Patras et al. (2010) (45)	sEMG	bipolar	according to SENIAM (Hermens et al., 2000 (93)) and Merletti & Hermens, 2004	signal bandwidth: 10–500 Hz sampling rate: 1500 Hz	full-wave	high-pass filtered (cut-off frequency at 20 Hz) with an 8th order Butterworth filter, smoothed with a 100 ms RMS algorithm	not performed
Pincheira et al. (2018) (46)	sEMG	bipolar	according to SENIAM (Hermens et al., 2000 (93))	signal bandwidth of 20-450 Hz sampling rate: 1000 Hz	full-wave	digital low-pass filtered at 50 Hz	n.m.
Rudolph et al. (2001) (47)	sEMG	bipolar	n.m.	sampling rate: 960 Hz	full-wave	low-pass filter (2nd order, phase corrected, Butterworth filter) with cut-off frequency of 20 Hz	to a maximum EMG, which was defined as the highest level of EMG over a 30-ms interval during any of the isometric, walking or jogging trials (%MVIC)
Rudolph et al. (2000) (48	sEMG	bipolar	n.m.	n.m.	full-wave	low pass filter (2nd order, phase corrected, Butterworth filter) with cut-off frequency of 20 Hz	peak EMG activity over 30-ms from either the dynamic or maximum isometric trials used to normalize EMG data in dynamic trials
Rudolph & Snyder-Mackler (2004) (49)	sEMG	bipolar	over the muscle bellies according to Delagi et al., 1981	sampling rate: 960 Hz	full-wave	phase corrected, 8th order, Butterworth filter, with high-pass cut-off frequency of 90 Hz, after rectification: low-pass filter with 2nd order, phase corrected, Butterworth filter with cut-off frequency of 20 Hz	maximum EMG defined as highest amplitude of EMG found during any of the trials (MVIC and dynamic tasks). Signals from step trials were then normalized by maximum value
Swanik et al. (2004) (50)	sEMG	bipolar	identified by bony landmarks and by palpating midlength of the contractile component during isometric contraction	single-ended amplifier (gain 500) with 4th order Butterworth filter (10–500 Hz), common mode rejection ratio of 130 db. sampling rate: 2500 Hz	full-wave	smoothing over a 15-ms moving window	peak muscle activity during landing used for amplitude normalization
Briem et al. (2016) (51)	sEMG	bipolar	according to SENIAM (Hermens et al., 2000 (93))	signal bandwidth of 16–500 Hz sampling rate: 1600 Hz	full-wave	high-pass filtered at 25 Hz, RMS derived using moving 250 ms window	peak values test jump normalized to maximum signal of two 5-s trials of MVIC (%MVIC)

Lessi et al. (2018) (52)	sEMG	bipolar	according to SENIAM (Hermens et al., 2000 (93))	preamplification (transmission frequency 2.4 GHz, common mode rejection ratio >80 dB; bandwidth of 450 Hz at >80 dB/s) sampling rate: 2400 Hz	full-wave	band-pass filtered at 20–400 Hz, smoothed by symmetrical moving RMS filter (20 ms time constant)	against peak RMS during landing phase → peak RMS during landing represented 100% of muscle activity (%peak RMS during landing task)
Lustosa et al. (2011) (53)	sEMG	bipolar	on the largest portion of the VL and BF muscles, according to the direction of the fibers	amplifiers with input impedance of 2 MΩ, common mode rejection ratio of 1000 MΩ signal bandwidth: 10 to 2000 Hz built-in high-gain amplifier with an integral 500 Hz low-pass filter sampling rate: 1000 Hz	full-wave	filtered with 500-Hz low-pass and 10 Hz high-pass filters	RMS used to quantify intensity of EMG signal during MVIC tests → values used to normalize the EMG signal (%MVIC)
Nyland et al. (2010) (54) Nyland et al. (2013) (55) Nyland et al. (2014) (56)	sEMG	bipolar	applied in parallel alignment to the muscle fibers at muscle belly	signal bandwith: 10 - 500 Hz, differential input impedance >10 MΩ, common mode rejection ratio of 100 dB at 50 or 60 Hz sampling rate: 1000 Hz	full-wave	60-Hz notch filter and 50 ms RMS-smoothing	mean EMG signal amplitudes collected during single-leg CMJ testing (54,55), single-leg hop for distance (56) respectively, normalized to MVIC
Boerboom et al. (2001) (57)	sEMG	n.m.	according to Perotto, 1994	n.m.	yes, not further specified	band-pass filtered 20 Hz–10 kHz and smoothed with a 25 Hz 3rd order Butterworth filter. Smoothed rectified EMGs were A/D converted at 100 Hz	individually averaged EMG pattern normalized to standard pattern of healthy control group (normative EMG profiles), several steps of calculations
Bulgheroni et al. (1997) (58)	sEMG	n.m.	n.m.	sampling rate: 500 Hz	yes, not further specified	High-pass filter to eliminate frequency components <10 Hz, after rectification: filtered to eliminate the components of the signal > 200 Hz	to the maximum recorded signal amplitude during a single walking cycle
Gokeler et al. (2010) (59)	sEMG	bipolar	according to SENIAM (Hermens et al., 2000 (93))	preamplifier with >110 dB common mode rejection, <2 microV RMS noise level, >500MΩ input impedance high-pass filter at 20 Hz with 3rd order digital Butterworth filter sampling rate: 800 Hz	yes, not further specified	Smoothing with 10 Hz zero-lag Butterworth filter	n.m.
Hansen et al. (2017) (60)	sEMG	n.m.	according to SENIAM (Hermens et al., 2000 (93))	sampling rate: 2000 Hz	n.m.	high-pass filter with 5 Hz cut-off, low-pass with 500 Hz cut-off	normalized to its respective maximal contraction value during 100% body weight running trials for each participant

Klyne et al. (2012) (61)	sEMG	n.m.	according to Kendall and McCleary, 1983	signal bandwidth of 20‐450 Hz ±10% (incorporated in electrodes) preamplifier (gain = 1000 V/V) differential input voltage range of ±10 V, resolution of 100 mV, max sampling rate of 100 kS/s, max gain of x500, common mode rejection rate 105 dB, input impedance of 1 GΩ, sampling rate: 1000 Hz	n.m.	2nd order, low-pass, Butterworth filter with cut-off frequency of 500 Hz	RMS collected during single leg hop test normalized to peak MVIC RMS recordings over a 150 ms epoch
Knoll et al. (2004) (62)	sEMG	bipolar	on the skin overlying the muscle belly	sampling rate: 1000 Hz	yes, not further specified	high-pass filter to eliminate frequency components <10 Hz, after rectification: filtered to eliminate the components of the signals > 200 Hz RMS and normalized	to average of peak EMG signal values of six gait cycles → EMG patterns during % of gait cycle
Kuster et al. (1995) (63)	sEMG	bipolar	n.m.	amplified, band-pass filtered (3 dB down at 3 Hz and 1 kHz) sampling rate: 500 Hz	full-wave	high-pass filtered at 4 Hz to eliminate movement artefacts	averages of 10-19 strides for each subject → representative group linear envelope of these averaged EMG records obtained by across-subject averaging following normalization of each individual's ensemble average to 100% of peak activity
Madhavan & Shields (2011) (64)	sEMG	bipolar	according to Cram et al., 1998	electrodes with on-site preamplification (gain x 35), further amplified at main frame by 10 K (high-impedance circuit with common mode rejection ratio of 87 dB at 60 Hz) signal bandwidth: 15‐4000 Hz sampling rate: 2000 Hz	n.m.	calculation of linear velocity by differentiating displacement signal (Tc = 10 ms) and low-pass filtering at 6 Hz using a 5th order zero phase lag Butterworth filter RMS processed with a time constant of 10 ms	analysis of MVICs by finding peak RMS during each muscle contractions → calculating mean RMS for 200ms on either side of the peak EMG (%MVIC)
Ortiz et al. (2008) (65) Ortiz et al. (2011) (66)	sEMG	bipolar	according to Cram et al. 1998	preamplified electrodes, overall gain 2000 mV filtered at a bandwidth of 10 to 500 Hz with 130 dB common-mode rejection within the transmitter sampling rate: n.m.	full-wave	n.m.	by using a dynamic normalization procedure in which the mean signal for each muscle group in the window of interest was divided by the maximum signal generated on the specific trial analyzed
Patras et al. (2012) (67)	sEMG	bipolar	according to SENIAM (Hermens et al., 2000 (93)) and Merletti & Hermens, 2004	signal bandwidth: 10–500 Hz sampling rate: 1500 Hz	full-wave	high-pass filtered (cut-off frequency at 20 Hz) with an 8th order Butterworth filter, smoothed with a 100 ms RMS algorithm	not performed
Swanik et al. (1999) (68)	sEMG	bipolar	according to Basmajian & De Luca, 1985	amplifier (gain 500) with Butterworth low-pass (15 Hz) and high-pass (500 Hz) filters, common mode rejection ratio of 130 dB, receiver (gain 500, total gain 1000) sampling rate: 2500 Hz	full-wave	integrated EMG data averaged over a 15 ms moving window with sampling rate of 1000 Hz	integrated EMG (microvolts x ms) normalized to mean amplitude of 3 - 6 consecutive test repetitions and for time
Zebis et al. (2017) (69)	sEMG	bipolar	according to SENIAM (Hermens et al., 2000 (93))	n.m.	n.m.	high-pass filtered at a 5Hz cut-off frequency (4th order zero-lag Butterworth filter), subsequently smoothed by symmetrical moving RMS filter of 30 ms	mean RMS amplitude normalized to peak RMS amplitude recorded during sidecutting maneuver (%maxEMG)

Legends: CMJ = countermovement jump(ing); EMG = electromyography; MVC = maximum voluntary contraction; MVIC = maximum voluntary isometric contraction; Hz = Hertz; ms = milliseconds; n.m. = not mentioned; RMS = root mean square; sEMG = surface electromyography; SENIAM = Surface ElectroMyoGraphy for the Non-Invasive Assessment of Muscles Project

Additional references (in order of apperance):

Daanen HA, Mazure M, Holewijn M, Van der Velde EA. Reproducibility of the mean power frequency of the surface electromyogram. Europ J Appl Physiol Occup Physiol. 1990;61(3–4):274–7.

De Luca CJ. The use of surface electromyography in biomechanics. J Appl Biomech. 1997;13:135–63.

Winter DA. Biomechanics and motor control of human movement. 2nd ed. New York: Wiley; 1990.

Cram JR, Kasman GS, Holtz J. Introduction to Surface Electromyography. Aspen: Gaithersburg; 1998.

Merletti R, Hermens HJ. Detection and conditioning of the surface EMG signal. In: Merletti R, Parker P (eds). Electromyography: physiology, engineering and non-invasive applications. New Jersey: Wiley; 2004.

Basmajian JV, DeLuca C. Muscles Alive: Their Functions Revealed in Electromyography. 5th ed. Baltimore: Williams & Wilkins; 1985.

Delagi EF, Iazzetti J, Perotto A, Morrison D. Anatomical Guide for the Electromyographer. Springfield: Charles C. Thomas; 1981.

Perotto AO. Anatomical guide for the electromyographer. The limbs and the trunk, 3rd ed. Springfield: Thomas; 1994.

Kendall FP, McCleary EK. Muscles: testing and function. Baltimore, USA: Williams and Wilkins; 1983

CHAPTER 4

STUDY 2

Neuromuscular control in acute ACL injury

Neuromuscular Control During Stair Descent and Artificial Tibial Translation After Acute ACL Rupture.

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Abstract

Background: Anterior cruciate ligament (ACL) rupture has direct effect on passive and active knee stability and, specifically, stretch-reflex excitability.
Purpose/Hypothesis: The purpose of this study was to investigate neuromuscular activity in patients with an acute ACL deficit (ACL-D group) compared with a matched control group with an intact ACL (ACL-I group) during stair descent and artificially induced anterior tibial translation. It was hypothesized that neuromuscular control would be impaired in the ACL-D group.
Study Design: Cross-sectional study; Level of evidence, 3.
Methods: Surface electromyographic (EMG) activity of the vastus medialis (VM), vastus lateralis (VL), biceps femoris (BF), and semitendinosus (ST) muscles was recorded bilaterally in 15 patients with ACL-D (mean, 13.8 days [range, 7-21 days] since injury) and 15 controls with ACL-I during stair descent and artificially induced anterior tibial translation. The movements of stair descent were divided into preactivity, weight acceptance, and push-off phases. Reflex activity during anterior tibial translation was split into preactivity and short, medium, and late latency responses. Walking on a treadmill was used for submaximal EMG normalization. Kruskal-Wallis test and post hoc analyses with Dunn-Bonferroni correction were used to compare normalized root mean square values for each muscle, limb, movement, and reflex phase between the ACL-D and ACL-I groups.
Results: During the preactivity phase of stair descent, the hamstrings of the involved leg of the ACL-D group showed 33% to 51% less activity compared with the matched leg and contralateral leg of the ACL-I group ($P < .05$). During the weight acceptance and push-off phases, the VL revealed a significant reduction (approximately 40%) in the involved leg of the ACL-D group compared with the ACL-I group. At short latency, the BF and ST of the involved leg of the ACL-D group showed a significant increase in EMG activity compared with the uninvolved leg of the ACL-I group, by a factor of 2.2 to 4.6.
Conclusion: In the acute phase after an ACL rupture, neuromuscular alterations were found mainly in the hamstrings of both limbs during stair descent and reflex activity. The potential role of prehabilitation needs to be further studied.
Keywords: anterior cruciate ligament; rupture; acute; neuromuscular control; tibial translation; stairs

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Background

Injuries of the anterior cruciate ligament (ACL) happen frequently and concern elite (0.15 injuries per 1000 athlete-exposures) but also recreational athletes.[27,30] Most ACL injuries occur during cutting and pivoting sports and are caused by a noncontact multiplane mechanism because of high knee valgus stress and foot abduction position.[26,32,57] The injury often leads to surgical reconstruction or repair. This applies especially to younger people with high demands on their knees at work or in sports or experiencing persistent giving-way episodes. It is known that patients with an ACL injury show neuromuscular adaptations due to altered sensorimotor control.[20,55] These changes in sensorimotor control are caused by altered afferent inputs to the central nervous system due to the loss of the mechano-receptors of the native (original) ACL.[46,60] In recent years, studies have reported findings of neuro-muscular control in patients after ACL reconstruction by investigating activities of daily living such as stair ambulation[10,23] or sport-specific tasks such as hop landing,[52] both of which demand high levels of neuro-muscular control. For example, increased neuro-muscular activity amplitude was found in the gluteus maximus of participants (1-18 years post- operatively) with ACL reconstruction compared with healthy controls during stair ascent and descent.[23] A pilot study with participants 1 year after ACL reconstruction reported a significantly increased activity of the semitendinosus (ST) in the surgically treated leg and of the vastus lateralis (VL) in the uninvolved leg compared with healthy controls during stair descent.[10] The same authors found a decreased activity in vastus medialis (VM) of the reconstructed knee compared with the uninvolved leg and matched limb of controls.[10]

Neuromuscular alterations in the hamstrings—in terms of increased hamstring activation in the recon-structed leg compared with the contralateral leg—have been found not only in the active population but also in athletes returning to sport after ACL recons-truction.[52] These alterations during landing persisted even 6 months after clearance for return to sport.[52] Moreover, different environmental conditions (cognitive dual-task, unpredictable perturbation of supporting surface) during a step-down task affected athletes' neuromuscular response of thigh muscles and adaptation to perturbed tasks in a negative way.[51] In contrast, there have been few studies investigating neuromuscular alterations in patients with ACL deficiency with nonoperative treatment only.[43-45,54] To date, only 3 studies have measured ACL deficiency in patients in the acute stage before any rehabilitative intervention.[11,16,24] Women with an ACL rupture (2-11 months after accident) showed altered neuro-muscular activation, and in general a lower quadri-ceps/hamstring ratio, in the injured leg compared with the uninvolved leg during single- and double-leg squats.[54] In that study, surface electromyographic (EMG) signals were collected, and ratios of average EMG amplitude between injured and uninjured sides, as well as between antagonistic muscles on the same side, were compared without prior normali-zation.[54] A pilot study with male and female participants with an acute ACL deficiency (1-3 weeks after accident) found an activation of only 35% to 50% in the thigh muscles of the injured leg compared with the uninvolved leg (with 100% of activation as reference) during stair ascent.[11] The authors used surface EMG signals during walking on a treadmill at a speed of 5 km/h (1.39 m/s) for submaximal EMG normalization, with stair ascent activity normalized and expressed as a percentage (EMG %) of respective level walking activity.[11] Furthermore, a systematic review reported an increased muscular activity of the hamstrings in patients with acute ACL deficiency during walking, but also a decreased quadriceps activation in the acute stage. A minority of included studies found prolonged duration of activity in patients with ACL deficiency compared with a control group.[48] Normalization procedures varied and included maximum isometric voluntary contraction, peak EMG activity during a gait cycle, mean EMG activity over the entire stride, or deviation from obtained standard muscle activity.[48]

Active joint stability is determined not only by neuromuscular activity (reflex-induced and voluntary activation), but also by muscular reaction times.[28] So far, mainly nonspecific tests, such as hop tests, have been used to test active joint stability. However, testing paradigms that assess neuromuscular control of the knee joint–stabilizing muscles in isolated situations can resemble much more precisely the physiological function of the involved muscle. During anterior tibial translation, the hamstrings, working synergistically with the ACL, respond to a sudden perturbation with a corresponding reflex activation (stretch reflex).[9] Only a few studies have shown that the extent of protective reflex activation of the hamstrings after immediate tibial translation results in increased active joint stiffness.[6,13] To date, neuromuscular control has mainly been assessed in patients with ACL reconstruction during functional or sport-specific tasks. Some authors have also investigated patients with ACL deficiency, but in the chronic stage, usually after nonoperative treatment; some authors have assessed reflex activity in healthy participants. However, literature investigating neuromuscular control and reflex activity in patients with an acute ACL deficiency is limited.

The objective of this cross-sectional study was to compare neuromuscular activity during (1) stair descent and (2) artificially induced anterior tibial translation while standing in patients with acute ACL rupture compared with a matched healthy control group. Based on the literature,[10,11,22,23] we hypothesized that neuromuscular control would be impaired in participants with acute ACL deficiency, meaning that they would show (1) a reduced quadriceps and enhanced hamstring activation and (2) a decreased and prolonged reflex activity of the hamstrings during artificially induced anterior tibial translation compared with healthy controls.

Methods

The protocol for this cross-sectional study received ethics committee approval, and the study was conducted in accordance with the Declaration of Helsinki.[58] All included patients provided written informed consent.

Sample Size Calculation

The a priori analysis of sample size was performed using the software G*Power (Version 3.1; University of Kiel).[15]

The effect size (ES) was calculated with data from a study that investigated the effect of maximal fatigue on reflex responses of the ST during the time interval 20 to 40 ms after tibial translation.[4] The difference was 20% with small variability and resulted in a large ES (1.098).[4] Based on this ES and the assumptions made, a total sample size of 30 patients (n = 15 per group) and a power of 0.82 was obtained. The following assumptions were used: protocol of sample size calculation: n =12; test family = t tests; statistical test = t test; differences between 2 independent means (2 groups); 2-tailed; type of power analysis = a priori; ES = 0.8; alpha-error probability = .05; power (1 – beta-error probability) = 0.8; number of groups = 2; number of measurements = 1.

Participants

Two groups were recruited for this study. One group consisted of patients with an acute (7-21 days after accident), isolated, complete ACL rupture, ACL deficiency, respectively (ACL-D) without any concomitant injuries, confirmed by clinical examination and magnetic resonance imaging scan. Furthermore, patients were included if they had no acute inflammatory signs, limited swelling (<2 cm difference in the circumferential measurement compared with the contralateral side), no acute pain on visual analog scale (VAS; score, <5 of 10),[50] and an approximately free range of motion in flexion and extension of <20° difference from the contralateral side and were able to walk on even ground and climb stairs without any walking aids such as crutches and orthoses.

The patients were recruited in collaboration with Philipp Henle MD, Sonnenhof Orthopaedic Center, Lindenhof Group, Bern, Switzerland, between February 2016 and February 2020. From the initial 19 patients recruited, 4 could not be measured for time reasons (not enough time before surgery or hospital stay), leaving 15 patients in this group.

The control group consisted of 15 healthy matched individuals with an intact ACL (ACL-I). The participants were recruited from local sport clubs and students and collaborators of the Bern University of Applied Sciences. Matching was based on sex, age, body height, body mass, and dominant leg (defined as the preferred leg for kicking a ball).

Inclusion criteria for all participants were age range between 18 and 60 years, being physically active for at least 45 minutes twice per week, and having a minimum Tegner activity score of 5, in which 0 represents disabled and 10 represents professional-level sports.[8,40] Exclusion criteria for all participants were cardiac problems, neurological diseases, peripheral vascular diseases, musculoskeletal complaints, acute infections, alcohol abuse, use of analgesic drugs, knee surgery beforehand, concomitant knee injuries (regarding menisci, medial or lateral collateral ligaments), other concomitant injuries of the lower limb (foot, hip), back pain, trunk injury, thrombosis, and pregnancy.

Measurements

All measurements were performed at the Bern Movement Laboratory. The same setup as for a pilot study was used,[10,11] including a retrospective analysis of pilot data of healthy matched controls.

For all participants, anthropometric data (age, body height, body mass, etc), limb dominance, and data regarding physical activity (type of sports, number of hours per week, Tegner activity score)[53] were collected with the aid of a standardized case report form. Moreover, the Knee injury and Osteoarthritis Outcome Score (KOOS)[41] was completed by every participant. Afterward, the skin was prepared (shaved, smoothed, and cleaned with alcohol) for bipolar, self-adhesive electrodes (Blue Sensor Type P-00-S; Ambu; interelectrode distance, 20 mm), which were applied to the VM, VL, ST, and biceps femoris (BF) muscle of both limbs according to Surface ElectroMyoGraphy for the Non- Invasive Assessment of Muscles standards.[25] The reference electrode was always placed on the right patella. Then, the interelectrode impedance was controlled (impedance meter D175; Digitimer) and accepted at <2 kOhm.

After the preparation and before the measurements started, the actual health status (general well-being) and actual pain level of the participants were assessed by using a 100-mm VAS.[47] This was done to test for inconvenience and pain from any measurements or the presence of the participant in our laboratory.

Each participant started with a warm-up on an instrumented treadmill (h/p/cosmos; sports & medical GmbH) for 10 minutes at 5 km/h (1.39 m/s). The initial contact of each gait cycle was detected by 2 force transducers (series KMB52, 10 kN; Megatron Elektronik) that had been mounted under the treadmill. Signals of electromyography of all 4 muscles on both limbs were recorded during walking at a speed of 5 km/h (1.39 m/s) for 2 minutes and were used for submaximal EMG normalization of stretch reflexes and root mean square (RMS) values of the gait phases during stair climbing.[2,3] After this warm-up, each participant completed 2 experimental situations in the same order: a functional task consisting of stair descent (Fig. 1) and a physiological experimental task, stretch-reflex measurements induced by artificial tibial translation (Fig. 2).

Figure 1. Experimental setup for stair descent.

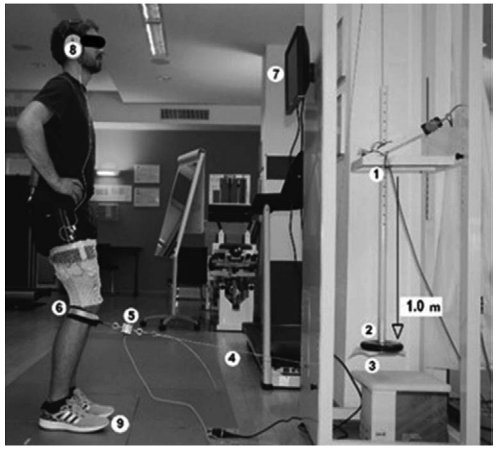

Figure 2. Experimental setup for stretch-reflex measurements (anterior tibial translation): (1) electromagnet, (2) falling barbell weight, (3) stopper, (4) wire rope, (5) force transducer, (6) brace, (7) computer screen for visual control of equal body weight distribution, (8) headphones and attenuator, and (9) 2 force plates.

Stair Descent

Participants were asked to descend a 6-step stairway 10 times at a self-selected speed without using the handrails. The custom-made wooden staircase (Fig. 1) was composed of 2 integrated multi-component force plates (type 9286BA; Kistler), which were embedded in the third and fourth step to identify gait cycles during stair climbing. The inclination was 30.6°, with a step height of 17.1 cm and a step depth of 29.0 cm. The configurations for vertical ground-reaction forces had been previously described and had shown adequate reliability.[34]

The cycle of stair descent was divided into the 3 movement phases: preactivity (PRE), weight acceptance (WA), and push-off (PO). The PRE phase was defined from 150 ms before initial foot-floor contact until initial contact with the force platform. The WA phase covered the period from initial contact until the lowest applied vertical ground-reaction force ("braking phase" until anterior-posterior force crosses the zero line). The PO phase followed the WA phase until the vertical ground-reaction forces declined to zero ("propulsion phase").

Artificial Tibial Translation

The participants were assessed in a relaxed, upright, bipedal stance with hands on hips and knees in 30° of flexion (Fig. 2). To guarantee a standardized standing position, participants stood with each foot on a force plate (type 9286BA; Kistler) and, to ensure equal distribution of the body weight, received visual feedback provided by a computer screen at eye level. In addition, the participants had to wear headphones with music and an attenuator to avoid any kind of acoustic anticipation. An online tool (www.randomization.com) was used to create a list for testing both legs in a randomized order. To evoke standardized tibial translation in the posterior-anterior direction, a reliable rope-and-pulley system[9] was used (Fig. 2). A standardized impulse was applied to the tibial shank and monitored by a force transducer (type KM1506, 2 kN; Megatron Elektronik), which was used as a trigger signal for the measurements of onset of tibial translation. As it has been shown that the neuromuscular hamstring reflex response is greatest to a high magnitude of impulse and a high rate of force development,[9] a barbell weight of 2.5 kg and a drop height of barbell weight of 1.0 m were applied.

Artificial tibial translation was elicited 30 times per lower extremity, with a short break after 15 repetitions to avoid excessive co-contraction or muscular fatigue. Between sets, participants were allowed to walk around and relax during the resting intervals (5 minutes). Between each stimulus, a break of about 30 seconds was taken to avoid impulse anticipation and to allow participants to adjust their standing position (interstimulus interval, 20-30 seconds). Basically, the participants were unaware of the point in time of the tibial translation.

After the measurements were completed, the actual health status (general well-being) and actual pain level of the participants were assessed once more by VAS.

Study Outcomes

As primary outcomes, the RMS values of the EMG signals after the activation of the stretch reflex (after onset of tibial translation) were calculated for 4 predefined time intervals: –50 to 0 ms background activity and preactivity (PRE_50); 20 to 40 ms, short latency response (SLR); 40 to 60 ms, medium latency response (MLR); and 60 to 95 ms, late latency response (LLR).[4,5,9] The RMS values of stair descent in the PRE, WA, and PO phases served as secondary outcomes.[2,3]

Signal Transmission, Data Processing, and Normalization

Transmission of the EMG signal occurred across a differential preamplifier (gain, 500; input impedance, 4000 MOhm; common mode rejection, 90 dB at 60 Hz) to a telemetric main amplifier (PowerPack; Pfitec; bandpass filter, 10 Hz to 1 kHz; gain, 5.0; resultant overall gain, 2500), in which it was recorded at 2000 Hz for walking or stair descent and at 4000 Hz for the stretch-reflex measurement.[35] Then, an analog-digital conversion was conducted (NI PCI 6255; 1.25 ms/s, 16 bit; National Instruments), and finally, LabVIEW-based software (Imago Record; Pfitec) was used to register the signals.

EMG data processing was performed using the same LabVIEW-based software. All corresponding raw EMG signals were full wave rectified. The raw EMG signals from the treadmill and stair descent were additionally band-pass filtered at 10 to 500 Hz (second-order Butterworth).

For interparticipant comparability, RMS values were normalized according to the corresponding time intervals retrieved during level walking. Level walking was expressed as 100% of neuromuscular activity, and reflex responses during tibial translation and stair descent were normalized and expressed as a percentage (EMG%) of respective level walking activity. This kind of evaluation has been used for related research.[2,3]

The RMS values were then exported into Excel spreadsheets (Windows 10; Microsoft Corp), in which individual means of 10 strides, 10 steps (stair descent), and 30 tibial translations per extremity for each muscle in each time interval were calculated and checked for plausibility. Individual values >2 standard deviations (SDs) for stair descent and >3 SDs for reflex measurement were traced back to the original data set and corrected if possible.

TABLE 1

Comparison of Characteristics Between the ACL-D and ACL-I Groups[a]

Characteristic	ACL-D (n ¼ 15)	ACL-I (n ¼ 15)	*P*
Age, y	32.67 ± 9.53	32.20 ± 6.78	.953
Body height, cm	174.0 ± 7.83	177.73 ± 7.27	.187
Body mass, kg	77.98 ± 12.14	73.55 ± 11.74	.512
Female sex, %	33	33	–
Leg dominance, right/left, n	14/1	14/1	–
Time since injury, d	13.8 ± 5.6	–	–
Physical activity, min/wk	340.67 ± 277.83	265.67 ± 126.36	.775
Preinjury Tegner score (10 points max)	6.20 ± 1.86	5.27 ± 1.10	.202
KOOS total score (168 points max)	102.53 ± 23.30	165.67 ± 1.92	<.0001
Pain (36 points max)	24.40 ± 5.73	35.80 ± 0.41	<.0001
Symptoms (28 points max)	18.07 ± 4.27	26.13 ± 1.60	<.0001
ADL (68 points max)	49.73 ± 10.41	68.0 ± 0.00	<.0001
Sport and Recreation (20 points max)	5.20 ± 4.40	19.87 ± 0.35	<.0001
HRQoL (16 points max)	5.13 ± 2.50	15.87 ± 0.52	<.0001
VAS pain			
Premeasurement	9.40 ± 11.84	0.67 ± 1.63	.045
Postmeasurement	17.40 ± 21.20	1.87 ± 3.14	.016
VAS well-being			
Premeasurement	14.07 ± 14.52	6.20 ± 8.76	.037
Postmeasurement	15.20 ± 15.17	5.73 ± 7.31	.001

[a]*Data are reported as mean ± SD unless otherwise indicated. Boldface P values indicate a statistically significant difference between groups (P < .05). Dashes indicate not applicable. ACL-D, anterior cruciate ligament deficient; ACL-I, anterior cruciate ligament intact; ADL, Activities of Daily Living; HRQoL, health-related Quality of Life; KOOS, Knee injury and Osteoarthritis Outcome Score; max, maximum; VAS, visual analog scale.*

Statistical Analysis

Data were transferred from the case report forms to Excel spreadsheets and later processed with SPSS software (Version 27; IBM Corp) and RStudio software (Version 4.1; PBC). Testing of normal distribution of the data was per- formed with the Shapiro-Wilk test. Most of the variables were not normally distributed. However, to allow comparison with other studies, means and SDs are reported. The Mann-Whitney *U* test was used to compare participant characteristics. To test for significant (α = .05) differences in nonparametric data between the ACL-D and ACL-I groups, a Kruskal-Wallis analysis of variance (ANOVA) (rank-based ANOVA, post hoc analyses with Dunn-Bonferroni correction) was conducted for between-group and within-group comparisons for the 4 recorded muscles (VM, VL, BF, and ST), the 3 different movement phases (PRE, WA, and PO) during stair descent, and the 4 reflex time windows (PRE_50, SLR, MLR, and LLR) during artificial tibial translation. The ES was calculated with the rank epsilon-square test, where 0.2 = small effect, 0.5 = medium effect, and 0.8 = large effect.[12]

Results

Characteristics of patients and healthy controls are displayed in Table 1. There were no significant differences in age, body height, body mass, physical activity, and Tegner score between the ACL-D and ACL-I groups. However, the 2 groups differed significantly in KOOS total scores and on each of the KOOS subscales (P < .0001 for all).

Stair Descent

During stair descent, post hoc analysis comparing neuromuscular activity revealed significant differences in the VL and the hamstrings in some of the movement phases. All data regarding comparisons are displayed in Table 2 and are graphically shown in Figure 3. During PRE, significantly less neuromuscular activity was found in the hamstrings of the ACL-D compared with the ACL-I group: the BF of the ACL-D involved leg had 44% less activity than the ACL-I involved leg (P = .0009; ES = 1.5) and 51% less activity than the ACL-I uninvolved leg (P < .0001; ES = 1.8). The ST of the ACL-D involved leg showed 35% and 33% less neuromuscular activity versus the ACL-I involved leg (P = .001; ES = 1.4) and ACL-I un-involved leg (P = .003; ES = 1.2), respectively.

During the WA phase, VL activity showed a 39% reduction in the ACL-D involved leg versus the ACL-I involved leg (P = .019; ES = 0.9). And during PO, there was 40% less activity in the VL of the involved leg compared with the uninvolved leg of ACL-D participants (P = .017; ES = 0.1).

TABLE 2

Between-Group and Within-Group Comparisons of Normalized RMS Values (%) for Stair Descent During the PRE, WA, and PO Phases[a]

	Stair Descent: PRE											
	ACL-D		ACL-I (Control)		*P*							
Muscle	(1) Involved	(2) Uninvolved	(3) Involved	(4) Uninvolved	ANOVA	(1) vs (2)	(1) vs (3)	(1) vs (4)	(2) vs (3)	(2) vs (4)	(3) vs (4)
VM	122.9 ± 50.8	144.6 ± 62.9	121 ± 41.4	113 ± 45.2	.389	—	—	—	—	—	—
VL	124.1 ± 55.6	155.5 ± 67.7	113.9 ± 33.5	108 ± 38.4	.059	—	—	—	—	—	—
BF	68.3 ± 32.8	81.8 ± 25.2	122.1 ± 34.7	140.8 ± 45.3	**<.0001**	>0.99	**.0009**	**<.0001**	**.02**	**.0002**	.96
							ES = 1.5	ES = 1.8	ES = 1.3	ES = 1.6	
ST	87.1 ± 34.4	71.5 ± 22.9	134.7 ± 32.7	130.8 ± 35.5	**<.0001**	>0.99	**.001**	**.003**	**<.0001**	**<.0001**	>.99
							ES = 1.4	ES = 1.2	ES = 2.2	ES = 1.9	

	Stair Descent: WA											
	ACL-D		ACL-I (Control)		*P*							
Muscle	(1) Involved	(2) Uninvolved	(3) Involved	(4) Uninvolved	ANOVA	(1) vs (2)	(1) vs (3)	(1) vs (4)	(2) vs (3)	(2) vs (4)	(3) vs (4)
VM	181.7 ± 70.6	193.4 ± 107.7	261.8 ± 97	222.2 ± 104.6	.149	—	—	—	—	—	—
VL	154.4 ± 61.4	160.4 ± 54.9	254.5 ± 114.9	200.6 ± 69.2	**.010**	>.99	**.019**	.736	**.034**	>.99	.765
							ES = 0.9		ES = 0.9		
BF	60.9 ± 40.4	67.1 ± 35.9	98.7 ± 55.6	92.4 ± 44.6	.119	—	—	—	—	—	—
ST	56.9 ± 27.2	42.1 ± 27.1	56.2 ± 47.2	75.6 ± 44	.139	—	—	—	—	—	—

	Stair Descent: PO											
	ACL-D		ACL-I (Control)		*P*							
Muscle	(1) Involved	(2) Uninvolved	(3) Involved	(4) Uninvolved	ANOVA	(1) vs (2)	(1) vs (3)	(1) vs (4)	(2) vs (3)	(2) vs (4)	(3) vs (4)
VM	193.6 ± 110.8	293.8 ± 126.5	231 ± 127.2	268.9 ± 125.3	.206	—	—	—	—	—	—
VL	149 ± 87.4	247 ± 54.5	177.6 ± 97.7	206.4 ± 83.2	**.018**	**.017**	>.99	.401	.168	>.99	>.99
						ES = 0.1					
BF	53.4 ± 23.5	78.1 ± 40	83.6 ± 35.5	73.9 ± 51	.1	—	—	—	—	—	—
ST	71.8 ± 30	51.9 ± 20.2	64.3 ± 35.3	54.5 ± 30.2	.229	—	—	—	—	—	—

[a]*Stair descent data are reported as mean ± SD. Boldface P values indicate a statistically significant difference between and within groups as indicated (P < .05). Dashes indicate not applicable. ACL-D, anterior cruciate ligament deficient; ACL-I, anterior cruciate ligament intact; ANOVA, analysis of variance; BF, biceps femoris; ES, effect size; involved, injured leg and respective matched leg of controls; PO, push-off; PRE, preactivity; RMS, root mean square; ST, semitendinosus; uninvolved, uninjured leg and respective matched leg of controls; VL, vastus lateralis; VM, vastus medialis; WA, weight acceptance.*

Artificial Tibial Translation

All data regarding comparisons of reflex activity during anterior tibial translation are displayed in Table 3 and are graphically shown in Figure 4. At PRE_50, ANOVA revealed overall significant differences for the VM and VL (P = .043 and .002, respectively) but not for within- and between-group comparisons (Table 3). During SLR, the hamstrings revealed significant differences (P = .009 for BF and P = .002 for ST) with ES values of 0.2 (for BF) and 0.4 (for ST) between the ACL-D involved leg and ACL-I uninvolved leg. Post hoc analysis of neuromuscular activity revealed that the BF of the ACL-D involved leg had an increase of 168% compared with the ACL-I uninvolved leg (P = .006; ES = 0.3), and the ST of the ACL-D involved leg showed an increase in activity of 221% compared with the ACL-I involved leg (P = .04; ES = 0.2) and an increase of 460% compared with the ACL-I uninvolved leg (P = .005; ES = 0.4). There were no significant between-group or within-group differences in reflex activity for any muscle during the MLR and LLR time windows.

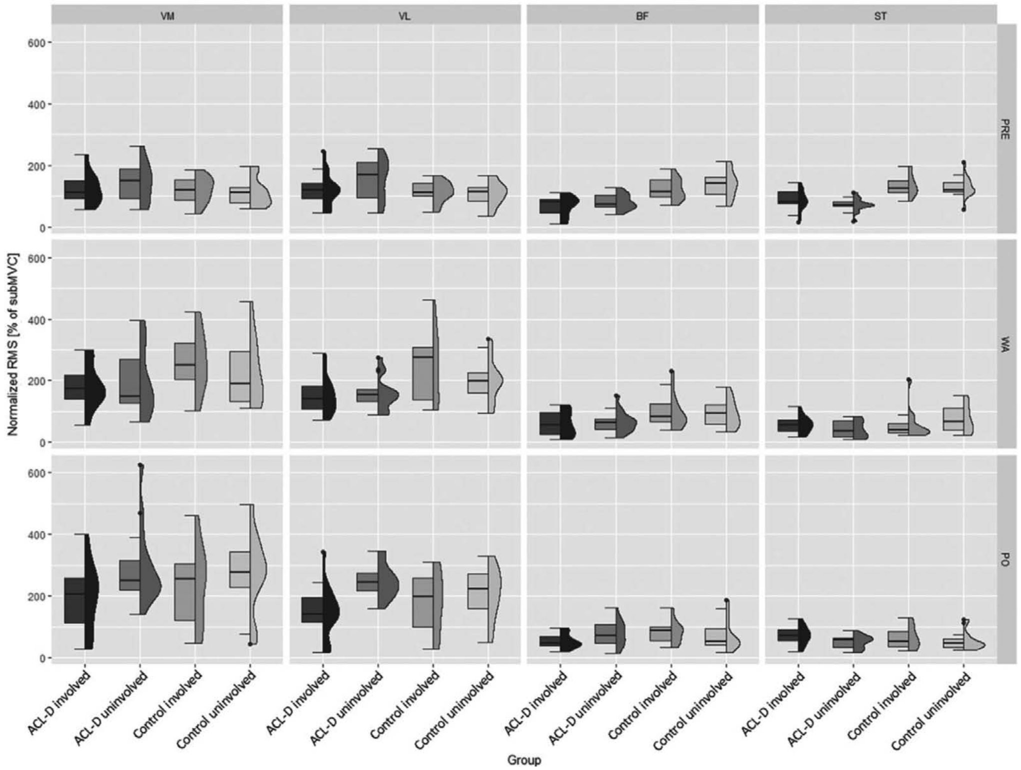

Figure 3. Violin plots of normalized root mean square (RMS) values for the involved and uninvolved legs of the participants in the anterior cruciate ligament–deficient (ACL-D) group and the matched respective legs of the control participants (ACL-I) in the 3 phases of stair descent: preactivity (PRE), weight acceptance (WA), and push-off (PO). BF, biceps femoris; involved, injured leg and respective matched leg of controls; ST, semitendinosus; %subMVC, percentage of submaximal values of maximum voluntary contraction; uninvolved, uninjured leg and respective matched leg of controls; VL, vastus lateralis; VM, vastus medialis.

TABLE 3
Between-Group and Within-Group Comparisons of Normalized RMS Values (%) for Reflex Activity During the PRE_50, SLR, MLR, and LLR Reflex Time Windows[a]

	Reflex Activity: PRE_50										
	ACL-D		ACL-I (Control)		*P*						
Muscle	(1) Involved	(2) Uninvolved	(3) Involved	(4) Uninvolved	ANOVA	(1) vs (2)	(1) vs (3)	(1) vs (4)	(2) vs (3)	(2) vs (4)	(3) vs (4)
VM	124.1 ± 52.1	113.8 ± 46.1	172.5 ± 84.2	165.6 ± 77.1	**.043**	>.99	.32	.57	.12	.23	>.99
VL	140.5 ± 28.6	108.4 ± 29.7	174.9 ± 73.3	154.6 ± 31.6	**.002**	.455	.317	>.99	**.001**	.062	>.99
									ES = 1.1		
BF	76.5 ± 48	71.6 ± 45.2	78.4 ± 40.4	73.1 ± 50.6	.938	—	—	—	—	—	—
ST	44.5 ± 26.8	43.9 ± 31.2	34.7 ± 27.1	44.7 ± 43.9	.648	—	—	—	—	—	—
	Reflex Activity: SLR										
	ACL-D		ACL-I (Control)		*P*						
Muscle	(1) Involved	(2) Uninvolved	(3) Involved	(4) Uninvolved	ANOVA	(1) vs (2)	(1) vs (3)	(1) vs (4)	(2) vs (3)	(2) vs (4)	(3) vs (4)
VM	171.9 ± 102.3	202.1 ± 116.7	157.6 ± 74.4	148.6 ± 52.1	.655	—	—	—	—	—	—
VL	126.9 ± 40	167.3 ± 97.6	156.9 ± 60.6	167.5 ± 88.2	.572	—	—	—	—	—	—
BF	439 ± 321.6	239.1 ± 136.5	204.9 ± 139.1	163.7 ± 105	**.009**	.893	.128	**.006**	>.99	.42	>.99
								ES = 0.3			
ST	456.5 ± 419.6	318.1 ± 253.2	141.9 ± 173.6	81.4 ± 637	**.002**	>.99	**.04**	**.005**	.349	.068	>.99
							ES = 0.2	ES = 0.4			
	Reflex Activity: MLR										
	ACL-D		ACL-I (Control)		*P*						
Muscle	(1) Involved	(2) Uninvolved	(3) Involved	(4) Uninvolved	ANOVA	(1) vs (2)	(1) vs (3)	(1) vs (4)	(2) vs (3)	(2) vs (4)	(3) vs (4)
VM	410.3 ± 223.8	395.6 ± 266.8	367.8 ± 196.3	326.8 ± 168.9	.865	—	—	—	—	—	—
VL	414.2 ± 195.2	322.3 ± 108.1	311.9 ± 168.3	289.7 ± 161.1	.276	—	—	—	—	—	—
BF	473.5 ± 210.9	354.4 ± 176.4	376.6 ± 299.8	348.8 ± 350.8	.103	—	—	—	—	—	—
ST	432 ± 226.2	231 ± 211	443.3 ± 396.8	273.2 ± 226.7	.124	—	—	—	—	—	—
	Reflex Activity: LLR										
	ACL-D		ACL-I (Control)		*P*						
Muscle	(1) Involved	(2) Uninvolved	(3) Involved	(4) Uninvolved	ANOVA	(1) vs (2)	(1) vs (3)	(1) vs (4)	(2) vs (3)	(2) vs (4)	(3) vs (4)
VM	334.2 ± 263.1	277.9 ± 233.9	242.3 ± 120.9	272.8 ± 183	.909	—	—	—	—	—	—
VL	245.9 ± 107.5	231.7 ± 167.7	208.1 ± 94.5	259.3 ± 154.9	.69	—	—	—	—	—	—
BF	233.9 ± 146.6	229.4 ± 132.3	241.7 ± 134.4	258 ± 154.1	.968	—	—	—	—	—	—
ST	229 ± 150.2	133.7 ± 87.9	203.7 ± 173.4	178.5 ± 116.1	.471	—	—	—	—	—	—

[a]Reflex activity data are reported as mean ± SD. Boldface P values indicate a statistically significant difference between and within groups as indicated ($P < .05$). Dashes indicate not applicable. ACL-D, anterior cruciate ligament deficient; ACL-I, anterior cruciate ligament intact; ANOVA, analysis of variance; BF, biceps femoris; ES, effect size; involved, injured leg and respective matched leg of controls; LLR, late latency response; MLR, medium latency response; PRE_50, preactivity; RMS, root mean square; SLR, short latency response; ST, semitendinosus; uninvolved, uninjured leg and respective matched leg of controls; VL, vastus lateralis; VM, vastus medialis.

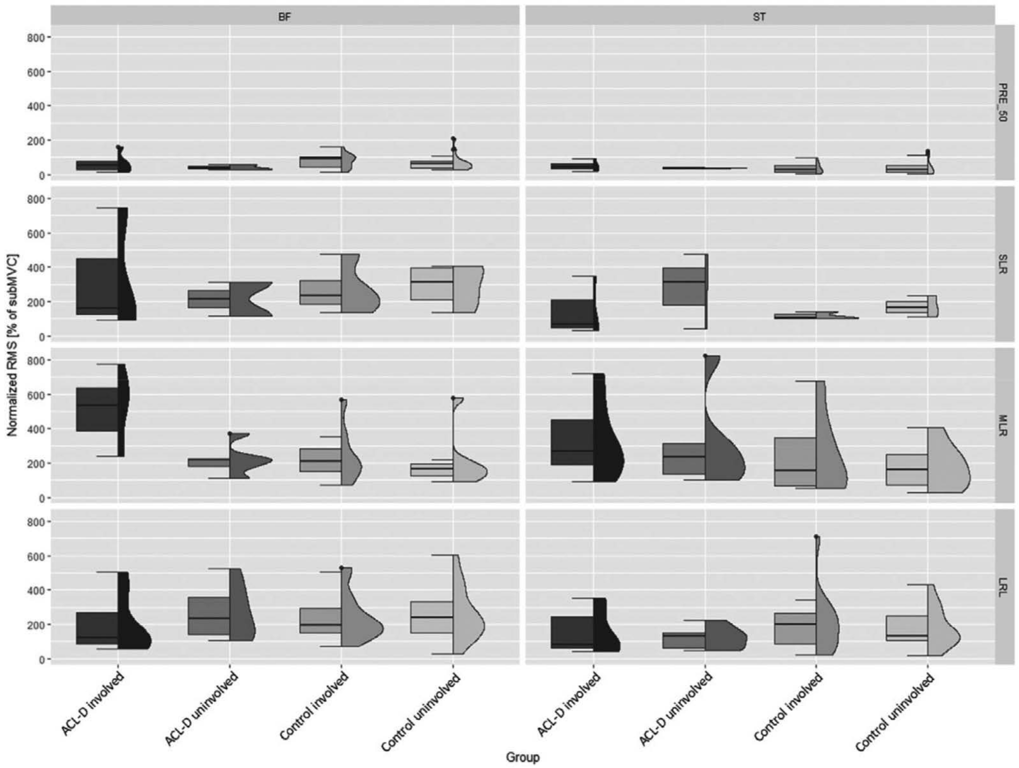

Figure 4. Violin plots of normalized root mean square (RMS) values of the hamstring muscles for the involved and uninvolved legs of the participants in the anterior cruciate ligament–deficient (ACL-D) group and the matched respective legs of the control participants (ACL-I) in the 4 reflex time windows: preactivity in time window from 50 ms before tibial translation (PRE_50), short latency response (SLR), medium latency response (MLR), and late latency response (LLR). BF, biceps femoris; involved, injured leg and respective matched leg of controls; ST, semitendinosus; %subMVC, percentage of submaximal values of maximum voluntary contraction; uninvolved, uninjured leg and respective matched leg of controls.

Discussion

So far, neuromuscular control has mainly been assessed in patients with ACL reconstruction during functional or sport-specific tasks. Only a few publications have reported neuromuscular control of patients with an ACL deficiency, but in the chronic stage, and usually after nonoperative treatment. In addition, some researchers assessed reflex activity in healthy participants. However, literature investigating neuromuscular control and reflex activity in patients with an acute ACL deficiency is limited. Therefore, this cross-sectional study investigated neuromuscular activity in patients with an acute ACL rupture during stair descent as a functional task and an artificially induced tibial translation while standing in comparison with a healthy matched control group. Beforehand, it was hypothesized that neuromuscular control would be impaired in the acute ACL-D group, meaning that the participants with acute ACL injury would show a reduced quadriceps and hamstring activation and a decreased and prolonged reflex activity of the hamstrings during tibial translation compared with healthy matched controls.

In general, we found a huge range of differences in activity patterns within and between groups in the investigated time frames and movement phases, indicating a large intraindividual variability, especially during artificial tibial translation. The hypothesis that neuromuscular control would be negatively affected in the ACL-D group was confirmed. This was the case on one hand by a significant decrease of hamstring activity during all 3 phases of stair descent and a decreased VL activity in the WA and PO phases and on the other hand by a larger neuromuscular activity of the hamstrings at SLR during artificial tibial translation.

The findings implicate bilateral consequences in the early, acute stage after ACL rupture. Therefore, it is questionable to use limb symmetry indices as objective outcomes throughout rehabilitation or even as return-to-sport criteria, even though they are widely used. A study with participants with ACL-D (acute injury; mean, 23 days after ACL rupture) revealed a significantly reduced quadriceps strength capacity of the uninvolved limb compared with the dominant leg of a healthy control group during a concentric contraction.[24] These results support the findings in the present study. Consequently, the uninvolved limb might not represent the condition of a healthy person, leading to an overestimation of knee function after ACL injury by using limb symmetry indices.[56] However, more research is needed to further develop and test evidence-based return-to-sport and competition criteria, as well as associated guidelines.[1,56] This aspect of bilateral alterations might be also used to conduct prehabilitation before surgery. After reconstruction, early rehabilitation with training interventions for the uninjured leg should be used to achieve an effect in that leg as well.[11] In addition, bilateral learning strategies and cross-educational effects should be further considered.[36]

Stair Descent

For stair ambulation, a high level of neuromuscular control is needed. The quadriceps is essential to decelerate body weight and to actively control flexion in the knee joint when descending stairs. In addition, the hamstrings are considered the most important muscle group to support the ACL in its knee-stabilizing function by limiting anterior tibial translation.[37,49] Tibial translation is controlled by hamstrings group 1 afferents in healthy persons, affirming that early onset of reflex activity of the hamstrings is crucial for a stable knee joint.[18] Furthermore, ACL load is significantly reduced with higher hamstring activity, which is far more effective than reduced VL activity.[49] Consequently, the activation of hamstrings can potentially reduce shear forces in the knee joint of a patient with ACL-D.[49] However, these findings are from computer modeling and cadaveric studies but have been supported by studies evaluating strength, reflexes, and activity of hamstrings in healthy humans.[18,21]

The decreased neuromuscular activity of all recorded muscles—with only the hamstrings showing significant changes—of the ACL-D compared with the ACL-I group during PRE can be interpreted that either the ACL rupture itself leads to an immediate change of the individual motor program or the short period of ≤3 weeks between rupture and measurements might have altered the preprogrammed movement pattern. This reduced neuromuscular activity may be explained by the sensorimotor control loop and result in a “loss of neurosensory information eventually leading to an altered central movement program.”[11] Several research groups who investigated brain activity after ACL reconstruction found altered cortical activation, indicating changes in the central nervous system, even years after surgery.[20,59] This neuroplasticity of the central nervous system provides further possible explanations for changed neuromuscular activity, which could also have affected our findings. However, to date and to our knowledge, there are no such investigations of brain activity with participants after an ACL rupture in the acute stage. Only 1 study was found with patients

≥6 months after ACL rupture[31] who showed reorganization of the central nervous system, suggesting that an ACL rupture should be seen as a "neurophysiologic dysfunction, not a simple peripheral musculoskeletal injury."[31] Hence, reduced neuromuscular activity before injury might be a risk factor for ACL rupture and cannot be ruled out by our data. Therefore, future studies should aim to confirm the findings from this study and, furthermore, consider subsequent changes in brain activity after an ACL rupture in the acute stage. Moreover, the adaptive possibilities of the central nervous system could be used during rehabilitation to prevent secondary injuries after an ACL rupture or reinjuries after ACL reconstruction.[23,31]

Artificial Tibial Translation

Reflex activity of the hamstrings after tibial translation is considered to contribute to knee joint stiffness. The direct reflex arc from the ACL to the hamstrings with a latency of 70 ms is not sufficiently fast to produce a substantial protective force for the ACL.[14] However, it is assumed that this ligament-muscle reflex is involved in the coordination of muscle activity and alteration of movement patterns.[14] Thus, after an ACL rupture, there might possibly be differences in proprioceptive information of the knee joint with subsequent alterations of muscle activity of the knee's surrounding muscles because of the lack of information from ACL afferents.[9] However, the biphasic reflex measured by our setting in the standing position seems to arise from the direct stretch of the hamstrings and may be sufficient to compensate for ACL deficiency.[17] After muscle fatigue, reduced hamstring SLR in association with increased tibial translation has been reported in a similar setting,[5] indicating a fatigue-related reflex reduction. This reduction might imply that a patient experiencing increased anterior tibial translation caused by ACL rupture needs more neuromuscular activity to stabilize the knee joint. Therefore, the increased reflex activity of the hamstrings as SLR and MLR (the latter not significant) might reflect an active compensation pattern of the hamstrings for higher, acute injury–related stability demands. In the case of ACL deficiency, a reduction of MLR was found to be related to "giving way" symptoms in the first few weeks after injury.[38] Therefore, sufficient reflex response in the MLR time frame is essential and seems to be the case for BF and ST when compared with the uninvolved limb and the limbs of healthy controls in our study.

During artificial tibial translation in the standing position, equal distribution of body mass between right and left was monitored, and the knees were kept at 30° of flexion. However, the anterior and posterior directions of the knee joint were uncontrolled, and besides "standing upright with hands on hips," no further instruction for the trunk position was given. If the body mass is shifted more onto the heel or forefoot, the center of mass changes and results in a more extended or flexed spine, pelvis ante-/retroversion, or trunk inclination/reclination, respectively.[7,33,42] This altered, individual upright starting position could influence the activity of the hamstrings and could have led to a different neuromuscular strategy. Furthermore, the band-sling was placed at the proximal part of the shank over the triceps surae muscle, which could influence the activation of the hamstring muscles due to mechanical stimuli in triceps surae 1a and 2 afferent pathways.[9]

Strengths and Limitations

This study is one of the few publications reporting neuro-muscular activity of thigh muscles in patients with an acutely injured ACL shortly after the accident. Moreover, to our current knowledge, it is the first study that has investigated reflex response after artificially induced tibial perturbation in this patient group. Another strength of this study is the relatively homogeneous patient sample, considering the diagnosis of an isolated complete ACL rupture without concomitant injuries. This strict diagnosis was chosen because, for example, patients with the frequent additional diagnosis of a bone bruise or subchondral fracture of the lateral femoral condyle show clinically relevant limitations[29]: they have longer-lasting and greater swelling, take longer to walk pain-free without crutches and achieve full range of motion in the knee joint, and report higher pain scores 1, 2, 3, and 4 weeks after injury compared with patients with an isolated ACL rupture.[29] Therefore, concomitant injuries were an exclusion criterion as these limitations would have hindered or even precluded the measurements. Furthermore, the matching was well-balanced, showing that no significant between-group differences regarding sex, age, body mass, body height, physical activity per week, Tegner score, and leg dominance were found. The fact that the patient group and the control group differed significantly in the overall KOOS and in each of its subscales is not surprising. Since the KOOS is used to assess self-reported pain, other symptoms, impairments in activities of daily living, sports and leisure, and health-related quality of life[41] in patients with knee problems, it could be assumed that the healthy control group would have no or hardly any problems and would score higher in all subscales.

Several study limitations should be considered. First, the overall sample size of 30 participants was rather small and limits the generalizability of the findings. In addition, only 15 patients after an ACL rupture in the acute stage could be included, despite the long recruitment phase of 4 years. This was mainly because of the strict inclusion and exclusion criteria, especially regarding the diagnosis (no concomitant injuries; isolated, complete rupture), functional status (able to descend stairs without using handrails or crutches), and short time frame between injury, recruitment, and medical appointment, as well as the date of surgery. Therefore, comparisons with other studies should be made with caution. Nevertheless, the results expand new fields of research in an interdisciplinary setting to better understand the short- and long-term consequences of an ACL rupture, especially for neuromuscular control.[11] Second, sex-specific differences might have influenced the results.[5] In this study, subgroup analysis for sex was not applicable with this small number of men and women. Third, the participants were allowed to descend the stairs at self-selected speed. This method was also used in another study with patients who had experienced an acute ACL rupture, but it has implications for the recorded EMG activities during exercise.[19] In addition, a prescribed, standardized stride frequency changes the normal gait pattern decisively.[39] Fourth, an effusion of up to a 2-cm circumference difference compared with the uninjured leg was accepted for inclusion. However, effusion might diminish quadriceps activation and could therefore influence the neuromuscular activity, especially in this early stage after injury. Fifth, electromyography during normal walking was recorded for normalization of EMG data of stair descent and tibial translation. It has been shown that electromyography during walking is enhanced in patients with ACL injury.[48] Thus, the normalized EMG data might be influenced by the effects of ACL rupture on stair descent and tibial translation as well as the effects of ACL rupture on walking.

Conclusion

The present study, investigating neuromuscular activity in participants with acute ACL deficiency and healthy matched controls, revealed that already in the first 3 weeks after an ACL rupture, neuromuscular alterations can be found mainly in the hamstrings during stair descent and reflex activity. These findings indicate an alteration in the preprogrammed activity and in the underlying voluntary movement control pattern. Furthermore, neuromuscular control seems to be impaired in both extremities after unilateral ACL rupture.

This is clinically relevant, as alterations of neuromuscular control in both legs in the acute phase of an ACL rupture emphasize the need for prehabilitation to possibly achieve better results in the long term after reconstruction or nonoperative treatment. Therefore, conservative therapy with a health professional specialized in sport physical therapy with an early focus on neuromuscular control and treatment of the injured but also the uninjured leg before surgery is strongly recommended. In addition, prehabilitation could also contribute to the decision-making process of whether to reconstruct the ACL or consider a nonoperative treatment pathway. However, recommendations mainly concern rehabilitation standards after reconstruction and do not focus on early treatment before surgery.

Future researchers should focus especially on the aspect of bilateral deficits after ACL rupture. In addition, research in the future should investigate whether the contralateral leg can be an adequate reference for functional evaluation of the injured extremity. As the limb symmetry index is still widely used but probably underestimates the functional deficits of both lower extremities, other outcome measures for neuromuscular function should be considered when deciding for clearance for a safe return to sport.

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References

1. Ardern CL, Glasgow P, Schneiders A, et al. 2016 Consensus statement on return to sport from the First World Congress in Sports Physical Therapy, Bern. *Br J Sports Med.* 2016;50(14):853-864.

2. Baur H, Hirschmuller A, Cassel M, Muller S, Mayer F. Gender-specific neuromuscular activity of the M. peroneus longus in healthy runners— a descriptive laboratory study. *Clin Biomech* (Bristol, Avon). 2010; 25(9):938-943.

3. Baur H, Muller S, Hirschmuller A, Cassel M, Weber J, Mayer F. Com- parison in lower leg neuromuscular activity between runners with uni- lateral mid-portion Achilles tendinopathy and healthy individuals. *J Electromyogr Kinesiol.* 2011;21(3):499-505.

4. Behrens M, Mau-Moeller A, Wassermann F, Bruhn S. Effect of fatigue on hamstring reflex responses and posterior-anterior tibial translation in men and women. *PLoS One.* 2013;8(2):e56988.

5. Behrens M, Mau-Moeller A, Wassermann F, Plewka A, Bader R, Bruhn S. Repetitive jumping and sprinting until exhaustion alters hamstring reflex responses and tibial translation in males and females. *J Orthop Res.* 2015;33(11):1687-1692.

6. Blackburn JT, Norcross MF, Padua DA. Influences of hamstring stiffness and strength on anterior knee joint stability. *Clin Biomech* (Bristol, Avon). 2011;26(3):278-283.

7. Blackburn JT, Padua DA. Sagittal-plane trunk position, landing forces, and quadriceps electromyographic activity. *J Athl Train.* 2009;44(2): 174-179.

8. Booth FW, Lees SJ. Physically active subjects should be the control group. *Med Sci Sports Exerc.* 2006;38(3):405-406.

9. Bruhn S, Leukel C, Gollhofer A. Differential effects of stimulus characteristics during knee joint perturbation on hamstring and quadriceps reflex responses. *Hum Mov Sci.* 2011;30(6):1079-1091.

10. Busch A, Blasimann A, Henle P, Baur H. Neuromuscular activity during stair descent in ACL reconstructed patients: a pilot study. *Knee.* 2019;26(2):310-316.

11. Busch A, Henle P, Boesch L, Blasimann A, Baur H. Neuromuscular control in patients with acute ACL injury during stair ascent—a pilot study. *Sports Orthop Traumatol.* 2019;35(2):158-165.

12. Cohen J. Statistical Power Analysis for the Behavioral Sciences. 2nd ed. *Lawrence Erlbaum Associates*; 1988.

13. Dhaher YY, Tsoumanis AD, Houle TT, Rymer WZ. Neuromuscular reflexes contribute to knee stiffness during valgus loading. *J Neuro- physiol.* 2005;93(5):2698-2709.

14. Dyhre-Poulsen P, Krogsgaard MR. Muscular reflexes elicited by electrical stimulation of the anterior cruciate ligament in humans. *J Appl Physiol* (1985). 2000;89(6): 2191-2195.

15. Faul F, Erdfelder E, Buchner A, Lang AG. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. *Behav Res Methods.* 2009;41(4): 1149-1160.

16. Frank RM, Lundberg H, Wimmer MA, et al. Hamstring activity in the anterior cruciate ligament injured patient: injury implications and com- parison with quadriceps activity. *Arthroscopy.* 2016;32(8):1651-1659.

17. Friemert B, Bumann-Melnyk M, Faist M, Schwarz W, Gerngross H, Claes L. Differentiation of hamstring short latency versus medium latency responses after tibia translation. *Exp Brain Res.* 2005;160(1):1-9.

18. Friemert B, Franke S, Gollhofer A, Claes L, Faist M. Group I afferent pathway contributes to functional knee stability. *J Neurophysiol.* 2010;103(2):616-622.

19. Gao B, Cordova ML, Nigel N. Human movement science three-dimensional joint kinematics of ACL-deficient and ACL-reconstructed knees during stair ascent and descent. *Hum Mov Sci.* 2012;31;222-235.

20. Grooms DR, Page SJ, Nichols-Larsen DS, Chaudhari AM, White SE, Onate JA. Neuroplasticity associated with anterior cruciate ligament reconstruction. *J Orthop Sports Phys Ther.* 2017;47(3):180-189.

21. Gruber M, Bruhn S, Gollhofer A. Specific adaptations of neuromuscular control and knee joint stiffness following sensorimotor training. *Int J Sports Med.* 2006; 27(8):636-641.

22. Hall M, Stevermer CA, Gillette JC. Gait analysis post anterior cruciate ligament reconstruction: knee osteo- arthritis perspective. *Gait Posture.* 2012;36(1):56-60.

23. Hall M, Stevermer CA, Gillette JC. Muscle activity amplitudes and co-contraction during stair ambulation following anterior cruciate ligament reconstruction. *J Electromyogr Kinesiol.* 2015;25(2):298-304.

24. Hannon J, Wang-Price S, Goto S, Garrison JC, Bothwell JM. Do mus- cle strength deficits of the uninvolved hip and knee exist in young athletes before anterior cruciate ligament reconstruction? *Orthop J Sports Med.* 2017;5(1):2325967116683941.

25. Hermens HJ, Freriks B, Disselhorst-Klug C, Rau G. Development of recommendations for SEMG sensors and sensor placement procedures. *J Electromyogr Kinesiol.* 2000;10(5):361-374.

26. Hewett TE, Zazulak BT, Myer GD. Effects of the menstrual cycle on anterior cruciate ligament injury risk: a systematic review. *Am J Sports Med.* 2007;35(4):659-668.

27. Hootman JM, Dick R, Agel J. Epidemiology of collegiate injuries for 15 sports: summary and recommendations for injury prevention initiatives. *J Athl Train.* 2007;42(2):311-319.

28. Hughes G, Watkins J. A risk-factor model for anterior cruciate ligament injury. *Sports Med.* 2006;36(5):411-428.

29. Johnson DL, Bealle DP, Brand JC Jr, Nyland J, Caborn DN. The effect of a geographic lateral bone bruise on knee inflammation after acute anterior cruciate ligament rupture. *Am J Sports Med.* 2000;28(2):152-155.

30. Kaeding CC, Leger-St-Jean B, Magnussen RA. Epidemiology and diagnosis of anterior cruciate ligament injuries. *Clin Sports Med.* 2017;36(1):1-8.

31. Kapreli E, Athanasopoulos S, Gliatis J, et al. Anterior cruciate ligament deficiency causes brain plasticity: a functional MRI study. *Am J Sports Med.* 2009;37(12):2419-2426.

32. Kobayashi H, Kanamura T, Koshida S, et al. Mechanisms of the anterior cruciate ligament injury in sports activities: a twenty-year clinical research of 1,700 athletes. *J Sports Sci Med.* 2010;9(4): 669-675.

33. Kulas AS, Hortobagyi T, Devita P. The interaction of trunk-load and trunk-position adaptations on knee anterior shear and hamstrings muscle forces during landing. *J Athl Train.* 2010;45(1):5-15.

34. Leitner M, Schmid S, Hilfiker R, Radlinger L. Test-retest reliability of vertical ground reaction forces during stair climbing in the elderly population. *Gait Posture.* 2011;34(3):421-425.

35. Leukel C, Lundbye-Jensen J, Gruber M, Zuur AT, Gollhofer A, Taube W. Short-term pressure induced suppression of the short-latency response: a new methodology for investigating stretch reflexes. *J Appl Physiol* (1985). 2009;107(4):1051-1058.

36. Manca A, Dragone D, Dvir Z, Deriu F. Cross-education of muscular strength following unilateral resistance training: a meta-analysis. *Eur J Appl Physiol.* 2017; 117(11):2335-2354.

37. Markolf KL, O'Neill G, Jackson SR, McAllister DR. Effects of applied quadriceps and hamstrings muscle loads on forces in the anterior and posterior cruciate ligaments. *Am J Sports Med.* 2004;32(5): 1144-1149.

38. Melnyk M, Faist M, Gothner M, Claes L, Friemert B. Changes in stretch reflex excitability are related to "giving way" symptoms in patients with anterior cruciate ligament rupture. *J Neurophysiol.* 2007;97(1):474-480.

39. Murray MP, Spurr GB, Sepic SB, Gardner GM, Mollinger LA. Treadmill vs. floor walking: kinematics, electromyogram, and heart rate. *J Appl Physiol* 1985;59(1):87-91.

40. Pollock ML, Gaesser GA, Butcher JD, et al. ACSM position stand: the recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. *Med Sci Sports Exerc.* 1998;30:975-991.

41. Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes.* 2003;1:64.

42. Roos PE, Button K, Sparkes V, van Deursen RW. Altered biomechanical strategies and medio-lateral control of the knee represent incomplete recovery of individuals with injury during single leg hop. *J Biomech.* 2014;47(3):675-680.

43. Rudolph KS, Axe MJ, Buchanan TS, Scholz JP, Snyder-Mackler L. Dynamic stability in the anterior cruciate ligament deficient knee. *Knee Surg Sports Traumatol Arthrosc.* 2001;9(2):62-71.

44. Rudolph KS, Axe MJ, Snyder-Mackler L. Dynamic stability after ACL injury: who can hop? *Knee Surg Sports Traumatol Arthrosc.* 2000;8(5): 262-269.

45. Rudolph KS, Snyder-Mackler L. Effect of dynamic stability on a step task in ACL deficient individuals. *J Electromyogr Kinesiol.* 2004;14(5): 565-575.

46. Schutte MJ, Dabezies EJ, Zimny ML, Happel LT. Neural anatomy of the human anterior cruciate ligament. *J Bone Joint Surg Am.* 1987; 69(2):243-247.

47. Scott J, Huskisson EC. Graphic representation of pain. *Pain.* 1976; 2(2):175-184.

48. Shanbehzadeh S, Mohseni Bandpei MA, Ehsani F. Knee muscle activity during gait in patients with anterior cruciate ligament injury: a systematic review of electromyographic studies. *Knee Surg Sports Traumatol Arthrosc.* 2017;25(5):1432-1442.

49. Shelburne KB, Torry MR, Pandy MG. Effect of muscle compensation on knee instability during ACL-deficient gait. *Med Sci Sports Exerc.* 2005;37(4):642-648.

50. Silbernagel KG, Thomee´ R, Eriksson BI, Karlsson J. Full symptomatic recovery does not ensure full recovery of muscle-tendon function in patients with Achilles tendinopathy. *Br J Sports Med.* 2007;41(4): 276-280.

51. Smeets A, Verschueren S, Staes F, Vandenneucker H, Claes S, Vanrenterghem J. Athletes with an ACL reconstruction show a different neuromuscular response to environmental challenges compared to uninjured athletes. *Gait Posture.* 2021;83:44-51.

52. Smeets A, Willems M, Gilson L, et al. Neuromuscular and biomechanical landing alterations persist in athletes returning to sport after anterior cruciate ligament reconstruction. *Knee.* 2021;33:305-317.

53. Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries. *Clin Orthop Relat Res.* 1985;198:43-49.

54. Trulsson A, Miller M, Hansson GA, Gummesson C, Garwicz M. Altered movement patterns and muscular activity during single and double leg squats in individuals with anterior cruciate ligament injury. *BMC Musculoskelet Disord.* 2015;16:28.

55. Ward S, Pearce AJ, Pietrosimone B, Bennell K, Clark R, Bryant AL. Neuromuscular deficits after peripheral joint injury: a neurophysiological hypothesis. *Muscle Nerve.* 2015; 51(3):327-332.

56. Wellsandt E, Failla MJ, Snyder-Mackler L. Limb symmetry indexes can overestimate knee function after anterior cruciate ligament injury. *J Orthop Sports Phys Ther.* 2017; 47(5):334-338.

57. Wiggins AJ, Grandhi RK, Schneider DK, Stanfield D, Webster KE, Myer GD. Risk of secondary injury in younger athletes after anterior cruciate ligament reconstruction: a systematic review and meta-analysis. *Am J Sports Med.* 2016;44(7):1861-1876.

58. World Medical Association. WMA Declaration of Helsinki—ethical principles for medical research involving humans. *Accessed* August 29, 2022. https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/

59. Zarzycki R, Morton SM, Charalambous CC, Marmon A, Snyder-Mackler L. Corticospinal and intracortical excitability differ between athletes early after ACLR and matched controls. *J Orthop Res.* 2018; 36(11):2941-2948.

60. Zimny ML, Schutte M, Dabezies E. Mechanoreceptors in the human anterior cruciate ligament. *Anat Rec.* 1986; 214(2):204-209.

CHAPTER 5

STUDY 3A

Sex and treatment effects 1 year after ACL rupture

Neuromuscular control in males and females
1 year after an anterior cruciate ligament
rupture or reconstruction during stair descent
and artificial tibial translation

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Abstract

Background: Neuromuscular alterations are reported in patients with anterior cruciate ligament reconstruction (ACL-R) and conservative treatment (copers with ACL deficiency, ACL-C). However, it is unclear whether sex influences neuromuscular control. The objective was to investigate differences in neuromuscular control regarding sex and treatment type one year after ACL rupture in comparison to a group with an intact ACL (ACL-I).

Methods: Electromyography of vastus medialis (VM) and lateralis, biceps femoris (BF) and semitendinosus (ST) was recorded in ACL-R (N = 38), ACL-C (N = 26), and ACL-I (N = 38) during stair descent and reflex activity by anterior tibial translation while standing. The movements of stair descent were divided into pre-activity, weight-acceptance and push-off phases, reflex activity in pre-activation, short, medium (MLR), and long latency responses (LLR). Normalized root mean squares for each muscle of involved and matched control limb per phase were calculated and analyzed with two-way ANOVA ($\alpha = 0.05$).

Results: During stair descent, neuromuscular differences of BF were significant during push-off only ($p = 0.001$). Males of ACL-R and ACL-C had higher BF activity compared to ACL-I ($p = 0.009$, 0.007 respectively). During reflex activity, VM and BF were significantly different between treatment groups for pre-activation ($p = 0.013$, 0.035 respectively). VM pre-activation of females was higher in ACL-R compared to ACL-C ($p = 0.018$), and lower in ACL-C compared to ACL-I ($p = 0.034$). Males of ACL-R showed higher VM and less BF pre-activation ($p = 0.025$, $p = 0.003$ respectively) compared to ACL-I. Males of ACL-C had less BF pre-activation compared to ACL-I ($p = 0.019$). During MLR, intra-group differences in ST were found for treatment ($p = 0.011$) and females of ACL-R compared to ACL-I ($p = 0.015$). During LLR, overall intra-group differences in VM were present for treatment ($p = 0.034$) and in females (ACL-R versus ACL-C ($p = 0.015$), ACL-I ($p = 0.049$)), respectively.

Conclusion: One year after an ACL rupture, neuromuscular alterations persist regardless of treatment and sex. Standard rehabilitation protocols may not be able to restore neuromuscular control. Future research should include long-term follow up and focus on exercises targeting neuromuscular function.

Keywords: anterior cruciate ligament, ACL, conservative treatment, reconstruction, neuromuscular control, sex

Introduction

Neuromuscular control includes volitional and reflexive activity before and during static and dynamic tasks, as it has been stated for a neuromuscular training to enhance unconscious motor responses by stimulating afferent signals and central mechanisms responsible for dynamic joint control.[1] Adequate neuromuscular control leads to active knee stability during controlled, known activities of daily living (ADL) but also in situations with sudden (tibial) perturbations. In these cases, neuromuscular control does not only consist of adequate neuromuscular answers after initial foot-floor contact but also appropriate pre-activation of knee stabilizing muscles before landing. Neuromuscular control during static and dynamic tasks can be directly assessed by electromyography (EMG), of which a wide range of outcome measures has been reported in the literature.[2]

After a rupture of the anterior cruciate ligament (ACL), altered sensorimotor control and neuromuscular adaptations,[3,4] due to the loss of the mechanoreceptors of the native (original) ACL leading to altered afferent inputs to the central nervous system,[5,6] have been reported. Patients with an ACL are treated either non-surgically (conservatively with rehabilitation alone) or surgically with different graft types for ACL reconstruction or suture.[7] A 5-year follow-up did not reveal any differences in patient-reported and objective outcomes between ACL patients with early reconstruction, conservative treatment followed by reconstruction or rehabilitation alone.[8] However, neuromuscular alterations – in terms of increased hamstrings activation in the reconstructed leg compared to the contralateral leg – were found in physically active people after ACL reconstruction during functional activities such as (stair) walking and stepdown tasks[9-12] or in athletes during sport-specific assessments such as landing after a hop.[11,13] Similar results were also reported in ACL deficient patients with conservative treatment during walking,[14] step tasks,[15] level walking and jogging.[16]

Clearance for return to sport (RTS) after ACL rupture is mainly based on clinical examinations, patient-reported outcome scores and widely used physical performance test batteries,[17-19] despite a wide range of EMG outcome measures for neuromuscular control reported in the literature.[2] Moreover, no consensus exists about gold standard for safe RTS assessments and cut-off points. [20-22] After RTS, failure rates of the graft up to 19% and contralateral ACL rupture postoperatively in up to 24% of the cases were reported.[23-25] The high rates of re-injury and secondary ACL rupture, and a lack of validity of RTS criteria after ACL reconstruction are inacceptable and indicate that more research is needed.[21,22,26]

Therefore, the purpose of this cross-sectional study was to investigate neuromuscular activity in participants one year after an ACL rupture or reconstruction, at the timepoint of unrestricted clearance for RTS after completion of rehabilitation. The study compared conservatively and surgically treated participants, females and males, during stair descent and artificially induced tibial translation while standing, in comparison to a healthy control group. Based on literature,[10-12,27,28] it is hypothesized that, because of altered afferent information, the neuromuscular quadriceps response will be downregulated and hamstring EMG activity will be upregulated in patient cohorts compared to controls. Subjects with former ACL injury may have developed different neuromuscular strategies than subjects who have never torn their ACL.[3] Therefore, it is hypothesized that neuromuscular control will still be impaired in conservatively (ACL-C) and surgically treated participants (ACL-R) one year after ACL rupture compared to healthy controls. Due to the controversial findings regarding sex-specific differences in neuromuscular control,[29] no hypothesis regarding subgroups of females and males are made.

Methods

A cross-sectional, experimental study design with two patient groups and a healthy control group was determined to investigate differences of neuromuscular control related to treatment for females and males one year after an ACL reconstruction or rehabilitation alone.

Sample size calculation

An a priori analysis of effect size and sample size was made for a desired power of 95% and an α-error of 0.05 (software G*Power, version 3.1, Heinrich Heine University of Duesseldorf, D),[30] based on own pilot data.[9,27] Considering the variability of data, an a priori necessary sample size for independent comparisons of $n = 10$ ($\alpha = 0.05$, actual power: 0.96, effect size d: 1.78) was set. To account for dropouts and subgroup analysis (treatment modality and sex as dependent samples), a total number of $n = 15$ females and males per group was planned to be recruited.

Participants

Persons could be included if they were between 16 and 60 years old, with unequivocally detectable, unilateral ACL status, physically active at least 2x/ week for 45min, and had a Tegner activity score of 5 or higher.[31-33] Magnetic resonance imaging was available in all participants with former ACL rupture. Patients could be included with any type of ACL reconstruction except dynamic intraligamentary stabilization (Ligamys, Mathys AG, Bettlach, CH) and similar techniques. Time since rupture, reconstruction respectively, had to be between 11 and 14 months. Status of ACL was clinically examined in all participants to allow for group allocation. This clinical examination included testing of active and passive range of motion of both the femorotibial and patellofemoral joint, Lachman test in 20° knee flexion, Anterior drawer test in 90° knee flexion and Pivot Shift Test by always the same experienced sports physical therapist. General exclusion criteria were former knee pathology before ACL rupture, other injury of the lower extremity, back pain, musculoskeletal disorders refraining from test protocol, cardiac, neurologic, or peripheral vascular disease, acute infection, alcohol abuse, current pain medication, thrombosis, pregnancy, dementia, and not being able to understand written or oral German.

Participants for the ACL-R and ACL-C group were mainly recruited through the Sonnenhof Orthopaedic Center, Lindenhof Group AG, Bern (Switzerland) by an orthopaedic surgeon between January 2018 and August 2021. In addition, surgically and conservatively treated patients were recruited through private physiotherapy practices, sports clubs, and private networks during the same period. Information was mainly spread by physiobern (official professional body of physiotherapists in the Cantone of Berne, Switzerland) through newsletters for members, social media, but also via word-of-mouth recommendation. The control group consisted of healthy people with an anamnestically intact ACL (ACL-I) who had been recruited from local sport clubs, and among members of the Bern University of Applied Sciences (Switzerland). Individual group matching for initially two control groups was based on sex, age, body height, body mass and dominant leg, defined as the preferred leg to kick a ball with.[31,32] For data analysis, the two matched control groups were combined to one, later named ACL-I with N = 38 healthy participants. In total, N = 185 participants volunteered for this study and were assigned to one of three groups, based on ACL status (Fig. 1).

Measurements

All measurements took place at the Bern Movement Lab (Bern University of Applied Sciences, Bern, Switzerland) by using a setup described in former publications [9,10,27].

Anthropometric data (age, height, body mass), limb dominance as well as data regarding physical activity such as type of sports, number of hours per week

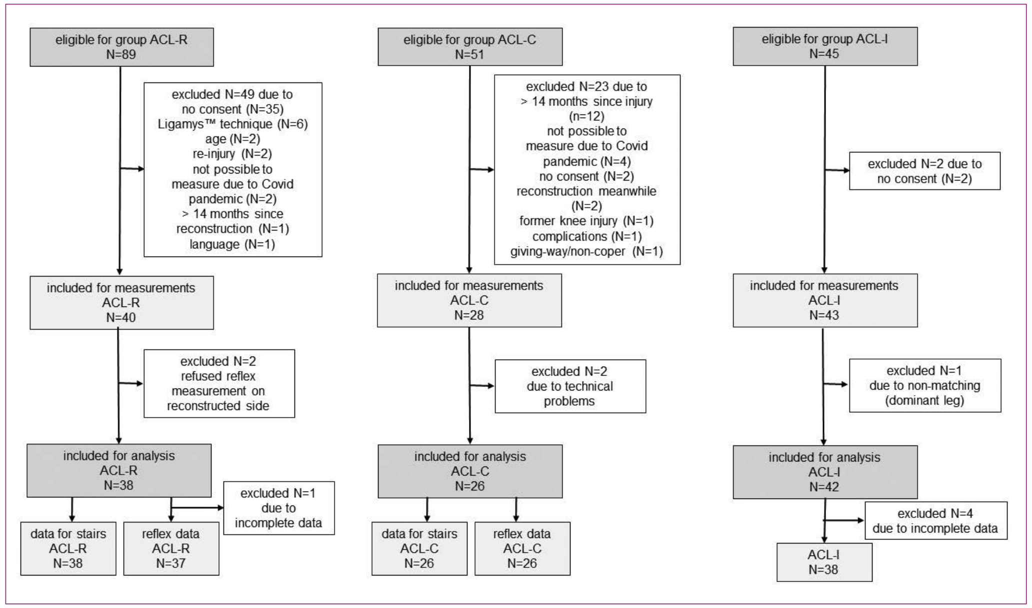

Figure 1: Flowchart describing number of participants during recruitment process and data sets analysed
Legend (Fig. 1): ACL-R = ACL reconstructed group; ACL-C = ACL group with conservative treatment; ACL-I = healthy control group with intact ACL; N = number of

and Tegner activity score[33] were collected with a standardized case report form (CRF). Moreover, patient-reported outcomes regarding pain, other symptoms, activities of daily life, sports and knee-related quality of life were assessed with the Knee injury and Osteoarthritis Outcome Score (KOOS).[34] Afterwards, the participants were prepared for the EMG measurements. The skin was shaved, smoothed, and cleaned with alcohol to prepare for bipolar, self-adhesive electrodes (Ambu BlueSensor, Ambu A/S, Ballerup, DK; Type P-00-S, inter-electrode distance: 20 mm) being applied on the vastus medialis (VM), vastus lateralis (VL), semitendinosus (ST) and biceps femoris (BF) muscle on both limbs according to SENIAM standards.[35] The inter-electrode impedance was controlled (D175 Electrode Impedance Meter, Digitimer, Herfordshire, UK) and accepted ≤ 2 kΩ. The reference electrode was placed on the right patella. Before the measurements started, the actual wellbeing and pain level of the participants were assessed by using a visual analogue scale (VAS).[36]

Each participant started with a warm-up on a treadmill (quasar med, h/p/cosmos sports & medical GmbH, Nussdorf-Traunstein, D) for ten minutes at 1.39 m/s (5km/h). Initial contact of each gait cycle was detected by two force transducers (type KMB52, 10kN, MEGATRON Elektronik GmbH & Co. KG, Putzbrunn, D) mounted under the treadmill. Surface electromyography (EMG) signals of VM, VL, BF and ST were recorded during treadmill walking at the above-mentioned speed for two minutes. These signals were used for submaximal EMG normalization.[37,38] Following this warm-up, each participant completed two experimental situations in the same order: stair descent (Fig. 2) and stretch reflex measurements induced by artificial tibial translation in posterior-anterior direction (Fig. 3).

Stair descent as functional task

Participants descended a six-step stairway ten times at self-selected speed without using the handrails. The custom-made wooden stairway (Fig. 2) with an inclination of 30.6°, a step height of 17.1 cm and a step depth of 29.0 cm[39] had two embedded multicomponent force plates (type 9286BA, Kistler Instrumente AG, Winterthur, CH) in the third and fourth step identifying gait cycles during stair climbing.

Figure 2: Functional task: walking downstairs on custom-made wooden stairway (©BFH Bern Movement Lab)

Movement cycles of stair descent were divided into pre-activation (PRE), weight acceptance (WA) and push-off (PO) phases. The PRE phase included 150 ms prior to initial foot-floor contact until initial contact. The WA phase was defined from initial contact to the lowest applied vertical ground reaction force (equal to "braking phase" until anterior–posterior force crosses the zero line). After the WA phase, the PO phase followed until vertical ground reaction forces decline to zero ("propulsion phase").

Stretch reflex measurements: Artificial tibial translation in posterior-anterior direction

The participants were standing upright with arms akimbo and knees slightly bent (30° flexion) (Fig. 3). To guarantee equal distribution of the body mass, participants placed each foot on a force plate (Type 9286BA, Kistler Instrumente AG, Winterthur, CH) and controlled body mass distribution by visual feedback provided by a computer screen at eye level. All participants were blinded to the time point of artificially induced tibial translation. Moreover, participants wore headphones for music and an attenuator to avoid any acoustic anticipation. Both legs were tested in randomized order (www.randomization.com).

A standardized impulse for tibial translation was applied to the tibia shank by a rope and pulley system in posterior-anterior direction,[40] monitored by a force transducer (type KM1506, 2KN, MEGATRON Elektronik GmbH & Co. KG, Putzbrunn, Germany) (Figure 3). The impulse was the trigger signal for the onset of tibial translation and was elicited 2x15 times per lower extremity. In between each stimulus, a break of about 30 seconds was performed to avoid impulse anticipation and to allow subjects to adjust the standardized position if necessary. Between the series, a short break allowed the participants to walk around and relax to avoid excessive co-contraction or muscular fatigue. After the measurements, the general wellbeing and actual pain levels of the participants were assessed again as described previously.

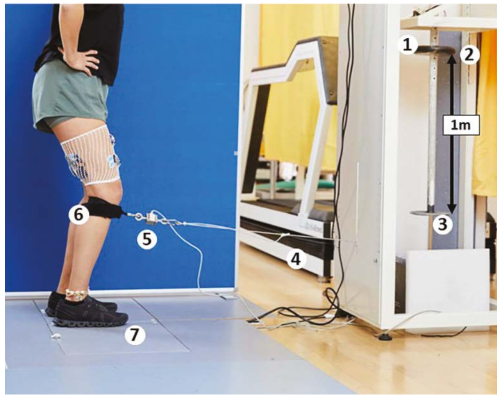

Figure 3: Stretch reflex measurements in upright standing position (©BFH Bern Movement Lab)
Legend (Fig. 3): 1) electromagnet, 2) falling barbell weight, 3) stopper, 4) wire rope, 5) force transducer, 6) brace, 7) two force plates

Outcomes

Root mean squares (RMS) values of EMG signals during stair descent in the respective pre-defined time intervals (PRE, WA, PO) were used as outcomes.[37,38] Moreover, RMS values of EMG signals after the activation of the stretch reflex (following onset of tibial translation) were calculated in four pre-defined time intervals: -50-0 ms background activity, pre-activation (PRE_50) respectively, 20-40 ms short latency response (SLR), 40-60 ms medium latency response (MLR) and 60-95 ms long latency response (LLR).[40-43]

Signal transmission, data processing and normalization

In general, there was no delay due to synchronization since all systems (force sensor signals from treadmill, rope-pulley system and stairs) were recorded together with the EMG signals in one LabVIEW-based software (IMAGO Record, pfitec, Endingen, D). No later synchronization during the post-processing was needed. EMG signals were transmitted across a differential-preamplifier to a telemetric main amplifier (PowerPack, pfitec, Endingen, D), band-pass filtered at 10 Hz - 1000 Hz and recorded at 2000 Hz for treadmill walking and stair descent, and at 4000 Hz for the stretch-reflex measurement.[44] Then, the signals were converted from analogue to digital (type NI PCI 6255, National Instruments, Austin, USA), registered and further processed with the same LabVIEW-based software (IMAGO Record, pfitec, Endingen, D). Afterwards, all raw EMG signals were full wave rectified. Additionally, raw EMG signals from treadmill walking and stair descent were band-pass filtered at 10 - 500Hz (Butterworth, 2nd order). RMS values were calculated for the defined time windows as described above.

Afterwards, RMS values were exported in Excel spreadsheets (Windows 10, Microsoft Corporation, Redmond WA, USA), where individual means out of 30 gait cycles (treadmill walking), ten steps (stair descent), and 30 tibial translations per extremity for each muscle in each time interval were calculated. RMS values were normalized according to the corresponding time intervals retrieved during treadmill walking – defined as 100% of neuromuscular activity – and used for inter-subject-comparability. Reflex responses during artificial tibial translation, and activations during stair descent were normalized and expressed as a percentage (% EMG) of respective treadmill walking activity.[37,38] For each normalized RMS, a plausibility check was done based on the mean RMS for each muscle per timeframe. If individual RMS values exceeded two standard deviations (SD) for stair descent and three SD for reflex measurement (due to high intra-individual variability), suspicious values were traced back to the original data set, recalculated and eventually excluded.

Statistical analysis

Data were transferred from CRFs to Excel spreadsheets (Windows 10, Microsoft Corporation, Redmond WA, USA) and later processed by the Statistical Package for the Social Science (SPSS) software (SPSS Statistics for Windows, version 28.0, IBM, Armonk NY, USA). Participants' characteristics were checked for normal distribution (Kolmogorov-Smirnov), followed by non-parametric t-tests (Mann-Whitney-U and Kruskal-Wallis) to evaluate age, body height, and weight, physical activity level, Tegner, KOOS, leg dominance, wellbeing, and pain level for significant differences between groups. Additionally, a parametric two-way analysis of variance (ANOVA) for repeated measures with the factors sex and treatment was performed.[45] All EMG outcomes (dependent variables) of all muscles (VM, VL, ST, BF) for the injured leg of ACL-R, ACL-C and the matched ACL-I leg during all movement phases of stair descent (PRE, WA, PO) and the reflex time windows (PRE_50, SLR, MLR, LLR) during artificial tibial translation were analyzed. If data were not normally distributed and heterogeneity of variances was present (Levene test not significant), non-parametric tests for analysis of variance (Kruskal-Wallis-test) were used alternatively. In addition, post-hoc tests (Bonferroni) were applied for the factor group assignment. Effect sizes (ES) were calculated for significant results by using the following equitation (n = total number of participants in the compared groups): $r=|z/\sqrt{n}|$ with $r < 0.3$ as small effect, $0.3 \leq r < 0.5$ as medium effect, and $r \geq 0.5$ as large effect 46. The alpha-level was set at 5%.

Results

Characteristics of participants

To allow comparison with other studies, mean values, and standard deviations (SD) are reported although not all data were normally distributed.

There were no significant differences in age ($p = 0.419$), body height ($p = 0.087$), body mass ($p = 0.507$), body mass index (BMI) ($p = 0.056$), sex ($p = 0.419$) and leg dominance ($p = 0.876$) between the groups of ACL-R, ACL-C and ACL-I. However, the three groups differed significantly in physical activity regarding weekly hours ($p = 0.014$) and level ($p = < 0.0001$), which was higher in the patient groups. The mean Tegner activity score of averaged 7 in the ACL-R and ACL-C group indicated a higher level of recreational sports such as alpine skiing, tennis, squash, running or competitive sports like basketball, rugby, ice-hockey, handball, frisbee and Swiss wrestling. Furthermore, also KOOS subscales and total scores ($p < 0.0001$ all) were significantly higher in ACL-R and ACL-C groups. The groups ACL-R and ACL-C were comparable regarding anthropometric data, time since rupture, weekly hours and level of physical activity (all $p > 0.05$). More details regarding characteristics of the two patient groups (ACL-R, ACL-C respectively), and healthy controls (ACL-I) are displayed in Table 1 below and in the Tables A.1 & A.2 (supplementary material).

Table 1: Characteristics of participants with an ACL reconstruction (ACL-R), with a conservatively treated ACL rupture (ACL-C) and healthy controls with an intact ACL (ACL-I). Means, ± standard deviations and p-values are reported.

	ACL-R	ACL-C	ACL-I	ACL-R vs. ACL-I	ACL-C vs. ACL-I	ACL-R vs. ACL-C	overall
Characteristics	**N = 38**	**N = 26**	**N = 38**	**p-value**	**p-value**	**p-value**	**p-value**
Age [years]	32.02 ± 12.21	38.38 ± 11.65	33.13 ± 9.16	0.391	0.099	0.031*	0.419
Body height [cm]	173.55 ± 6.25	170.23 ± 7.59	173.66 ± 6.96	0.831	0.033*	0.075	0.087
Body mass [kg]	71.71 ± 11.19	71.06 ± 14.88	68.38 ± 9.43	0.244	0.942	0.456	0.507
BMI [kg/m^2]	23.94 ± 2.73	24.47 ± 4.64	22.64 ± 2.02	0.015*	0.305	0.305	0.056
Time since injury (months)	12.7 ± 1.4	12.5 ± 1.1	--	< 0.0001*	--	0.579	--
Sex: Ratio of ♀:♂ (%)	17:21 (44.7:55.3)	16:10 (61.5:38.5)	20:18 (52.6:47.4)	0.494	0.848	0.190	0.419
Physical activity [min/week]	425.96 ± 265.10	373.02 ± 158.18	293.26 ± 182.81	0.014*	0.011*	0.811	0.014*
Tegner score (max. 10 points)°	6.71 ± 1.45	6.96 ± 1.18	5.53 ± 1.31	0.001*	< 0.0001*	0.273	< 0.0001*

*Legend: If not otherwise stated means, ± standard deviations and p-values are reported. Dashed lines indicate not applicable * indicates significant p-values (p<0.05). ACL-R = anterior cruciate ligament reconstructed (=patients); ACL-C = anterior cruciate ligament rupture conservatively treated; ACL-I = anterior cruciate ligament intact (= healthy controls); °Tegner activity score (preinjury) ranging from 0 (sick leave or disability pension) to 10 (competitive sport on a professional level)*

Stair descent

An overview containing mean EMG values, SD and analysis of variance presented for sex and group (treatment option) can be found in Table A.3 (supplementary material).

During stair descent, post-hoc analysis comparing neuromuscular activity of the formerly injured, involved leg of ACL-R, ACL-C, and the matched leg of ACL-I (based on side of injury) revealed significant differences of the BF in PO phase only (p = 0.001). Significantly higher neuromuscular activity was found for the BF of ACL-R males in comparison to ACL-I males (p = 0.009, ES 0.43) and of ACL-C males compared to males in the ACL-I group (p = 0.007, ES 0.52). Figure 4 shows bar plots for significant results of BF during PO, provided for group allocation (a) and sex (b). All other comparisons of muscles, phases and group members were not significant (Table A.3, supplementary material).

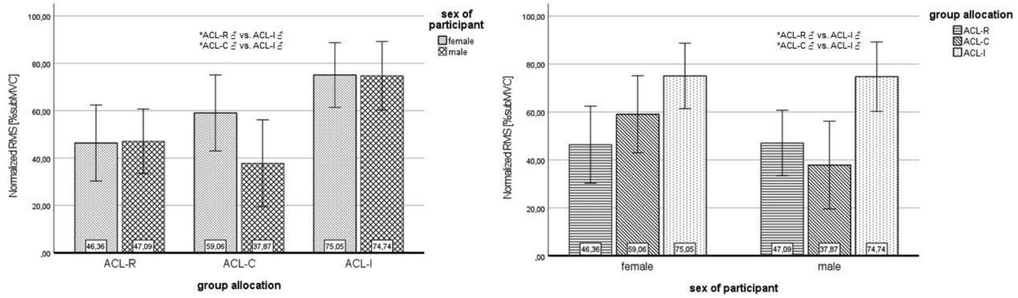

Figure 4: Bar plots of significant results for stair descent

*Legend (Fig. 4): Results are presented for group allocation (left side) and sex (right side); error bars = 95% confidence interval; *significant differences between subgroups (p<0.05); ACL = anterior cruciate ligament; ACL-C = group with conservative treatment after ACL rupture; ACL-I = healthy controls with intact ACL; ACL-R = group with ACL reconstruction; BF = biceps femoris; CI = confidence interval involved = formerly injured or reconstructed side, respective matched leg of controls; PO = push-off phase during stair descent; RMS = root mean square values; subMVC = submaximal voluntary contraction (normalized values with treadmill walking = 100% subMVC)*

Artificial tibial translation

Table A.4 (supplementary material) provides an overview of mean EMG values expressed as %RMS, SD, analysis of variance and effect sizes presented for sex and group. Significant results of respective muscles, phases and groups are graphically edited in Fig. 5A-D. During pre-activation (PRE_50), VM and BF showed overall significant differences comparing ACL-R, ACL-C and ACL-I (p = 0.013, p = 0.035 respectively). Females of ACL-R differed from ACL-C and ACL-I and showed higher RMS values in VM, but only the comparison with females of ACL-C was significant (p = 0.018, ES 0.43) (Fig.5A). Females of ACL-C differed significantly from ACL-I (p = 0.034, ES 0.36) with lower neuromuscular activity of VM compared to their controls and ACL-R (Fig.5A). Moreover, males of ACL-R had a significantly higher pre-activation in VM (p = 0.025, ES 0.41) compared to males in ACL-I (Fig.5A). Regarding BF during PRE_50 only males of ACL-R and ACL-C showed significantly less activity compared to their controls (p = 0.003, ES 0.48; p = 0.019, ES 0.44, respectively) (Fig.5B). The comparison between male participants after ACL injury was not significantly different (p = 0.860). All additional comparisons between muscles and groups in this phase revealed no significant differences.

No significant comparisons were observed for SLR.

In the time window of MLR, ST showed overall significant results (p = 0.011). Females of ACL-R had significantly lower mean reflex activity compared to the female controls (p = 0.015, ES 0.43) (Fig.5C). All other comparisons were not significant.

During LLR, significant results were found for VM only (p = 0.034). Neuromuscular activity of VM of ACL-R females was significantly higher than those of ACL-C females (p = 0.015, ES 0.45) but also higher than in females of the control group (p = 0.049, ES 0.34) (Fig. 5D). No significant differences between treatment options or sex were observed for VL or hamstrings during this phase (Table A.4, supplementary material).

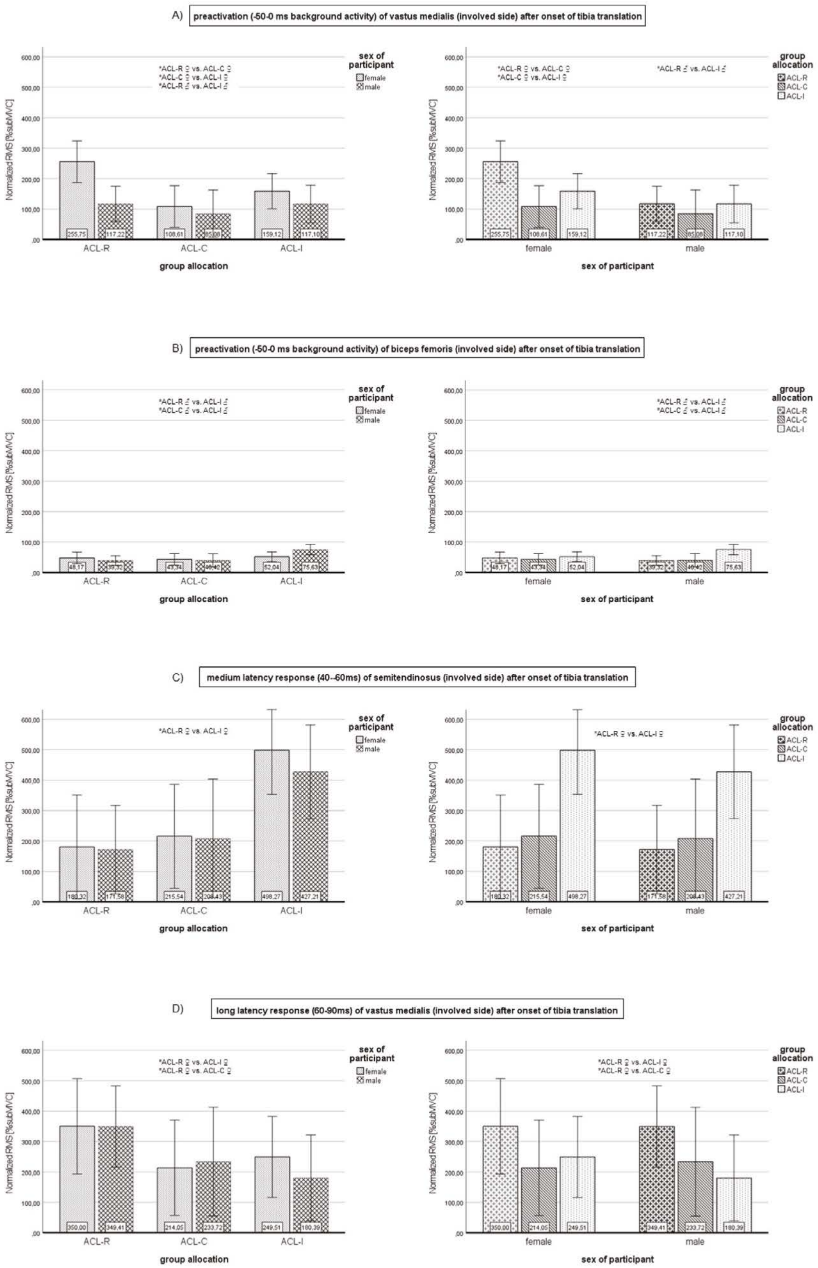

Figure 5A-D: Bar plots of significant results for artificial tibial translation
*Legend (Fig. 5A-D): Results are presented for group allocation (left side) and sex (right side); error bars = 95% confidence interval; *significant differences between subgroups (p<0.05); ACL = anterior cruciate ligament; ACL-C = group with conservative treatment after ACL rupture; ACL-I = healthy controls with intact ACL; ACL-R = group with ACL reconstruction; BF = biceps femoris; CI = confidence interval involved = formerly injured or reconstructed side, respective matched leg of controls; PRE_50 = pre-activation (background activity); MLR = medium latency response; LLR = long latency response; RMS = root mean square values; subMVC = submaximal voluntary contraction (normalized values with treadmill walking = 100% subMVC); VM = vastus medialis; ST = semitendinosus*

More statistical values are provided as supplementary material (Table A.5).

Discussion

This cross-sectional study investigated neuromuscular activity in patients one year after an ACL rupture with reconstruction or conservative treatment in comparison to a healthy control group. Neuromuscular control was assessed during stair descent as functional task and an artificially induced tibial translation while standing. Beforehand, it was hypothesized that neuromuscular control would still be impaired in conservatively (ACL-C) and surgically treated participants (ACL-R) one year after ACL rupture compared to healthy controls.

In general, we found a large range of differences in activity patterns within and between groups in the investigated timeframes and movement phases indicating a large intra-individual variability, especially during artificial tibial translation. This was in line with further research assessing patients with an acute rupture of the ACL.[9] However, the hypothesis that neuro-muscular control would be negatively affected even one year after reconstruction or conservatively treated rupture had been confirmed.

Stair descent

A significant decrease in neuromuscular activity was found in the BF muscle of male patients during PO in comparison to healthy controls. The altered neuromuscular activity can be interpreted that afferent feedback is still affected one year after ACL rupture or reconstruction, regardless of treatment. At least in conservatively treated patients, this might be a functional adaptation to altered mechanical properties. Obviously, the changes in the brain leading to impaired neuromuscular control in people after ACL rupture may not be sufficiently targeted by current rehabilitation programs which is in line with present findings.[47] During stair descent, Hall and colleagues also found higher hamstrings activity in patients after ACL-R compared to healthy controls.[11] However, the higher activity was found in the medial hamstrings (ST) and the group consisted of males and females with an ACL reconstruction 1-18 years ago.[11] In an early study investigating a one-step climbing and descending task, a significantly earlier onset and longer total duration of lateral hamstrings was observed in copers compared to a healthy control group.[15] Also this group consisted of males and females but was tested one year after ACL injury.[15]

Altered cortical activation after ACL reconstruction had been reported previously: Patients six or more months after ACL rupture showed reorganization of the central nervous system, indicating that an ACL rupture is not only a peripheral musculoskeletal injury but rather a neurophysiologic dysfunction,[48] which is present even years after ACL surgery.[3,49] ACL injury may alter intracortical facilitation[49] and lead to increased intracortical inhibition. The latter is correlated with decreased capability to voluntarily activate the quadriceps.[50] In our study, the findings regarding quadriceps activation were controversial, and only significant in the following situations and comparisons: females after ACL-R had significantly higher VM activity compared to ACL-C during WA, males of ACL-C showed lower VL activity compared to ACL-I. During PO, males of ACL-R had lower VM and VL activity compared to ACL-C, males of ACL-C had higher VM and VL activity compared to ACL-I, and females of ACL-R had higher VL activity compared to ACL-C.

Artificial tibial translation

In a similar setting as in the present study, a reduced SLR of hamstrings in combination with increased tibial translation had been reported.[42] However, those measurements had been done after muscle fatigue, indicating a fatigue-related reflex reduction. This reduction could point at the need for more neural "drive" in patients suffering from increased anterior tibial translation caused by ACL rupture, resulting in higher neuromuscular activity to stabilize the knee joint. Therefore, the increased pre-activation in VM and BF as well as reflex activity of the ST during MLR might reflect an active compensation pattern of the hams-trings for higher stability demands. Sufficient reflex response in the MLR timeframe is essential and seems to be better after conservative treatment than after surgical reconstruction when compared to healthy controls in our study. In case of ACL deficiency few weeks after injury, a reduction of MLR was found to be related to "giving-way" symptoms.[51] However, as our participants in the ACL-C group were copers, "giving-way" symptoms had not been assessed previously. In addition, the increased activity during MLR in this group can be seen as compensatory mechanism to guarantee active knee stability.

ST was significantly and highly reduced in female ACL-R compared to female ACL-I, but hamstrings in general tended to be less active in all patient groups. Sex-specific neuromuscular adaptations such as activation timing, differences in force intensity of knee stabilizing muscles[52-57] and a dominance of the quadriceps over the hamstring muscles in women, which could increase anterior tibial translation, had been reported previously.[55,56,58,59] In contrast, these findings had been contradicted by a systematic review about sex differences in landing and cutting manoeuvres which reported that no proof for quadriceps dominance during the described activities was present.[60]

Methodological aspects

Stair descent and artificial tibial translation have been selected as representing tasks for important, functionally relevant, and demanding situations.

Stairway walking (ascent and descent) as an ADL activity requires preactivity (joint stiffening) before initial contact to guarantee active joint stability, and eccentric contraction[61] while 346% of the bodyweight loads the knee joint.[62]Additionally, it has been shown that an anterior-posterior tibial translation occurs during ambulation.[63] Previously published preliminary studies from our research group had shown the feasibility and reliability of this method, and the discriminatory power between different cohorts.[39,64] With this task, which is relevant to everyday life, sensorimotor competence can be assessed in applied situations.

Artificially induced tibial perturbation was chosen as reflex activity and simulation of injury mechanism. Monitoring neuromuscular control during the corresponding time window from pre-activity to perturbation onset and time windows for reflex responses after perturbation give insight into sensorimotor control mechanisms to guarantee knee joint stability.[40-42] During tibial translation in posterior-anterior direction (relatively to the femur), the ACL comes under tension. In healthy subjects with an intact ACL, the hamstring muscles (BF, ST, semimembranosus muscle) act synergistically to this translational movement.[40] This synergistic contraction occurs reflexively during appropriately rapid tibial translation, e.g., by the rope-pulley system triggering sudden tibial perturbations which induce a reflex response of the hamstring muscles.[40] After a sudden, anterior tibial translation, the magnitude of protective reflex activation of the hamstrings results in increased active joint stability of the knee; this mechanism protects against injury.[65] This indicates that the extent of the dynamic neuromuscular joint control of the knee stabilizing muscles can be measured closely to the physiological injury mechanism by surface EMG during standardized tibial perturbations.[40,66]

Eighty percent of all ACL injuries are due to non-contact episodes[67] while deceleration and acceleration motions with excessive quadriceps contraction or insufficient hamstrings activation at or near full knee extension are seen.[68,69] Thereby, the tibia is translated anteriorly relatively to the femur and stresses the ACL. With an intact ACL, the hamstring muscles act synergistically to this translational movement whereas the quadriceps muscles are ACL antagonist.[40] It has been shown that non-contact ACL ruptures happen 17-50ms after initial contact,[67] leaving a short time frame for mechanosensory feedback (e.g., reflex response). Pre-activity and reactive neuromuscular responses regulate muscle and joint stiffness, which is influencing dynamic joint stability, consequently influencing ACL injury risk.[70] Monitoring neuromuscular control during exactly this time window from preactivity to onset of perturbation and reflexive time windows after tibial translation give insight into sensorimotor control mechanisms establishing knee joint stability.[40-42]

During artificial tibial translation in standing position, equal distribution of body mass under the right and left foot was monitored. However, if the body mass would shifted more onto the heel or forefoot, the center of mass changed and would lead to more degrees of flexion or extension of the spine, pelvis ante-/retroversion or trunk inclination/reclination.[71-73] With this altered upright starting position, the participants could have unconsciously influenced the activity of the hamstrings which could led to a different neuromuscular strategy due to changes in the length of the superficial back line, a myofascial meridian.[74] Furthermore, the band-sling was placed at the proximal part of the shank over the triceps surae, which could influence the activation of the hamstring muscles due to mechanical stimuli in triceps surae Ia and II afferent pathways.[40]

Strengths and limitations

This study is one of the few publications reporting neuromuscular activity of thigh muscles comparing two ACL patient groups with different treatment modalities one year after injury. Moreover, to current knowledge, it is the first study which investigated reflex response after artificial induced tibial perturbation in participants with ACL-R or rehabilitation alone (ACL-C). A narrow time frame (11 – 14 months post-injury, after reconstruction respectively) was chosen for both patient groups where all participants had full clearance for RTS. In addition, the applied methods were standardized and used before. Monitoring neuromuscular control during exactly the time window from pre-activity to perturbation onset and reflexive time windows after joint (stability) perturbation give insight into sensorimotor control mechanisms establishing knee joint stability.[40-42] This method could lead to define outcomes for neuromuscular control to be integrated into current RTS criteria which has already been stated.[26,75] However, the assessment of neuromuscular control as presented in this study is sophisticated but not ready to be used in a clinical setting yet.

Several study limitations should be considered: It was planned a priori to recruit 30 participants per group, 15 females and 15 males. However, we could include fewer participants in the ACL-C group despite the extended recruitment phase. This was mainly due to Covid pandemic, during which the movement laboratory had to be closed for several weeks. By the time the laboratory was accessible again, six subjects – among which four for the ACL-C group – were outside the time window of 14 months post-injury and could no longer be included. As sex seems to affect neuromuscular patterns,[41,42,76] an equal sex distribution in the groups was aimed but could not be reached.

The ACL-R group was heterogenous regarding choice of graft and surgical techniques as participants from more than one orthopaedic surgeon had been included. This led to different treatment modalities regarding duration and quality of rehabilitation as rehabilitation after ACL rupture or ACL reconstruction is not standardized. Moreover, no specialization in sports physical therapy for physiotherapists is needed to treat ACL patients which sometimes negatively affects quality of rehabilitation. Although all included patients were cleared for unrestricted RTS, their physical condition and psychological readiness to participate in sport varied widely when they were measured at the lab: Some participants of the patient groups showed atrophy in the operated leg, experienced painful episodes, had limited knee flexion, were hypermobile in one or both knee joints, or had not returned to the sport level before ACL rupture. Furthermore, the subjects had very different levels of sport, ranging from recreational activities to competitive sport at a national level. Accordingly, the mean EMG values during stair climbing and the reflex activities during tibial translation varied largely which was in line with former research from our group.[9,10,27]

In summary, this heterogeneity in ACL injured participants' physical and mental state, quality and duration of rehabilitation, experience and training of physical therapist could have influenced our results and limits generalizability of the findings. Nevertheless, the results help to better understand long-term consequences of an ACL rupture, especially for neuromuscular control after RTS.[27]

Another limitation was that we decided to use two-way parametric ANOVA to analyze the factors "group" and "sex" despite non-parametric distribution of most of the variables tested. According to published recommendations,[77] parametric ANOVA may be used in those situations. Furthermore, adjusted linear models including age, physical activity and BMI as covariates were used to check whether the effects of sex and group changed substantially (> 10% difference in effect sizes). Only the effect of group was substantially different in the adjusted model for the outcome variable "MLR of ST" when age, physical activity and BMI had been included. Both non-adjusted and adjusted effect sizes were still medium, and the effect of confounding was not further investigated.

Conclusions

The present study revealed that neuromuscular alterations are still present in the involved leg one year after ACL rupture or reconstruction compared to healthy controls. Standard rehabilitation protocols may not be able to restore neuromuscular control. In addition, neuromuscular control seems to be impaired independently from sex after unilateral ACL rupture but influenced by treatment. Therefore, it is important to assess neuromuscular control directly by surface EMG to detect deficits despite fulfilled clinical and physical performance test for RTS.

Future research should aim at more homogenous participant groups, include long-term follow up and standardized rehabilitation programs which focus on exercises targeting neuromuscular function. Another aspect of future research interest are bilateral deficits after ACL rupture to investigate whether the contralateral leg can be an adequate reference for functional evaluation of the injured extremity. As the limb symmetry index is still widely used, but probably underestimating the functional deficits of both lower extremities, other outcome measures for neuromuscular function should be considered when deciding for a safe RTS.

Data availability

The datasets used and analysed during the current study are available from the corresponding author upon reasonable request and are stored on servers owned by the Bern University of Applied Sciences.

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Contributions

An.B. participated in the design of the study, was responsible for data collection, contributed to data analysis and interpretation of results, and was responsible for writing the manuscript; Ag.B. supported during measurements, was responsible for data reduction and contributed to data analysis and interpretation; P.H. was responsible for patient recruitment and clinical assessment, subscribed magnetic resonance imaging for patients if necessary and contributed to the design of the study; S.B. was consultant for methods and contributed to the interpretation of results; D.V. contributed to the interpretation of data; H.B. designed the study, was project leader and responsible for funding, contributed to data analysis and interpretation of results. All authors contributed to the manuscript writing, have read and approved the final version of the manuscript and agree with the order of authors as listed.

Competing interests

Angela Blasimann, Aglaja Busch, Philipp Henle, Sven Bruhn, Dirk Vissers and Heiner Baur declare that they have no competing interests.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Canton of Bern (Switzerland), KEK No. 2017-02282, and was conducted in accordance with the Declaration of Helsinki[78]. Written informed consent was obtained from every participant.

Consent for publication

All participants in this study provided written informed consent for publication.

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Table A.1: Additional clinical characteristics of participants with an ACL reconstruction (ACL-R), with a conservatively treated ACL rupture (ACL-C) and healthy controls with an intact ACL (ACL-I).

	ACL-R	ACL-C	ACL-I	ACL-R vs. ACL-I	ACL-C vs. ACL-I	ACL-R vs. ACL-C	overall
Characteristics	**N = 38**	**N = 26**	**N = 38**	**p-value**	**p-value**	**p-value**	**p-value**
Leg dominance (N=)							
right:left [%]	35:3 (92.1:7.9)	23:3 (88.5:11.5)	34:4 (89.5:10.5)	0.694	0.899	0.626	0.876
Prehabilitation (N=)							
yes:no [%]	13:25 (34.2:65.8)	--	--	< 0.0001*	--	< 0.0001*	--
PT after surgery/injury (N=)							
yes:no [%]	38:0 (100:0)	26:0 (100:0)	--	< 0.0001*	--	< 0.0001*	--
KOOS subscale (absolute values)							
pain (9 items, max. 36 p.)	4.47 ± 3.32	3.35 ± 2.99	0.37 ± 0.71	< 0.0001*	< 0.0001*	0.119	< 0.0001*
other symptoms (7 items, max. 28 p.)	5.95 ± 3.80	5.08 ± 3.12	1.58 ± 1.52	< 0.0001*	< 0.0001*	0.532	< 0.0001*
ADL (17 items, max. 68 p.)	2.50 ± 3.42	2.23 ± 4.03	0.08 ± 0.36	< 0.0001*	< 0.0001*	0.380	< 0.0001*
sports & leisure (5 items, max. 20 p.)	3.63 ± 2.88	2.69 ± 2.77	0.21 ± 0.70	< 0.0001*	< 0.0001*	0.151	< 0.0001*
HRQoL (4 items, max. 16 p.)	4.73 ± 3.29	3.81 ± 2.90	0.37 ± 1.00	< 0.0001*	< 0.0001*	0.259	< 0.0001*
VAS							
wellbeing pre [mm]	5.53 ± 8.60	5.35 ± 10.31	5.29 ± 6.90	0.643	0.666	0.972	0.870
wellbeing post [mm]	7.29 ± 9.00	5.58 ± 9.91	6.55 ± 7.39	0.937	0.355	0.402	0.612
pain pre [mm]	3.08 ± 4.08	4.35 ± 8.89	1.08 ± 2.06	0.026*	0.037*	0.977	0.045*
pain post [mm]	6.18 ± 13.25	6.42 ± 10.57	3.42 ± 7.88	0.264	0.082	0.486	0.209
Medial meniscal tears (N=)							
conservative treatment [%]	2 (5.3)	4 (15.4)	--	--	--	--	--
suture [%]	15 (39.5)	0	--	--	--	--	--
resection [%]	7 (18.4)	0	--	--	--	--	--
none [%]	14 (36.8)	22 (84.6)	--	--	--	--	--

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Lateral meniscal tears (N=)								
conservative treatment [%]	1 (2.6)	5 (19.2)	--	--	--	--	--	--
suture [%]	8 (21.1)	0	--	--	--	--	--	--
resection [%]	1 (2.6)	0	--	--	--	--	--	--
none [%]	28 (73.7)	21 (80.8)	--	--	--	--	--	--
Medial collateral ligament injury (N=)								
conservative treatment [%]	8 (21.1)	8 (30.8)	--	--	--	--	--	--
surgery [%]	1 (2.6)	0	--	--	--	--	--	--
none [%]	29 (76.3)	18 (69.2)	--	--	--	--	--	--
Lateral collateral ligament injury (N=)								
conservative treatment [%]	2 (5.3)	4 (15.4)	--	--	--	--	--	--
surgery [%]	0	0	--	--	--	--	--	--
none [%]	36 (94.7)	22 (84.6)	--	--	--	--	--	--
Bone bruise (N=)								
yes:no [%]	0:38 (0:100)	7:19 (26.9:73.1)	--	--	--	--	--	--
Cartilage defect (N=)								
yes:no [%]	2:36 (5.3:94.7)	2:24 (7.7:92.3)	--	--	--	--	--	--
Graft types (N=)								
Quadriceps tendon [%]	26 (68.4)	--	--	--	--	--	--	--
Hamstrings tendon [%]	8 (21.1)	--	--	--	--	--	--	--
Patellar tendon [%]	3 (7.9)	--	--	--	--	--	--	--
Unknown [%]	1 (2.6)	--	--	--	--	--	--	--

*Data are presented as mean ± standard deviation (SD) unless otherwise stated. * Indicates significant p-values (p<0.05); dashed lines indicate not applicable.*
Legend: ACL-C = anterior cruciate ligament rupture conservatively treated; ACL-I = anterior cruciate ligament intact (= healthy controls); ACL-R = anterior cruciate ligament reconstructed (=patients); ADL = activity of daily life; HRQoL = health-related quality of life; KOOS = Knee injury and Osteoarthritis Outcome Score (scoring per item: 0 = no problems; 4 = extreme problems); max. = maximum; p = points; N= number of; post = after the measurements; pre = before the measurements started; PT = physiotherapy; VAS = visual analogue scale from 0 to 100mm

Table A.2: Characteristics of females and males for all three groups

Characteristics	**ACL-R (N = 38)**		**ACL-C (N = 26)**		**ACL-I (N = 38)**		ACL-R vs. ACL-I	ACL-C vs. ACL-I	ACL-R vs. ACL-C	overall
sex	**females**	**males**	**females**	**males**	**females**	**males**	p-value	p-value	p-value	p-value
number of participants	**N = 17**	**N = 21**	**N = 16**	**N = 10**	**N = 20**	**N = 18**				
Age [years]	31.71 ± 11.64	32.29 ± 12.94	39.25 ± 11.48	37.00 ± 12.40	31.80 ± 9.44	34.61 ± 8.87	0.391	0.099	0.031	0.419
Body height [cm]	169.12 ± 5.53	177.14 ± 4.20	165.81 ± 5.39	177.30 ± 4.62	169.35 ± 6.40	178.44 ± 3.70	0.831	0.033	0.075	0.087
Body mass [kg]	63.68 ± 8.53	78.22 ± 8.61	66.76 ± 13.34	77.95 ± 15.27	62.17 ± 7.82	75.29 ± 5.41	0.244	0.942	0.456	0.507
BMI [kg/m^2]	22.4 ± 2.39	25.13 ± 2.43	24.26 ± 4.64	24.82 ± 4.87	21.64 ± 2.03	23.76 ± 1.35	0.015	0.305	0.305	0.056
Time since injury (months)	12.29 ± 0.77	13.10 ± 1.67	12.63 ± 1.15	12.30 ± 0.95	--	--	< 0.0001	--	0.579	--
Sex ♀:♂ (%)	17:21 (44.7:55.3)		16:10 (61.5:38.5)		20:18 (52.6:47.4)		0.494	0.848	0.19	0.419
Leg dominance (right:left)	16:1	19:2	15:1	8:2	19:1	15:3	0.694	0.899	0.626	0.876
Prehabilitation (yes:no) (% of subgroup)	8:9 (47.1:52.9)	5:16 (23.8:76.2)	--	--	--	--	--	--	--	--
Prehabilitation (yes:no) (% of subgroup)	13:25 (34.2:65.8)		--		--		< 0.0001	--	< 0.0001	--
PT after surgery/injury (yes:no)	17:0	21:0	16:0	10:0	--	--	--	--	--	--
PT after surgery/injury (yes:no)	38:0		26:0		--		< 0.0001	--	< 0.0001	--
Physical activity [min/week]	447.68 ± 213.66	408.38 ± 304.58	362.41 ± 168.87	390.00 ± 146.46	293.80 ± 213.21	292.67 ± 148.10	0.014	0.011	0.811	0.014
Tegner score (max. 10 points)°	6.53 ± 1.55	6.86 ± 1.39	6.56 ± 0.81	7.60 ± 1.43	5.40 ± 1.54	5.67 ± 1.03	0.001	< 0.0001	0.273	< 0.0001

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KOOS subscale										
(absolute values)										
pain (9 items, max. 36 p.)	31.82 ± 3.30	31.29 ± 3.40	32.63 ± 3.40	32.70 ± 2.36	35.85 ± 0.49	35.44 ± 0.86	< 0.0001	< 0.0001	0.119	< 0.0001
other symptoms (7 items, max. 28 p.)	21.94 ± 2.75	22.14 ± 4.54	22.70 ± 3.42	23.30 ± 2.71	26.40 ± 1.31	26.44 ± 1.76	< 0.0001	< 0.0001	0.532	< 0.0001
ADL (17 items, max. 68 p.)	65.18 ± 3.70	65.76 ± 3.24	65.25 ± 4.77	66.60 ±2.46	67.90 ± 0.45	67.94 ± 0.24	< 0.0001	< 0.0001	0.380	< 0.0001
sports & leisure (5 items, max. 20 p.)	16.12 ± 3.02	16.57 ±2.82	17.06 ± 3.07	17.70 ± 2.31	19.95 ± 0.22	19.61 ± 0.98	< 0.0001	< 0.0001	0.151	< 0.0001
HRQoL (4 items, max. 16 p.)	12.00 ± 2.81	10.67 ± 3.58	11.63 ± 3.12	13.10 ± 2.38	15.70 ± 0.92	15.56 ± 1.10	< 0.0001	< 0.0001	0.259	< 0.0001
VAS										
wellbeing pre [mm]	6.12 ± 10.27	5.05 ± 7.21	7.94 ± 12.50	1.20 ± 1.99	4.50 ± 5.48	6.17 ± 8.28	0.643	0.666	0.972	0.870
wellbeing post [mm]	6.71 ± 10.69	7.76 ± 7.60	8.13 ± 11.93	1.50 ± 2.42	6.85 ± 8.11	6.22 ± 6.72	0.937	0.355	0.402	0.612
pain pre [mm]	3.41 ± 5.23	2.81 ± 2.94	6.25 ± 10.93	1.30 ± 1.95	0.95 ± 1.76	1.22 ± 2.39	0.026	0.037	0.977	0.045
pain post [mm]	6.65 ± 11.26	5.81 ± 14.94	9.25 ± 12.64	1.90 ± 2.73	4.75 ± 10.44	1.94 ± 3.02	0.264	0.082	0.486	0.209
Medial meniscal tears (N=)										
conservative treatment	0	2	3	1	--	--	--	--	--	--
suture	7	8	0	0	--	--	--	--	--	--
resection	1	6	0	0	--	--	--	--	--	--
Lateral meniscal tears (N=)										
conservative treatment	1	0	4	1	--	--	--	--	--	--
suture	3	5	0	0	--	--	--	--	--	--
resection	0	1	0	0	--	--	--	--	--	--

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Medial collateral ligament injury (N=)										
conservative treatment	3	5	5	3	--	--	--	--	--	--
surgery	1	0	0	0	--	--	--	--	--	--
Lateral collateral ligament injury (N=)										
conservative treatment	1	1	3	1	--	--	--	--	--	--
surgery	0	0	0	0	--	--	--	--	--	--
Bone bruise					--	--	--	--	--	--
(N=) (% of subgroup)	0 (0)	0 (0)	6 (37.5)	1 (6.3)						
Cartilage defect					--	--	--	--	--	--
(N=) (% of subgroup)	0 (0)	2 (9.5)	2 (12.5)	0 (0)						
Graft types (N=) (%)										
Quadriceps tendon	10 (58.8)	16 (76.2)	--	--	--	--	--	--	--	--
Hamstrings tendon	5 (29.4)	3 (14.3)	--	--	--	--	--	--	--	--
Patellar tendon	1 (5.9)	2 (9.5)	--	--	--	--	--	--	--	--
Unknown	1 (5.9)	0 (0)	--	--	--	--	--	--	--	--

If not otherwise stated means, ± standard deviations and p-values are reported. Dashed lines indicate not applicable.
Legend: ACL-R = anterior cruciate ligament reconstructed (=patients); ACL-C = anterior cruciate ligament rupture conservatively treated; ACL-I = anterior cruciate ligament intact (= healthy controls); KOOS = Knee injury and Osteoarthritis Outcome Score; ADL = activity of daily life; HRQoL = health-related quality of life; N= number of; pre = before the measurements started; PT = physiotherapy; post = after the measurements; VAS = visual analogue scale from 0 to 100mm; % = percentage of subgroup; °Tegner activity score (preinjury) ranging from 0 (sick leave or disability pension) to 10 (competitive sport on a professional level)

Table A.3: Stair descent: Neuromuscular activity for females and males per group for the involved (injured), matched limb respectively

Muscle	Group: ACL-R females [1]	ACL-R males [2]	ACL-C females [3]	ACL-C males [4]	ACL-I = Control females [5]	ACL-I = Control males [6]	p-values: overall*	[1]vs[3]°	[1]vs[5]°	[3]vs[5]°	[2]vs[4]°	[2]vs[6]°	[4]vs[6]°	Effect size: [1]vs[3]°	[1]vs[5]°	[3]vs[5]°	[2]vs[4]°	[2]vs[6]°	[4]vs[6]°
VM	131.8 (38.9)	125.6 (32.1)	116.1 (31.9)	118.2 (41.5)	117.5 (38.4)	110.5 (42.5)	0.328	0.234	0.448	0.745	0.538	0.273	0.688	--	--	--	--	--	--
VL	126.3 (26.1)	124.6 (28.8)	127.4 (24.2)	118.6 (24.3)	133.3 (44.1)	108.1 (41.0)	0.806	0.865	0.503	0.617	0.598	0.094	0.482	--	--	--	--	--	--
BF	96.8 (36.7)	100.5 (37.0)	115.3 (43.7)	90.8 (40.5)	117.4 (45.3)	108.9 (43.1)	0.362	0.167	0.134	0.975	0.735	0.693	0.388	--	--	--	--	--	--
ST	102.3 (34.5)	96.8 (39.7)	107.7 (33.7)	107.8 (42.0)	124.6 (40.4)	114.1 (52.3)	0.174	0.64	0.106	0.121	0.605	0.274	0.647	--	--	--	--	--	--
Stair descent, weight acceptance, involved/matched side																			
Muscle	**females [1]**	**males [2]**	**females [3]**	**males [4]**	**females [5]**	**males [6]**	**overall***	**[1]vs[3]°**	**[1]vs[5]°**	**[3]vs[5]°**	**[2]vs[4]°**	**[2]vs[6]°**	**[4]vs[6]°**	**[1]vs[3]°**	**[1]vs[5]°**	**[3]vs[5]°**	**[2]vs[4]°**	**[2]vs[6]°**	**[4]vs[6]°**
VM	274.9 (76.3)	251.4 (105.0)	213.9 (75.6)	254.0 (50.1)	274.3 (104.4)	252.0 (136.2)	0.654	**0.038**	0.951	0.083	0.235	0.626	0.451	--	--	--	--	--	--
VL	258.6 (60.0)	238.6 (75.8)	243.2 (53.7)	152.3 (46.2)	250.8 (86.6)	201.7 (77.5)	0.331	0.234	0.670	0.806	0.356	0.135	**0.031**	--	--	--	--	--	--

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Muscle	Group: ACL-R females [1]	ACL-R males [2]	ACL-C females [3]	ACL-C males [4]	ACL-I = Control females [5]	ACL-I = Control males [6]	p-values: overall*	[1]vs[3]°	[1]vs[5]°	[3]vs[5]°	[2]vs[4]°	[2]vs[6]°	[4]vs[6]°	Effect size: [1]vs[3]°	[1]vs[5]°	[3]vs[5]°	[2]vs[4]°	[2]vs[6]°	[4]vs[6]°
BF	73.1 (30.9)	77.6 (26.8)	59.2 (22.6)	55.2 (19.3)	82.2 (61.4)	91.4 (50.2)	0.051	0.117	0.831	0.790	**0.039**	0.503	0.056	--	--	--	--	--	--
ST	40.1 (14.8)	51.4 (21.9)	51.6 (21.7)	38.1 (19.2)	59.8 (39.6)	54.6 (35.0)	0.693	0.114	0.136	0.959	0.215	0.716	0.317	--	--	--	--	--	--
Stair descent, push-off, involved/matched side																			
Muscle	**females [1]**	**males [2]**	**females [3]**	**males [4]**	**females [5]**	**males [6]**	**overall***	**[1]vs[3]°**	**[1]vs[5]°**	**[3]vs[5]°**	**[2]vs[4]°**	**[2]vs[6]°**	**[4]vs[6]°**	**[1]vs[3]°**	**[1]vs[5]°**	**[3]vs[5]°**	**[2]vs[4]°**	**[2]vs[6]°**	**[4]vs[6]°**
VM	336.4 (145.8)	251.9 (118.0)	269.5 (143.2)	414.8 (115.2)	262.2 (123.7)	207.9 (92.6)	0.081	0.097	0.233	0.665	**0.002**	0.273	**< 0.001**	--	--	--	--	--	--
VL	297.0 (95.4)	216.8 (104.2)	216.9 (70.5)	309.3 (65.8)	236.0 (100.4)	162.6 (79.4)	0.069	**0.043**	0.211	0.345	**0.014**	0.135	**< 0.001**	--	--	--	--	--	--
BF	49.0 (17.2)	48.4 (19.7)	57.6 (26.9)	37.9 (18.2)	76.0 (36.9)	82.1 (48.3)	**0.001**	0.777	0.055	0.131	0.218	**0.009**	**0.007**	--	--	--	--	0.43	0.52
ST	52.1 (19.7)	52.9 (26.2)	65.3 (24.4)	47.5 (29.6)	70.4 (33.1)	59.0 (22.3)	0.146	0.136	0.084	0.822	0.628	0.265	0.14	--	--	--	--	--	--

*Legend: Normalized root mean square (RMS) values, expressed as % of submaximal voluntary contraction (during treadmill walking), are reported per muscle and movement phase during stair descent. If not otherwise stated means, standard deviations (in brackets) and p-values are reported. *Kruskal-Wallis test; °Mann-Whitney-U test. Boldface p-values indicate statistically significant differences between subgroups (p<0.05). Dashes indicate not applicable. ACL = anterior cruciate ligament; ACL-R = anterior cruciate ligament reconstructed (=patients); ACL-C = anterior cruciate ligament rupture conservatively treated; ACL-I = anterior cruciate ligament intact (= healthy controls); BF = biceps femoris; involved = injured leg, respective matched leg of controls (based on side of injury); PO = push-off; PRE = pre-activity; RMS = root mean square; SD = standard deviation; ST = semitendinosus; VM = vastus medialis; VL = vastus lateralis; WA = weight acceptance*

Table A.4: Artificial tibial translation: Reflex activity for females and males per group per phase for the involved (injured), matched limb respectively

Reflex activity, pre-activation 50ms (PRE_50), involved/matched side

Muscle	Group						p-values							Effect size					
	ACL-R		ACL-C		ACL-I = Control														
	females	males	females	males	females	males													
	[1]	[2]	[3]	[4]	[5]	[6]	overall*	[1]vs[3]°	[1]vs[5]°	[3]vs[5]°	[2]vs[4]°	[2]vs[6]°	[4]vs[6]°	[1]vs[3]°	[1]vs[5]°	[3]vs[5]°	[2]vs[4]°	[2]vs[6]°	[4]vs[6]°
VM	243.6 (288.3)	127.7 (57.1)	111.2 (39.1)	85.1 (28.2)	153.0 (66.7)	125.3 (66.5)	**0.013**	**0.018**	0.466	**0.034**	**0.025**	0.599	0.164	0.43	--	0.36	0.41	--	--
VL	199.7 (138.0)	126.5 (60.3)	126.0 (33.1)	117.7 (39.5)	152.4 (49.9)	140.6 (64.1)	0.229	**0.010**	0.229	0.120	0.966	0.297	0.362	--	--	--	--	--	--
BF	56.8 (52.5)	41.1 (22.4)	43.3 (28.1)	40.4 (28.3)	53.9 (39.0)	79.1 (40.6)	**0.035**	0.827	0.636	0.435	0.860	**0.003**	**0.019**	--	--	--	--	0.48	0.44
ST	57.3 (21.1)	62.6 (34.6)	62.6 (27.5)	54.8 (31.6)	56.5 (30.8)	35.4 (29.1)	0.099	0.647	0.716	0.716	0.538	**0.009**	0.084	--	--	--	--	--	--

Reflex activity, short latency response (SLR), involved/matched side

Muscle	Group						p-values							Effect size					
	ACL-R		ACL-C		ACL-I = Control														
	females	males	females	males	females	males													
	[1]	[2]	[3]	[4]	[5]	[6]	overall*	[1]vs[3]°	[1]vs[5]°	[3]vs[5]°	[2]vs[4]°	[2]vs[6]°	[4]vs[6]°	[1]vs[3]°	[1]vs[5]°	[3]vs[5]°	[2]vs[4]°	[2]vs[6]°	[4]vs[6]°
VM	377.7 (289.1)	181.0 (114.4)	202.6 (131.8)	181.8 (140.3)	205.0 (75.8)	177.1 (128.3)	0.582	0.088	0.126	0.667	0.692	0.661	0.962	--	--	--	--	--	--

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VL	315.1 (149.4)	139.5 (65.5)	178.1 (101.4)	159.4 (69.1)	170.4 (48.4)	162.3 (96.5)	0.643	**0.007**	**0.003**	0.817	0.402	0.509	0.808	--	--	--	--	--	--
BF	292.9 (442.0)	237.0 (327.4)	215.8 (136.7)	172.6 (153.7)	192.7 (124.6)	220.3 (166.9)	0.570	0.570	0.732	0.800	0.860	0.279	0.231	--	--	--	--	--	--
ST	215.4 (204.7)	256.3 (238.6)	219.9 (181.2)	185.2 (141.1)	272.3 (343.0)	189.4 (259.4)	0.351	0.694	0.799	0.544	0.455	0.077	0.366	--	--	--	--	--	--

Reflex activity, medium latency response (MLR), involved/matched side

Muscle	Group						p-values							Effect size					
	ACL-R		ACL-C		ACL-I = Control														
	females	males	females	males	females	males													
	[1]	[2]	[3]	[4]	[5]	[6]	overall*	[1]vs[3]°	[1]vs[5]°	[3]vs[5]°	[2]vs[4]°	[2]vs[6]°	[4]vs[6]°	[1]vs[3]°	[1]vs[5]°	[3]vs[5]°	[2]vs[4]°	[2]vs[6]°	[4]vs[6]°
VM	516.6 (319.9)	372.4 (461.1)	239.0 (98.5)	313.3 (207.2)	340.7 (155.2)	317.7 (202.8)	0.097	**0.001**	0.117	**0.040**	0.888	0.599	1.000	--	--	--	--	--	--
VL	511.8 (279.9)	300.7 (186.0)	301.4 (128.5)	298.8 (128.9)	305.3 (133.3)	321.3 (196.0)	0.472	**0.031**	**0.028**	0.945	0.769	0.735	0.797	--	--	--	--	--	--
BF	294.9 (190.3)	234.3 (213.7)	268.8 (147.4)	252.3 (127.7)	391.3 (347.1)	362.4 (280.6)	0.325	0.792	0.687	0.551	0.567	0.152	0.472	--	--	--	--	--	--
ST	180.3 (120.5)	208.8 (213.7)	216.9 (143.6)	208.4 (87.3)	500.3 (499.4)	418.1 (408.9)	**0.011**	0.475	**0.015**	0.042	0.312	0.161	0.422	--	0.43	--	--	--	--

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Reflex activity, long latency response (LLR), involved/matched side																			
Muscle	Group						p-values							Effect size					
	ACL-R		ACL-C		ACL-I = Control														
	females	males	females	males	females	males	overall*	[1]vs[3]°	[1]vs[5]°	[3]vs[5]°	[2]vs[4]°	[2]vs[6]°	[4]vs[6]°	[1]vs[3]°	[1]vs[5]°	[3]vs[5]°	[2]vs[4]°	[2]vs[6]°	[4]vs[6]°
	[1]	[2]	[3]	[4]	[5]	[6]													
VM	435.1 (368.1)	387.5 (553.5)	212.3 (145.0)	233.7 (166.9)	238.3 (139.7)	186.9 (142.6)	**0.034**	**0.015**	**0.049**	0.591	0.538	0.075	0.388	0.45	0.34	--	--	--	--
VL	311.5 (162.7)	272.4 (203.3)	258.3 (180.7)	199.9 (122.9)	233.7 (129.9)	174.9 (102.5)	0.110	0.313	0.199	0.947	0.272	0.055	0.632	--	--	--	--	--	--
BF	233.7 (118.3)	186.4 (134.1)	225.0 (114.6)	233.3 (127.9)	230.0 (139.5)	266.0 (112.1)	0.624	0.730	0.841	0.885	0.272	0.215	0.848	--	--	--	--	--	--
ST	233.1 (132.9)	267.9 (265.0)	260.6 (190.8)	379.3 (231.7)	225.7 (144.7)	227.5 (178.7)	0.457	0.930	0.893	0.716	0.190	0.941	0.108	--	--	--	--	--	--

*Legend: Normalized root mean square (RMS) values, expressed as % of submaximal voluntary contraction (during treadmill walking), are reported per muscle and reflex window. If not otherwise stated means, standard deviations (in brackets) and p-values are reported. *Kruskal-Wallis test; °Mann-Whitney-U test. Boldface p-values indicate statistically significant differences between subgroups (p<0.05). Dashes indicate not applicable. ACL = anterior cruciate ligament; ACL-R = anterior cruciate ligament reconstructed (=patients); ACL-C = anterior cruciate ligament rupture conservatively treated; ACL-I = anterior cruciate ligament intact (= healthy controls); BF = biceps femoris; involved = injured leg, respective matched leg of controls (based on side of injury); LLR = long latency response; MLR = medium latency response; PRE_50 = pre-activity; SLR = short latency response; ST = semitendinosus; VM = vastus medialis; VL = vastus lateralis*

Table A.5a: Tests of between-subjects effects by two-way parametric ANOVA (significant results for involved side)

Factor	Dependent variable	Typ III sum of squares	df	Means of squares	F	Sig.	Partial eta square
group	PO of BF during stair descent	15557.87	2	7778.93	9.191	< 0.0001	0.183
	PRE_50 of VM during reflex measurements	105944.80	2	52972.40	3.471	0.036	0.078
	PRE_50 of BF during reflex measurements	9052.15	2	4526.08	3.840	0.025	0.086
	MLR of ST during reflex measurements	1536569.94	2	768284.97	8.020	0.001	0.164
	LLR of VM for reflex measurements	339665.53	2	169832.76	2.104	0.129	0.049
sex	PO of BF during stair descent	1010.30	1	1010.30	1.194	0.278	0.014
	PRE_50 of VM during reflex measurements	97430.24	1	97430.24	6.385	0.013	0.072
	PRE_50 of BF during reflex measurements	326.36	1	326.36	0.277	0.600	0.003
	MLR of ST during reflex measurements	17664.55	1	17664.55	0.184	0.669	0.002
	LLR of VM for reflex measurements	5858.91	1	5858.91	0.073	0.788	0.001
group * sex	PO of BF during stair descent	1911.09	2	955.55	1.129	0.328	0.027
	PRE_50 of VM during reflex measurements	54267.71	2	27133.85	1.778	0.175	0.042
	PRE_50 of BF during reflex measurements	4727.81	2	2363.91	2.006	0.141	0.047
	MLR of ST during reflex measurements	20500.00	2	10250.00	0.107	0.899	0.003
	LLR of VM for reflex measurements	32076.96	2	16038.48	0.199	0.820	0.005

Legend: BF = biceps femoris; df = degrees of freedom; F = F-value; involved side = injured leg, respective matched leg of controls (based on side of injury); LLR = long latency response; MLR = medium latency; PO = push-off; PRE_50 = pre-activation (-50-0 ms background activity); Sig. = significance (p-value); ST = semitendinosus; VM = vastus medialis

Table A.5b: Stair descent: Neuromuscular activity for females and males per group, including values for calculation of effect sizes (for significant results)

Stair descent, push-off, involved/matched side																				
Muscle	Group						p-values							Effect size (Z-value) *N*=						
	ACL-R		ACL-C		ACL-I = Control															
	females	males	females	males	females	males	overall*	[1]vs[3]°	[1]vs[5]°	[3]vs[5]°	[2]vs[4]°	[2]vs[6]°	[4]vs[6]°	[1]vs[3]°	[1]vs[5]°	[3]vs[5]°	[2]vs[4]°	[2]vs[6]°	[4]vs[6]°
	[1]	[2]	[3]	[4]	[5]	[6]														
BF	49.0 (17.2)	48.4 (19.7)	57.6 (26.9)	37.9 (18.2)	76.0 (36.9)	82.1 (48.3)	**0.001**	0.777	0.055	0.131	0.218	**0.009**	**0.007**	--	--	--	--	0.43 (-2.621) *N=37*	0.52 (-2.711) *N=27*

*Legend: Normalized root mean square (RMS) values, expressed as % of submaximal voluntary contraction (during treadmill walking), are reported per muscle and movement phase during stair descent. If not otherwise stated means, standard deviations (in brackets) and p-values are reported. *Kruskal-Wallis test; °Mann-Whitney-U test. Boldface p-values indicate statistically significant differences between subgroups (p<0.05). Dashes indicate not applicable. ACL = anterior cruciate ligament; ACL-R = anterior cruciate ligament reconstructed (=patients); ACL-C = anterior cruciate ligament rupture conservatively treated; ACL-I = anterior cruciate ligament intact (= healthy controls); BF = biceps femoris; involved = injured leg, respective matched leg of controls (based on side of injury); N= number of ; RMS = root mean square; SD = standard deviation*

Table A.5c: Reflex activity: Neuromuscular activity for females and males per group, including values for calculation of effect sizes (for significant results)

Muscle	ACL-R females [1]	ACL-R males [2]	ACL-C females [3]	ACL-C males [4]	ACL-I = Control females [5]	ACL-I = Control males [6]	p overall*	p [1]vs[3]°	p [1]vs[5]°	p [3]vs[5]°	p [2]vs[4]°	p [2]vs[6]°	p [4]vs[6]°	ES [1]vs[3]°	ES [1]vs[5]°	ES [3]vs[5]°	ES [2]vs[4]°	ES [2]vs[6]°	ES [4]vs[6]°
Reflex activity, pre-activation 50ms (PRE_50), involved/matched side																			
VM	243.6 (288.3)	127.7 (57.1)	111.2 (39.1)	85.1 (28.2)	153.0 (66.7)	125.3 (66.5)	**0.013**	**0.018**	0.466	**0.034**	**0.025**	0.599	0.164	0.43 (-2,370) *N=30*	--	0.36 (-2,119) *N=35*	0.41 (-2.244) *N=30*	--	--
BF	56.8 (52.5)	41.1 (22.4)	43.3 (28.1)	40.4 (28.3)	53.9 (39.0)	79.1 (40.6)	**0.035**	0.827	0.636	0.435	0.860	**0.003**	**0.019**	--	--	--	--	0.48 (-2,953) *N=38*	0.44 (-2,349) *N=28*
Reflex activity, medium latency response (MLR), involved/matched side																			
ST	180.3 (120.5)	208.8 (213.7)	216.9 (143.6)	208.4 (87.3)	500.3 (499.4)	418.1 (408.9)	**0.011**	0.475	**0.015**	0.042	0.312	0.161	0.422	--	0.43 (-2,436) *N=32*	--	--	--	--
Reflex activity, long latency response (LLR), involved/matched side																			
VM	435.1 (368.1)	387.5 (553.5)	212.3 (145.0)	233.7 (166.9)	238.3 (139.7)	186.9 (142.6)	**0.034**	**0.015**	**0.049**	0.591	0.538	0.075	0.388	0.45 (-2,444) *N=29*	0.34 (-1,967) *N=33*	--	--	--	--

*Legend: Normalized root mean square (RMS) values, expressed as % of submaximal voluntary contraction (during treadmill walking), are reported per muscle and reflex window. If not otherwise stated means, standard deviations (in brackets) and p-values are reported. *Kruskal-Wallis test; °Mann-Whitney-U test. Boldface p-values indicate statistically significant differences between subgroups (p<0.05). Dashes indicate not applicable. ACL = anterior cruciate ligament; ACL-R = anterior cruciate ligament reconstructed (=patients); ACL-C = anterior cruciate ligament rupture conservatively treated; ACL-I = anterior cruciate ligament intact (= healthy controls); BF = biceps femoris; involved = injured leg, respective matched leg of controls (based on side of injury); LLR = long latency response; MLR = medium latency response; PRE_50 = pre-activity; ST = semitendinosus; VM = vastus medialis*

References

1. Risberg, M. A., Mork, M., Jenssen, H. K. & Holm, I. Design and implementation of a neuromuscular training program following anterior cruciate ligament reconstruction. *J Orthop Sports Phys Ther* 31, 620-631, doi:10.2519/jospt.2001.31.11.620 (2001).

2. Blasimann, A., Koenig, I., Baert, I., Baur, H. & Vissers, D. Which assessments are used to analyze neuromuscular control by electromyography after an anterior cruciate ligament injury to determine readiness to return to sports? A systematic review. *BMC Sports Sci Med Rehabil* 13, 142, doi:10.1186/s13102-021-00370-5 (2021).

3. Grooms, D. R. et al. Neuroplasticity Associated With Anterior Cruciate Ligament Reconstruction. *J Orthop Sports Phys Ther* 47, 180-189, doi:10.2519/jospt.2017.7003 (2017a).

4. Ward, S. et al. Neuromuscular deficits after peripheral joint injury: a neurophysiological hypothesis. *Muscle Nerve* 51, 327-332, doi:10.1002/mus.24463 (2015).

5. Schutte, M. J., Dabezies, E. J., Zimny, M. L. & Happel, L. T. Neural anatomy of the human anterior cruciate ligament. *J Bone Joint Surg Am* 69, 243-247 (1987).

6. Zimny, M. L., Schutte, M. & Dabezies, E. Mechanoreceptors in the human anterior cruciate ligament. Anat Rec 214, 204-209, doi:10.1002/ar.1092140216 (1986).

7. Frobell, R. B., Roos, E. M., Roos, H. P., Ranstam, J. & Lohmander, L. S. A randomized trial of treatment for acute anterior cruciate ligament tears. *N Engl J Med* 363, 331-342, doi:10.1056/NEJMoa0907797 (2010).

8. Frobell, R. B. et al. Treatment for acute anterior cruciate ligament tear: five year outcome of randomised trial. *BMJ* 346, f232, doi:10.1136/bmj.f232 (2013).

9. Blasimann, A. et al. Acute anterior cruciate ligament injury: neuromuscular control during stair descent and artificial tibia translation. *Orthop J Sports Med*, doi:https://doi.org/10.1177/23259671221123299 (2022).

10. Busch, A., Blasimann, A., Henle, P. & Baur, H. Neuromuscular activity during stair descent in ACL reconstructed patients: A pilot study. *Knee* 26, 310-316, doi:10.1016/j.knee.2018.12.011 (2019).

11. Hall, M., Stevermer, C. A. & Gillette, J. C. Muscle activity amplitudes and co-contraction during stair ambulation following anterior cruciate ligament reconstruction. *Journal of electromyography and kinesiology : official journal of the International Society of Electrophysiological Kinesiology* 25, 298-304, doi:10.1016/j.jelekin.2015.01.007 (2015).

12. Smeets, A. et al. Athletes with an ACL reconstruction show a different neuromuscular response to environmental challenges compared to uninjured athletes. *Gait Posture* 83, 44-51, doi:10.1016/j.gaitpost.2020.09.032 (2021).

13. Smeets, A. et al. Neuromuscular and biomechanical landing alterations persist in athletes returning to sport after anterior cruciate ligament reconstruction. *Knee* 33, 305-317, doi:10.1016/j.knee.2021.10.020 (2021).

14. Shanbehzadeh, S., Mohseni Bandpei, M. A. & Ehsani, F. Knee muscle activity during gait in patients with anterior cruciate ligament injury: a systematic review of electromyographic studies. *Knee Surg Sports Traumatol Arthrosc* 25, 1432-1442, doi:10.1007/s00167-015-3925-9 (2017).

15. Rudolph, K. S. & Snyder-Mackler, L. Effect of dynamic stability on a step task in ACL deficient individuals. *Journal of electromyography and kinesiology* 14, 565-575 (2004).

16. Rudolph, K. S., Axe, M. J., Buchanan, T. S., Scholz, J. P. & Snyder-Mackler, L. Dynamic stability in the anterior cruciate ligament deficient knee. *Knee Surg Sports Traumatol Arthrosc* 9, 62-71 (2001).

17. Meredith, S. J. et al. Return to Sport After Anterior Cruciate Ligament Injury: Panther Symposium ACL Injury Return to Sport Consensus Group. *Orthop J Sports Med* 8, 2325967120930829, doi:10.1177/2325967120930829 (2020).

18. Wellsandt, E., Failla, M. J. & Snyder-Mackler, L. Limb Symmetry Indexes Can Overestimate Knee Function After Anterior Cruciate Ligament Injury. *J Orthop Sports Phys Ther* 47, 334-338, doi:10.2519/jospt.2017.7285 (2017).

19. Wilk, K. E. & Arrigo, C. A. Rehabilitation Principles of the Anterior Cruciate Ligament Reconstructed Knee: Twelve Steps for Successful Progression and Return to Play. *Clin Sports Med* 36, 189-232, doi:10.1016/j.csm.2016.08.012 (2017).

20. Ardern, C. L. et al. 2016 Consensus statement on return to sport from the First World Congress in Sports Physical Therapy, Bern. *Br J Sports Med* 50, 853-864, doi:10.1136/bjsports-2016-096278 (2016).

21. Buckthorpe, M. Optimising the Late-Stage Rehabilitation and Return-to-Sport Training and Testing Process After ACL Reconstruction. *Sports medicine* (Auckland, N.Z.) 49, 1043-1058, doi:10.1007/s40279-019-01102-z (2019).

22. Dingenen, B. & Gokeler, A. Optimization of the Return-to-Sport Paradigm After Anterior Cruciate Ligament Reconstruction: A Critical Step Back to Move Forward. *Sports medicine* (Auckland, N.Z.) 47, 1487-1500, doi:10.1007/s40279-017-0674-6 (2017).

23. Deehan, D. J., Salmon, L. J., Webb, V. J., Davies, A. & Pinczewski, L. A. Endoscopic reconstruction of the anterior cruciate ligament with an ipsilateral patellar tendon autograft. A prospective longitudinal five-year study. *J Bone Joint Surg Br* 82, 984-991, doi:10.1302/0301-620x.82b7.10573 (2000).

24. Hui, C. et al. Fifteen-year outcome of endoscopic anterior cruciate ligament reconstruction with patellar tendon autograft for „isolated“ anterior cruciate ligament tear. *Am J Sports Med* 39, 89-98, doi:10.1177/0363546510379975 (2011).

25. Pinczewski, L. A. et al. A 10-year comparison of anterior cruciate ligament reconstructions with hamstring tendon and patellar tendon autograft: a controlled, prospective trial. *Am J Sports Med* 35, 564-574, doi:10.1177/0363546506296042 (2007).

26. Gokeler, A., Dingenen, B. & Hewett, T. E. Rehabilitation and Return to Sport Testing After Anterior Cruciate Ligament Reconstruction: Where Are We in 2022? *Arthrosc Sports Med Rehabil* 4, e77-e82, doi:10.1016/j.asmr.2021.10.025 (2022).

27. Busch, A., Henle, P., Boesch, L., Blasimann, A. & Baur, H. Neuromuscular control in patients with acute ACL injury during stair ascent – A pilot study. *Sports Orthopaedics and Traumatology* 35, 158-165, doi:10.1016/j.orthtr.2019.04.002 (2019).

28. Hall, M., Stevermer, C. A. & Gillette, J. C. Gait analysis post anterior cruciate ligament reconstruction: knee osteoarthritis perspective. *Gait Posture* 36, 56-60, doi:10.1016/j.gaitpost.2012.01.003 (2012).

29. Steiner, M., Baur, H. & Blasimann, A. Sex-specific differences in neuromuscular activation of the knee stabilizing muscles in adults - a systematic review. *Arch Physiother* 13, 4, doi:10.1186/s40945-022-00158-x (2023).

30. Faul, F., Erdfelder, E., Buchner, A. & Lang, A. G. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. *Behav Res Methods* 41, 1149-1160, doi:10.3758/BRM.41.4.1149 (2009).

31. Booth, F. W. & Lees, S. J. Physically active subjects should be the control group. *Med Sci Sports Exerc* 38, 405-406, doi:10.1249/01.mss.0000205117.11882.65 (2006).

32. Pollock, M. L. et al. ACSM Position Stand: The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. *Med Sci Sports Exerc* 30, 975-991 (1998).

33. Tegner, Y. & Lysholm, J. Rating systems in the evaluation of knee ligament injuries. *Clin Orthop Relat Res*, 43-49 (1985).

34. Roos, E. M. & Lohmander, L. S. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes* 1, 64, doi:10.1186/1477-7525-1-64 (2003).

35. Hermens, H. J., Freriks, B., Disselhorst-Klug, C. & Rau, G. Development of recommendations for SEMG sensors and sensor placement procedures. Journal of electromyography and kinesiology : *official journal of the International Society of Electrophysiological Kinesiology* 10, 361-374, doi:10.1016/s1050-6411(00)00027-4 (2000).

36. Scott, J. & Huskisson, E. C. Graphic representation of pain. *Pain* 2, 175-184, doi:10.1016/0304-3959(76)90113-5 (1976).

37. Baur, H., Hirschmuller, A., Cassel, M., Muller, S. & Mayer, F. Gender-specific neuromuscular activity of the M. peroneus longus in healthy runners - A descriptive laboratory study. *Clin Biomech* (Bristol, Avon) 25, 938-943, doi:10.1016/j.clinbiomech.2010.06.009 (2010).

38. Baur, H. et al. Comparison in lower leg neuromuscular activity between runners with unilateral mid-portion Achilles tendinopathy and healthy individuals. Journal of electromyography and kinesiology : *official journal of the International Society of Electrophysiological Kinesiology* 21, 499-505, doi:10.1016/j.jelekin.2010.11.010 (2011).

39. Leitner, M., Schmid, S., Hilfiker, R. & Radlinger, L. Test-retest reliability of vertical ground reaction forces during stair climbing in the elderly population. *Gait Posture* 34, 421-425, doi:10.1016/j.gaitpost.2011.06.014 (2011).

40. Bruhn, S., Leukel, C. & Gollhofer, A. Differential effects of stimulus characteristics during knee joint perturbation on hamstring and quadriceps reflex responses. *Human movement science* 30, 1079-1091, doi:10.1016/j.humov.2011.07.015 (2011).

41. Behrens, M., Mau-Moeller, A., Wassermann, F. & Bruhn, S. Effect of fatigue on hamstring reflex responses and posterior-anterior tibial translation in men and women. *PLoS One* 8, e56988, doi:10.1371/journal.pone.0056988 (2013).

42. Behrens, M. et al. Repetitive jumping and sprinting until exhaustion alters hamstring reflex responses and tibial translation in males and females. *J Orthop Res* 33, 1687-1692, doi:10.1002/jor.22935 (2015).

43. Haas, G., Diener, H. C., Bacher, M. & Dichgans, J. Development of postural control in children: short-, medium-, and long latency EMG responses of leg muscles after perturbation of stance. *Experimental brain research* 64, 127-132, doi:10.1007/BF00238208 (1986).

44. Leukel, C. et al. Short-term pressure induced suppression of the short-latency response: a new methodology for investigating stretch reflexes. *J Appl Physiol* (1985) 107, 1051-1058, doi:10.1152/japplphysiol.00301.2009 (2009).

45. Kirkwood, B. R. & Sterne, J. A. C. *Essential medical statistics*. 2nd edn, 83-85 (Blackwell Publishing, 2006).

46. Cohen, *J. Statistical Power Analysis for the Behavioral Sciences*. 2 edn, (Lawrence Erlbaum Associates, 1988).

47. Gokeler, A., Neuhaus, D., Benjaminse, A., Grooms, D. R. & Baumeister, J. Principles of Motor Learning to Support Neuroplasticity After ACL Injury: Implications for Optimizing Performance and Reducing Risk of Second ACL Injury. *Sports medicine* (Auckland, N.Z.) 49, 853-865, doi:10.1007/s40279-019-01058-0 (2019).

48. Kapreli, E. et al. Anterior cruciate ligament deficiency causes brain plasticity: a functional MRI study. *Am J Sports Med* 37, 2419-2426, doi:10.1177/0363546509343201 (2009).

49. Zarzycki, R., Morton, S. M., Charalambous, C. C., Marmon, A. & Snyder-Mackler, L. Corticospinal and intracortical excitability differ between athletes early after ACLR and matched controls. *J Orthop Res* 36, 2941-2948, doi:10.1002/jor.24062 (2018).

50. Luc-Harkey, B. A. et al. Greater intracortical inhibition associates with lower quadriceps voluntary activation in individuals with ACL reconstruction. *Experimental brain research* 235, 1129-1137, doi:10.1007/s00221-017-4877-8 (2017).

51. Melnyk, M., Faist, M., Gothner, M., Claes, L. & Friemert, B. Changes in stretch reflex excitability are related to „giving way" symptoms in patients with anterior cruciate ligament rupture. *J Neurophysiol* 97, 474-480, doi:10.1152/jn.00529.2006 (2007).

52. Del Bel, M. J. et al. A hierarchy in functional muscle roles at the knee is influenced by sex and anterior cruciate ligament deficiency. *Clin Biomech* (Bristol, Avon) 57, 129-136, doi:10.1016/j.clinbiomech.2018.06.014 (2018).

53. Huston, L. J. & Wojtys, E. M. Neuromuscular performance characteristics in elite female athletes. *Am J Sports Med* 24, 427-436, doi:10.1177/036354659602400405 (1996).

54. Shultz, S. J. et al. Neuromuscular Response Characteristics in Men and Women After Knee Perturbation in a Single-Leg, Weight-Bearing Stance. *J Athl Train* 36, 37-43 (2001).

55. Sigward, S. M. & Powers, C. M. The influence of gender on knee kinematics, kinetics and muscle activation patterns during side-step cutting. *Clin Biomech* (Bristol, Avon) 21, 41-48, doi:10.1016/j.clinbiomech.2005.08.001 (2006).

56. Urabe, Y. et al. Electromyographic analysis of the knee during jump landing in male and female athletes. *Knee* 12, 129-134, doi:10.1016/j.knee.2004.05.002 (2005).

57. White, K. K., Lee, S. S., Cutuk, A., Hargens, A. R. & Pedowitz, R. A. EMG power spectra of intercollegiate athletes and anterior cruciate ligament injury risk in females. *Med Sci Sports Exerc* 35, 371-376, doi:10.1249/01.MSS.0000053703.65057.31 (2003).

58. Chappell, J. D., Creighton, R. A., Giuliani, C., Yu, B. & Garrett, W. E. Kinematics and electromyography of landing preparation in vertical stop-jump: risks for noncontact anterior cruciate ligament injury. *Am J Sports Med* 35, 235-241, doi:10.1177/0363546506294077 (2007).

59. Hanson, A. M., Padua, D. A., Troy Blackburn, J., Prentice, W. E. & Hirth, C. J. Muscle activation during side-step cutting maneuvers in male and female soccer athletes. *J Athl Train* 43, 133-143, doi:10.4085/1062-6050-43.2.133 (2008).

60. Benjaminse, A., Gokeler, A., Fleisig, G. S., Sell, T. C. & Otten, B. What is the true evidence for gender-related differences during plant and cut maneuvers? A systematic review. *Knee Surg Sports Traumatol Arthrosc* 19, 42-54, doi:10.1007/s00167-010-1233-y (2011).

61. McFadyen, B. J. & Winter, D. A. An integrated biomechanical analysis of normal stair ascent and descent. *J Biomech* 21, 733-744, doi:10.1016/0021-9290(88)90282-5 (1988).

62. Kutzner, I. et al. Loading of the knee joint during activities of daily living measured in vivo in five subjects. *J Biomech* 43, 2164-2173, doi:10.1016/j.jbiomech.2010.03.046 (2010).

63. Vergis, A. & Gillquist, J. Sagittal Plane Translation of the Knee During Stair Walking. *The American Journal of Sports Medicine* 26, 841-846, doi:10.1177/03635465980260061801 (1998).

64. Luder, G. et al. Stair climbing - an insight and comparison between women with and without joint hypermobility: a descriptive study. Journal of electromyography and kinesiology : *official journal of the International Society of Electrophysiological Kinesiology* 25, 161-167, doi:10.1016/j.jelekin.2014.07.005 (2015).

65. Dai, B., Herman, D., Liu, H., Garrett, W. E. & Yu, B. Prevention of ACL Injury, Part I: Injury Characteristics, Risk Factors, and Loading Mechanism. *Research in Sports Medicine* 20, 180-197, doi:10.1080/15438627.2012.680990 (2012).

66. Quatman, C. E., Quatman-Yates, C. C. & Hewett, T. E. A ‚plane' explanation of anterior cruciate ligament injury mechanisms: a systematic review. *Sports medicine* (Auckland, N.Z.) 40, 729-746, doi:10.2165/11534950-000000000-00000 (2010).

67. Krosshaug, T. et al. Mechanisms of anterior cruciate ligament injury in basketball: video analysis of 39 cases. *Am J Sports Med* 35, 359-367, doi:10.1177/0363546506293899 (2007).

68. Boden, B. P., Dean, G. S., Feagin, J. A., Jr. & Garrett, W. E., Jr. Mechanisms of anterior cruciate ligament injury. *Orthopedics* 23, 573-578, doi:10.3928/0147-7447-20000601-15 (2000).

69. Shimokochi, Y. & Shultz, S. J. Mechanisms of noncontact anterior cruciate ligament injury. *J Athl Train* 43, 396-408, doi:10.4085/1062-6050-43.4.396 (2008).

70. Hughes, G. & Watkins, J. A risk-factor model for anterior cruciate ligament injury. *Sports medicine* (Auckland, N.Z.) 36, 411-428, doi:10.2165/00007256-200636050-00004 (2006).

71. Blackburn, J. T. & Padua, D. A. Sagittal-plane trunk position, landing forces, and quadriceps electromyographic activity. *J Athl Train* 44, 174-179, doi:10.4085/1062-6050-44.2.174 (2009).

72. Kulas, A. S., Hortobagyi, T. & Devita, P. The interaction of trunk-load and trunk-position adaptations on knee anterior shear and hamstrings muscle forces during landing. *J Athl Train* 45, 5-15, doi:10.4085/1062-6050-45.1.5 (2010).

73. Roos, P. E., Button, K., Sparkes, V. & van Deursen, R. W. Altered biomechanical strategies and medio-lateral control of the knee represent incomplete recovery of individuals with injury during single leg hop. *J Biomech* 47, 675-680, doi:10.1016/j.jbiomech.2013.11.046 (2014).

74. Myers, T. M. *Anatomy Trains. Myofascial Meridians for Manual Therapists and Movement Professionals*. . 4th edn, 360 (Elsevier, 2020).

75. Buckthorpe, M. Recommendations for Movement Re-training After ACL Reconstruction. *Sports medicine* (Auckland, N.Z.) 51, 1601-1618, doi:10.1007/s40279-021-01454-5 (2021).

76. Webster, K. E. & Feller, J. A. Exploring the High Reinjury Rate in Younger Patients Undergoing Anterior Cruciate Ligament Reconstruction. *Am J Sports Med* 44, 2827-2832, doi:10.1177/0363546516651845 (2016).

77. Blanca, M. J., Alarcon, R., Arnau, J., Bono, R. & Bendayan, R. Non-normal data: Is ANOVA still a valid option? *Psicothema* 29, 552-557, doi:10.7334/psicothema2016.383 (2017).

78. WMA. World Medical Association: Declaration of Helsinki – Ethical principles for medical research involving humans. https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/ (2018).

CHAPTER 6

STUDY 3B

Leg differences
1 year after ACL rupture

Neuromuscular control of both legs in
surgically and conservatively treated
patients one year after unilateral
ACL rupture.
A cross-sectional study

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Abstract

Background: Neuromuscular alterations are present in patients after anterior cruciate ligament (ACL) rupture or reconstruction, even in the long run. ACL rupture seems to affect neuromuscular control of the involved, injured leg but also of the non-involved limb. Therefore, this study aims at comparing neuromuscular control of both lower limbs in patients 1 year after reconstruction of the anterior cruciate ligament (ACL-R) or conservative treatment (ACL-C) to healthy controls with an intact ACL (ACL-I).
Methods: Electromyography of vastus medialis (VM) and lateralis (VL), biceps femoris (BF) and semitendinosus (ST) was recorded in ACL-R (N = 38), ACL-C (N = 26), and ACL-I (N = 38) during stair descent and artificially induced anterior tibial translation. Each step of stair descent was divided into pre-activity, weight-acceptance and push-off phase. Pre-activation, short, medium and long latency responses were defined for reflex activity. For each muscle and phase, normalized root mean squares were calculated ($\alpha = 0.05$).
Results: During stair descent, BF differed significantly comparing each patient group with ACL-I during push-off. Significant interlimb differences of the quadriceps were found in ACL-R in all phases, of BF in ACL-C during weight-acceptance and during pre-activity in ACL-I. Reflexes revealed significant differences in pre-activation for VM between ACL-R and ACL-C, between ACL-C and ACL-I and for BF between each patient group and ACL-I. Medium latency response of ST differed significantly between each of the patient groups and ACL-I. Long latency response of VM were significantly different in ACL-R versus ACL-C, and ACL-R versus ACL-I.
Conclusion: One year after unilateral ACL rupture, bilateral neuromuscular alterations are present regardless of treatment option. Current rehabilitation protocols do not seem to restore neuromuscular control to the level of healthy controls. Future research should include standardized rehabilitation programs with neuromuscular exercises to restore bilateral, normal function.

Keywords: Anterior Cruciate Ligament; Knee Injuries; Reconstruction; Conservative Treatment

Abstract

Objectives: To compare bilateral neuromuscular control in patients one year after anterior cruciate ligament reconstruction (ACL-R) or conservative treatment (ACL-C) to healthy controls (ACL-I).

Design: Cross-sectional study.

Setting: Electromyography of vastus medialis (VM) and lateralis (VL), biceps femoris (BF) and semitendinosus (ST) was recorded during stair descent and anterior tibial translation. Each step of stair descent was divided into pre-activity, weight-acceptance and push-off phase. Pre-activation, short, medium (MLR) and long latency responses (LLR) were defined for reflex activity.

Participants: N = 38 ACL-R, N = 26 ACL-C, N = 38 ACL-I

Main Outcome Measures: Normalized root mean squares per muscle and phase ($\alpha = 0.05$).

Results: During stair descent, within-group leg differences were found for the quadriceps in ACL-R during all phases and for the BF in ACL-C during weight-acceptance. Between-group leg differences were found for BF in both patient groups compared to ACL-I during push-off. Between-group differences in pre-activation for VM between ACL-R and ACL-C, and between ACL-C and ACL-I were found, and as LLR between patients and ACL-R versus ACL-I. Pre-activation of BF and MLR of ST differed for each patient group compared to ACL-I.

Conclusions: Bilateral neuromuscular alterations are still present one year after ACL rupture or reconstruction.

Keywords: Anterior Cruciate Ligament; Knee Injuries; Reconstruction; Conservative Treatment

Introduction

Ruptures of the anterior cruciate ligament (ACL) are multifactorial[1] and are mainly classified as non-contact injuries.[2] Most non-contact ACL ruptures happen shortly (17-50ms) after initial foot-ground contact within a time frame which is too short for adequate mechanosensory feedback (e.g., reflex response).[2]
Treatment of ACL ruptures can be surgically or conservatively, depending on patient's activity level, type of sports and occupation, former knee injuries etc.[3] At 2- and 5-year follow-up, no differences in patient-reported knee function and incidence of knee osteoarthritis between ACL patients with early reconstruction, conservative treatment followed by reconstruction or conservative treatment alone were found.[4] Nonetheless, this study was limited in reported functional outcomes and demands for further research.
Altered sensorimotor control and neuromuscular adaptations in patients after ACL reconstruction have been stated previously.[5] Deficits in voluntary activation with medium to large effect sizes and limited to moderate evidence as well as increased long-term spinal excitability with limited effect sizes and strong evidence have been summarized.[6] Neuromuscular alterations have been reported to be bilateral in various functional tasks.[7-9] However, these studies are limited to either reconstructed or conservatively treated patients with an ACL rupture and may vary greatly in their included measurement time points.
Therefore, the purpose of this cross-sectional study was to investigate the neuromuscular activity in the involved and non-involved leg of participants one year after surgical or conservative treatment of an ACL rupture compared to a healthy control group during stair descent and artificially induced anterior tibial translation. Based on literature, we hypothesized that altered neuromuscular control in form of lower activity of the quadriceps and of higher activity of the hamstrings is present in the involved as well as in the contralateral leg of patients after an ACL reconstruction (ACL-R) or conservative treatment (ACL-C) compared to healthy controls with an intact ACL (ACL-I).[8,9]

Methods

Study design, sample size calculation, and ethical considerations

A cross-sectional, experimental study design with two patient groups and a healthy asymptomatic control group was determined to investigate neuromuscular control one year after an ACL reconstruction or conservative treatment, rehabilitation alone, respectively. One group consisted of participants after an ACL reconstruction (ACL-R), one of participants with conservative treatment (ACL-C) after ACL rupture, and one of healthy controls with an intact ACL (ACL-I).

A priori sample size calculation based on own pilot data[7] revealed a sample size for independent comparisons of n = 10 participants per group ($\alpha = 0.05$, actual power: 0.96, effect size d: 1.78; G*Power, version 3.1, Heinrich-Heine University, Düsseldorf, Germany).[10]

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Canton of Bern (Switzerland), KEK No. 2017-02282. Every participant provided written informed consent.

Participants

Participants for the ACL-R and ACL-C group had been recruited via an orthopedic surgeon, private physiotherapy practices or sports clubs between January 2018 and August 2021. Healthy people for the control group (ACL-I) had been recruited from local sport clubs, and among members of the Bern University of Applied Sciences (Switzerland). Matching was based on sex, age, body height, body mass and dominant leg, defined as the preferred leg to kick a ball with. The following inclusion criteria were applicable for all participants: age between 16 and 60 years, physically active at least 2x/week for 45min, Tegner activity score of ≥ 5. From participants in the ACL-R or ACL-C group, magnetic resonance imaging was available, and time since rupture, reconstruction respectively, had to be between 11 and 14 months. Any type of ACL reconstruction was included. Exclusion criteria for all participants were former knee pathology, other injury of the lower extremity, back pain, musculo-skeletal disorders refraining from test protocol, cardiac, neurologic, or peripheral vascular disease, acute infection, alcohol abuse, current pain medication, thrombosis, pregnancy, dementia, and not being able to understand written or oral German.

In total, N = 185 people volunteered for this study and were assigned to 1 of the 3 groups, based on ACL status. Data from 38 subjects each for the ACL-R and ACL-I groups as well as 26 subjects for the ACL-C were included in the final analysis. Details regarding the recruitment process can be found in Figure A.1.

Measurements

All measurements took place at the Bern Movement Lab (Bern University of Applied Sciences, Bern, Switzerland) by using a formerly described setup.[7 11]

In brief, clinical examination, anthropometric data, limb dominance, type of sports, number of hours per week of physical activity, Tegner score[12] and Knee Osteoarthritis Outcome Score (KOOS)[13] were collected as described before.[11] The EMG electrodes were applied on the vastus medialis (VM), vastus lateralis (VL), semitendinosus (ST) and biceps femoris (BF) muscle on both limbs according to SENIAM preparation standards and guidelines[14] including a reference electrode placed on the right patella and inter-electrode impedance kept ≤ 2 kΩ. Before and after the measurements, the actual wellbeing and pain were assessed by using a visual analogue scale (VAS).[15]

The measurements started with a warm-up on an instrumented treadmill for 10 minutes at 1.39 m/s (5km/h) and additional 2 minutes treadmill-walking at the same speed with recordings of the EMG signals for submaximal EMG normalization.[11] Afterwards, each participant completed 2 experimental situations in the same order: stair descent and stretch reflex measurements.[11]

Stair descent

Participants descended a custom-made wooden stairway with six steps 10 times at self-selected speed without using the railings.[11] To identify gait cycles, the stairway had two embedded multicomponent force plates in the third and fourth step. Stair descent was divided into three movement cycles: The pre-activation phase (PRE) covered 150 ms prior to initial foot-floor contact until initial contact. The weight acceptance phase (WA) included initial contact to the lowest applied vertical ground reaction force. The push-off phase (PO), followed the WA phase until vertical ground reaction forces declined to zero.[11]

Stretch reflex measurements

To assess stretch reflexes, artificial anterior tibial translation was applied on both legs in randomized order. Starting position was standing upright with the hands placed at the pelvis, knees in 30° flexion and equal body mass distribution, controlled by bipedal stand on two force plates.[11] To be blinded to the time point of artificially induced tibial translation and avoid any acoustic anticipation, participants wore headphones with music and ear protection.

A rope and pulley system applied a standardized impulse to the tibia shank inducing an anterior tibial translation.[16] Onset of the applied force monitored by a force transducer was considered as trigger signal for the tibial translation.[16] Further details describing the setup can be found elsewhere.[11 16] Artificial tibial translation was elicited in two series with 15 repetitions per lower extremity. Between the series, the participants got a short break to minimize fatigue or excessive co-contraction. Four pre-defined time intervals were used as outcomes: -50-0 ms pre-activation (PRE_50), 20-40 ms short latency response (SLR), 40-60 ms medium latency response (MLR) and 60-95 ms long latency response (LLR).[11 17]

Statistical analysis

Data analysis was done by using the Statistical Package for the Social Science (SPSS) software (SPSS Statistics for Windows, version 28.0, IBM, Armonk NY, USA). The level of significance was set at 0.05. Participants' characteristics (anthropometric data, physical activity, KOOS, TAS) were tested for normal distribution by using Kolmogorov-Smirnov test, followed by non-parametric t-tests (Mann-Whitney-U and Kruskal-Wallis) to detect differences between the groups (ACL-R, ACL-C and ACL-I). To evaluate group differences of the neuromuscular activity, all EMG outcomes of each muscle (VM, VL, BF, ST) per phase during stair descent (PRE, WA, PO) and artificial tibial translation (PRE_50, SLR, MLR, LLR) were analyzed separated in the involved (reconstructed, conservatively treated, or matched knee based on side of injury) and the non-involved leg (contralateral knee) using Kruskal-Wallis tests since the requirements for a parametric procedure were not fulfilled (Shapiro Wilk and Levene test). For pair-wise post-hoc comparisons, the Mann-Whitney-U test for independent samples and for intra-individual leg comparison, the Wilcoxon test for dependent samples was carried out, including Dunn Bonferroni correction for multiple testing. Although not all data were normally distributed, mean values and standard deviations (SD) are reported to allow comparison with other studies.

Effect sizes (ES) were calculated based on Pearson's correlation.[18] An ES below 0.3 was interpreted as small effect, $0.3 \leq r < 0.5$ as medium effect, and equal 0.5 or higher as large effect.[19]

Results

Characteristics of participants

Patient groups had significantly higher weekly hours of physical activity ($p = 0.014$, 0.011 respectively) and activity level ($p = 0.001$, $p < 0.0001$ respectively) compared to the healthy controls (ACL-I). No other significant differences were found for anthropometric data (Table 1). Details on concomitant injuries, type of treatment and autograft for reconstruction (if applicable) are described in Table A.1.

*Table 1: Characteristics of 38 participants with an ACL reconstruction (ACL-R), 26 participants with a conservatively treated ACL rupture (ACL-C) and 38 healthy controls with an intact ACL (ACL-I), matched by sex, age, body height, body mass and leg dominance. Data are presented as mean ± standard deviation (SD) unless otherwise stated. * Indicates significant p-values (p<0.05); dashed lines indicate not applicable.*

	Mean ± SD if not otherwise stated			p-value			
Characteristics	**ACL-R N = 38**	**ACL-C N = 26**	**ACL-I N = 38**	**ACL-R vs. ACL-I**	**ACL-C vs. ACL-I**	**ACL-R vs. ACL-C**	**overall**
Age [years]	32.02 ± 12.21	38.38 ± 11.65	33.13 ± 9.16	0.391	0.099	0.031*	0.074
Body height [cm]	173.55 ± 6.25	170.23 ± 7.59	173.66 ± 6.96	0.831	0.033*	0.075	0.087
Body mass [kg]	71.71 ± 11.19	71.06 ± 14.88	68.38 ± 9.43	0.244	0.942	0.456	0.507
BMI [kg/m²]	23.94 ± 2.73	24.47 ± 4.64	22.64 ± 2.02	0.015*	0.305	0.305	0.056
Time since injury (months)	12.7 ± 1.4	12.5 ± 1.1	--	< 0.0001*	--	0.579	--
Sex: Ratio of ♀:♂ (%)	17:21 (44.7:55.3)	16:10 (61.5:38.5)	20:18 (52.6:47.4)	0.494	0.848	0.190	0.419
Leg dominance (right:left)	35:3	23:3	34:4	0.694	0.899	0.626	0.876
Prehabilitation (yes:no)	13:25	--	--	< 0.0001*	--	< 0.0001*	--
PT after surgery/injury (yes:no)	38:0	26:0	--	< 0.0001*	--	< 0.0001*	--
Physical activity [min/week]	425.96 ± 265.10	373.02 ± 158.18	293.26 ± 182.81	0.014*	0.011	0.811	0.014*
Tegner score (max. 10 points)	6.71 ± 1.45	6.96 ± 1.18	5.53 ± 1.31	0.001*	< 0.0001*	0.273	< 0.0001*
KOOS subscale (absolute values)							
pain (9 items, max. 36 p.)	4.47 ± 3.32	3.35 ± 2.99	0.37 ± 0.71	< 0.0001*	< 0.0001*	0.119	< 0.0001*
other symptoms (7 items, max. 28 p.)	5.95 ± 3.80	5.08 ± 3.12	1.58 ± 1.52	< 0.0001*	< 0.0001*	0.532	< 0.0001*
ADL (17 items, max. 68 p.)	2.50 ± 3.42	2.23 ± 4.03	0.08 ± 0.36	< 0.0001*	< 0.0001*	0.380	< 0.0001*
sports & leisure (5 items, max. 20 p.)	3.63 ± 2.88	2.69 ± 2.77	0.21 ± 0.70	< 0.0001*	< 0.0001*	0.151	< 0.0001*
HRQoL (4 items, max. 16 p.)	4.73 ± 3.29	3.81 ± 2.90	0.37 ± 1.00	< 0.0001*	< 0.0001*	0.259	< 0.0001*
VAS							
wellbeing pre [mm]	5.53 ± 8.60	5.35 ± 10.31	5.29 ± 6.90	0.643	0.666	0.972	0.870
wellbeing post [mm]	7.29 ± 9.00	5.58 ± 9.91	6.55 ± 7.39	0.937	0.355	0.402	0.612
pain pre [mm]	3.08 ± 4.08	4.35 ± 8.89	1.08 ± 2.06	0.026*	0.037*	0.977	0.045*
pain post [mm]	6.18 ± 13.25	6.42 ± 10.57	3.42 ± 7.88	0.264	0.082	0.486	0.209

*Abbreviations: ACL-C = anterior cruciate ligament rupture conservatively treated; ACL-I = anterior cruciate ligament intact (= healthy controls); ACL-R = anterior cruciate ligament reconstructed (=patients); ADL = activity of daily life; HRQoL = health-related quality of life; KOOS = Knee injury and Osteoarthritis Outcome Score; max. = maximum; post = after the measurements; pre = before the measurements started; PT = physiotherapy; *Tegner activity score (preinjury) ranging from 0 (sick leave or disability pension) to 10 (competitive sport on a professional level); VAS = visual analogue scale from 0 to 100mm*

Stair descent

Figur 1 provides box plots for all four muscles and all three phases during stair descent, presented separately for legs and groups. Significant results of involved and non-involved leg comparison between a nd within groups are summarized below and all mean and SD values as well as results of inferential statistics are presented in the Table A.2.

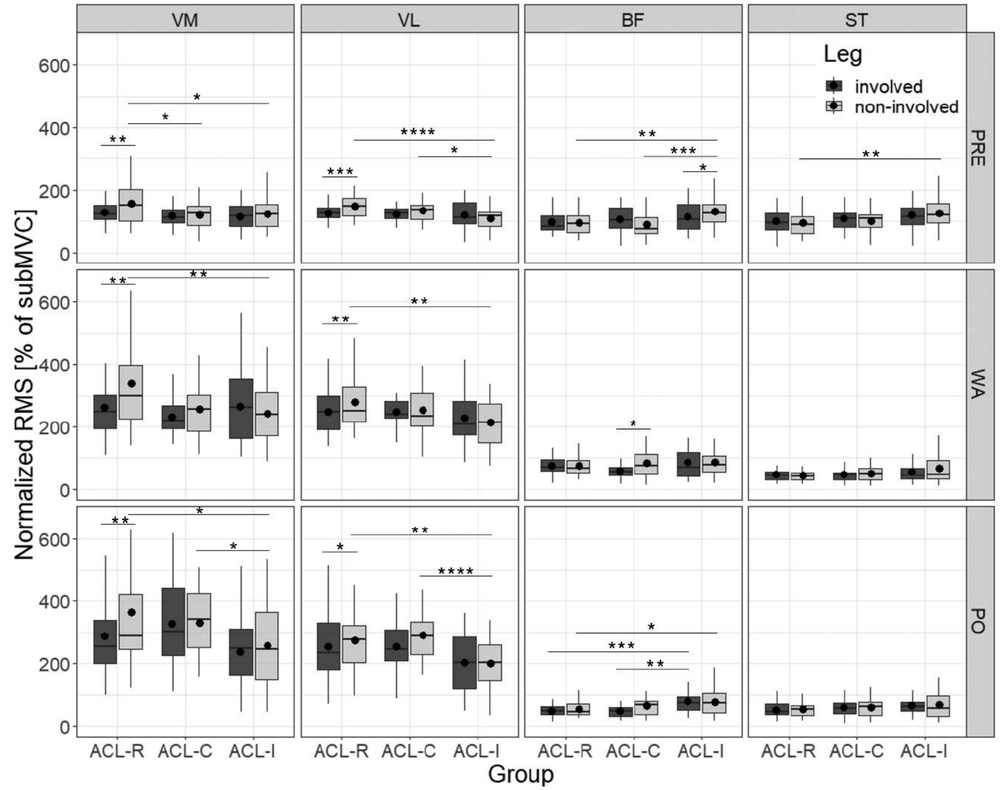

Figure 1: Stair descent: Box plots of all four muscles of the involved and non-involved leg for pre-activity, weight-acceptance and push-off phase (from top to bottom)

*Legend (Fig.1): Results are presented for all three phases of stair descent as median and interquartile ranges including mean value expressed as black dot; *p<0.05; **p<0.01; ***p<0.001; ****p<0.0001; ACL = anterior cruciate ligament; ACL-C = group with conservative treatment after ACL rupture; ACL-I = healthy controls with intact ACL; ACL-R = group with ACL reconstruction; BF = biceps femoris; CI = confidence interval; involved = formerly injured or reconstructed side, respective matched leg of controls (based on side of injury); PRE = pre-activity; PO = push-off phase during stair descent; RMS = root mean square values; ST = semitendinosus; subMVC = submaximal voluntary contraction (normalized values with treadmill walking = 100% subMVC); VM = vastus medialis; VL = vastus lateralis; WA = weight-acceptance phase*

Leg comparisons within groups

Intragroup comparisons revealed that neuromuscular activity of the involved compared to non-involved leg of ACL-R was significantly lower for the quadriceps in all three movement phases: during PRE (for VM: Δ-18.7%, ES 0.34, p = 0.004; for VL: Δ-15.8%, ES 0.37, p = 0.001), WA (for VM: Δ-22.7%, ES 0.34, p = 0.004; for VL: Δ-11.2%, ES 0.35, p = 0.003) and PO (for VM: Δ-20.8%, ES 0.31, p = 0.008; for VL: Δ-7.9%, ES 0.28, p = 0.018).

The involved leg of ACL-C group demonstrated significantly lower activities in BF during WA only compared to the contralateral leg (Δ-32.2%, ES 0.34, p = 0.015).

Significant leg differences of the healthy controls were present in the BF during PRE only (Δ-13.1%, ES 0.29, p = 0.014).

Leg comparisons between groups

For intergroup comparisons, the following results were found: Post-hoc analysis comparing neuromuscular activity revealed significant differences for ACL-R compared to ACL-I in the non-involved leg for both quadriceps and hamstrings for PRE phase: for VM (Δ+29.1%, ES 0.30, p = 0.011), VL (Δ+38.2%, ES 0.47, p < 0.0001), BF (Δ-26.7%, ES 0.36, p = 0.002) and ST (Δ-23.7%, ES 0.32, p = 0.007). During WA phase, significantly higher activities in the quadriceps were present in the non-involved leg comparing ACL-R to ACL-I: for VM (Δ+40.1%, ES 0.31, p = 0.008), and for VL (Δ+30.4%, ES 0.31, p = 0.007). During PO phase, significantly higher neuromuscular activity in ACL-R was found in the non-involved leg for the VM (Δ+41.6%, ES 0.27, p = 0.019) and VL (Δ+37.1%, ES 0.36, p = 0.002), and decreased neuromuscular activity in ACL-R for BF in both legs (involved: Δ-38.4%, ES 0.39, p = 0.001; non-involved: Δ-29.5%, ES 0.29, p = 0.014) compared to ACL-I.

Post-hoc analysis in the non-involved leg revealed significantly higher activities for VL (Δ+21.1%, ES 0.31, p = 0.016) in ACL-C and significantly lower for BF (Δ-32.5%, ES 0.42, p = 0.001) for ACL-C compared to ACL-I during PRE. During PO, significantly higher activities were present for VM (Δ+28.5%, ES 0.26, p = 0.040) and VL (Δ+45.4%, ES 0.48, p < 0.0001) in the ACL-C group. In the involved leg, significantly lower neuromuscular activity in ACL-C compared to ACL-I was found for BF (Δ-37%, ES 0.37, p = 0.004).

Post-hoc analysis comparing both former patient groups (ACL-R versus ACL-C) revealed significantly higher neuromuscular activity in VM of the non-involved limb (Δ+31.1%, ES 0.27, p = 0.030) during PRE for ACL-R compared to ACL-C.

Artificial tibial translation

Figure 2 provides box plots for all four muscles and all four phases during artificial tibial translation, presented separately for legs and groups. Significant results of involved and non-involved leg comparison between and within groups are summarized below and all mean and SD values as well as results of inferential statistics are presented in the Table A.3.

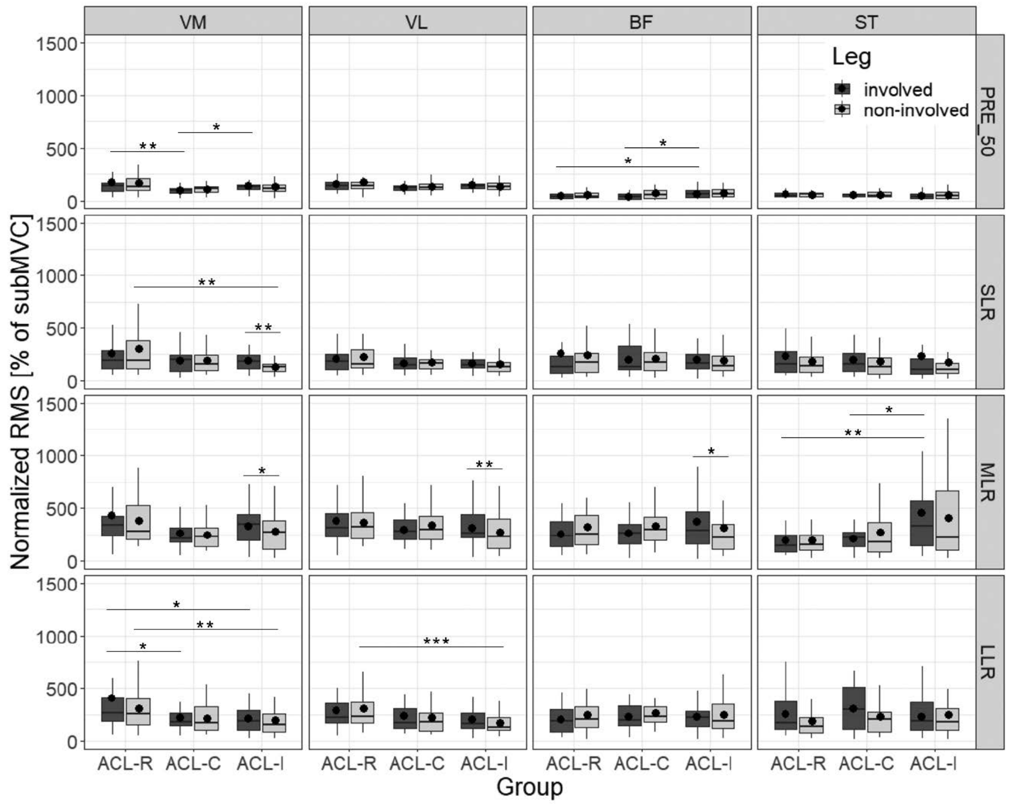

Figure 2: Reflex measurements: Box plots of all four muscles of the involved and non-involved for pre-activation, short, medium, and long latency response during artificial tibia translation (from top to bottom)

*Legend (Fig.2): Results are presented for all four phases of reflex measurements as median and interquartile ranges including mean value expressed as black dot; *p<0.05; **p<0.01; ***p<0.001; ****p<0.0001; ACL = anterior cruciate ligament; ACL-C = group with conservative treatment after ACL rupture; ACL-I = healthy controls with intact ACL; ACL-R = group with ACL reconstruction; BF = biceps femoris; CI = confidence interval; involved = formerly injured or reconstructed side, respective matched leg of controls (based on side of injury); LLR = long latency response; MLR = medium latency response; PRE_50 = pre-activation (background activity); RMS = root mean square values; ST = semitendinosus; subMVC = submaximal voluntary contraction (normalized values with treadmill walking = 100% subMVC); VM = vastus medialis; VL = vastus lateralis; WA = weight-acceptance phase*

Leg comparisons within groups

In both former patient groups, no significant within-group leg differences were found for any of the investigated muscles and time windows during artificial tibial translation. However, in the group of healthy controls (ACL-I), neuromuscular activity was significantly higher in the matched "involved" leg, based on side of injury, compared to the contralateral leg in two phases: during SLR for VM (Δ+39%, ES 0.34, p = 0.004) and during MLR for VM (Δ+19.1%, ES 0.25, p = 0.033), VL (Δ+15.7%, ES 0.31, p = 0.008) and BF (Δ+18.7%, ES 0.23, p = 0.044).

Leg comparisons between groups

Post-hoc analysis for intergroup comparisons revealed significant lower pre-activation in the involved leg of ACL-R compared to ACL-I for BF (Δ-28.1%, ES 0.25, p = 0.035). During SLR, significantly higher activity was found for VM of the non-involved limb of ACL-R (Δ+119.2%, ES 0.34, p = 0.04). During MLR, ST of the involved leg showed significantly less activity in ACL-R subjects (Δ-57.2%, ES 0.33, p = 0.007). During LLR, VM of both the involved (Δ+90.9%, ES 0.28, p = 0.021) and the non-involved leg (Δ+58.5%, ES 0.31, p = 0.008), and VL of the non-involved leg (Δ+83.1%, ES 0.38, p = 0.001) presented significantly higher neuromuscular activation in ACL-R compared to ACL-I.

Significantly lower pre-activation in the involved leg for VM (Δ-27.5%, ES 0.31, p = 0.013) and BF (Δ-36.2%, ES 0.29, p = 0.022) as well as during MLR for ST (Δ-53.7%, ES 0.27, p = 0.037) was present in the ACL-C compared to ACL-I.

Post-hoc analysis comparing both former patient groups revealed significantly higher neuromuscular pre-activation for VM of the involved limb (Δ+73.5%, ES 0.35, p = 0.007) and higher neuromuscular activation during LLR (Δ+84.4%, ES 0.28, p = 0.034) in patients after ACL reconstruction.

Discussion

This cross-sectional study compared bilateral neuromuscular activity in patients one year after an ACL rupture with surgical reconstruction or conservative treatment in comparison to a healthy control group during stair descent and an artificially induced anterior tibial translation. One year after an ACL rupture, neuromuscular alterations were still present in both legs of ACL patients, regardless of treatment option.

Reported results are in line with former research [7 11] representing a large range of EMG activity patterns within and between groups in the investigated time-frames and movement phases.

The hypothesis that neuromuscular control would be altered – lower quadriceps and higher hamstrings activity during voluntary activation – in the involved and non-involved leg even one year after an ACL reconstruction in comparison to healthy controls with an intact ACL had been partially confirmed. This altered muscle activity strategy has been described as arthrogenic muscle response meaning a natural mechanism of reflex inhibition and/or muscular facilitation to stabilize and therefore protect the injured joint.[20] In patients with an ACL injury, arthrogenic muscle response might be due to a loss of mechanoreceptors by the ruptured ACL and altered discharge of sensory receptors induced by inflammatory signs and joint laxity.[20] This arthrogenic muscle response with decrease of the quadriceps activity (as ACL antagonist) and increased excitability of the hamstrings (as ACL agonists) reduces potentially dangerous movements for the injured knee joint as it has been shown in ACL-R patients.[21] In the acute phase after ACL rupture or reconstruction, the combination of both low quadriceps and high hamstrings activation in the involved leg compared to the matched leg of the healthy control group could be advantageous as this strategy improves dynamic stability of the knee joint.[22] However, if this altered muscle strategy persists, it might negatively influence joint biomechanics and articular cartilage loading, potentially leading to post-traumatic knee osteoarthritis.[8 22]

During stair descent, both legs showed significant less neuromuscular activity of BF during PO. Opposite to our results, athletes after ACL-R (mean time post-surgery 8.5 months) demonstrated lower activity levels of the VM and larger hamstrings activation during a step-down task.[9] However, these participants had ST autografts while participants from our study mainly had quadriceps autografts, and EMG signals were analysed in one time interval after step down landings (50ms to 250ms after initial contact). In the present study, significant differences were found mainly during pre-activity and in PO phase, where adequate neuromuscular control by the quadriceps is essential to eccentrically decelerate the body weight in knee flexion. It is known that ACL injury may negatively influence intracortical facilitation[23] leading to larger intracortical inhibition which is correlated with decreased capability to voluntarily activate the quadriceps.[24] However, it remains unclear if this strategy with upregulation of the quadriceps and lower activation of the hamstrings has more beneficial long-term effects as the stress on the ACL in posterior-anterior direction could be increased due to the impaired protective effect by lower hamstrings activation.

Significant interlimb differences during stair descent in ACL-R participants were found, demonstrating decreased activity of the quadriceps in the involved limb compared to the non-involved limb in all examined phases. This may be explained by the artificial injury due to graft harvesting, especially autografts with quadriceps tendon, which must also be compensated accordingly.[25] In our study, two thirds of all patients of the ACL-R group got a quadriceps tendon autograft. Differences between graft types and reconstructive techniques should be investigated to give specific recommendations for individualized rehabilitation.[25] However, further comparisons of graft types were out of the scope of the present study.

Alterations in neuromuscular activity have been found during artificial tibial translation, as well. From a physiological point of view, the MLR is most relevant as it has been recognized as the most vulnerable phase due to the homonymous interconnection of cruciate ligament receptors and hamstring muscles.[16] This means that the hamstrings need to be specifically targeted during rehabilitation to be sufficiently activated before and during dynamic activities.

Participants after conservative treatment (ACL-C) showed altered neuromuscular control in both legs in both tasks, but not for all muscles and phases. Overall, neuromuscular control in those participants differed less from healthy controls than those of ACL-R participants. Present findings were in line with changes in neuromuscular control of males with an ACL deficiency (mean time since injury 19.8 months) compared to healthy controls during landings from a 30cm height.[26] The authors reported a reduction in lateral hamstrings activation of the affected leg compared to the matched limb of healthy individuals at SLR.[26] Post-landing EMG of VL was reduced in the involved and non-involved side of ACL deficient participants compared to the control limb during SLR and MLR. Our study confirms findings in the literature demonstrating that current rehabilitation programs may not sufficiently target the impaired neuromuscular control after ACL rupture,[27] independently from treatment chosen. During artificial tibial translation, no significant within-group differences were found in both former patient groups, which indicates similar bilateral consequences after ACL rupture – either deterioration or improvement of neuromuscular control. These findings indicate that the non-involved, "healthy" leg is not a good reference to decide upon a safe RTS and does not mean reaching the sports ability as before ACL rupture.[28] As the function of the contralateral limb worsens in ACL-R patients one and five years after reconstruction,[29] lower limb indices could overestimate current sensorimotor competence and therefore, should not be used in isolation to evaluate functional performance.[28 29] Ideally, and for athletes probably the case, pre-injury reference values would exist which would consider age, physical and professional activity as well as type and level of sports participation. Moreover, artificial tibial translation gives insight into sensorimotor control mechanisms for knee joint stability.[16 17] This method could help defining outcomes for neuromuscular control to be integrated into current RTS criteria as it has been stated before.[30]

Strengths and limitations

There are some strengths and limitations to be considered. This study is one of only few publications reporting neuromuscular activity of thigh muscles comparing [2] ACL patient groups after different treatments one year after injury with a healthy control group. According to current knowledge, it is one of the first studies that investigated reflex response after artificial induced tibial perturbation in participants with different treatment modalities after ACL injury.

However, study limitations include the following aspects: As the inclusion of ACL-R participants was not limited to one orthopedic surgeon and/or one surgical technique, the group presented itself heterogeneous regarding choice of graft and surgical techniques. Participants were not randomly allocated to either surgical technique or conservatively treatment. Therefore, a selection bias cannot be neglected. Furthermore, different treatment modalities (type, duration, content), as no consensus of rehabilitation after ACL rupture exist, might have influenced the results. Moreover, suffering from concomitant injuries was not an exclusion criterium and could have altered or even prolonged rehabilitation. Nonetheless, a narrow time frame for measurements was chosen to reduce these possible influences.

At the time of measurements, all included patients had got medical clearance for RTS. However, not every patient had full, bilaterally comparable active and passive end range of motion in the knee joint. Some ACL-R participants presented with atrophy in the involved, operated leg, reported experienced painful episodes or were hypermobile in one or both knee joints.

In summary, the heterogeneity within and between patient groups regarding age, physical and mental state, as well as choice of graft, type and duration of rehabilitation, could have influenced the results and limits the generalizability. Finally, the presented methods to assess neuromuscular control are complex and not yet ready to be easily included in physical performance test batteries or used in other clinical settings for follow-up assessment.

Conclusion

The present study showed that neuromuscular alterations are still present in both lower limbs one year after ACL rupture in comparison to healthy controls, independently from treatment chosen. As both legs are affected, widely used limb symmetry indices should not be used in isolation to decide upon a safe RTS.

Future research should assess both lower limbs and include other outcomes than limb symmetry indices alone to decide upon a safe return to sports despite of treatment path chosen. In addition, it is necessary to evaluate evidence-based, standardized rehabilitation programs for reconstructed and conservatively treated patients. These programs should include neuromuscular, biomechanical, sensorimotor, and neurocognitive factors to restore movement quality and performance as it had already been stated for ACL reconstruction.[27 30] Moreover, studies with long-term follow-up after clearance for RTS are needed to proof positive effects such rehabilitation programs with special focus on improvement of neuromuscular control.

Declaration of interest

None declared.

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Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used the translator DeepL SE (https://www.deepl.com/translator) in order to check some words being correctly translated and written in English. After using this translating tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Highlights

- Patients after ACL rupture, reconstruction and healthy controls were compared
- Neuromuscular function is still affected in both legs one year after ACL rupture
- Neuromuscular alterations are present independent from treatment chosen
- Limb symmetry indices should not be used in isolation for return to sport decisions

Supplementary material

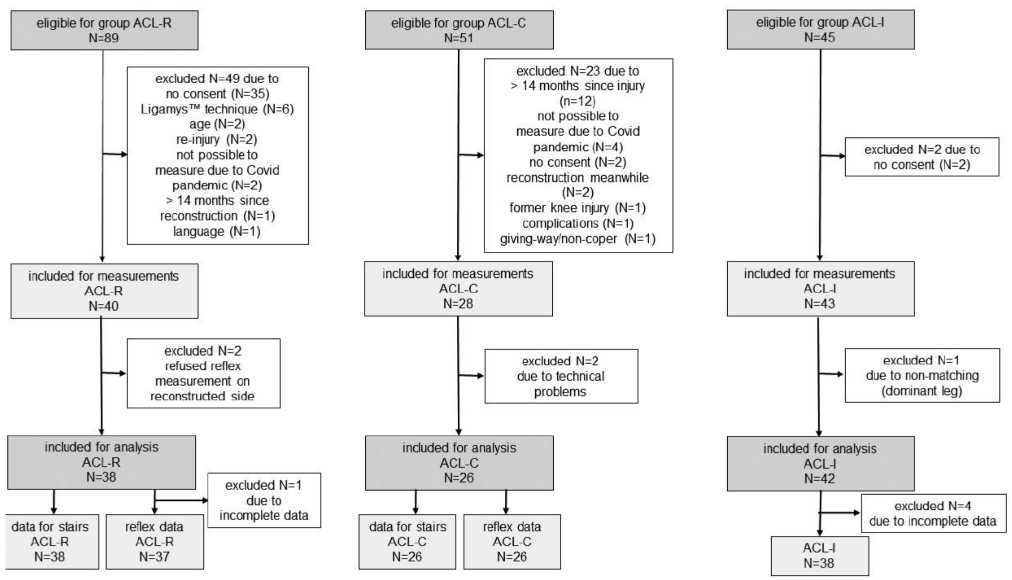

Figure A.1: Flowchart of eligibility, recruitment process and inclusion of participants for all three groups

Legend (Fig.A.1): ACL-C = anterior cruciate ligament rupture conservatively treated; ACL-I = anterior cruciate ligament intact (= healthy controls); ACL-R = anterior cruciate ligament reconstructed (=patients); N = number of

Table A.1: Frequencies of concomitant injuries, types of treatment and graft (if applicable) of participants with an ACL reconstruction (ACL-R) and participants with a conservatively treated ACL rupture (ACL-C).

	ACL-R (N = 38)	ACL-C (N = 26)
Medial meniscal tears		
conservative treatment	2 (5.3%)	4 (15.4%)
suture	15 (39.5%)	0
resection	7 (18.4%)	0
none	14 (36.8%)	22 (84.6%)
Lateral meniscal tears		
conservative treatment	1 (2.6%)	5 (19.2%)
suture	8 (21.1%)	0
resection	1 (2.6%)	0
none	28 (73.7%)	21 (80.8%)
Medial collateral ligament injury		
conservative treatment	8 (21.1%)	8 (30.8%)
surgery	1 (2.6%)	0
none	29 (76.3%)	18 (69.2%)
Lateral collateral ligament injury		
conservative treatment	2 (5.3%)	4 (15.4%)
surgery	0	0
none	36 (94.7%)	22 (84.6%)
Bone bruise		
yes	0	7 (26.9%)
none	38 (100%)	19 (73.1%)
Cartilage defect		
yes	2 (5.3%)	2 (7.7%)
none	36 (94.7%)	24 (92.3%)
Graft types		
Quadriceps tendon	26 (68.4%)	n.a.
Hamstrings tendon	8 (21.1%)	n.a.
Patellar tendon	3 (7.9%)	n.a.
unknown	1 (2.6%)	n.a.

Legend and abbreviations (Tab.A.1): ACL-R = group with ACL reconstruction; ACL-C = group with conservatively treated ACL rupture; n.a. = not applicable

Table A.2: Stair descent: Mean (standard deviations), p-values and effect sizes of normalized RMS values for the involved (injured) and non-involved (contralateral) limb of ACL-R and ACL-C participants, ACL-I with matched legs (based on side of injury) as controls in the 3 phases pre-activation (PRE), weight acceptance (WA) and push-off (PO).

Stair descent, pre-activity (PRE)

Muscle	Group						p-values										
	ACL-R		ACL-C		ACL-I = Control		ACL-R	ACL-C	ACL-I	all 3 groups		ACL-R vs. ACL-I		ACL-C vs. ACL-I		ACL-R vs. ACL-C	
	involved	non-involved	involved	non-involved	involved	non-involved	between legs	between legs	between legs	involved	non-involved	involved	non-involved	involved	non-involved	involved	non-involved
	[1]	[2]	[3]	[4]	[5]	[6]	[1]vs[2]^	[3]vs[4]^	[5]vs[6]^	overall~	overall~	[1]vs[5]°	[2]vs[6]°	[3]vs[5]°	[4]vs[6]°	[1]vs[3]°	[2]vs[4]°
VM	128.5 (35.0)	158.0 (63.1)	116.9 (35.2)	120.5 (47.4)	114.1 (40.0)	122.4 (49.0)	0.004* ES 0.34	0.619	0.566	0.328	0.020*	0.209	0.011* ES 0.30	0.875	0.978	0.199	0.030* ES 0.27
VL	125.4 (27.2)	149.0 (36.6)	123.9 (24.2)	133.1 (33.6)	121.7 (44.0)	107.8 (37.9)	0.001* ES 0.37	0.170	0.404	0.806	< 0.0001*	0.520	< 0.0001* ES 0.47	0.736	0.116* ES 0.31	0.780	0.106
BF	99.0 (36.4)	95.6 (38.0)	105.9 (43.4)	88.1 (42.0)	113.4 (43.9)	130.5 (49.2)	0.765	0.174	0.014* ES 0.29	0.362	0.001*	0.170	0.002* ES 0.36	0.652	0.001* ES 0.42	0.369	0.403
ST	99.4 (36.9)	95.4 (45.7)	107.7 (36.0)	99.4 (43.5)	119.5 (46.2)	125.0 (47.2)	0.164	0.493	0.235	0.174	0.016*	0.075	0.007* ES 0.32	0.245	0.052	0.491	0.417

Stair descent, weight acceptance (WA)

Muscle	Group						p-values										
	ACL-R		ACL-C		ACL-I = Control		ACL-R	ACL-C	ACL-I	all 3 groups		ACL-R vs. ACL-I		ACL-C vs. ACL-I		ACL-R vs. ACL-C	
	involved	non-involved	involved	non-involved	involved	non-involved	between legs	between legs	between legs	involved	non-involved	involved	non-involved	involved	non-involved	involved	non-involved
	[1]	[2]	[3]	[4]	[5]	[6]	[1]vs[2]^	[3]vs[4]^	[5]vs[6]^	overall~	overall~	[1]vs[5]°	[2]vs[6]°	[3]vs[5]°	[4]vs[6]°	[1]vs[3]°	[2]vs[4]°
VM	262.2 (92.4)	339.2 (174.4)	231.3 (67.5)	257.4 (87.7)	264.1 (118.8)	242.4 (92.2)	0.004* ES 0.34	0.935	0.706	0.654	0.025*	0.858	0.008* ES 0.31	0.443	0.538	0.390	0.079
VL	247.8 (68.8)	279.2 (82.9)	247.0 (49.9)	253.2 (71.2)	228.3 (85.1)	214.2 (76.3)	0.003* ES 0.35	0.568	0.474	0.331	0.016*	0.228	0.007* ES 0.31	0.179	0.083	0.988	0.243
BF	75.5 (28.4)	75.8 (31.4)	57.6 (21.0)	85.0 (43.7)	86.4 (55.9)	86.9 (44.6)	0.626	0.015* ES 0.34	0.870	0.051	0.612	0.901	0.321	0.089	0.920	0.008*	0.530
ST	46.2 (19.6)	43.6 (16.7)	46.2 (21.4)	50.5 (25.2)	57.4 (37.1)	67.5 (51.8)	0.612	0.903	0.993	0.693	0.308	0.442	0.171	0.495	0.507	0.970	0.281

Stair descent, push-off (PO)

Muscle	Group						p-values										
	ACL-R		ACL-C		ACL-I = Control		ACL-R	ACL-C	ACL-I	all 3 groups		ACL-R vs. ACL-I		ACL-C vs. ACL-I		ACL-R vs. ACL-C	
	involved	non-involved	involved	non-involved	involved	non-involved	between legs	between legs	between legs	involved	non-involved	involved	non-involved	involved	non-involved	involved	non-involved
	[1]	[2]	[3]	[4]	[5]	[6]	[1]vs[2]^	[3]vs[4]^	[5]vs[6]^	overall~	overall~	[1]vs[5]°	[2]vs[6]°	[3]vs[5]°	[4]vs[6]°	[1]vs[3]°	[2]vs[4]°
VM	289.4 (136.0)	365.6 (192.7)	327.6 (149.0)	331.8 (104.0)	236.6 (112.0)	258.2 (140.2)	0.008* ES 0.31	0.798	0.719	0.081	0.034*	0.166	0.019* ES 0.27	0.032*	0.040* ES 0.26	0.291	0.944
VL	253.6 (106.9)	275.5 (93.4)	255.4 (81.7)	292.2 (73.2)	202.3 (97.4)	201.0 (85.5)	0.018* ES 0.28	0.063	0.994	0.069	< 0.0001*	0.067	0.002* ES 0.36	0.039*	< 0.0001* ES 0.48	0.637	0.357
BF	48.6 (18.3)	54.3 (22.0)	49.7 (25.4)	64.1 (33.0)	78.9 (42.2)	77.0 (41.0)	0.145	0.097	0.647	0.001*	0.048*	0.001* ES 0.39	0.014* ES 0.29	0.004* ES 0.37	0.204	0.693	0.348
ST	52.5 (23.1)	54.8 (24.4)	58.2 (27.5)	58.5 (28.1)	65.2 (28.9)	67.0 (41.3)	0.481	0.954	0.911	0.146	0.670	0.048*	0.414	0.341	0.647	0.443	0.584

*Legend and abbreviations (Tab.A.2): ~Kruskal-Wallis test; ^Wilcoxon signed-rank test; °Mann-Whitney-U test; *indicate statistically significant differences between groups or legs (p<0.05); dashes indicate not applicable; ACL = anterior cruciate ligament; BF = biceps femoris; involved = injured leg, respective matched leg of controls; PO = push-off; PRE = pre-activity; RMS = root mean square; SD = standard deviation; ST = semitendinosus; non-involved = non-injured leg, respective contralateral leg; VM = vastus medialis; VL = vastus lateralis; WA = weight acceptance*

Table A.3: Reflex activity: Mean (standard deviations), p-values and effect sizes of normalized RMS values for the involved (injured) and non-involved (contralateral) limb of ACL-R and ACL-C participants, ACL-I with matched legs (based on side of injury) as controls in the 4 reflex windows pre-activation (PRE_50), short latency response (SLR), medium latency response (MLR) and long latency response (LLR).

Reflex activity, pre-activation 50ms (PRE_50)

Muscle	Group						p-values										
	ACL-R		ACL-C		ACL-I = Control		ACL-R	ACL-C	ACL-I	all 3 groups	all 3 groups	ACL-R vs. ACL-I		ACL-C vs. ACL-I		ACL-R vs. ACL-C	
	involved	non-involved	involved	non-involved	involved	non-involved	between legs	between legs	between legs	involved	non-involved	involved	non-involved	involved	non-involved	involved	non-involved
	[1]	[2]	[3]	[4]	[5]	[6]	[1]vs[2]^	[3]vs[4]^	[5]vs[6]^	overall~	overall~	[1]vs[5]°	[2]vs[6]°	[3]vs[5]°	[4]vs[6]°	[1]vs[3]°	[2]vs[4]°
VM	175.4 (194.9)	168.5 (105.5)	101.1 (37.0)	110.8 (39.9)	139.5 (67.1)	133.2 (70.0)	0.248	0.238	0.323	0.013*	0.103	0.645	0.207	0.013* ES 0.31	0.312	0.007* ES 0.35	0.038*
VL	155.8 (103.7)	171.9 (103.6)	122.8 (35.1)	130.2 (50.9)	146.7 (56.7)	134.6 (44.1)	0.105	0.603	0.307	0.229	0.338	0.723	0.344	0.081	0.577	0.232	0.150
BF	47.6 (37.9)	56.7 (40.7)	42.2 (27.6)	69.6 (55.8)	66.2 (41.3)	73.5 (48.3)	0.614	0.061	0.405	0.035*	0.336	0.035* ES 0.25	0.136	0.022* ES 0.29	0.596	0.854	0.450
ST	60.4 (29.5)	60.2 (27.1)	59.6 (28.8)	58.1 (28.9)	46.3 (31.4)	53.3 (38.7)	0.726	0.713	0.084	0.099	0.413	0.040*	0.176	0.121	0.436	0.964	0.819

Reflex activity, short latency response (SLR)

Muscle	Group						p-values										
	ACL-R		ACL-C		ACL-I = Control		ACL-R	ACL-C	ACL-I	all 3 groups		ACL-R vs. ACL-I		ACL-C vs. ACL-I		ACL-R vs. ACL-C	
	involved	non-involved	involved	non-involved	involved	non-involved	between legs	between legs	between legs	involved	non-involved	involved	non-involved	involved	non-involved	involved	non-involved
	[1]	[2]	[3]	[4]	[5]	[6]	[1]vs[2]^	[3]vs[4]^	[5]vs[6]^	overall~	overall~	[1]vs[5]°	[2]vs[6]°	[3]vs[5]°	[4]vs[6]°	[1]vs[3]°	[2]vs[4]°
VM	262.0 (223.9)	300.5 (274.2)	194.6 (132.7)	192.5 (113.2)	191.4 (104.2)	137.1 (74.5)	0.728	0.990	0.004* ES 0.34	0.582	0.011*	0.427	0.004* ES 0.34	0.823	0.073	0.332	0.260
VL	209.7 (136.7)	223.6 (155.1)	171.4 (90.0)	179.0 (95.8)	166.5 (74.0)	160.0 (94.0)	0.544	0.568	0.359	0.643	0.124	0.401	0.039*	0.988	0.356	0.449	0.387
BF	260.0 (373.4)	242.8 (233.8)	198.6 (142.2)	210.6 (156.9)	206.5 (145.9)	192.4 (162.1)	0.922	0.946	0.272	0.570	0.769	0.307	0.551	0.557	0.521	0.645	0.977
ST	239.5 (222.9)	183.4 (144.4)	206.0 (164.5)	181.8 (160.5)	233.1 (305.0)	174.2 (201.5)	0.166	0.278	0.149	0.351	0.490	0.169	0.205	0.312	0.693	0.818	0.626

Further table on the next page

Table A.3: Reflex activity: Mean (standard deviations), p-values and effect sizes of normalized RMS values for the involved (injured) and noninvolved (contralateral) limb of ACL-R and ACL-C participants, ACL-I with matched legs (based on side of injury) as controls in the 4 reflex windows pre-activation (PRE_50), short latency response (SLR), medium latency response (MLR) and long latency response (LLR).

Reflex activity, medium latency response (MLR)

Muscle	Group						p-values										
	ACL-R		ACL-C		ACL-I = Control		ACL-R	ACL-C	ACL-I	all 3 groups		ACL-R vs. ACL-I		ACL-C vs. ACL-I		ACL-R vs. ACL-C	
	involved	non-involved	involved	non-involved	involved	non-involved	between legs	between legs	between legs	involved	non-involved	involved	non-involved	involved	non-involved	involved	non-involved
	[1]	[2]	[3]	[4]	[5]	[6]	[1]vs[2]^	[3]vs[4]^	[5]vs[6]^	overall~	overall~	[1]vs[5]°	[2]vs[6]°	[3]vs[5]°	[4]vs[6]°	[1]vs[3]°	[2]vs[4]°
VM	431.8 (409.8)	380.3 (257.8)	265.8 (147.3)	249.3 (128.3)	329.5 (177.8)	276.6 (188.9)	0.376	0.797	0.033* ES 0.25	0.097	0.078	0.645	0.092	0.137	0.888	0.025*	0.027*
VL	385.1 (247.6)	365.4 (218.5)	300.5 (125.9)	341.5 (212.8)	313.3 (165.4)	270.9 (186.3)	0.765	0.264	0.008* ES 0.31	0.472	0.069	0.317	0.030*	0.814	0.119	0.284	0.503
BF	258.2 (162.4)	320.4 (257.0)	262.4 (137.7)	329.8 (204.0)	377.2 (312.4)	317.9 (299.5)	0.400	0.238	0.044* ES 0.23	0.325	0.504	0.167	0.494	0.276	0.258	0.737	0.568
ST	197.6 (181.0)	196.0 (144.6)	213.5 (122.1)	269.3 (271.3)	461.5 (454.3)	409.5 (440.9)	0.808	0.510	0.145	0.011*	0.146	0.007* ES 0.33	0.050*	0.037* ES 0.27	0.272	0.224	0.577

Reflex activity, long latency response (LLR)

Muscle	Group						p-values										
	ACL-R		ACL-C		ACL-I = Control		ACL-R	ACL-C	ACL-I	all 3 groups		ACL-R vs. ACL-I		ACL-C vs. ACL-I		ACL-R vs. ACL-C	
	involved	non-involved	involved	non-involved	involved	non-involved	between legs	between legs	between legs	involved	non-involved	involved	non-involved	involved	non-involved	involved	non-involved
	[1]	[2]	[3]	[4]	[5]	[6]	[1]vs[2]^	[3]vs[4]^	[5]vs[6]^	overall~	overall~	[1]vs[5]°	[2]vs[6]°	[3]vs[5]°	[4]vs[6]°	[1]vs[3]°	[2]vs[4]°
VM	407.1 (480.0)	311.2 (215.8)	220.8 (151.1)	215.1 (140.0)	213.3 (141.6)	196.4 (152.8)	0.741	0.412	0.208	0.034*	0.023*	0.021* ES 0.28	0.008* ES 0.31	0.824	0.444	0.034* ES 0.28	0.082
VL	287.4 (187.2)	307.2 (209.9)	235.8 (160.8)	219.0 (147.1)	205.1 (119.5)	167.8 (89.9)	0.952	0.439	0.066	0.110	0.005*	0.040*	0.001* ES 0.38	0.645	0.289	0.165	0.074
BF	204.5 (128.6)	247.9 (220.6)	228.3 (117.6)	265.1 (127.2)	228.0 (124.7)	243.9 (171.5)	0.586	0.104	0.900	0.624	0.368	0.417	0.983	0.883	0.189	0.399	0.231
ST	254.6 (222.0)	191.5 (172.0)	306.3 (211.3)	228.0 (173.4)	231.3 (159.4)	247.9 (233.1)	0.091	0.122	0.900	0.457	0.340	0.963	0.166	0.209	0.911	0.347	0.284

*Legend and abbreviations (Tab.A.3): ~Kruskal-Wallis test; ^Wilcoxon signed-rank test; °Mann-Whitney-U test; *indicate statistically significant differences between groups or legs (p<0.05); dashes indicate not applicable; ACL = anterior cruciate ligament; BF = biceps femoris; involved = injured leg, respective matched leg of controls; PO = push-off; PRE_50 = pre-activation 50ms before; RMS = root mean square; SD = standard deviation; ST = semitendinosus; non-involved = non-injured leg, respective contralateral leg; VM = vastus medialis; VL = vastus lateralis*

References

1. Shultz SJ, Schmitz RJ, Benjaminse A, et al. ACL Research Retreat VI: an update on ACL injury risk and prevention. *J Athl Train* 2012;47(5):591-603. doi: 10.4085/1062-6050-47.5.13 [published Online First: 2012/10/17]

2. Krosshaug T, Nakamae A, Boden BP, et al. Mechanisms of anterior cruciate ligament injury in basketball: video analysis of 39 cases. *Am J Sports Med* 2007;35(3):359-67. doi: 10.1177/0363546506293899 [published Online First: 2006/11/10]

3. Frobell RB, Roos EM, Roos HP, et al. A randomized trial of treatment for acute anterior cruciate ligament tears. *N Engl J Med* 2010; 363(4):331-42. doi: 10.1056/NEJMoa0907797 [published Online First: 2010/07/28]

4. Monk AP, Davies LJ, Hopewell S, et al. Surgical versus conservative interventions for treating anterior cruciate ligament injuries. *Cochrane Database Syst Rev*2016;4:CD011166. doi: 10.1002/14651858.CD011166.pub2 [published Online First: 2016/04/04]

5. Grooms DR, Page SJ, Nichols-Larsen DS, et al. Neuroplasticity Associated With Anterior Cruciate Ligament Reconstruction. *J Orthop Sports Phys Ther* 2017;47(3):180-89. doi: 10.2519/jospt.2017.7003 [published Online First: 2016/11/08]

6. Tayfur B, Charuphongsa C, Morrissey D, et al. Neuromuscular Function of the Knee Joint Following Knee Injuries: Does It Ever Get Back to Normal? A Systematic Review with Meta-Analyses. *Sports Med.* (Auckland, NZ) 2021; 51(2):321-38. doi: 10.1007/s40279-020-01386-6 [published Online First: 2020/11/29]

7. Busch A, Henle P, Boesch L, et al. Neuromuscular control in patients with acute ACL injury during stair ascent – A pilot study. *Sports Orthop Traumatol* 2019;35(2):158-65. doi: 10.1016/j.orthtr.2019.04.002

8. Hall M, Stevermer CA, Gillette JC. Muscle activity amplitudes and co-contraction during stair ambulation following anterior cruciate ligament reconstruction. *J Electromyogr Kinesiol* 2015; 25(2):298-304. doi: 10.1016/j.jelekin.2015.01.007 [published Online First: 2015/02/27]

9. Smeets A, Verschueren S, Staes F, et al. Athletes with an ACL reconstruction show a different neuromuscular response to environmental challenges compared to uninjured athletes. *Gait Posture* 2021;83:44-51. doi: 10.1016/j.gaitpost.2020.09.032 [published Online First: 2020/10/20]

10. Faul F, Erdfelder E, Buchner A, et al. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. *Behav Res Methods* 2009;41(4):1149-60. doi: 10.3758/BRM.41.4.1149 [published Online First: 2009/11/10]

11. Blasimann A, Busch A, Henle P, et al. Acute anterior cruciate ligament injury: neuromuscular control during stair descent and artificial tibia translation. *Orthop J Sports Med* 2022 doi: https://doi.org/10.1177/23259671221123299

12. Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries. *Clin Orthop Relat Res* 1985(198):43-9. [published Online First: 1985/09/01]

13. Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes* 2003;1:64. doi: 10.1186/1477-7525-1-64 [published Online First: 2003/11/14]

14. Hermens HJ, Freriks B, Disselhorst-Klug C, et al. Development of recommendations for SEMG sensors and sensor placement procedures. *J Electromyogr Kinesiol*2000;10(5):361-74. doi: 10.1016/s1050-6411(00)00027-4 [published Online First: 2000/10/06]

15. Scott J, Huskisson EC. Graphic representation of pain. *Pain* 1976;2(2):175-84. doi: 10.1016/0304-3959(76)90113-5 [published Online First: 1976/06/01]

16. Bruhn S, Leukel C, Gollhofer A. Differential effects of stimulus characteristics during knee joint perturbation on hamstring and quadriceps reflex responses. *Hum Mov Sci* 2011;30(6): 1079-91. doi: 10.1016/j.humov.2011.07.015 [published Online First: 2011/11/02]

17. Behrens M, Mau-Moeller A, Wassermann F, et al. Effect of fatigue on hamstring reflex responses and posterior-anterior tibial translation in men and women. *PLoS One* 2013;8(2):e56988. doi: 10.1371/journal.pone.0056988 [published Online First: 2013/04/11]

18. Tomczak M, Tomczak E. The need to report effect size estimates revisited. An overview of some recommended measures of effect size. *Sport Sci* 2014;1(21):19-25

19. Cohen J. Statistical Power Analysis for the Behavioral Sciences. 2 ed. Hillsdale, New Jersey: *Lawrence Erlbaum Associates* 1988

20. Rice DA, McNair PJ. Quadriceps arthrogenic muscle inhibition: neural mechanisms and treatment perspectives. *Semin Arthritis Rheum* 2010;40(3):250-66.doi:10.1016/j.semarthrit.2009.10.001 [published Online First: 2009/12/04]

21. Pamukoff DN, Pietrosimone BG, Ryan ED, et al. Quadriceps Function and Hamstrings Co-Activation After Anterior Cruciate Ligament Reconstruction. *J Athl Train* 2017;52(5):422-28. doi: 10.4085/1062-6050-52.3.05 [published Online First: 2017/04/08]

22. Tsai LC, McLean S, Colletti PM, et al. Greater muscle co-contraction results in increased tibiofemoral compressive forces in females who have undergone anterior cruciate ligament reconstruction. *J Orthop Res* 2012;30(12):2007-14. doi: 10.1002/jor.22176 [published Online First: 2012/06/26]

23. Zarzycki R, Morton SM, Charalambous CC, et al. Corticospinal and intracortical excitability differ between athletes early after ACLR and matched controls. *J Orthop Res* 2018;36(11):2941-48. doi: 10.1002/jor.24062 [published Online First: 2018/05/31]

24. Luc-Harkey BA, Harkey MS, Pamukoff DN, et al. Greater intracortical inhibition associates with lower quadriceps voluntary activation in individuals with ACL reconstruction. *Exp Brain Res* 2017;235(4):1129-37. doi: 10.1007/s00221-017-4877-8 [published Online First: 2017/02/02]

25. Dai W, Leng X, Wang J, et al. Quadriceps Tendon Autograft Versus Bone-Patellar Tendon-Bone and Hamstring Tendon Autografts for Anterior Cruciate Ligament Reconstruction: A Systematic Review and Meta-analysis. *Am J Sports Med* 2022; 50(12):3425-39.doi:10.1177/03635465211030259 [published Online First: 2021/09/09]

26. Konishi Y, McNair PJ, Rice DA, et al. Stretch reflex changes in ACL-deficient individuals and healthy controls during normal and surprise landings. *Scand J Med Sci Sports* 2020;30(12):2342-51. doi: 10.1111/sms.13810 [published Online First: 2020/08/28]

27. Gokeler A, Neuhaus D, Benjaminse A, et al. Principles of Motor Learning to Support Neuroplasticity After ACL Injury: Implications for Optimizing Performance and Reducing Risk of Second ACL Injury. *Sports Med* (Auckland, NZ) 2019;49(6):853-65. doi: 10.1007/s40279-019-01058-0 [published Online First: 2019/02/06]

28. Wellsandt E, Failla MJ, Snyder-Mackler L. Limb Symmetry Indexes Can Overestimate Knee Function After Anterior Cruciate Ligament Injury. *J Orthop Sports Phys Ther* 2017;47(5):334-38. doi: 10.2519/jospt.2017.7285 [published Online First: 2017/03/31]

29. Patterson BE, Crossley KM, Perraton LG, et al. Limb symmetry index on a functional test battery improves between one and five years after anterior cruciate ligament reconstruction, primarily due to worsening contralateral limb function. *Phys Ther Sport* 2020;44:67-74. doi: 10.1016/j.ptsp.2020.04.031 [published Online First: 2020/05/25]

30. Buckthorpe M. Recommendations for Movement Re-training After ACL Reconstruction. *Sports Med* (Auckland, NZ) 2021;51(8):1601-18. doi: 10.1007/s40279-021-01454-5 [published Online First: 2021/04/12]

CHAPTER 7

GENERAL DISCUSSION & CONCLUSION

Abstract

What we found out:

- So far, no outcomes related to electromyography (EMG) for neuromuscular control in patients after rupture of the anterior cruciate ligament (ACL) have been reported in the literature.
- Neuromuscular alterations are present not only in the injured but also in the contralateral leg shortly after ACL rupture.
- Former patients, who have returned to sport (RTS), do not reach the level of neuromuscular control in comparison to healthy matched controls, regardless of treatment and sex.
- The impairments and alterations of neuromuscular control persist in both legs, even one year after the injury or surgical reconstruction.
- However, due to missing baseline data as reference, we do not know whether different neuromuscular activation patterns and levels had been present in patients before ACL rupture occurred.

What is recommended for research and practice:

- Future research should aim at homogenous groups including matched healthy subjects for comparison, evaluate sex differences, and use sport-specific tasks.
- Moreover, investigations regarding neuromuscular control should include long-term follow up with EMG-related assessments for muscle physiology, patient's perspective but also psychological, social, and contextual factors.
- Further studies should assess both lower limbs and rely more on other outcomes than limb symmetry indices alone to decide upon a safe RTS. This applies equally for practice.
- Use of rehabilitation programs with neuromuscular exercises focusing on restoring bilateral neuromuscular function at best is highly recommended.

In this doctoral thesis, we aimed to provide an overview of EMG-related outcomes for neuromuscular control in patients after an ACL rupture and to analyze whether those outcomes were used to judge upon RTS. As no such outcomes were found, we aimed to define objective, EMG-related criteria for sensorimotor competence. Therefore, we collected and analyzed data regarding neuromuscular control of the knee stabilizing muscles in patients suffering from an ACL rupture. Patients were assessed either immediately after the injury, or one year after the ACL rupture treated with surgical reconstruction or with rehabilitation alone. The research questions had been investigated with a systematic literature review (Chapter 3) and cross-sectional studies at the Bern Movement Lab, with different ACL cohorts and subgroups for sex and treatment (Chapters 4, 5, 6). All patient data were compared to a healthy, matched control group.

Neuromuscular control was assessed with EMG in two different tasks, in stair walking as a demanding ADL for volitional neuromuscular activity and in anterior tibial translation during stance for reflexive neuromuscular answers.

The main findings are summarized in the first subchapter. In the following subchapters, several aspects related to methodological approaches, patient selection, recruitment and rehabilitation are discussed and critically reviewed. Furthermore, limitations and strengths of this PhD projects are mentioned. Finally, suggestions for practical implications and further research are presented.

7.1 Main findings and general discussion

Outcomes of neuromuscular control in patients with ACL rupture (Chapter 3)

First, we conducted a systematic review including 38 mainly cross-sectional, case-controlled studies with 1236 subjects – 809 participants with ACL-R or ACL deficiency and 427 healthy controls (Chapter 3). All studies were qualitatively analysed. Risk of bias was medium to high due to an unclear description of participants and prior interventions, confounding factors and incompletely reported results. Most studies provided EMG outcomes of thigh and/or calf muscles during jumping, running, or squatting. In addition, outcome measures of neuromuscular control of the knee in domains of time, amplitude, or activity were described. None of the included studies used the surface EMG measurements to decide upon readiness for RTS. However, about one third of the studies (31.6%, 12 studies) provided useful information about assessed groups and comparisons, such as copers versus non-copers, intervention and control group from the same team or level, data from pre-injury/-surgery including post-surgical follow up, or about participants with full RTS versus limited RTS. Two studies even investigated the influence of fatigue on neuromuscular control. (Chapter 3).[1]
In summary, we concluded that despite a wide range of EMG outcome measures for neuromuscular control reported, none was used to decide upon RTS in these patients. Therefore, further research should aim at finding reliable and valid, EMG-related variables to be used as diagnostic tool for neuromuscular control. This would add to the appraisal for RTS decision making in addition to the widely used physical performance test.

In addition, we conducted a second systematic literature review to evaluate potential sex-related differences in neuromuscular control assessed with EMG.[2] Fifteen studies with 462 healthy participants, 233 women and 299 men, were included. Surface EMG measurements with outcomes such as integral, RMS, mean values, analysis of time and amplitude of the knee stabilizing muscles were summarized. From only seven studies reporting EMG activity expressed as %MVC, three research groups found a significantly higher activity of the VL and VM in females.[3-5] Two studies reported significantly lower neuromuscular activity in the BF and ST in females.[5 6] Two research teams found no significant sex-related differences[7 8] or reported even contradicting results with significant higher activation in the hamstrings for females.[9] The methodological quality of the studies was mostly rated "fair".[2]
In summary, the controversial findings did not allow for a concluding decision regarding sex-specific neuromuscular activation.[2]

Neuromuscular control in patients with an acute ACL rupture (Chapter 4)

Secondly, we investigated neuromuscular activity in patients with an acute ACL deficiency (ACL-D) compared to a matched, control group with an intact ACL (ACL-I) during stair descent and artificially induced, anterior tibia translation (Chapter 4).[10] For this cross-sectional study in a laboratory setting, 15 acutely injured ACL patients and 15 healthy controls were included. All participants had to descend stairs and undergo measurements of reflex activity induced by artificial anterior tibial translation in upright standing position. Surface EMG of VM, VL, BF and ST was recorded bilaterally. The movements of stair descent were divided into PRE, WA and PO phases; reflex activity in preactivation, SLR, MLR and LLR responses. During PRE while going downstairs, hamstrings of the involved leg of ACL-D showed approximately 30 – 50% significant less activity compared to the matched involved and non-involved leg of ACL-I. During WA and PO, VL revealed a significant reduction of approximately 40% of the involved leg of ACL-D compared to ACL-I. For SLR response, BF and ST of the involved leg of ACL-D showed a twice to five times increase compared to the matched, non-involved leg of ACL-I (both significant). All other comparisons were not significant.
In summary, acutely injured ACL patients revealed less neuromuscular activity during stair descent and an upregulation of reflex activity, mainly in the hamstrings of both limbs in comparison to healthy controls (Chapter 4).[10]

Effect of sex and treatment (Chapter 5) and leg comparison (Chapter 6) one year after ACL rupture

Thirdly and fourthly, we investigated neuromuscular activity in patients one year after ACL rupture, either treated surgically with reconstruction or rehabilitation alone, and compared to a control group of healthy, matched participants. All patients had full clearance for RTS at measurement time point, between 11 and 14 months after ACL rupture or surgical reconstruction. Again, the study design was cross-sectional and the same measurements as for study 2 (Chapter 4)[10] were done at Bern Movement Lab. We were interested in a) effects of sex and treatment (Chapter 5) and b) in leg differences within and between groups (Chapter 6).[11] For both analyses (Study 3a, Chapter 5; Study 3b, Chapter 6) data from 38 patients after ACL-R (N = 17 women, N = 11 men), 26 patients with conservative treatment (ACL-C; N = 16 women, N = 10 men) and 38 healthy controls (ACL-I; N = 20 women, N = 18 men) were included.
Results for the effects of sex and treatment (Chapter 5, Study 3a) were as follows: During stair descent, neuromuscular differences of BF were significant during PO phase only. Males of ACL-R and ACL-C had significantly higher BF activity compared to ACL-I. During reflex activity, VM and BF were significantly different between treatment groups for pre-activation. VM pre-activation of females was significantly higher in ACL-R compared to ACL-C, and lower in ACL-C compared to ACL-I. Males after ACL-R showed higher VM and less BF pre-activation compared to ACL-I. Males of ACL-C had significantly less BF pre-activation compared to ACL-I. During MLR, significant intra-group differences in ST were found for treatment and females of ACL-R compared to ACL-I. During LLR, overall significant intra-group differences in VM were present for treatment and in females (ACL-R versus ACL-C, and ACL-R versus ACL-I) (Chapter 5).

Results for the comparison between legs (Chapter 6, Study 3b) were as follows: During stair descent, BF differed significantly comparing each patient group with ACL-I during PO. Significant interlimb differences of the quadriceps were found in ACL-R in all phases, of BF in ACL-C during WA and during PRE in ACL-I. Reflex measurements revealed significant differences in pre-activation for VM between ACL-R and ACL-C, between ACL-C and ACL-I, and for BF between each patient group and ACL-I. MLR of ST differed significantly between each of the patient groups and ACL-I. LLR of VM were significantly different in ACL-R versus ACL-C, and ACL-R versus ACL-I (Chapter 6).[11]

In summary, neuromuscular alterations were still present in both patient groups compared to healthy individuals, regardless of treatment and sex, even one year after ACL rupture or reconstruction. Standard rehabilitation protocols may not be able to restore normal neuromuscular control to the level of healthy controls (Chapter 5).
In addition, the analysis of data from both limbs revealed that neuromuscular alterations, in terms of a down-regulation of activation, were still present in both lower limbs one year after ACL rupture in comparison to healthy controls. These decreased activation levels were independently from treatment chosen. As both legs are affected, widely used limb symmetry indices should not be used in isolation to decide upon a safe RTS as they overestimate present sensorimotor ability even after having returned to sport (Chapter 6).[11]

Discussion of methodological aspects

Participants

As the inclusion of ACL-R participants was not limited to one orthopedic surgeon and/or one surgical technique, the group presented itself heterogeneous regarding choice of graft and surgical procedures (Chapter 5 & 6). Participants were not randomly allocated to either surgical technique or conservatively treatment. Therefore, a selection bias cannot be neglected. The fact that several physiotherapists were among ACL-C participants could be seen as another potential selection bias. Being physiotherapists and health professionals, they were well informed about treatment options and rehabilitation protocols. Therefore, these physiotherapists, patients respectively, were more open for the conservative approach. It can be assumed that these patients benefited from their own professional knowledge and probably had longer, qualitatively better rehabilitation which could have positively influenced neuromuscular control. In addition, the rate of females was higher in the ACL-C group. Moreover, the mean age was higher in this group compared to the mean age of participants in the ACL-R and ACL-I group. This is in line with current recommendations to rather opt for conservative treatment at higher age when no severe concomitant injuries are present, and the patients are not highly active (anymore).

Suffering from concomitant injuries was not an exclusion criterium and could have altered or even prolonged rehabilitation. Nonetheless, a narrow time frame for measurements was chosen to reduce these possible influences.

A new tool to rate the magnitude of structural tissue damage in patients suffering from an ACL injury has been published recently.[12] The research group proposed the ACL Injury Severity Scale (ACLISS) which identifies easily and rapidly different injury severity profiles in patients undergoing primary ACL-R.[12] According to the authors, the ACLISS represents a feasible grading and documentation tool and therefore, allows reproducible comparison of clinical data in ACL injured patients.[12] The use of this tool could help to compare between studies having included heterogenous patient groups regarding concomitant injuries and severity of ACL injury.

It can be assumed that different types of graft led to different surgical techniques and probably to different rehabilitation pathways. However, equal and comparable clinical outcomes have been shown for ST grafts, QT and BPTB grafts for ACL-R.[13-15] In addition, similar patient-reported outcomes after ACL-R with QT autografts compared with HT autografts[16] and between BPTB and HT autografts have been reported previously.[17] Moreover, similar RTS rates[17] and clinical and functional outcomes two years after ACL-R were found comparing different types of grafts.[16, 18] From the perspective of RTS and patient-reported outcomes, it was feasible to include patients with different ACL-R techniques in this PhD project (Chapters 5 & 6). Therefore, clinical outcomes and PROMs are likely to be similar in the patients in our two different treatment groups. However, concerning the choice of grafts and neuromuscular control, it is obvious that different harvesting sites for grafts led to different donor site morbidities, such as weakness of the hamstrings or quadriceps, which might have influenced the neuromuscular activation of either agonists or antagonists of the ACL.[19] These negative consequences were seen in several participants after ACL-R with QT autograft who presented with clearly visible quadriceps atrophy and evasive movements when walking in Study 3a and 3b. Nonetheless, all patients in our studies had returned to sport at the time of measurements at the movement laboratory.

Regarding type of grafts, patients with BPTB autografts suffered from lower quadriceps strength compared to those with HT autografts.[20] In cases with QT tendon autografts, it was shown that knee extensor strength had not been restored before 24 months after ACL-R.[21] In addition, use of QT autograft resulted in more pronounced impairments in knee extensor strength compared to hamstring autografts affecting both, knee extensor and flexor strength.[18] These findings are in line with our results that impairments in neuromuscular activation of the quadriceps are not restored one year after ACL injury.[22] However, we did not analyze neuromuscular alterations in different subgroups for grafts due to too few participants.

Persistent retraction of the ST muscle (larger than 10mm) was observed following harvest of the ST tendon for ACL autograft and does not seem to be a natural variation.[19] This may have implications for generation of muscle force and for the ST being able to serve as a knee stabilizing muscle with the same efficiency as prior to tendon harvest. It has been stated that muscle retraction of medial hamstrings in the affected leg compared to the healthy leg is correlated to decreased strength in knee flexion.[23] The same authors found that the weakness of the donor muscle (medial hamstrings) was compensated by hypertrophy of the lateral hamstrings leading to an imbalance in rotational strength of the knee.[23] Thus, changes in muscle morphology and corresponding loss of strength could have implications for the risk of re-rupture. It is known that the ST muscle serves as an important ACL synergist in the stabilization of the knee.[24] The degree of recovery of the muscle from which the tendon is harvested could, therefore, potentially be important for knee function. Most of our patients with an ACL-R in Study 3a (Chapter 5) and Study 3b (Chapter 6) were treated with an QT autograft. The sample size was too small to stratify for graft type and to analyze those subgroups. To our knowledge and to date, there is no evidence published regarding consequences of harvesting the QT on knee extensor strength and active knee stability. Nevertheless, quadriceps weakness after ACL-R is well documented, however with large variations regarding the magnitude of weakness. Full recovery from quadriceps weakness post ACL-R seems to need much more time than time for wound healing of the connective tissue, as a time span of 54-59 months has been reported.[20] In addition to time, sex and type of graft influence quadriceps strength after ACL-R.[20] Compared to the contralateral side, male participants alone had greater deficits than groups with both sexes; when compared to healthy controls, the opposite was found.[20] Our findings from Study 3a (Chapter 5) revealed that males of both treatment groups had significantly higher BF activity compared to healthy controls during push-off phase while descending stairs. During anterior tibial translation, VM and BF were significantly different between treatment groups for pre-activation. VM pre-activation of females with ACL-R was significantly higher compared to rehabilitation alone, and lower with rehabilitation alone compared to the healthy group. Males after ACL-R showed higher VM compared to healthy controls. Males of both patient groups had significantly less BF pre-activation compared to people with an intact ACL.

At the time of measurements, all included patients had received medical clearance for RTS. However, not every patient in the Study 3a and 3b had full, bilaterally comparable active and passive end range of motion in the knee joint. Some ACL-R participants presented with atrophy of thigh muscles in the involved, operated leg, reported experienced painful episodes or were hypermobile in one or both knee joints. It was obvious that physical deficits persisted, and that not all patients had fully recovered from the severe knee injury, despite full medical clearance for RTS.

Different treatment modalities (type, duration, content), as no consensus of rehabilitation after ACL rupture exist, might have influenced our findings. We did not standardize the type or duration of the sessions, and did not specify the choice of exercises, training variables or duration of rehabilitation. As we had patients recruited from different orthopedic surgeons sending patients to different physical therapy practices, our study population represents the reality of the patient population that many physical therapists see in daily practice. In addition, we did not prescribe the professional background of physiotherapists. It can be assumed that a higher professional degree (e.g., Master of Science) or specialized training (e.g., in sports physical therapy) leads to a higher quality of treatment that will benefit patients with an ACL injury. Close follow-up and high-quality sports physiotherapy interventions have been reported to increase the likelihood of RTS.[25] It is obvious that better results in ACL patients can be achieved by using a high-quality, structured, and progressive rehabilitation program, combined with clear goalsetting, repeated testing, and patient education.[25] Therefore, taking all those aspects into account, we recruited patients not only via specialized orthopedic surgeons but also through physiotherapy practices with special knowledge in sports physical therapy.

In addition, we had anamnestically assessed the content of physiotherapy and had several patients reporting that they never had exercises including jumps, hopping or cutting; elements which are recommended during ACL rehabilitation by different researchers.[26 27] A lot of patients did not have any RTS testing before returning to sports, some even reported that RTS was based on time-criterion which is not adequate anymore. This was surprising as we were aware of potential huge differences in rehabilitation quality and therefore, we chose physiotherapy practices specialized in sports physical therapy in addition to orthopedic knee surgeons to recruit patients, as mentioned above.

Applied methods and assessments

Regarding influence of myofascial meridians during standing position, Dischiavi and colleagues[28 29] provided an interesting viewpoint regarding three-dimensional (3-D) positioning of the body affecting the global tension in the musculoskeletal system. They stated that an individual muscle was only as strong as the position in which it currently was in, together with the accompanying tension.[29] This 3-D position of the entire musculoskeletal system is responsible for the amount of tension being maintained throughout the body[28 29] as described by the term tensional integrity structure, "(bio)tensegrity" respectively.[28 30] Consequently, system tension can affect performance in the lower extremity:[31 32] rotation of pelvis on the femur (so called anterior or posterior tilt of the pelvis in sagittal plane) alters tension in the entire myofascial/musculoskeletal system, like wringing out a towel.[33] A study comparing activation of myofascial meridians during single leg vertical drop jump in patients with ACL-R and healthy participants found that patients after ACL-R may present altered muscle activations in the functional frontal and back line. Muscles integrated in these two myofascial meridians may therefore negatively influence positioning of lower extremity and could therefore increase ACL injury risk.[34] During upright standing position as we asked participants to do in Study 2, 3a and 3b, it is likely that positioning of the pelvis in relation to the spine and the hip joints influenced tension of myofascial meridians. An anterior pelvic tilt leads to the biceps femoris being more under tension which consequently affects part of the spiral line and the superficial back line. Therefore, altered 3-D position of the pelvis, spine and trunk could have influenced the reflex answers by altered myofascial tension as we only controlled the 30°-angle of knee flexion and gave the instruction to stand upright with body weight equally distributed under both feet. Altered posture during standing might influence excitability of reflexes in hamstring muscles via altered tension of myofascial meridians and fascial connections, especially the superficial back line.[35 36] In Study 2, 3a and 3b, this aspect was considered by correcting verbally and manually the posture of participants by the assessor. Additionally, participants controlled equal bilateral loading visually by checking the screen where data from two force plates had been projected.

Alterations of neuromuscular control and consequences for rehabilitation

Altered sensorimotor control and neuromuscular adaptations in patients after ACL reconstruction have been stated previously.[37 38] Deficits in voluntary activation with medium to large effect sizes and limited to moderate evidence have been reported.[39] Moreover, it has been stated that increased long-term spinal excitability with limited effect sizes and strong evidence were present in patients with ACL injury.[39] Neuromuscular alterations have been found to be bilateral and indifferent of surgical or conservative treatment in various functional tasks.[22 40-46] However, these studies are limited to either reconstructed or conservatively treated ACL patients and may vary greatly in their included measurement time points. We could confirm the reported findings regarding alterations in neuromuscular control in acutely injured patients with an ACL rupture,[10] but also in patients one year after the injury with different treatments at full clearance regarding RTS (Study 3a). In addition, we analyzed subgroups for sex and treatment, and made leg comparisons within and between groups with the same methodological approach (Study 3b). In all these patient subgroups, mainly lower neuromuscular activation levels were present compared to the control group, as well as bilateral deficits were confirmed.

Ultimately, the cerebral cortex is planning and regulating motor control. It is known that reactive muscle activation is associated with involuntary muscular reflexes that can be pre-planned, modulated or even distinguished by corticospinal regions.[47 48] After ACL-R, an increased excitability of the spinal-reflex pathways and decreased excitability of the corticospinal pathways was found.[49] These changes were accompanied by decreased strength and voluntary activation of the quadriceps.[49] However, increased spinal reflex activity of the leg muscles may assist the recovery of central feed forward control.[49] Therefore, the afferent pathways of the hamstring reflex and their influence on muscle stiffness seem to be part of developing central feed forward control which is crucial for a protective knee stiffness.[50 51] As a consequence, it is recommended to address these impairments during rehabilitation by focusing on neural pathways to target quadriceps inhibition after ACL-R.[49] Furthermore, the brain activation profile found after ACL-R in relation to neuroplasticity might indicate a shift from a sensory-motor strategy towards a visual-motor strategy to engage in knee movement.[37] Therefore, a specific rehabilitation program for all patients after ACL injury is needed to target those impairments. This can be done by implementing multidimensional exercises with impaired visual feedback as it has been reported before.[52-55] In addition, unplanned, complex, multi-directional movements, cognitive-visual-motor interactions, changing tasks and environments, exercises for adaptability, and variation in progression should be included as well.[48 52-57] Even though these recommendations are based on findings after ACL-R, it can be assumed that patients with ACL deficiency would benefit as well from that specific rehabilitation program.

It has been reported previously that patients with a deficient ACL showed different neuromuscular strategies during walking.[44] In the acute phase after ACL rupture or reconstruction, the combination of both low quadriceps and high hamstrings activation in the involved leg compared to the matched leg of the healthy control group could be advantageous as this strategy improves dynamic stability of the knee joint.[58] These findings could be confirmed by our research group in the cross-sectional study with acutely injured patients (Chapter 4),[10] and in patients with chronic ACL deficiency after one year (Chapter 5 & 6).

Conservatively treated individuals at different time points from ACL injury, did not show any differences in EMG activity or latency in comparison to healthy controls.[59] In contrast, our findings in patients with acute and chronic ACL deficiency revealed that neuromuscular control of patients differed from matched healthy controls.[10] This increased hamstring activity can be interpreted as a protective mechanism after acute ACL injury as the hamstrings act as synergists to the ACL.[47 60]

There is evidence for bilateral biomechanical changes and neuromuscular alterations in both legs after a unilateral ACL injury,[61] as confirmed by our results in patients with acute and chronic ACL deficiency (Chapter 4 & 6),[10] but also after ACL-R one year after the injury (Chapter 6) . As a consequence, widely used limb symmetry indices may overestimate the actual state and performance of the non-injured, but nevertheless affected leg.[62 63] Therefore, it is necessary to compare ACL patients to a healthy control group instead of using the contralateral limb of injured participants as reference only.[63] However, it is rarely the case to have pre-injury data as reference in "normal" patients. Norm or baseline data are difficult to generate in clinical settings with non-professional athletes or patients.

It is probably not realistic to reach the same level of performance as before the injury because sensori-motor competence is influenced by the injury itself, the management of injury (surgical treatment or rehabilitation alone) as well as type, quality, and quantity of interventions during rehabilitation. Short- and long-term consequences of neuromuscular control regarding strength, voluntary activation, cortical and spinal excitability, timing and control of muscle force production have been found in patients after knee injury.[39] These long-term alterations may be specific for patients after ACL injury as no evidence was found for other knee injuries.[39] Further-more, it remains unclear whether full restoration of neuromuscular control will be achieved. In addition, it might not be realistic to reach 100% of pre-injury state as most of the patients as presented in daily clinical practice do not have pre-injury data. There-fore, the aim should be to increase neuromuscular control of the injured side as highly as possible as the contralateral side gets worse, too. These alterations in neuromuscular control are not restored one year after injury or reconstruction as found in Study 3a and 3b.[11]

7.2 Limitations and strengths

Several limitations must be considered.
As recruitment was quite challenging, especially for conservatively treated patients and during Covid pandemic, we included participants not only from our co-author and collaborator MD Philipp Henle but also from other orthopedic surgeons. As it is common in Switzerland to go to a physiotherapist by own choice or on recommendation by the treating surgeon, the heterogeneity regarding amount and quality of rehab was large. We recruited via P. Henle but also via private physiotherapy and clinic networks. Likewise, we had several physiotherapy practices and ambulatories with different profes-sional background of the physiotherapists in terms of specialization, knowledge, experience, sports-specific knowhow, or equipment etc. A cross-sectional study analyzing outcomes of an online survey among US American physiotherapists found considerable variation in practice regarding rehabili-tation following ACL-R.[64] This variability in practice may contribute to suboptimal outcomes in patients after an ACL-R.[64] However, as we were aware of potential heterogeneity of the patient group and rehabilitation protocols, we only recruited patients from specialized sports physiotherapy practices to guarantee a certain level of knowledge and further education of treating physiotherapists. Consequently, we did not prescribe any rehabilitation protocol or standardized treatment for Study 3a and 3b. We did not analyze any treatment protocols provided by the physiotherapists but only asked the patients about frequency, type, intensity, and other training variables. This anamnestic data collection is likely prone to recall bias by the patients as at the time point of measurements (one-year after ACL-R or ACL rupture), most participants had finished rehabilitation already months ago. Although all patients had full clearance for RTS, some presented with quadriceps atrophy, which was still evident after one year. It is possible that these patients had different neuro-muscular activation patterns and were more likely to use neuromuscular compensatory mechanisms as it has been reported even years after the injury or post-ACL-R.[39] This may have had an influence on our measurement results and may be partly responsible for the large heterogeneity of the data.

Meniscal injuries occur in approximately 64% to 77% of ACL injuries.[65] If a patient needed surgical repair for a meniscal tear, alteration of the reha-bilitation program was warranted, according to the recommendations of Wilk and Arrigo.[27] In contrast, an arthroscopic partial meniscectomy does not significantly influence the rehabilitation protocol after ACL injury with or without reconstruction. However, running or jumping may be allowed at a later time point in rehabilitation.[27] Consequently, this delay in progression together with a less accelerated rehabilitation might have altered neuromuscular control in included patients with concomitant injuries. Nonetheless, all participants in Study 3a and 3b had received full clearance for RTS and had returned to the preferred sport before testing. In addition, the measurement time point of 11 - 14 months after injury or ACL-R assumed that participants could perform all tasks in the laboratory without restriction.
In summary, the heterogeneity within and between patient groups regarding age, physical state, as well as choice of graft, type and duration of reha-bilitation, could have influenced the results and limits the generalizability. Finally, the presented methods to assess neuromuscular control are complex and not yet ready to be easily included in physical performance test batteries or used in clinical settings for therapy progression, RTS or follow-up assessment. For the cross-sectional studies, we don't have any baseline measurements which could give insight in potential preexisting differences between humans regarding neuromuscular control. This was a question, MD Philipp Henle raised regarding individual interlimb-differences: „Couldn't it also be that the differences between the two treatment groups and ACL-I is not a result of the injury, but that these people simply have a different neuro-muscular pattern that may increase their risk for ACL injury?". To answer the question, preinjury data would be needed as being the best reference. In an ideal world – maybe possible in professional soccer teams – data are assessed before injury occurs to set an individual risk profile and to target these deficits by established, effective and evidence-based prevention programs. However, in clinics and for patients who are normally seen and treated in physiotherapy practice, it is not realistic to have measurements as baseline data before injury occurs. Our best reference for all cross-sectional studies (Chapters 4 – 6) was the matched, healthy control group. Therefore, we can conclude that the closer the patients' values are to the reference values of the healthy control group, the better the sensorimotor competence of the patients is. This would signify that the closer the values for neuromuscular control to the reference data of healthy controls are reached, the better - the more the neuromuscular control of the affected limb is restored towards the healthy reference group.

A strength of this PhD was that unlike many published studies including only professional or semiprofessional athletes after ACL ruptures, we allowed participants with a wide range of sports and levels. In this regard, our study population represents the reality of the patient population that many physical therapists see in practice. Accordingly, our results represent the average athletic patient, which may be an advantage in translating the results into clinical practice. In addition, all patients should have resumed desired activities and sports 12 months after ACL rupture, regardless of the type of conco-mitant injury, treatment management and type and level of activity. Consequently, our study sample represents real daily patients for most, clinically active physical therapists in practice.

Another strength is the selection and assessment of acutely injured patients for Study 2 (Chapter 4) who had very narrow in- and exclusion criteria. So far, studies assessing ACL deficient patients described neuromuscular asymmetries but within seven months after injury,[66] investigated the influence of different factors on knee stability[67] or the choice of surgical techniques.[68] Only one study was found which reported on muscular activity and altered movement patterns in acutely injured ACL patients.[67] However, time since ACL rupture in those patients was on average 11 weeks, compared to three weeks in our patients. In Study 2, we were able to show that deterioration of the neuromuscular control of contralateral limb is present already within the first weeks after injury (Chapter 4).[10]

Moreover, our method is a direct approach to measure muscle physiology by established EMG-related outcomes for neuromuscular activation for reflex answers and ADL. So far, current RTS testing assess physical function but fail to include neuromuscular aspects in relation to muscle physiology and cortical alterations, as stated recently.[69] These measurements, as included in our studies, are used to assess active knee stability directly by analyzing neuromuscular answers to physical activity or artificial induced tibial translation. They are advantageous to indirect measures by video analysis of leg alignment during landing or hop performance as surrogate for active knee stability. Those currently used assessments may mask the actual state of knee stabilizing muscles by overestimating function as they do not measure close to the injury mechanism. In contrast, we could assess timing and amount of (pre-)reflex responses by eliciting anterior tibial translation. Therefore, we have a deeper insight in what happens at neuromuscular level as we measure directly and close to one of the injury mechanisms.

7.3 Practical implications and future perspectives

Practical implications

Regardless of the treatment chosen, physiotherapy plays an important role in patients with an ACL rupture whether as conservative treatment, as pre-habilitation before surgery and/or rehabilitation directly after ACL-R.[70-72]
Bilateral neuromuscular alterations are present in both legs after a unilateral ACL injury.[10 61] Consequently, widely used limb symmetry indices may overestimate the actual state and performance of the non-injured, but nevertheless affected leg.[62 63] When comparison between limbs is made, LSI should not be used alone to assess readiness for RTS. As the contralateral, non-involved limb gets worse as well, it might not be helpful to aim at reaching the level of the "healthy" side as we have demonstrated with the research projects involving ACL patients at the Bern Movement Lab.

Monitoring rehabilitation progress is key, not only for care providers but especially for the patients. In addition, physiotherapist would benefit from additional knowledge about neuromuscular control and state of fatigue while exercises are monitored with EMG to target risk factors as fatigue induces higher levels of neuromuscular activation.
Rehabilitation after ACL rupture should target neuromuscular activation to improve strategies for active joint stability during all kind of tasks. The often-mentioned neuromuscular training to be included in rehabilitation after ACL rupture is defined as a training to enhance unconscious motor responses by stimulating afferent signals and central mechanisms responsible for dynamic joint control.[73] These exercises are designed to induce compensatory changes in muscle activation patterns and facilitate dynamic joint stability.[73] "Train the brain, not only the knee, the lower leg or other bodily parts – efficient rehabilitation after ACL injury should address all levels of sensorimotor control and be as individual, sport-specific and impairment-centered as possible", was stated by Dr. Bart Dingenen, sports physical therapist and researcher, at the Swiss Sportfisio Symposium, held online in November 2020. Consequently, neuromuscular training should be integrated and include e.g., perturbation, and multi-dimensional exercises with impaired visual feedback as it has been reported before.[52-55] Therefore, the following aspects should be mandatorily included during rehabilitation: unplanned, complex, multi-directional movements, cognitive-visual-motor interactions, changing tasks and environments, exercises for adaptability, and variation in progression.[48 52-57] This induces that detecting and monitoring neuromuscular deficits early after injury, assessing and evaluating rehabilitation progress with direct insights into muscle physiology as done in our studies ,[10 22 74] and providing adequate feedback to the patient (e.g., via real-time surface EMG-biofeedback) is important.

Derived from our findings and concerning clinical practice, guidelines for rehabilitation after ACL injury should be more specific regarding treatment and sex due to potentially different neuromuscular activation. In addition, rehabilitation guidelines should allow for individualized therapy with a patient- or person-/athlete-centered approach which integrates the domains of the biopsychosocial model.[75] It is mandatory to consider not only the patient and the ACL injury with its physical consequences but also consider psychological, social and contextual factors.[76] The latter could be socioeconomic status, sport environment or perceptions shaped by ethnicity.[76] A patient-centered approach would be facilitated by a close interprofessional and interdisciplinary collaboration (e.g., orthopedic surgeon, physiotherapist, psychologist, athletic coach), however, this is rarely the case in an every-day setting for average athletic patients. In addition, a better understanding of these patient-related factors at the time of injury and during rehabilitation could support to optimize injury management, achieving RTS, and long-term HRQoL.[76]

Further evidence to optimize rehabilitation and RTS in relation to our findings

It is important to bring physiotherapy in rehabilitation to a superior level, such as from experience-led to evidence-based to data-driven methods by translating research into practice. Therefore, further aspects related to our findings should be considered to optimize rehabilitation and RTS of ACL patients.

A systematic review concerning clinical practice guidelines and their applicability found good quality of rehabilitation guidelines for ACL-R.[77] However, all six included clinical practice guidelines showed poor applicability. In summary, immediate mobilization of the knee joint, strength and neuromuscular training should be included, continuous passive motion and functional bracing should be omitted.[71 77] Therefore, it is important for all involved health professionals to respect current clinical rehabilitation guidelines and follow evidence-based recommendations. As we heard from our included patients in Study 2, 3a and 3b, content, quality and RTS criteria were broad and might contribute to the high risk of recurrence or re-injury after ACL rupture. This underpins that often used clinical guidelines for RTS are designed for athletes in a professional setting or patients in an "ideal world" and not for non-professional athletes or non-athletes, but (highly) physically active people such as most of our included patients. This aspect could influence quality of rehabilitation, length of rehabilitation, quality or even applicability of criteria for return to activity, RTS or even return to competition. In addition, patients as non-professional athletes are expected to be back to work soon leading to less time for rehabilitation besides occupational activities. Moreover, Swiss insurances agencies are not willing to pay as much physiotherapy sessions as needed and mainly rely on time-based criteria for RTS clearance. This could partly be solved by us, clinically working physiotherapist, who should shift from a strict supervised therapy using all prescribed sessions to a more person-centered approach with shared-decision making and home-based exercises, eventually supervised by telerehabilitation or app-based approaches. The patient could profit from educational resources and coping strategies to take over more responsibility during the rehabilitation process. For instance, the patient can train him-/herself with supervised sessions at a later stage of rehabilitation.

It is essential "not to forget the brain", not only to target deficits in neuromuscular control but also to think of psychological barriers for successful RTS.[76] Assessing psychological factors such as fear of movement (kinesiophobia) or self-efficacy/readiness for RTS could be helpful in these patient groups after ACL rupture. It is known that psychological factors have a significant impact on the physical factors and on RTS.[78] Therefore, it is recommended to complement the test batteries for physical performance with assessments of psychological readiness to RTS.[26] However, psychological factors should not only be assessed for RTS but even more important throughout the rehabilitation process to identify psychological factors and their influence on recovery.[71] The Anterior Cruciate Ligament-Return to Sport Injury Scale (ACL-RSI) and the Tampa Scale for Kinesiophobia (TSK) questionnaire are assessments for psychological factors in patients after ACL rupture.

The ACL-RSI is a recommended, valid and reliable PROM for psychological readiness after ACL injury during rehabilitation.[79-84] It is easy to use, translated into different languages, also to Dutch,[81] French[79] and German.[80] Since 2018, there is also a short form of the ACL-RSI available.[85] Physical function and psychological readiness for RTS after ACL-R seem to be correlated: Patients with a cut-off value of 60 points and above in the ACL-RSI had significantly higher knee flexor strength, better outcomes in the Y-Balance test in anterior direction, a more favorable hamstrings-quadriceps strength ratio and higher limb symmetry indices (LSI) of single-leg-hop tests in lateral and medial direction.[86]

The TSK is available as original version with 17 questions[87] and short version containing 11 questions (TSK-11).[88-90] The TSK-11 has been used in patients after ACL-R.[91-93] However, despite adequate reliability, the TSK-11 has low validity in examining psychological readiness regarding RTS after ACL surgery.[94] Additionally, low significance of the TSK-11 compared with the ACL-RSI was reported.[80] Therefore, the TSK-11 should better be used to elicit pain-related kinesiophobia[90] instead of psychological readiness in these patient population. This is important as a lower activity level, decreased strength of the hamstring muscles, lower performance in hop tests and lower self-assessment of knee function after ACL-R are related to pronounced kinesiophobia.[95]

Preoperative rehabilitation (so-called prehabilitation, short "prehab") is known under the term "Better in, better out".[96] There is evidence, albeit of low-quality, that prehab including muscular strength training, balance and perturbation training improve partly quadriceps strength and single leg hop scores three months after ACL-R compared to no prehab done.[70] However, there is no consensus so far on the optimum content, frequency, and length of such prehabilitation programs, but it is recommended to include psychosocial factors and relevant assessments for psychological readiness and RTS.[70] Prehab could efficiently target strength deficits of the quadriceps before surgery as it is known that those patients will likely suffer from decreased knee function post-surgery, even two years after reconstruction.[97 98] In addition, quadriceps strength levels have been found to be predictive for self-reported knee function 6 months after ACL-R.[99] Therefore, prehab is an important field for physiotherapists, and can be used just as usefully for „surgery yes/no" decision-making time. Unfortunately, however, prehab still does not receive much approval from health insurance companies.

To target bilateral consequences after ACL injury as reported as our findings in acutely injured, conservatively and surgically treated patients, cross-educational training is often recommended and used in practice. However, there are discussions ongoing: After ACL-R, cross-education showed beneficial effects and improved quadriceps strength recovery.[100 101] and attenuated muscle performance loss.[102] In contrast, it was stated that contralateral training did not accelerate the rehabilitation of neuromuscular functions,[103] or that early and late-phase rehabilitation outcomes did not improve after ACL-R.[104] in summary, there is moderate to high quality of evidence that the addition of unilateral training to standard rehabilitation improves significantly the cross-education of quadriceps strength after ACL-R.[105]

After ACL-R with hamstring autografts, it is important to choose the most efficient exercises to target weakness and muscular retraction of medial hamstrings. Nordic Hamstring exercises and Kettlebell Swing with initial movement from the hip joints (knees fixed closed to full extension) are proven to be adequate for impaired hamstrings function in those patients.[106 107]

Future perspectives and research

In Study 3a and 3b, we collected data regarding neuromuscular control one year after the injury or reconstruction, at time point when patients are expected to be back to sport respectively. However, we were not checking for readiness towards RTS or investigating RTS. As stated before, current RTS testing assesses and quantifies physical function but fails to detect important neural compensations.[69] Consequently, assessments for neuromuscular control and neural compensations are needed, not only in research but also in a clinical setting. Recently, it has been recommended "to evaluate athletes' neurocognitive reliance by augmenting RTS testing with combined neurocognitive and motor dual-task challenges".[69] Therefore, future research should compare physiologic aspects, such as neuromuscular control assessed by EMG, to outcomes as used in current physical performance test batteries. This could be done in patients at the end of the rehabilitation to decide whether RTS is safe, but also as longitudinal study assessing patients several times during rehabilitation. Consequently, further research projects should aim at transferring our findings into practice and define valid and reliable outcomes for successful rehabilitation and restoration of neuromuscular control. Our research group will start a new ACL project, funded by the Swiss National Science Foundation, in autumn 2023. The aims of this new research project are twofold: 1) to investigate sensorimotor deficits throughout current standard rehabilitation (longitudinal diagnostics) and 2) to evaluate an intervention addressing deficits of neuromuscular control with usual therapy content (intervention study).

In addition, long-term observational studies over 10 to 15 years could be helpful to see whether the level of restoration of neuromuscular control is sufficient. This should be done by elaborating not only EMG outcomes (aspect of physiology) but also multiple outcomes for successful rehabilitation and restoration to have a multidimensional picture of the patient after his/her ACL injury. To cover more dimensions, other aspects such as patient's view (e.g., satisfaction, PASS, HRQoL), psychological aspects (fear of movement, readiness to RTS), physical performance, biomechanics (gait patterns, compensation strategies through altered recruitment), socioeconomic evaluation and other aspects (occupation, club/federation if professional athlete) could be included. Furthermore, cut-off values and/or minimal important differences are needed to assess rehabilitation progress, optimize individual rehabilitation and safe RTS. In addition, reaching a certain value could be a predictor of good QoL for a patient in the long run after ACL injury. Future research should also assess neuromuscular control as long-term follow-up over several years after injury or reconstruction as it is not clear whether full restoration after ACL rupture is realistic to achieve.[39] Furthermore, comparison of test batteries with results from assessments for neuromuscular control (such as reflex answers and neuromuscular control by surface EMG) should be made to evaluate the most important parameters or criteria for a safe RTS.

Analysis of neuromuscular control should ideally be on an individual patient level, and not for a whole group of females and males with different grafts or treatments. This could support a more person-centered assessment and rehabilitation and help to guide individual RTS process.[108] Person-centered rehabilitation is reflexive and adaptive to the situation, collaborative, empowering and enabling, focuses on meanings, hope and strengths, and includes a person-health professional relationship which is respectful of and tailored to the person.[108] However, larger, and more homogenous groups regarding sex and treatment are needed in research to support current evidence regarding differences in neuromuscular control as seen in our studies. It is important to consider the selection of graft as the graft harvesting site has consequences for neuromuscular activity and strength. It has been shown that medial hamstrings contribute to rotational stability and retract after being harvested with long-term consequences for muscle length, cross-section and neuromuscular activation.[19,23,109,110] As both limbs show neuromuscular and bio-mechanical alterations after ACL rupture, it is necessary to compare ACL patients to a healthy control group instead of using the contralateral limb of injured participants as reference only. However, reference data is usually not available. Therefore, we should also consider attaining values that "guarantee" a safe RTS with a maximum HRQoL after an economically sound rehabilitation program. Moreover, patient groups should be controlled for differences in rehabilitation, ideally follow standardized protocols under the supervision of well-trained and experienced physiotherapists and other health professionals in an interprofessional and interdisciplinary setting.

The test batteries should include psychological assessments for readiness to RTS and kinesiophobia to see if impaired neuromuscular control is linked to lower scores in theses questionnaires. In addition, role of rehabilitation (structured, criterion-based, specific) and prehab in post-operatively outcomes and long-term follow-up should be investigated. As rehabilitation after ACL injury is criterion-based, clearance for RTS should be as well. Furthermore, RTS should be based on neuromuscular strategies, e.g., side-cutting maneuvers with EMG outcomes and 3-D motion capture should be analyzed to identify risk factors.[110] The setting and chosen exercises are preferably close to the injury mechanism, assessed with surface EMG in combination with 3-D motion capture.

In the future, it is desirable to have affordable, easy applicable, valid, and reliable assessments for neuro-muscular control, which are ready for on-field use, for screening, monitoring, and assessing. This means that also quick, easy-accessible EMG processing should be available for clinical practice. Additionally, patients could benefit from real-time biofeedback to better understand, acquire, and apply different neuromuscular strategies to improve neuromuscular control and active stability for the whole-body. Since 2001, development of garments with textile EMG electrodes are reported, however despite proven validity and reliability in special settings[111] and similar level of sensitivity to force variation as gel-based electrodes,1[12,113] surface EMG included in garments has not yet become established.

In future studies, the effect of proposed, novel training strategies on neuromuscular control[37,53,54] could be assessed with our device and analyzed whether sensorimotor competence increased in ACL patients. This is planned with a new ACL-related project from our research group, starting in autumn 2023. With this new research project, we aim 1) to investigate sensorimotor deficits throug-hout current standard rehabilitation (longitudinal diagnostics) and 2) to evaluate an intervention addressing deficits of neuromuscular control with usual therapy content (intervention study).

7.4 General conclusion

Consequences after an ACL injury can be severe and include reduced ROM, impaired physical activity, pain and long-term joint degeneration like post-traumatic knee osteoarthritis.[114] ACL injury may lead to instability, secondary meniscal injury or even knee osteoarthritis in the long run.[115-118] Consequently, this injury means several weeks or even months of physical impairment with wide consequences for the patients concerning return to work, RTS or even return to competition. Furthermore, the recurrence rates even after successful surgery and subsequent rehabilitation are high, with an injury of the opposite leg after successful rehabilitation of first ACL injury, muscle injuries following ACL repair/ rehabilitation on the ipsilateral side, bilateral consequences or even an increased risk for post-traumatic knee osteoarthritis.[115] The prevalence for posttraumatic osteoarthritis is reported to be as high as 80% 10 years or longer after an ACL injury.[39] This underlines the need for not only for primary but also for secondary prevention measures.

It is known that ACL ruptures induce altered kinematics and kinetics[119] - these changes are referred to neuromuscular adaptations due to altered sensori-motor control.[37] However, current assessments, such as widely used surgical scores, patient-reported outcome scores including health-related quality of life, psychosocial aspects, as well as physical performance tests do not adequately reflect the level of knee stability needed for a safe return to activity or even RTS. In addition, the rates for re-injury after ACL rupture are high despite apparently fulfilled criteria for RTS. Meaningful, reliable, valid, and accurate diagnostic tools for ACL patients are needed and may aid clinical decision-making to optimize sports participation following ACL-R.

Neuromuscular control is rarely directly assessed by surface EMG in test batteries for RTS nor monitored during rehabilitation. However, bio-mechanical and neuromuscular characteristics are modifiable risk factors for non-contact knee injury mechanisms.[120] Therefore, this PhD project provided first an overview of currently used, EMG-related assessments for neuromuscular control in patients after ACL injury to judge upon readiness for RTS. Secondly, neuromuscular control in patients with an acute ACL rupture was compared to healthy individuals during stair descent and reflex measure-ments during stance. Thirdly, the same tasks were used for patients after ACL-R or rehabilitation alone to investigate effects of treatment and sex on neuro-muscular control in comparison to a healthy control group. Fourthly, neuromuscular control of both, the injured and non-injured leg, of the two patient groups was assessed, analyzed, and comparisons made to the matched leg of controls with an intact ACL. In summary, we found out that neuromuscular alterations were present not only in the injured but also in the contralateral leg shortly after the injury. Furthermore, we could show that the impairments and alterations of neuromuscular control persist in both legs, even one year after the injury or ACL-R regardless of treatment and sex. As both legs are affected, widely used limb symmetry indices should not be used in isolation to decide upon a safe RTS. We concluded that standard rehabilitation protocols might not be able to restore normal neuro-muscular control as former patients do not reach the level of neuromuscular control in comparison to healthy matched controls. However, due to missing baseline data as reference, we do not know whether different neuromuscular activation patterns and levels were present in patients before ACL rupture has occurred.

Future research should aim at more homogenous groups including adequately matched healthy subjects, evaluate sex differences, and use sport-specific tasks. As neuromuscular alterations were found in both legs of acutely injured patients, the potential role of prehabilitation needs to be further studied. In addition, further studies should assess both lower limbs and rely more on other outcomes than limb symmetry indices alone to decide upon a safe RTS. Furthermore, it is necessary to evaluate evidence-based, standardized rehabilitation programs targeting neuromuscular deficits for reconstructed and conservatively treated patients. Current standard rehabilitation protocols may not be able restore neuromuscular control of ACL patients to the level of healthy controls, despite treatment chosen. Therefore, those programs should include neuro-muscular, biomechanical, sensorimotor, and neuro-cognitive factors to restore movement quality and performance. This is addressed with a new study being conducted by our research team. Moreover, investigations regarding neuromuscular control should include long-term follow up with assessments for muscle physiology by EMG, patient's perspective (HRQoL) but also psychological, social, and contextual factors. In addition, use of rehabilitation programs with neuromuscular exercises focusing on restoring bilateral neuromuscular function at best is highly recommended. Based on our findings, future rehabilitation guidelines may be adapted to treatment and sex, leading to a more specific rehabilitation plan to include an individual's physical, psychological, social and contextual factors. With this individualized, patient-centered rehabilitation plan, the needs, wishes and plans for future activities and (sports) participation of patients with ACL injury can hopefully better be targeted.

References

1. Blasimann A, Koenig I, Baert I, et al. Which assessments are used to analyze neuromuscular control by electromyography after an anterior cruciate ligament injury to determine readiness to return to sports? A systematic review. *BMC Sports Sci Med Rehabil* 2021;13(1):142. doi: 10.1186/s13102-021-00370-5 [published Online First: 2021/11/10]

2. Steiner M, Baur H, Blasimann A. Sex-specific differences in neuromuscular activation of the knee stabilizing muscles in adults - a systematic review. *Arch Physiother* 2023;13(1):4. doi: 10.1186/s40945-022-00158-x [published On line First: 2023/02/16]

3. Hanson AM, Padua DA, Troy Blackburn J, et al. Muscle activation during side-step cutting maneuvers in male and female soccer athletes. *J Athl Train* 2008;43(2):133-43. doi: 10.4085/1062-6050-43.2.133 [published Online First: 2008/03/18]

4. Padua DA, Carcia CR, Arnold BL, et al. Gender differences in leg stiffness and stiffness recruitment strategy during two-legged hopping. *J Mot Behav* 2005;37(2):111-25. doi: 10.3200/JMBR.37.2.111-126 [published Online First: 2005/02/26]

5. Urabe Y, Kobayashi R, Sumida S, et al. Electromyographic analysis of the knee during jump landing in male and female athletes. *Knee* 2005;12(2):129-34. doi: 10.1016/j.knee.2004.05.002 [published Online First: 2005/03/08]

6. Bencke J, Zebis MK. The influence of gender on neuromuscular pre-activity during side-cutting. *J Electromyogr Kinesiol* 2011;21(2):371-5. doi: 10.1016/j.jelekin.2010.10.008 [published Online First: 2010/11/30]

7. Kim AS, Needle AR, Thomas SJ, et al. A sex comparison of reactive knee stiffness regulation strategies under cognitive loads. *Clin Biomech* (Bristol, Avon) 2016;35:86-92. doi: 10.1016/j.clinbiomech.2016.04.010 [published Online First: 2016/05/03]

8. Palmieri-Smith RM, Wojtys EM, Ashton-Miller JA. Association between preparatory muscle activation and peak valgus knee angle. *J Electromyogr Kinesiol* 2008;18(6):973-9. doi: 10.1016/j.jelekin. 2007.03.007 [published Online First: 2007/05/15]

9. DeMont RG, Lephart SM. Effect of sex on preactivation of the gastrocnemius and hamstring muscles. *Br J Sports Med* 2004;38(2):120-4. doi: 10.1136/bjsm.2002.000195 [published Online First: 2004/03/25]

10. Blasimann A, Busch A, Henle P, et al. Acute anterior cruciate ligament injury: neuromuscular control during stair descent and artificial tibia translation. *Orthop J Sports Med* 2022 doi: https://doi.org/10.1177/23259671221123299

11. Blasimann A, Busch A, Henle P, et al. Bilateral neuromuscular control one year after anterior cruciate ligament reconstruction or conservative treatment. *Orthop Traumatol* 2023;39(2):208-09

12. Seil R, Pioger C, Siboni R, et al. The anterior cruciate ligament injury severity scale (ACLISS) is an effective tool to document and categorize the magnitude of associated tissue damage in knees after primary ACL injury and reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2023 doi: 10.1007/s00167-023-07311-4 [published Online First: 2023/01/12]

13. Barenius B, Ponzer S, Shalabi A, et al. Increased risk of osteoarthritis after anterior cruciate ligament reconstruction: a 14-year follow-up study of a randomized controlled trial. *Am J Sports Med* 2014;42(5):1049-57. doi: 10.1177/0363546514526139 [published Online First: 2014/03/20]

14. Sajovic M, Strahovnik A, Dernovsek MZ, et al. Quality of life and clinical outcome comparison of semitendinosus and gracilis tendon versus patellar tendon autografts for anterior cruciate ligament reconstruction: an 11-year follow-up of a randomized controlled trial. *Am J Sports Med* 2011;39(10):2161-9. doi: 10.1177/0363546511411702 [published Online First: 2011/06/30]

15. Slone HS, Romine SE, Premkumar A, et al. Quadriceps tendon autograft for anterior cruciate ligament reconstruction: a comprehensive review of current literature and systematic review of clinical results. *Arthroscopy* 2015;31(3):541-54. doi: 10.1016/j.arthro.2014.11.010 [published Online First: 2014/12/30]

16. Runer A, Csapo R, Hepperger C, et al. Anterior Cruciate Ligament Reconstructions With Quadriceps Tendon Autograft Result in Lower Graft Rupture Rates but Similar Patient-Reported Outcomes as Compared With Hamstring Tendon Autograft: A Comparison of 875 Patients. *Am J Sports Med* 2020;48(9):2195-204. doi: 10.1177/0363546520931829 [published Online First: 2020/07/16]

17. DeFazio MW, Curry EJ, Gustin MJ, et al. Return to Sport After ACL Reconstruction With a BTB Versus Hamstring Tendon Autograft: A Systematic Review and Meta-analysis. *Orthop J Sports Med* 2020;8(12):2325967120964919. doi: 10.1177/2325967120964919 [published Online First: 2021/01/07]

18. Sinding KS, Nielsen TG, Hvid LG, et al. Effects of Autograft Types on Muscle Strength and Functional Capacity in Patients Having Anterior Cruciate Ligament Reconstruction: A Randomized Controlled Trial. *Sports Med* (Auckland, NZ) 2020;50(7):1393-403. doi: 10.1007/s40279-020-01276-x [published Online First: 2020/03/04]

19. Speedtsberg MB, Zebis MK, Lauridsen HB, et al. Anatomical retraction of the semitendinosus muscle following harvest of the distal semitendinosus tendon for ACL reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2022;30(5):1706-10. doi: 10.1007/s00167-021-06718-1 [published Online First: 2021/09/03]

20. Tsai LC, Jeanfreau CM, Hamblin KA, et al. Time, graft, sex, geographic location, and isokinetic speed influence the degree of quadriceps weakness after anterior cruciate ligament reconstruction: a systematic review and meta-analysis. *Knee Surg Sports Traumatol Arthrosc* 2022;30(10):3367-76. doi: 10.1007/s00167-022-06906-7 [published Online First: 2022/03/01]

21. Johnston PT, McClelland JA, Feller JA, et al. Knee muscle strength after quadriceps tendon autograft anterior cruciate ligament reconstruction: systematic review and meta-analysis. *Knee Surg Sports Traumatol Arthrosc* 2021;29(9):2918-33. doi: 10.1007/s00167-020-06311-y [published Online First: 2020/10/08]

22. Busch A, Blasimann A, Henle P, et al. Neuromuscular activity during stair descent in ACL reconstructed patients: A pilot study. *Knee* 2019;26(2):310-16. doi: 10.1016/j.knee.2018.12.011 [published Online First: 2019/02/09]

23. Konrath JM, Vertullo CJ, Kennedy BA, et al. Morphologic Characteristics and Strength of the Hamstring Muscles Remain Altered at 2 Years After Use of a Hamstring Tendon Graft in Anterior Cruciate Ligament Reconstruction. *Am J Sports Med* 2016;44(10):2589-98. doi: 10.1177/0363546516651441 [published Online First: 2016/07/20]

24. Flaxman TE, Alkjaer T, Simonsen EB, et al. Predicting the Functional Roles of Knee Joint Muscles from Internal Joint Moments. *Med Sci Sports Exerc* 2017;49(3):527-37. doi: 10.1249/MSS.0000000000001125 [published Online First: 2016/10/19]

25. Grindem H, Risberg MA, Eitzen I. Two factors that may underpin outstanding outcomes after ACL rehabilitation. *Br J Sports Med* 2015;49(22):1425. doi: 10.1136/bjsports-2015-095194 [published Online First: 2015/08/05]

26. Ardern CL, Glasgow P, Schneiders A, et al. 2016 Consensus statement on return to sport from the First World Congress in Sports Physical Therapy, Bern. *Br J Sports Med* 2016;50(14):853-64. doi: 10.1136/bjsports-2016-096278 [published Online First: 2016/05/27]

27. Wilk KE, Arrigo CA. Rehabilitation Principles of the Anterior Cruciate Ligament Reconstructed Knee: Twelve Steps for Successful Progression and Return to Play. *Clin Sports Med* 2017;36(1):189-232. doi: 10.1016/j.csm.2016.08.012 [published Online First: 2016/11/23]

28. Dischiavi SL, Wright AA, Hegedus EJ, et al. Biotensegrity and myofascial chains: A global approach to an integrated kinetic chain. *Med Hypotheses* 2018;110:90-96. doi: 10.1016/j.mehy.2017.11.008 [published Online First: 2018/01/11]

29. Dischiavi SL, Wright AA, Hegedus EJ, et al. Rethinking Dynamic Knee Valgus and Its Relation to Knee Injury: Normal Movement Requiring Control, Not Avoidance. *J Orthop Sports Phys Ther* 2019;49(4):216-18. doi: 10.2519/jospt.2019.0606 [published Online First: 2019/04/02]

30. Chen YH, Chai HM, Shau YW, et al. Increased sliding of transverse abdominis during contraction after myofascial release in patients with chronic low back pain. *Man Ther* 2016;23:69-75. doi: 10.1016/j.math.2015.10.004 [published Online First: 2015/12/09]

31. Tak IJR. Hip and groin pain in athletes: morphology, function and injury from a clinical perspective. *Br J Sports Med* 2018;52(16):1024-25. doi: 10.1136/bjsports-2017-098618 [published Online First: 2018/01/27]

32. Tak IJR. Hip and groin pain in athletes: Morphology, function and injury from a clinical perspective. [Thesis, fully internal]. *Universiteit van Amsterdam*, 2017.

33. Zugel M, Maganaris CN, Wilke J, et al. Fascial tissue research in sports medicine: from molecules to tissue adaptation, injury and diagnostics: consensus statement. *Br J Sports Med* 2018;52(23):1497. doi: 10.1136/bjsports-2018-099308 [published Online First: 2018/08/04]

34. Sheikhi B, Letafatkar A, Thomas AC. Comparing myofascial meridian activation during single leg vertical drop jump in patients with anterior cruciate ligament reconstruction and healthy participants. *Gait Posture* 2021;88:66-71. doi: 10.1016/j.gaitpost.2021.05.006 [published Online First: 2021/05/19]

35. Wilke J, Krause F, Vogt L, et al. What is evidence-based about myofascial chains: a systematic review. *Arch Phys Med Rehabil* 2016;97:454-61. doi: 0.1016/j. apmr.2015.07.023

36. Myers TM. Anatomy Trains. Myofascial Meridians for Manual Therapists and Movement Professionals. 4th ed: *Elsevier* 2020:360.

37. Grooms DR, Page SJ, Nichols-Larsen DS, et al. Neuroplasticity Associated With Anterior Cruciate Ligament Reconstruction. *J Orthop Sports Phys Ther* 2017a;47(3):180-89. doi: 10.2519/jospt.2017.7003 [published Online First: 2016/11/08]

38. Ward S, Pearce AJ, Pietrosimone B, et al. Neuromuscular deficits after peripheral joint injury: a neurophysiological hypothesis. *Muscle Nerve* 2015;51(3):327-32. doi: 10.1002/mus.24463 [published Online First: 2014/09/27]

39. Tayfur B, Charuphongsa C, Morrissey D, et al. Neuromuscular Function of the Knee Joint Following Knee Injuries: Does It Ever Get Back to Normal? A Systematic Review with Meta-Analyses. *Sports Med* (Auckland, NZ) 2021;51(2):321-38. doi: 10.1007/s40279-020-01386-6 [published Online First: 2020/11/29]

40. Hall M, Stevermer CA, Gillette JC. Muscle activity amplitudes and co-contraction during stair ambulation following anterior cruciate ligament reconstruction. *J Electromyogr Kinesiol* 2015;25(2):298-304. doi: 10.1016/j.jelekin.2015.01.007 [published Online First: 2015/02/27]

41. Rudolph KS, Axe MJ, Buchanan TS, et al. Dynamic stability in the anterior cruciate ligament deficient knee. *Knee Surg Sports Traumatol Arthrosc* 2001;9(2):62-71.

42. Rudolph KS, Axe MJ, Snyder-Mackler L. Dynamic stability after ACL injury: who can hop? *Knee Surg Sports Traumatol Arthrosc* 2000;8(5):262-69.

43. Rudolph KS, Snyder-Mackler L. Effect of dynamic stability on a step task in ACL deficient individuals. *J Electromyogr Kinesiol* 2004;14(5):565-75.

44. Shanbehzadeh S, Mohseni Bandpei MA, Ehsani F. Knee muscle activity during gait in patients with anterior cruciate ligament injury: a systematic review of electromyographic studies. *Knee Surg Sports Traumatol Arthrosc* 2017;25(5):1432-42. doi: 10.1007/s00167-015-3925-9 [published Online First: 2015/12/26]

45. Smeets A, Verschueren S, Staes F, et al. Athletes with an ACL reconstruction show a different neuromuscular response to environmental challenges compared to uninjured athletes. *Gait Posture* 2021;83:44-51. doi: 10.1016/j.gaitpost.2020.09.032 [published Online First: 2020/10/20]

46. Smeets A, Willems M, Gilson L, et al. Neuromuscular and biomechanical landing alterations persist in athletes returning to sport after anterior cruciate ligament reconstruction. *Knee* 2021;33:305-17. doi: 10.1016/j.knee.2021.10.020 [published Online First: 2021/11/07]

47. Duncan A, McDonagh MJ. Stretch reflex distinguished from pre-programmed muscle activations following landing impacts in man. *J Physiol* 2000;526 Pt 2(Pt 2):457-68. doi: 10.1111/j.1469-7793.2000.t01-1-00457.x [published Online First: 2000/07/15]

48. Swanik CB. Brains and Sprains: The Brain's Role in Noncontact Anterior Cruciate Ligament Injuries. *J Athl Train* 2015;50(10):1100-2. doi: 10.4085/1062-6050-50.10.08 [published Online First: 2015/09/05]

49. Rodriguez KM, Palmieri-Smith RM, Krishnan C. How does anterior cruciate ligament reconstruction affect the functioning of the brain and spinal cord? A systematic review with meta-analysis. *J Sport Health Sci* 2021;10(2):172-81. doi: 10.1016/j.jshs.2020.07.005 [published Online First: 2020/07/25]

50. Krogsgaard MR, Dyhre-Poulsen P, Fischer-Rasmussen T. Cruciate ligament reflexes. *J Electromyogr Kinesiol* 2002;12(3):177-82. doi: 10.1016/s1050-6411(02)00018-4 [published Online First: 2002/06/28]

51. Melnyk M, Faist M, Gothner M, et al. Changes in stretch reflex excitability are related to „giving way" symptoms in patients with anterior cruciate ligament rupture. *J Neurophysiol* 2007;97(1):474-80. doi: 10.1152/jn.00529.2006 [published Online First: 2006/09/01]

52. Dingenen B, Gokeler A. Optimization of the Return-to-Sport Paradigm After Anterior Cruciate Ligament Reconstruction: A Critical Step Back to Move Forward. *Sports Med* (Auckland, NZ) 2017;47(8):1487-500. doi: 10.1007/s40279-017-0674-6 [published Online First: 2017/01/13]

53. Gokeler A, Neuhaus D, Benjaminse A, et al. Principles of Motor Learning to Support Neuroplasticity After ACL Injury: Implications for Optimizing Performance and Reducing Risk of Second ACL Injury. *Sports Med* (Auckland, NZ) 2019a;49(6):853-65. doi: 10.1007/s40279-019-01058-0 [published Online First: 2019/02/06]

54. Gokeler A, Neuhaus D, Benjaminse A, et al. Correction to: Principles of Motor Learning to Support Neuroplasticity After ACL Injury: Implications for Optimizing Performance and Reducing Risk of Second ACL Injury. *Sports Med* (Auckland, NZ) 2019b;49(6):979. doi: 10.1007/s40279-019-01078-w [published Online First: 2019/02/23]

55. Grooms D, Appelbaum G, Onate J. Neuroplasticity following anterior cruciate ligament injury: a framework for visual-motor training approaches in rehabilitation. *J Orthop Sports Phys Ther* 2015;45(5):381-93. doi: 10.2519/jospt.2015.5549 [published Online First: 2015/01/13]

56. Benjaminse A, Gokeler A, Dowling AV, et al. Optimization of the anterior cruciate ligament injury prevention paradigm: novel feedback techniques to enhance motor learning and reduce injury risk. *J Orthop Sports Phys Ther* 2015;45(3):170-82. doi: 10.2519/jospt.2015.4986 [published Online First: 2015/01/30]

57. Diekfuss JA, Grooms DR, Nissen KS, et al. Alterations in knee sensorimotor brain functional connectivity contributes to ACL injury in male high-school football players: a prospective neuroimaging analysis. *Braz J Phys Ther* 2020;24(5):415-23. doi: 10.1016/j.bjpt.2019.07.004 [published Online First: 2019/08/05]

58. Tsai LC, McLean S, Colletti PM, et al. Greater muscle co-contraction results in increased tibiofemoral compressive forces in females who have undergone anterior cruciate ligament reconstruction. *J Orthop Res* 2012;30(12):2007-14. doi: 10.1002/jor.22176 [published Online First: 2012/06/26]

59. Swanik CB, Lephart SM, Swanik KA, et al. Neuromuscular dynamic restraint in women with anterior cruciate ligament injuries. *Clin Orthop Relat Res* 2004(425):189-99. [published Online First: 2004/08/05]

60. Lepley AS, Ericksen HM, Sohn DH, et al. Contributions of neural excitability and voluntary activation to quadriceps muscle strength following anterior cruciate ligament reconstruction. *Knee* 2014;21(3):736-42. doi: 10.1016/j.knee.2014.02.008 [published Online First: 2014/03/13]

61. Grooms DR, Myer GD. Upgraded hardware horizontal line What about the software? Brain updates for return to play following ACL reconstruction. *Br J Sports Med* 2017;51(5):418-19. doi: 10.1136/bjsports-2016-096658 [published Online First: 2016/11/01]

62. Patterson BE, Crossley KM, Perraton LG, et al. Limb symmetry index on a functional test battery improves between one and five years after anterior cruciate ligament reconstruction, primarily due to worsening contralateral limb function. *Phys Ther Sport* 2020;44:67-74. doi: 10.1016/j.ptsp.2020.04.031 [published Online First: 2020/05/25]

63. Wellsandt E, Failla MJ, Snyder-Mackler L. Limb Symmetry Indexes Can Overestimate Knee Function After Anterior Cruciate Ligament Injury. *J Orthop Sports Phys Ther* 2017;47(5):334-38. doi: 10.2519/jospt.2017.7285 [published Online First: 2017/03/31]

64. Greenberg EM, Greenberg ET, Albaugh J, et al. Rehabilitation Practice Patterns Following Anterior Cruciate Ligament Reconstruction: A Survey of Physical Therapists. *J Orthop Sports Phys Ther* 2018;48(10):801-11. doi: 10.2519/jospt.2018.8264 [published Online First: 2018/05/23]

65. Cerabona F, Sherman MF, Bonamo JR, et al. Patterns of meniscal injury with acute anterior cruciate ligament tears. *Am J Sports Med* 1988;16(6):603-9. doi: 10.1177/036354658801600609 [published Online First: 1988/11/01]

66. Gardinier ES, Manal K, Buchanan TS, et al. Gait and neuromuscular asymmetries after acute anterior cruciate ligament rupture. *Med Sci Sports Exerc* 2012;44(8):1490-6. doi: 10.1249/MSS.0b013e31824d2783 [published Online First: 2012/02/15]

67. Hurd WI, Snyder-Mackler L. Knee instability after acute ACL rupture affects movement patterns during the mid-stance phase of gait. *J Orthop Res*2007;25(10):1369-77.

68. Kohl S, Stock A, Ahmad SS, et al. Dynamic intraligamentary stabilization and primary repair: a new concept for the treatment of knee dislocation. *Injury* 2015;46(4):724-8. doi: 10.1016/j.injury.2014.10.012 [published Online First: 2014/12/03]

69. Grooms DR, Chaput M, Simon JE, et al. Combining Neurocognitive and Functional Tests to Improve Return to Sport Decisions Following ACL Reconstruction. *J Orthop Sports Phys Ther* 2023(0):1-14.

70. Carter HM, Littlewood C, Webster KE, et al. The effectiveness of preoperative rehabilitation programmes on postoperative outcomes following anterior cruciate ligament (ACL) reconstruction: a systematic review. *BMC Musculoskelet Disord* 2020;21(1):647. doi: 10.1186/s12891-020-03676-6 [published Online First: 2020/10/05]

71. Jenkins SM, Guzman A, Gardner BB, et al. Rehabilitation After Anterior Cruciate Ligament Injury: Review of Current Literature and Recommendations. *Curr Rev Musculoskelet Med* 2022;15(3):170-79. doi: 10.1007/s12178-022-09752-9 [published Online First: 2022/04/07]

72. Risberg MA, Holm I, Myklebust G, et al. Neuromuscular training versus strength training during first 6 months after anterior cruciate ligament reconstruction: a randomized clinical trial. *Phys Ther* 2007;87(6):737-50. doi: 10.2522/ptj.20060041
[published Online First: 2007/04/20]

73. Risberg MA, Mork M, Jenssen HK, et al. Design and implementation of a neuromuscular training program following anterior cruciate ligament reconstruction. *J Orthop Sports Phys Ther* 2001;31(11):620-31. doi:10.2519/jospt.2001.31.11.620 [published Online First: 2001/11/27]

74. Busch A, Henle P, Boesch L, et al. Neuromuscular control in patients with acute ACL injury during stair ascent – A pilot study. *Sports Orthop Traumatol* 2019;35(2):158-65. doi: 10.1016/j.orthtr.2019.04.002

75. de Queiroz JHM, Murakawa YAB, de Castro SS, et al. Biopsychosocial Model Domains in Clinical Practice Guidelines for Return to Sport After ACL Injury: Systematic Review Using the AGREE II Checklist. *Sports Health* 2023;15(2):165-75. doi: 10.1177/19417381221094582 [published Online First: 2022/05/19]

76. Truong LK, Mosewich AD, Holt CJ, et al. Psychological, social and contextual factors across recovery stages following a sport-related knee injury: a scoping review. *Br J Sports Med* 2020;54(19):1149-56. doi: 10.1136/bjsports-2019-101206 [published Online First: 2020/02/16]

77. Andrade R, Pereira R, van Cingel R, et al. How should clinicians rehabilitate patients after ACL reconstruction? A systematic review of clinical practice guidelines (CPGs) with a focus on quality appraisal (AGREE II). *Br J Sports Med* 2020;54(9):512-19. doi: 10.1136/bjsports-2018-100310 [published Online First: 2019/06/09]

78. Ardern CL. Anterior cruciate ligament reconstruction—not exactly a one-way ticket back to the preinjury level: a review of contextual factors affecting return to sport after surgery. *Sports Health* 2015;7(3):224-30.

79. Bohu Y, Klouche S, Lefevre N, et al. Translation, cross-cultural adaptation and validation of the French version of the Anterior Cruciate Ligament-Return to Sport after Injury (ACL-RSI) scale. *Knee Surg Sports Traumatol Arthrosc* 2015;23(4):1192-6. doi: 10.1007/s00167-014-2942-4 [published Online First: 2014/03/29]

80. Müller U, Schmidt M, Krüger-Franke M, et al. Die ACL-Return to sport after Injury Skala als wichtiger Parameter bei der Beurteilung Rückkehr zum Sport Level I und II nach Rekonstruktion des vorderen Kreuzbandes (deutsche Version). *Sports Orthop Traumatol* 2014;30 (2):188-95.

81. Slagers AJ, Reininga IH, van den Akker-Scheek I. The Dutch language anterior cruciate ligament return to sport after injury scale (ACL-RSI) - validity and reliability. *J Sports Sci* 2017;35(4):393-401. doi: 10.1080/02640414.2016.1167230 [published Online First: 2016/04/16]

82. Webster KE, Feller JA, Lambros C. Development and preliminary validation of a scale to measure the psychological impact of returning t o sport following anterior cruciate ligament reconstruction surgery. *Phys Ther Sport* 2008;9(1):9-15. doi: 10.1016/j.ptsp.2007.09.003 [published Online First: 2008/12/17]

83. Meredith SJ, Rauer T, Chmielewski TL, et al. Return to Sport After Anterior Cruciate Ligament Injury: Panther Symposium ACL Injury Return to Sport Consensus Group. *Orthop J Sports Med* 2020;8(6):2325967120930829. doi: 10.1177/2325967120930829 [published Online First: 2020/07/11]

84. Webster KE, Feller JA. Evaluation of the Responsiveness of the Anterior Cruciate Ligament Return to Sport After Injury (ACL-RSI) Scale. *Orthop J Sports Med* 2021;9(8):23259671211031240. doi: 10.1177/23259671211031240 [published Online First: 2021/08/24]

85. Webster KE, Feller JA. Development and Validation of a Short Version of the Anterior Cruciate Ligament Return to Sport After Injury (ACL-RSI) Scale. *Orthop J Sports Med* 2018;6(4): 2325967118763763. doi: 10.1177/2325967118763763 [published Online First: 2018/04/18]

86. Aizawa J, Hirohata K, Ohji S, et al. Cross-sectional study on relationships between physical function and psychological readiness to return to sport after anterior cruciate ligament reconstruction. *BMC Sports Sci Med Rehabil* 2022;14(1): 97. doi: 10.1186/s13102-022-00491-5 [published Online First: 2022/06/02]

87. Clark ME. Kinesiophobia and chronic pain: psychometric characteristics and factor analysis of the Tampa Scale. *Paper presented at: The 15th Annual Scientific Meeting of the American Pain Society. Washington, DC,*

88. Archer KR, Phelps KD, Seebach CL, et al. Comparative study of short forms of the Tampa Scale for Kinesiophobia: fear of movement in a surgical spine population. *Arch Phys Med Rehabil* 2012;93(8):1460-2. doi: 10.1016/j.apmr.2012.03.024 [published Online First: 2012/04/07]

89. Rusu AC, Kreddig N, Hallner D, et al. Fear of movement/(Re)injury in low back pain: confirmatory validation of a German version of the Tampa Scale for Kinesiophobia. *BMC Musculoskelet Disord* 2014;15:280. doi: 10.1186/1471-2474-15-280 [published Online First: 2014/08/21]

90. Weermeijer JD, Meulders A. Clinimetrics: Tampa Scale for Kinesiophobia. *J Physiother* 2018;64(2): 126. doi: 10.1016/j.jphys.2018.01.001 [published Online First: 2018/03/24]

91. Chmielewski TL, George SZ. Fear avoidance and self-efficacy at 4 weeks after ACL reconstruction are associated with early impairment resolution and readiness for advanced rehabilitation. *Knee Surg Sports Traumatol Arthrosc* 2019;27(2):397-404. doi: 10.1007/s00167-018-5048-6 [published Online First: 2018/07/05]

92. Chmielewski TL, Zeppieri G, Jr., Lentz TA, et al. Longitudinal changes in psychosocial factors and their association with knee pain and function after anterior cruciate ligament reconstruction. *Phys Ther* 2011;91(9):1355-66. doi: 10.2522/ptj.20100277 [published Online First: 2011/06/28]

93. Kvist J, Ek A, Sporrstedt K, et al. Fear of re-injury: a hindrance for returning to sports after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2005;13(5):393-7. doi: 10.1007/s00167-004-0591-8 [published Online First: 2005/02/11]

94. Huang H, Nagao M, Arita H, et al. Reproducibility, responsiveness and validation of the Tampa Scale for Kinesiophobia in patients with ACL injuries. *Health Qual Life Outcomes* 2019; 17(1):150. doi: 10.1186/s12955-019-1217-7 [published Online First: 2019/09/12]

95. Norte GE, Solaas H, Saliba SA, et al. The relationships between kinesiophobia and clinical outcomes after ACL reconstruction differ by self-reported physical activity engagement. *Phys Ther Sport* 2019;40:1-9. doi: 10.1016/j.ptsp.2019.08.002 [published Online First: 2019/08/20]

96. Hoogeboom TJ, Dronkers JJ, Hulzebos EH, et al. Merits of exercise therapy before and after major surgery. *Curr Opin Anaesthesiol* 2014;27(2): 161-6. doi: 10.1097/ACO.0000000000000062 [published Online First: 2014/02/07]

97. de Jong SN, van Caspel DR, van Haeff MJ, et al. Functional assessment and muscle strength before and after reconstruction of chronic anterior cruciate ligament lesions. *Arthroscopy* 2007;23(1):21-8, 28 e1-3. doi: 10.1016/j.arthro.2006.08.024 [published Online First: 2007/01/11]

98. Eitzen I, Holm I, Risberg MA. Preoperative quadriceps strength is a significant predictor of knee function two years after anterior cruciate ligament reconstruction. *Br J Sports Med* 2009; 43(5):371-6. doi: 10.1136/bjsm.2008.057059 [published Online First: 2009/02/20]

99. Logerstedt D, Lynch A, Axe MJ, et al. Pre-operative quadriceps strength predicts IKDC2000 scores 6 months after anterior cruciate ligament reconstruction. *Knee* 2013;20(3):208-12. doi: 10.1016/j.knee.2012.07.011 [published Online First: 2012/10/02]

100. Harput G, Ulusoy B, Yildiz TI, et al. Cross-education improves quadriceps strength recovery after ACL reconstruction: a randomized controlled trial. *Knee Surg Sports Traumatol Arthrosc* 2019; 27(1):68-75. doi: 10.1007/s00167-018-5040-1 [published Online First: 2018/07/01]

101. Lepley LK, Palmieri-Smith RM. Cross-Education Strength and Activation After Eccentric Exercise. *J Athl Train* 2014;49(5):582-89. doi: 10.4085/1062-6050-49.3.24

102. Minshull C, Gallacher P, Roberts S, et al. Contralateral strength training attenuates muscle performance loss following anterior cruciate ligament (ACL) reconstruction: a randomised-controlled trial. *Eur J Appl Physiol* 2021; 121(12):3551-59. doi: 10.1007/s00421-021-04812-3 [published Online First: 2021/09/21]

103. Zult T, Gokeler A, van Raay J, et al. Cross-education does not accelerate the rehabilitation of neuromuscular functions after ACL reconstruction: a randomized controlled clinical trial. *Eur J Appl Physiol* 2018;118(8):1609-23. doi: 10.1007/s00421-018-3892-1 [published Online First: 2018/05/26]

104. Zult T, Gokeler A, van Raay J, et al. Cross-education does not improve early and late-phase rehabilitation outcomes after ACL reconstruction: a randomized controlled clinical trial. *Knee Surg Sports Traumatol Arthrosc* 2019;27(2):478-90. doi: 10.1007/s00167-018-5116-y [published Online First: 2018/09/06]

105. Cuyul-Vasquez I, Alvarez E, Riquelme A, et al. Effectiveness of Unilateral Training of the Uninjured Limb on Muscle Strength and Knee Function of Patients With Anterior Cruciate Ligament Reconstruction: A Systematic Review and Meta-Analysis of Cross-Education. *J Sport Rehabil* 2022;31(5):605-16. doi: 10.1123/jsr.2021-0204 [published Online First: 2022/03/13]

106. Krommes K, Jakobsen MD, Bandholm T, et al. Cross-sectional Study of EMG and EMG Rise During Fast and Slow Hamstring Exercises. *Int J Sports Phys Ther* 2021;16(4):1033-42. doi: 10.26603/001c.25364 [published Online First: 2021/08/14]

107. Zebis MK, Andersen CH, Bencke J, et al. Neuromuscular Coordination Deficit Persists 12 Months after ACL Reconstruction But Can Be Modulated by 6 Weeks of Kettlebell Training: A Case Study in Women's Elite Soccer. *Case Rep Orthop* 2017;2017:4269575.

108. Jesus TS, Bright FA, Pinho CS, et al. Scoping review of the person-centered literature in adult physical rehabilitation. *Disabil Rehabil* 2021;43(11):1626-36. doi: 10.1080/09638288.2019.1668483 [published Online First: 2019/09/26]

109. Bencke J, Curtis D, Krogshede C, et al. Biomechanical evaluation of the side-cutting manoeuvre associated with ACL injury in young female handball players. *Knee Surg Sports Traumatol Arthrosc* 2013;21(8):1876-81. doi: 10.1007/s00167-012-2199-8

110. Zebis MK, Aagaard P, Andersen LL, et al. First-time anterior cruciate ligament injury in adolescent female elite athletes: a prospective cohort study to identify modifiable risk factors. *Knee Surg Sports Traumatol Arthrosc* 2022;30(4):1341-51. doi: 10.1007/s00167-021-06595-8 [published Online First: 2021/05/08]

111. Lynn SK, Watkins CM, Wong MA, et al. Validity and Reliability of Surface Electromyography Measurements from a Wearable Athlete Performance System. *J Sports Sci Med* 2018;17(2):205-15. [published Online First: 2018/05/18]

112. Designing embroidered electrodes for wearable surface electromyography. *2016 IEEE International conference on robotics and automation (ICRA) 2016: 172-77*.

113. Shafti A, Ribas Manero RB, Borg AM, et al. Embroidered Electromyography: A Systematic Design Guide. *IEEE Trans Neural Syst Rehabil Eng* 2017;25(9):1472-80. doi: 10.1109/TNSRE.2016.2633506 [published Online First: 2016/12/04]

114. Lohmander LS, Ostenberg A, Englund M, et al. High prevalence of knee osteoarthritis, pain, and functional limitations in female soccer players twelve years after anterior cruciate ligament injury. Arthritis Rheum 2004;50(10):3145-52. doi: 10.1002/art.20589 [published Online First: 2004/10/12]

115. Friel NA, Chu CR. The role of ACL injury in the development of posttraumatic knee osteoarthritis. *Clin Sports Med* 2013;32(1):1-12. doi: 10.1016/j.csm.2012.08.017 [published Online First: 2012/11/28]

116. Lohmander LS, Englund PM, Dahl LL, et al. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. *Am J Sports Med* 2007;35(10):1756-69. doi: 10.1177/0363546507307396 [published Online First: 2007/09/01]

117. Oiestad BE, Engebretsen L, Storheim K, et al. Knee osteoarthritis after anterior cruciate ligament injury: a systematic review. *Am J Sports Med* 2009;37(7):1434-43. doi: 10.1177/0363546509338827 [published Online First: 2009/07/02]

118. Spindler KP, Wright RW. Clinical practice. Anterior cruciate ligament tear. *N Engl J Med* 2008;359(20):2135-42. doi: 10.1056/NEJMcp0804745 [published Online First: 2008/11/14]

119. Hall M, Stevermer CA, Gillette JC. Gait analysis post anterior cruciate ligament reconstruction: knee osteoarthritis perspective. *Gait Posture* 2012;36(1):56-60. doi: 10.1016/j.gaitpost.2012.01.003 [published Online First: 2012/02/09]

120. Ferrer A, Twycross-Lewis R, Maffulli N. Anterior cruciate ligament deficiency: rotational instability in the transverse plane. A preliminary laboratory in vivo study. *MLTJ* 2019;9(1)

CHAPTER 8

SUMMARY / SAMENVATTING

Abstract

The whole PhD project is summarized regarding background, methods, results, and conclusions and provided in English and in Dutch.

Het hele doctoraatsproject wordt samengevat wat betreft achtergrond, methoden, resultaten en conclusies en verstrekt in het Engels en het Nederlands.

8.1 Summary

Background

A rupture of the anterior cruciate ligament (ACL) is a frequent injury in physically active people with young females at highest risk. The reasons for sex-related differences in injury rates for ACL ruptures are multifactorial, but altered neuromuscular control is stated to be the most important factor.

ACL ruptures are treated either surgically or non-surgically, conservatively respectively. Physiotherapy comes into play either directly in non-surgical treatment approaches or in rehabilitation after reconstructive surgery. Regardless of treatment modality, the consequences after ACL rupture are often poor knee related quality of life, decreased knee function, lower activity level, detrimental effects on adjacent structures, or even posttraumatic knee osteoarthritis in the long run.

Most (80%) of all ACL injuries are non-contact episodes happening during deceleration and acceleration motions with excessive quadriceps contraction or insufficient hamstrings activation at or near full knee extension. Thereby, the tibia is t ranslated anteriorly relatively to the femur and stresses the ACL. Normally, the hamstring muscles act synergistically to this translational movement, whereas the quadriceps muscles are antagonists to the ACL and the hamstrings. It has been shown that non-contact ACL ruptures happen within the first 60ms after initial contact, leaving a short time frame for mechanosensory feedback (e.g., reflex response). Pre-activity and reactive neuromuscular responses regulate muscle and joint stiffness, which is influencing dynamic joint stability, consequently influencing ACL (re-)injury risk. Monitoring neuromuscular control of ACL-synergists and antagonists during exactly this time window from preactivity to perturbation onset and after perturbation give insight into sensorimotor control mechanisms for knee joint stability.

Almost all patients return to sport (RTS) after ACL rupture, however, not every athlete returns to the pre-injury level of physical activity or to competition despite successful achievement of clinical and surgical outcomes. In addition, the recurrence rates to sustain an ACL rupture in the contralateral knee, a re-rupture of the autograft or muscle injuries sums up to 20 – 40%. Currently, RTS decisions are mainly based on subjective clinical assessments (passive stability), patient-reported outcome measures (e.g., questionnaires) and physical performance test batteries (e.g., hop tests). Many guidelines and test batteries are published, but most tests show a lack of psychometric properties and do not adequately reflect the level of knee stability needed for a safe return to sport or even return to competition. This is because surrogate parameters, such as dynamic knee valgus during landing from a jump, are used to assess active knee stability that are not close enough to muscle physiology. Another gap is the lack of basic knowledge concerning neuromuscular control of the knee for functional stability during activities of daily life, at work or in doing sports. It is known that ACL ruptures induce altered kinematics and kinetics - these changes are referred to neuromuscular adaptations due to altered sensorimotor control. However, evidence regarding neuromuscular alterations is sparse.

Therefore, the aims of this PhD thesis were to give an overview of assessments for neuromuscular control, to assess neuromuscular control of the knee in acutely injured ACL patients, and to evaluate treatment-, sex-, and leg-related differences of neuromuscular control one year after ACL rupture or reconstruction. As the comparison with the contralateral, non-involved leg leads to an overestimation of current neuromuscular control, healthy matched participants were assessed additionally.

Methods and results

Thirty-eight mainly cross-sectional, case-controlled studies were included for qualitative analysis in the systematic literature review. Most studies provided EMG outcomes of thigh muscles during jumping, running or squatting, and described neuromuscular control in domains of time, amplitude or activity. Risk of bias (assessed with Downs and Black checklist) was medium to high due to an unclear description of participants and prior interventions, confounding factors and incompletely reported results.
In the cross-sectional studies, patients were assessed either within three weeks after ACL or one year after rupture, with surgical reconstruction or conservative treatment alone. Matched healthy participants served as control group. The same methods were used at the Bern Movement Laboratory (Bern University of Applied Sciences): Patients were assessed during stair walking (functional task, activity of daily life) and during artificially induced tibial perturbation (reflex activity, simulation of injury mechanism) in upright standing position. Surface EMG of four thigh muscles vastus medialis and lateralis, biceps femoris and semitendinosus were recorded and normalized to level walking on a treadmill.

In the acute phase after an ACL rupture, neuromuscular alterations (increased activity) were found mainly in the hamstrings of both limbs during stair descent and reflex activity.

One year after an ACL rupture, neuromuscular alterations are still present, regardless of treatment and sex. However, differences were present between females and males, between patient groups and compared to healthy participants but not for all muscles and phases of tasks. Regarding inter-limb differences, bilateral neuromuscular alterations were found in both tasks one year after unilateral ACL rupture, regardless of treatment option.

Conclusions

Further research should aim at more homogenous groups including matched healthy subjects, evaluate sex differences, and use sport-specific tasks. As neuromuscular alterations were found in both legs of acutely injured patients, the potential role of prehabilitation needs to be further studied. Moreover, current standard rehabilitation protocols may not be able to restore neuromuscular control to the level of healthy controls as they are not specific enough. Future research should include long-term follow up, assess neuromuscular control directly and not by surrogates, and use standardized rehabilitation programs focusing on restoring bilateral neuromuscular function. Furthermore, future rehabilitation guidelines may be adapted to treatment and sex.

8.2 Dutch summary (Samenvatting)

Achtergrond

Voorste kruisband (VKB) ruptuur is een frequent letsel bij fysiek actieve mensen, waarbij jonge vrouwen het grootste risico lopen. Meerdere factoren spelen een rol bij gender-gerelateerde verschillen in letselpercentages voor VKB-rupturen; veranderde neuromusculaire controle wordt als de belangrijkste factor beschouwd.

VKB-rupturen worden operatief of conservatief behandeld. Kinesitherapie speelt een rol bij de niet-operatieve behandeling of bij de revalidatie na reconstructie. Een slechte levenskwaliteit van de knie, een verminderde kniefunctie, een lager activiteitenniveau, nadelige effecten op aangrenzende structuren of zelfs posttraumatische knieartrose op lange termijn zijn gevolgen van een VKB-ruptuur, ongeacht de type behandeling.

De meeste (80%) VKB-letsels gebeuren zonder contact, en doen zich voor tijdens vertragende en versnellende bewegingen met overmatige contractie van de quadriceps of onvoldoende activering van de hamstrings in (bijna) volledige knie extensie. Daarbij wordt de tibia ten opzichte van het femur naar voren verplaatst en wordt de VKB belast. Normaal werken de hamstring spieren synergetisch op deze translatiebeweging, terwijl de quadricepsspieren antagonisten zijn van de VKB en de hamstrings. Er is aangetoond dat VKB-rupturen zonder contact plaatsvinden binnen de eerste 60 ms na het eerste contact, waardoor er weinig tijd overblijft voor mechanosensorische feedback (bv. reflexrespons). Pre-actieve en reactieve neuromusculaire reacties reguleren spier- en gewrichtsstijfheid, wat de dynamische gewrichtsstabiliteit beïnvloedt en bijgevolg het risico op VKB (her)letsel beïnvloedt. Het monitoren van de neuromusculaire controle van VKB-synergisten en -antagonisten gedurende dit exacte tijdsinterval van pre-activiteit tot het begin van de perturbatie en na de perturbatie geeft inzicht in sensomotorische controlemechanismen voor de stabiliteit van het kniegewricht.

Bijna alle patiënten keren na een VKB-ruptuur terug naar de sport, maar niet elke sporter keert terug naar het niveau van voor het letsel of naar volledige sportparticipatie, ondanks succesvolle klinische en chirurgische resultaten. Bovendien bedraagt het recidiefpercentage van een VKB-ruptuur in de contralaterale knie, een re-ruptuur van het autograft of spierletsels 20 tot 40%. Momenteel zijn RTS-beslissingen voornamelijk gebaseerd op subjectieve klinische beoordelingen (passieve stabiliteit), door de patiënt gerapporteerde uitkomstmaten (bv. vragenlijsten) en testbatterijen voor fysieke prestaties (bv. hoptests). Er zijn veel richtlijnen en testbatterijen gepubliceerd, maar de meeste tests vertonen een gebrek aan klinimetrische eigenschappen en weerspiegelen niet adequaat het niveau van kniestabiliteit dat nodig is voor een veilige RTS of zelfs terugkeer naar volledige wedstrijdparticipatie; omdat actieve kniestabiliteit beoordeelt wordt door middel van surrogaatparameters - zoals de dynamische knie valgus tijdens de landing - die niet dicht genoeg bij de spierfysiologie liggen.

Een ander hiaat is het gebrek aan basiskennis over de neuromusculaire controle van de knie voor functionele stabiliteit tijdens activiteiten in het dagelijks leven, op het werk of bij het sporten. Het is bekend dat VKB-scheuren een veranderde kinematica en kinetica veroorzaken - deze veranderingen worden neuromusculaire aanpassingen genoemd ten gevolge van een veranderde sensomotorische controle. Het bewijs voor neuromusculaire veranderingen is echter schaars.

Daarom waren de doelstellingen van dit proefschrift: 1) het geven van een overzicht van beoordelingen voor neuromusculaire controle; 2) het beoordelen van neuromusculaire controle van de knie bij patiënten met een acute VKB-letsel; 3) het evalueren van behandel-, geslachts- en been gerelateerde verschillen van neuromusculaire controle één jaar na VKB-ruptuur of reconstructie. Aangezien de vergelijking met het contralaterale, niet-betrokken been leidt tot een overschatting van de huidige neuromusculaire controle, werden aanvullend gezonde deelnemers beoordeeld.

Methoden en resultaten

Achtendertig studies (voornamelijk cross-sectioneel en case-controlled) werden geïncludeerd voor kwalitatieve analyse in de systematische literatuurstudie. De meeste studies gaven EMG-uitkomsten van dijspieren tijdens het springen, rennen of hurken, en beschreven neuromusculaire controle op het gebied van tijd, amplitude of activiteit. Het risico van vertekening (beoordeeld met de checklist van Downs en Black) was gemiddeld tot hoog door een onduidelijke beschrijving van deelnemers, voorafgaande interventies, verstorende factoren en onvolledig gerapporteerde resultaten.

In de cross-sectionele studies werden patiënten beoordeeld binnen drie weken na VKB of één jaar na ruptuur, met chirurgische reconstructie of alleen conservatieve behandeling. Gezonde deelnemers met een gelijkaardig profiel dienden als controlegroep. Dezelfde methoden werden gebruikt in het bewegingslaboratorium van Bern (Bern University of Applied Sciences): patiënten werden beoordeeld tijdens traplopen (functionele taak, activiteit van het dagelijks leven) en tijdens kunstmatig geïnduceerde tibia-perturbatie (reflexactiviteit, simulatie van het letselmechanisme) in staande positie. Oppervlakte-EMG van vier dijspieren Vastus Medialis, Vastus Lateralis, Biceps Femoris en Semitendinosus werden geregistreerd en genormaliseerd voor het lopen op een loopband. In de acute fase na een VKB-ruptuur werden neuromusculaire veranderingen (verhoogde activiteit) voornamelijk gevonden in de hamstrings van beide ledematen tijdens het afdalen van de trap en reflexactiviteit.

Een jaar na een VKB-ruptuur zijn de neuromusculaire veranderingen nog steeds aanwezig, ongeacht de behandeling en het geslacht. Er waren echter verschillen tussen vrouwen en mannen, tussen patiëntengroepen en in vergelijking met gezonde deelnemers, maar niet voor alle spieren en taakfasen. Wat de verschillen tussen de ledematen betreft, werden een jaar na een unilaterale VKB-ruptuur bilaterale neuromusculaire veranderingen gevonden in beide taken, ongeacht de behandelingsoptie.

Conclusies

Verder onderzoek moet zich richten op meer homogene groepen, waaronder gezonde proefpersonen met een gelijkaardig profiel, om geslachtsverschillen te evalueren en sport specifieke taken gebruikt worden. Aangezien neuromusculaire veranderingen werden gevonden in beide benen van acuut geblesseerde patiënten, moet de mogelijke rol van pre-revalidatie verder worden bestudeerd. Bovendien zijn de huidige standaard revalidatieprotocollen mogelijk niet in staat de neuromusculaire controle te herstellen tot het niveau van gezonde controles, omdat zij niet specifiek genoeg zijn. Toekomstig onderzoek moet een langdurige follow-up omvatten, de neuromusculaire controle rechtstreeks beoordelen - niet met behulp van surrogaten - en gestandaardiseerde revalidatieprogramma's gebruiken die gericht zijn op het herstel van de bilaterale neuromusculaire functie. Bovendien kunnen toekomstige revalidatierichtlijnen worden aangepast aan de behandeling en het geslacht.

List of abbreviations

Abbreviation	Definition
ACL-D	anterior cruciate ligament deficiency
ACL-I	healthy participants with an intact ACL
ACL-R	ACL patients with reconstruction (surgical treatment)
ACLISS	ACL Injury Severity Scale
ADL	activities of daily life
AE	athletic exposure
ALL	antero-lateral ligament
AMB	anterior-medial bundle of the ACL
ANOVA	analysis of variance
BE	Belgium
BF	biceps femoris muscle
BFH	Bern University of Applied Sciences (in German: Berner Fachhochschule)
BMI	body mass index
BPTB	bone-patella-tendon-bone graft for ACL reconstruction
CH	Confoederatio Helvetica (Switzerland)
CI	confidence interval
CMJ	countermovement jump(ing)
CNS	central nervous system
CRF	case report form
DK	Denmark
DE	Deutschland (Germany)
EMG	electromyography
ES	effect size
ESP	European Network for Sports Physiotherapy
GCP	Good Clinical Practice
HRQoL	health-related quality of life
HT	hamstrings tendon graft (for ACL reconstruction)
Hz	Hertz
ICC	Intraclass Correlation Coefficient
ICF	International Classification of Functioning, Disability and Health

Abbreviation	Definition
IE	Northern Ireland
IKDC	International Knee Documentation Committee 2000 Subjective Knee Form
IT	Italy
JP	Japan
km/h	kilometer per hour
KOOS	Knee injury and Osteoarthritis Outcome Score
LCL	lateral (fibular) collateral ligament
LLR	long latency response (60-95 ms after onset of tibia translation)
LU	Luxembourg
m	meter
MC	Monaco
m/s	meter per second
MCL	medial collateral ligament
MIC	minimal important change
MID	minimal important difference
MLR	medium latency response (40-60 ms after onset of tibia translation)
mm	millimeter
MRI	magnetic resonance imaging
ms	milliseconds
mv	millivolts
MVC	maximum voluntary contraction
MVIC	maximum voluntary isometric contraction
N	Newton or number of participants
NL	The Netherlands
PASS	Patient Accetable Symptom State
P or p	p-value
PCL	posterior cruciate ligament
PEDro	Physiotherapy Evidence Database
PL	Poland
PLB	posterior-lateral bundle of the ACL
PO	push-off phase during stair descent
post	after the measurements

Abbreviation	Definition
pre	before the measurements started
PRE	pre-activity phase before initial contact during stair descent
PRE_50	pre-activation (-50 – 0ms background activity before onset of tibia translation)
PRISMA	Preferred Reporting of Items for Systematic reviews and Meta-Analyses
PROM	patient-reported outcome measure
PROSPERO	international prospective register of systematic reviews
QF	quadriceps femoris muscle
QT	quadriceps tendon graft for ACL reconstruction
RMS	root mean square
RoB	risk of bias
ROM	range of motion
RTS	return to sport
s	second
SART	Swiss Working Group for Rehabilitation and Training
SD	standard deviation
SENIAM	Surface ElectroMyoGraphy for the Non-Invasive Assessment of Muscles Project
SG	Singapore
SLHD	single-leg hop for distance test
SLR	short latency response (20-40 ms after onset of tibia translation)
ST	semitendinosus muscle
TAS	Tegner Activity Score
TSK	Tampa Scale for Kinesiophobia
USA	United States of America
VAS	visual analogue scale
VKB	voorste kruisband (in English ACL: anterior cruciate ligament)
VL	vastus lateralis muscle
VM	vastus medialis muscle
WA	weight-acceptance phase during stair descent
WHO	World Health Organization
ZA	South Africa
%subMVC	percentage of submaximal values of maximum voluntary contraction
3-D	three-dimensional

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Date of Birth	26/01/1975
Nationality	Swiss
Married	to Stefan Schwarz, 3 children (born in 2010, 2011, 2014)
Affiliations	Bern University of Applied Sciences (BFH) School of Health Professions Division of Physiotherapy Murtenstrasse 10, CH-3008 Bern E-mail: angela.blasimann@bfh.ch University of Antwerp (UA) Faculty of Medicine and Health Sciences Department of Rehabilitation Sciences and Physiotherapy Universiteitsplein 1 BE-2610 Wilrijk E-mail: angela.blasimannschwarz@students.uantwerpen.be

EMPLOYMENTS

2021	2nd Assessor for vocational baccalaureate, direction health and social work, subject biology, written final examinations, vocational baccalaureate schools, Canton of Bern (CH)
2020 – present	Head of BSc Physiotherapy, Bern University of Applied Sciences (CH), locations Bern and Basel (Basel since 01/2022)
2020 – present	Deputy Head of Research Focus „Neuromuscular Control", Applied Research & Development Physiotherapy, Bern University of Applied Sciences, Bern (CH)
2020 – present	Lecturer MSc Physiotherapy and MSc Nursing, Bern University of Applied Sciences, Bern (CH)
2019 – 2020	Physiotherapist, Regional Hospital Emmental, Langnau (CH)
2016 – present	External expert for Bachelor theses, BSc Physiotherapy, Haute Ecole de Santé Suisse Occidentale (HES-SO), Leukerbad (CH)
2013 – 2020	Supervisor/instructor for female referees and linesmen, Swiss Ice Hockey Federation
2012 – 2014	Representative mid-level faculty, Bern University of Applied Sciences, School of Health Professions (former Department of Economics, Social Work and Health), Bern (CH)
2010 – present	Senior lecturer and assessor, art of motion training in movement®, Bern (CH)
2009 – 2020	Research associate (including supervision for Bachelor theses in Physiotherapy, lecturing/assessing in BSc and MSc programs), Bern University of Applied Sciences, School of Health Professions, Applied Research & Development in Physiotherapy, Bern (CH)
2003 – 2009	Physiotherapist and supervising tutor for practical training, responsible expert, project leader for workplace health promotion, Salem Hospital, Hirslanden Group Bern (CH)
2000 – 2003	Physiotherapist and supervising tutor for practical training, Center for Physiotherapy, M. Knol, Langnau (CH)
2000	Physiotherapist, Cantonal Hospital Winterthur (CH)
1995 – 1995	Patient care traineeship, Regional Hospital Emmental, Langnau (CH)
1991 – 2011	Referee and Linesman in ice hockey, on a national (Swiss Ice Hockey Federation) and international level (International Ice Hockey Federation)

EDUCATION

2018 – present	**PhD in Medical Sciences** University of Antwerp, Wilrijk (Belgium) Supervisors: Prof. Dirk Vissers, PhD, PT (University of Antwerp, Faculty of Medicine and Health Sciences) and Prof. Heiner Baur, PhD (Bern University of Applied Sciences, School of Health Professions)
2012 – 2015	**Master of Science in Physiotherapy** Bern University of Applied Sciences, Bern (CH)
2005 – 2008	**Master of Physiotherapy Sciences** University of Maastricht, Maastricht (NL)
2009	**Bachelor of Science in Physiotherapy** (subsequent acquisition of title) Bern University of Applied Sciences, Bern (CH)
2001 – 2002	**Diploma in Sport Physiotherapy** European Network for Sports Physiotherapy (ESP), Education Center, Zurzach (CH)
1996 – 2000	**Diploma in Physiotherapy (Swiss Red Cross approved)** School for Physiotherapy, Leukerbad (CH)
1995 - 1996	**Studies in Human Medicine** University of Bern (CH)
1991 - 1995	**Academic High School (Gymnasium),** Matura Typus B (Latin and English) Gymnasium Burgdorf (CH)

ACADEMIC THESES

2018 – present PhD thesis: Evaluation of neuromuscular control after anterior cruciate ligament rupture: Development of objective criteria to assess sensorimotor competence
University of Antwerp (BE), Faculty of Medicine and Health Sciences
Promotors: Prof. Dr. D. Vissers, PD Dr. H. Baur
Counsellors: Dr. I. Baert, PD Dr. med. P. Henle

2015 Navicular Rise – a possibility to describe dynamic foot function during stance? A descriptive, cross-sectional laboratory study.
Bern University of Applied Sciences, Bern (CH)
Promotors: PD Dr. H. Baur, Dr. P. Eichelberger

2008 Translation, cross-cultural adaptation, reliability and validity of the German version of the Hip Osteoarthritis Outcome Score.
Maastricht University, Maastricht (NL)
Promotors: Prof. Dr. S. Wood-Dauphinee, Prof. Dr. B. Staal

2000 [Regenerative procedures in Swiss ice hockey leagues]. German.
School for Physiotherapy, Leukerbad; today:
Haute Ecole de Santé Suisse Occidentale (HES-SO), Leukerbad (CH)
Promotor: H.R. Steuri, Co-author: M. Spiess

GRANTS, PRIZES AND AWARDS

Grant

2018 – 2020 Grant for non-tenured staff, Bern University of Applied Sciences, School of Health Professions (former Department of Health Professions)

Prizes and awards

2023 1. GOTS-Sporlastic Poster Prize at the 38th Annual Congress of GOTS in Luxembourg (LU) as first/presenting author for the poster: Bilateral neuromuscular control one year after anterior cruciate ligament reconstruction or conservative treatment. (Co-authors: Busch, A., Henle, P., Bruhn, S., Vissers, D., Baur, H.)

2022 Travel Award 2022 for PhD students, issued by the journal "Sports"

2017 Nominated for the Swiss Olympic Science Award during the coaches' conference of Swiss Olympic in Magglingen (CH): **Blasimann, A.**, Henle, P., Busch, A., Boesch, L., Baur, H. (2017). [Neuromuscular control of patient with an anterior cruciate ligament tear during stair walking] (Poster presentation, peer-reviewed). German.

2015 Boday Bulloni Prize for best Master thesis of the study program MSc Physiotherapy at the Bern University of Applied Sciences, Bern, Switzerland

Prize of the Physiotherapy Sciences Foundation for best Master thesis in physiotherapy, class of 2012

Prizes and awards for co-authorship

2022 Two BSc physiotherapy students, Jan Rothenbuehler and Syra Schmid, supervised by **A. Blasimann**, were among the three finalists for the Young Scientist Award of the Swiss Association for Sports Physiotherapy with the Bachelor thesis [Influence of supplemental Pilates training in adolescents and young adults on jump height in volleyball and basketball. A systematic review with meta-analysis] German.

Heiner Baur won the 2. GOTS-Sporlastic Poster Prize at the 37th Annual Congress of GOTS in Berlin (DE) as first/presenting author for the poster: Baur, H., Busch, A., Boesch, L., Schmidt, A., Henle, P., **Blasimann, A.** [Changes in reflex activity of hamstring muscles during rehabilitation after rupture of the anterior cruciate ligament (ACL)] German.

2021 Master student Sabrina Imhof, supervised by A. Blasimann was nominated for poster prize at 36th Annual Congress of the GOTS online, 01.-02.07.2021 as first/presenting author: Imhof, S., Hanusch, K.-U., Neuenschwander-Blaser, S., Baur, H., **Blasimann, A.** [Validity of the test protocol for ACL patients of the Emmental Hospital] German.

2018 Aglaja Busch won the GOTS-Sporlastic Poster Prize at the 1st German Olympic Congress for Sports Medicine Specialists in Hamburg (Germany) as first/presenting author for the poster: Busch, A., Henle, P., Boesch, L., **Blasimann, A.**, Baur, H. [Neuromuscular control in patients with acute ACL injury during stair ascent - a pilot study] German.

2015 Two BSc physiotherapy students, Simon Eberle and Manuel Megert, supervised by **A. Blasimann**, won the Young Scientist Award of the Swiss Association for Sports Physiotherapy with the Bachelor thesis [Effect of core strengthening programs on injury rates of male adult soccer players: a systematic review] German.

CERTIFICATES AND COURSES

2023	Internal training on REDcap software - Bern University of Applied Sciences in collaboration with University of Applied Sciences Western Switzerland (CH) Training course „Social Media: LinkedIn" - Bern University of Applied Sciences (CH)
2022	Good Clinical Practice (GCP) Refresher course online – Clinical Trial Unit, University of Bern (CH) Online course «Back Health: Short course rehearsal" – art of motion Switzerland Guest lecture "Rehabilitation and return to sport after muscle injuries of the lower extremity", Bern University of Applied Sciences (CH), online
2021 – 2022	Certificate of Advanced Studies "Neuromuscular Function – Movement Analysis and Training", University of Freiburg i.Br. (DE), online and on campus
2021	Short Course "Research Data Management" online – Bern University of Applied Sciences, Bern (CH) Organization of webinar in cooperation with BFH Centre for Health Technologies, Swiss Federal Institute of Sport Magglingen and Swiss Society for Sports Sciences; topic: „Wearables Technologies for Sports", online and on site in Magglingen (CH) Webinar «Fascia-focused movement & functional anatomy" – art of motion Switzerland
2020	Ultrasound for musculoskeletal problems, Sonoskills Switzerland (inhouse) Webinar "Masterclass Slings in Motion combined with temporary Pilates" – art of motion Switzerland
2018	Good Clinical Practice: Refresher course, University of Bern (CH) Practical course "Rehabilitation after ACL injury", Center for further education, Bern Cantonal Association for Physiotherapy, Bern (CH)
2017	Diploma Slings Myofascial Training®, certified as Slings Myofascial Practitioner - art of motion Switzerland Slings in Motion 3 – art of motion Switzerland
2016	Slings in Motion 2 – art of motion Switzerland Slings in Motion 1 – art of motion Switzerland Anatomy Trains in Motion – art of motion Switzerland
2015	Slings Essentials – art of motion Switzerland Good Clinical Practice: Advanced course, University of Bern (CH)
2013	Good Clinical Practice: Basic course, University of Bern (CH)
2011	Pilates during pregnancy and after birth – art of motion Switzerland Pilates props (Magic Circle) – art of motion Switzerland Pilates props (Toning balls) – art of motion Switzerland Pilates props (Foam Roller) – art of motion Switzerland Adaptations of the skeletal muscles – SART, Basel (CH)

2010	Pilates Flow matwork – art of motion Switzerland Surface Electromyography course – University of Applied Sciences of Southern Switzerland (SUPSI), Manno (CH)
2009	Certificate Pilates Essentials Matwork – art of motion Switzerland Pilates Essentials matwork – art of motion Switzerland Leukotape K Basics – Simon Keller AG, Burgdorf (CH) Lymphological treatment of postoperative and post-traumatic oedema – Lymphbildung A. Sonderegger, Zurich (CH)
2008	ESP Update "Sports and Movement for children and adolescents", rehastudy Zurzach (CH) ESP Update „Sports and Movement for elderly people", rehastudy Zurzach (CH) Basic Life Support refresher course for health professionals – corconsult GmbH, Bern (CH)
2007	Basic Life Support refresher course for health professionals – corconsult GmbH, Bern (CH)
2006	Nordic Walking instructor course – Swiss Nordic Fitness Organisation (SNO), Olten (CH) Basic Life Support refresher course for health professionals – corconsult GmbH, Bern (CH)
2005	Basic Life Support basic course for health professionals – corconsult GmbH, Bern (CH) Diploma Spiraldynamics® practicioner – Spiraldynamics Academy, Thalwil (CH) Spiraldynamics® basic course 1 for physiotherapists – Spiraldynamics Academy, Thalwil (CH) Mobilization of the peripheral neural system 1 – Zurich University of Applied Sciences, Winterthur (CH)
2004	Rehabilitation in physiotherapy practice – Center for Further Education Emmenhof, Derendingen (CH)
2003 – 2004	ESP Update „Applied performance physiology", rehastudy Zurzach (CH)
2003	Course "Strengthening with the Swissball" – EHSM Magglingen (CH)
2002	Course "From foot to back" – FEUSI Physiotherapy School, Bern (CH)
2001	Sport Physiotherapy Course PRT Level A – International Academy for Sportscience (IAS)/Education Center, Zurzach (CH)

2000	Diploma Aquafit Instructor – Ryffel Running Bern, Leukerbad (CH) Med Coach 2 advanced level – Jack Eugster Med Coaching, Zurich (CH)
1999	Med Coach 1 basic level – Jack Eugster Med Coaching, Zurich (CH)
1998	Taping course – Regional Hospital Martigny (CH) Manual therapy for peripheral joints – SAMT/Physiotherapy School, Leukerbad (CH)

SCIENTIFIC PUBLICATIONS

Peer-reviewed scientific articles

Blasimann, A., Busch, A., Henle, P., Bruhn, S., Vissers, D., Baur, H. (2023). Neuromuscular control in males and females 1 year after an anterior cruciate ligament rupture or reconstruction during stair descent and artificial tibial translation. Sci Rep 13, 15316. https://doi.org/10.1038/s41598-023-42491-6

Steiner, M., Baur, H., **Blasimann, A.** (2023). Sex-specific differences in neuromuscular activation of the knee stabilizing muscles in adults - a systematic review. *Arch Physiother*, 13(1), 1-15.

Grand-Guillaume-Perrenoud, J.A., Geese, F., Uhlmann, K., **Blasimann, A.**, Wagner, F.L., Neubauer, F.B., Huwendiek, S., Hahn, S., Schmitt, K.-U. (2023). Mixed methods instrument validation: Evaluation procedures for practitioners developed from the validation of the Swiss Instrument for Evaluating Interprofessional Collaboration. *BMC Health Serv Res* 23, 83. Epub 2023 January 25th. https://doi:10.1186/s12913-023-04090-3

Blasimann, A., Busch, A., Henle, P., Bruhn, S., Vissers, D., Baur, H. (2022). Neuromuscular control during stair descent and artificial tibia translation after acute anterior cruciate ligament injury. *Orthop J Sports Med*, 2022;10(10). https://doi:10.1177/23259671221123299

Blasimann, A., Koenig, I., Baert, I., Baur, H., Vissers, D. (2021). Which assessments are used to analyze neuromuscular control by electromyography after an anterior cruciate ligament injury to determine readiness to return to sports? A systematic review. *BMC Sports Sci Med Rehabil*13, 142. Epub 2021 November 8. https://doi.org/10.1186/s13102-021-00370-5

Busch, A., **Blasimann, A.,** Mayer, F., Baur, H. (2021). Alterations in sensorimotor function after ACL reconstruction during active joint position sense testing. A systematic review. *PLoS One*. Epub 2021 June 25. https://doi.org/10.1371/journal.pone.0253503

Busch, A., Henle, P., Boesch, L., **Blasimann, A.,** Baur, H. (2019). Neuromuscular control in patients with acute ACL injury during stair ascent – A pilot study. *Sports Orthop Traumatol* 35:158-165.

Busch, A., **Blasimann, A.,** Henle, P., Baur H (2019). Neuromuscular activity during stair descent in ACL reconstructed patients: A pilot study. *Knee*. 2019 Mar;26(2):310-316. doi: 10.1016/j.knee.2018.12.011. Epub 2019 Feb 4.

König, I., Eichelberger, P., **Blasimann, A.**, Hauswirth, A., Bayens, J.P., Radlinger, L. (2018). Wavelet analyses of electromyographic signals derived from lower extremity muscles while walking or running: A systematic review. *PLoS One* 13(11): e0206549. https://doi.org/10.1371/journal.pone.0206549

Blasimann, A., Eichelberger, P., Lutz, N., Radlinger, L., Baur, H. (2018). Intra- and interday reliability of the dynamic navicular rise, a new measure for dynamic foot function: A descriptive, cross-sectional laboratory study. *Foot* Dec 2018;37:48-53. https://doi.org/10.1016/j.foot.2018.08.002

Faes, Y., Banz, N., Buscher, N., **Blasimann, A.**, Radlinger, L., Eichelberger, P., Elfering, A. (2018). Acute effects of partial-body vibration in sitting position. *World J Orthop* 2018 Sep 18;9(9):156-164. doi: 10.5312/wjo.v9.i9.156. eCollection 2018 Sep 18.

Eichelberger, P., **Blasimann, A.**, Lutz, N., Krause, F., Baur, H. (2018). A minimal markerset for three-dimensional foot function assessment: measuring navicular drop and drift under dynamic conditions. *J Foot Ankle Res* 2018 Apr 18;11:15. doi: 10.1186/s13047-018-0257-2. eCollection 2018

Blasimann, A., Eberle, S., Scuderi, M.M. (2018). [Effect of Core Muscle Strengthening Exercises (Including Plank and Side Plank) on Injury Rate in Male Adult Soccer Players: A Systematic Review]. *Sportverletz Sportschaden* 2018 Mar;32(1):35-46. doi: 10.1055/a-0575-2324. Epub 2018 Mar 20. German.

Bachem, R., Metzler, P., **Blasimann, A.**, Baur, H. (2018). [Helmet therapy – therapy of choice for babies with plagiocephaly or bradycephaly? A retrospective study]. *kinderärzte.schweiz NEWS*.. 2018;1:38-40. (e-paper) http://epaper.vsdruck.ch/kinderaerzteschweiz/kis201801/ German.

Baur, H., Grebner, S., **Blasimann, A.**, Hirschmuller, A., Kubosch, E.J., Elfering, A. (2016). Work-family conflict and neck and back pain in surgical nurses. *Int J Occup Saf Ergon*. 2016:1-23.

Eichelberger, P., Ferraro, M., Minder, U., Denton, T., **Blasimann, A.**, Krause, F., Baur, H. (2016). Analysis of accuracy in optival motion capture - A protocol for laboratory setup evaluation. *J Biomech*. 2016 Jul 5;49(10):2085-8. doi:10.1016/j.jbiomech.2016.05.007. Epub 2016 May 10.

Juchler, I., **Blasimann, A.**, Baur, H., Radlinger, L. (2016). Effect of kinesio tape on neuromuscular activity of the peroneus longus during downhill running. *Physiother Theory Pract*. 2016;32(2):124-9.

Blasimann, A., Eichelberger, P., Brülhart, Y., El-Masri, I., Flückiger, G., Frauchiger, L., Huber, M., Weber, M., Krause, F.G., Baur, H. (2015). Non-surgical treatment of pain associated with posterior tibial tendon dysfunction: study protocol for a randomized clinical trial. *J Foot Ankle Res*, Aug 14;8:37. doi: 10.1186/s13047-015-0095-4. eCollection 2015.

Blasimann, A., Fleuti, U., Rufener, M., Elfering, A., Radlinger, L. (2014). Electromyographic activity of back muscles during stochastic whole body vibration. *J Musculoskelet Neuronal Interact*, 14(3); 311-317.

Blasimann, A., Wood Dauphine, S., Staal, J.B. (2014). Translation, cross-cultural adaptation, and psychometric properties of the German version of the Hip Osteoarthritis Outcome Score. *J Orthop Sports Phys Ther,* Nov 13:1-24. [Epub ahead of print]. 44(12); 989-997.

Rogan, S., **Blasimann, A.**, Nyffenegger, D., Zimmerli, N., Radlinger, L. (2013). Die Bedeutung der Rumpfkraft im Eishockey: eine Machbarkeitsstudie. [The relevance of core muscles in ice hockey players: a feasibility study]. *Sportverletz Sportschaden*, 27(4); 212-218. German.

Elfering, A., Zahno, J., Taeymans, J., **Blasimann, A.**, Radlinger, R. (2013). Acute Effects of Stochastic Resonance Whole Body Vibration. *World J Orthop* 2013: October 18, 4(4); 291-298.

Blasimann, A., Klingler, R., Leuenberger, S., Radlinger, L. (2013). [Diurnal variation in Fingertip-to-Floor Test in young, healthy females: observational study]. manuelletherapie, 17, 232- 238. German.
Rogan, S., **Blasimann, A.**, Steiger, M., Torre, A., Radlinger, L. (2012). [Acute effects of fast dynamic stretching on rate of force development in ice hockey players: a pilot study]. *Sportverletz Sportschaden*, 2012: 26; 207-211. German.

Rogan, S., **Blasimann, A.**, Steiger, M., Torre, A., Radlinger, L. (2012). [Acute effects of fast dynamic stretching on rate of force development in ice hockey players: a pilot study]. *Sportverletz Sportschaden*, 2012: 26; 207-211. German.

Non-peer reviewed scientific articles

Schmitt, K.-U., Geese, F., Grand-Guillaume Perrenoud, J.A., Linhart, M., Hahn, S., Uhlmann, K., Ritschard, K., **Blasimann, A.**, Stricker, D., Wagner, F., Huwendiek, S. (2020). [Application and optimization of the Swiss Interprofessionality Evaluation Instrument SIPEI. Final report] German. Retrievable from https://www.bag.admin.ch/bag/de/home/das-bag/publikationen/forschungsberichte/forschungsberichte-interprofessionalitaet-im-gesundheitswesen/forschungsberichte-interprofessionalitaet-M7-SIPEI.html

Blasimann, A., Luginbuehl, H. (2021). Nachhaltige Partnerschaften fördern das doppelte Kompetenzprofil. [Sustainable partnerships promote dual competence profile.] German. *frequenz* 2021, 1:21-22. "frequenz": magazine of the Department of Health Professions (today School of Health Professions), Bern University of Applied Sciences. Retrievable from http://www.bfh.ch/gesundheit/de/aktuell/magazine/frequenz/

Blasimann, A. (2016). [Read and comment on: Patient education and physiotherapy before total knee arthroplasty: is it worth it? A systematic literature review] physioscience 2016; 12: 35-36. German.

Blasimann, A. (2016). [Read and comment on: Patient education and physiotherapy before total knee arthroplasty: is it worth it? A systematic literature review] physioscience 2016; 12: 35-36. German.

Manuscripts under consideration

Blasimann, A., Busch, A., Henle, P., Bruhn, S., Vissers, D., Baur, H. (202x). Neuromuscular control during stair descent and artificial tibia translation: Neuromuscular control of both legs in surgically and conservatively treated patients one year after unilateral ACL rupture. A cross-sectional study. submitted

Gentsch, A., **Blasimann, A.**, Busch, A., Henle, P., Alfuth, M., Baur, H. (202x). Neuromuscular activity during volitional tasks differs from reflex responses. submitted

Abaecherli, K., **Blasimann, A.**, Busch, A., Henle, P., Baur, H. (202x). Neuromuscular activity during stair descent in conservatively and surgically treated ACL-injured participants - a cross-sectional study. submitted

Koecker, S., **Blasimann, A.**, Busch, A., Boesch, L., Henle, P., Bruhn, S., Baur, H. (202x). Hamstrings stretch reflex activity in healthy, ACL reconstructed and conservatively treated ACL participants. A cross-sectional-study. submitted

Peer-reviewed published abstracts

Blasimann, A., Busch, A., Henle, P., Bruhn, S., Vissers, D., & Baur, H. (2023). Bilateral neuromuscular control one year after anterior cruciate ligament reconstruction or conservative treatment. *Sports Orthop Traumatol.* 39(2), 208-209. http://dx.doi.org/10.1016/j.orthtr.2023.03.041

Baur, H., Busch, A., Boesch, L., Schmidt, A., Henle, P., **Blasimann, A.** (2022). Veränderungen der Reflexaktivität der Hamstring-Muskulatur im Verlauf der Rehabilitation nach Ruptur des vorderen Kreuzbandes (VKB). *Sports Orthop Traumatol.* 38, 220-221 (2022). http://dx.doi.org/10.1016/j.orthtr.2022.02.055

Köcker, S., **Blasimann, A.,** Busch, A., Boesch, L., Henle, P., Bruhn, S., Baur, H. (2022). Hamstring Reflex Aktivität bei gesunden, VKB konservativ und VKB operativ behandelten Probanden. *Sports Orthop Traumatol.* 38, 220-221 (2022). http://dx.doi.org/10.1016/j.orthtr.2022.02.055

Blasimann, A., Koenig, I., Baert, I., Baur, H., Vissers, D. (2021). 192 Assessments for neuromuscular control after an anterior cruciate ligament injury to decide upon return to sports. *Br J Sports Med* Nov 2021, 55 (Suppl 1) A75; http://dx.doi.org/10.1136/bjsports-2021-IOC.177

Steiner, M., **Blasimann, A.**, Baur, H. (2021). 211 Gender-specific differences in neuromuscular activation in the knee stabilizing muscles in adults – a systematic review. *Br J Sports Med* Nov 2021, 55 (Suppl 1) A82; http://dx.doi.org/10.1136/bjsports-2021-IOC.194

Blasimann, A., Gisler, D., Schwammberger, H. (2018). Effect of activity trackers on weight reduction and movement behavior of overweight adults. A systematic literature review. *Swiss Sports & Exerc Med* 2018;66(4):43

Schmidt A., **Blasimann, A.**, Boesch, L., Henle, P., Baur, H. (2018). Comparison of neuromuscular hamstring activity of people with acute anterior cruciate ligament rupture and at one-year follow-up - a pilot study. *Swiss Sports & Exerc Med* 2018;66(4):44

Busch, A., Henle, P., Boesch, L., **Blasimann, A.**, Baur, H. (2018). Neuromuscular control in patients with acute ACL injury during stair ascent – a pilot study. *Deut Z Sportmed* 2018;68(5):159.

Blasimann, A., Busch, A., Boesch, L., Henle, P., Baur, H. (2017). Muscle activity in patients with ACL tear during stair descent. *Phys Ther Sport* 28 (2017) e1-e25.

Baur, H., Busch, A., Boesch, L., **Blasimann, A.**, Henle, P. (2017). [Neuromuscular control in patients with acute ACL injury during stair ascent - a pilot study.] *Kinesither Rev*, December 2017:17(192);34-35. http://dx.doi.org/10.1016/j.kine.2017.09.050. French.

Blasimann, A., Freiburghaus, S., Marolf, M., Busch, A., Boesch, L., Henle, P., Baur, H. (2017). [Altered muscle activity in patients with ACL tear compared to healthy controls during stair descent.] *Kinesither Rev* December 2017:17(192);36. http://dx.doi.org/10.1016/j.kine.2017.09.051. French.

Blasimann, A., Burgener, S., Taraschewski, K. (2017). [Effects of Pilates on physical symptoms in patients with multiple sclerosis: a systematic review.] *Kinesither Rev*, December 2017:17(192);43. http://dx.doi.org/10.1016/j.kine.2017.09.06. French.

Eichelberger, P., **Blasimann, A.**, Woodtly, S.I., McEvoy J.C., Bohnenblust, M., Kaufmann, E., Krause, F., Baur, H. (2017). [Coupling of navicular mobility and foot length change during walking.] *Kinesither Rev* December 2017:17(192);39-40. http://dx.doi.org/10.1016/j.kine.2017.09.057. French.

König, I., **Blasimann, A.,** Hauswirth, A., Eichelberger, P., Baeyens, J.P., Radlinger, L. (2017). [Wavelet analysis of muscle activity of lower extremities and pelvic floor muscles in women while walking or running: a systematic review.] *Kinesither Rev*, December 2017:17(192);22-23. http://dx.doi.org/10.1016/j.kine.2017.09.024. French.

Eichelberger, P., Lutz, N., **Blasimann, A.**, Krause, F., Baur, H. (2016). [Reliability of a new foot model for dynamic navicular drop measurement.] *Kinesither Rev*, June 2016:16(174);34-35. French.

Blasimann, A., Eichelberger, P., Lutz, N., Radlinger, L., Baur, H. (2016). [Navicular Rise: a possibility to describe dynamic foot function during stance?] *Kinesither Rev*, June 2016:16(174);32. French.

Eberle, S., Scuderi, M.M., **Blasimann, A.** (2016). [Effect of core muscle strengthening for injury prevention in male adult soccer players: a systematic review.] *Kinésithérapie la Revue*, May 2016:54. respectively June 2016:16(174);54. http://dx.doi.org/10.1016/j.kine.2016.02.004. French.

Blasimann, A., Nötzli, A., Schaffner, L., Baur, H. (2015). Non-surgical treatment of pes planovalgus associated pain - a systematic review. World Conference for Physiotherapy in Singapore, 05.2015 (Poster presentation, peer-reviewed), *J Physiother* 2015;101:e130-131. http://dx.doi.org/10.1016/j.physio.2015.03.273

Blasimann, A., Wood-Dauphinee, S., Staal, B. J. (2011). Translation, cross-cultural adaptation, reliability and validity of the German version of the Hip Osteoarthritis Outcome Score. *J Physiother.* 2011; 97(Supplement):eS139-140.

ORAL PRESENTATIONS

National conferences

Blasimann, A., König, I., Baert, I., Baur, H., Vissers, D. (2021). Assessments for neuromuscular control for return to sport after an anterior cruciate ligament tear. 2nd Cooperation Congress reha schweiz & Physioswiss online 06./07.05.2021 (oral presentation, peer-reviewed)

Blasimann, A., Eichelberger, P., Lutz, N., Radlinger, L., Baur, H. (2016). [Navicular Rise – a possibility to describe dynamic foot function during stance?] 11th Clinical Research Forum in Zurich (CH), 29.10.2016 (teaser platform presentation & Poster). German.

Blasimann, A., Eichelberger, P., Lutz, N., Radlinger, L., Baur, H. (2016). Navicular Rise - a possibility to describe dynamic foot function during stance? physiocongress 2016 (Swiss Association for Physiotherapy) in Basel (CH), 17./18.06.2016 (oral platform presentation, peer-reviewed)

Blasimann, A., Wood-Dauphinee, S., Staal, B. J. (2012). [Translation, reliability and validity of the Hip Osteoarthritis Outcome Score.] physiocongress 2012 (Swiss Association for Physiotherapy) in Geneva (CH), 10./11.05.2012 (oral podium presentation, peer-reviewed). German.

International conferences

Blasimann, A., Busch, A., Henle, P., Bruhn, S., Vissers, D., Baur, H. (2023). Bilateral neuromuscular control one year after anterior cruciate ligament reconstruction or conservative treatment. 38th Annual Congress of GOTS in Luxembourg (LU) 15.-17.06.2023 (oral presentation, peer-reviewed).

Blasimann, A., Baur, H. (2019). Kann die Evaluation der neuromuskulären Kontrolle nach Verletzungen des vorderen Kreuzbandes zu besseren Return-to-Sport-Entscheidungen beitragen? [Does the evaluation of neuromuscular control after ACL injuries contribute to better return-to-sport decisions?] physiokongress West in Essen (DE), 28.09.2019 (oral presentation, invited keynote speaker).

Blasimann, A., Abgottspon, C., Schwab, C. (2019). Effect of different movement velocities during resistance training on strength gain – a systematic review. World Conference for Physiotherapy in Geneva (CH), 10.-13.05.2019 (oral presentation "classic platform", peer-reviewed).

Blasimann, A., Fleuti, U., Rufener, M., Elfering, A., Baur, H., Radlinger, L. (2014). Electromyographic activity of back muscles during stochastic whole-body vibration. AHFE International (5th International Conference on Applied Human Factors and Ergonomics, 3rd International Conference on Human Factors and Ergonomics in Health Care) in Krakow (PL), 19.-23.07.2014 (oral podium presentation, peer-reviewed)

POSTER PRESENTATIONS

First/presenting author

Blasimann, A., Busch, A., Henle, P., Bruhn, S., Vissers, D., Baur, H. (2023). Bilateral neuromuscular control one year after anterior cruciate ligament reconstruction or conservative treatment. 38th Annual Congress of GOTS in Luxembourg (LU) 15.-17.06.2023 (poster presentation, peer-reviewed).

Blasimann, A., Busch, A., Henle, P., Bruhn, S., Vissers, D., Baur, H. (2023). Neuromuscular control one year after ACL rupture: Influence of sex and treatment in comparison to healthy controls. A cross-sectional study. Scandinavian Sports Medicine Congress in Copenhagen (DK) 02.02. – 04.02.02.2023 (poster presentation, peer-reviewed)

Blasimann, A., Busch, A., Henle, P., Bruhn, S., Vissers, D., Baur, H. (2022). Acute anterior cruciate ligament rupture: neuromuscular control during stair descent and anterior tibia translation. 4th World Congress of Sports Physical Therapy – IFSPT in Nyborg (DK) 26./27.08.2022 (poster presentation, peer-reviewed)

Blasimann, A., Koenig, I., Baert, I., Baur, H., Vissers, D. (2021). Assessments for neuromuscular control after an anterior cruciate ligament injury to decide upon return to sport. IOC World Conference (Prevention of injury and illness in Sport) in Monaco (MC) 25. – 27.11.2021 (poster presentation, peer-reviewed)

Abgottspon, C., Schwab, C., **Blasimann, A.** (2021). Effect of muscle time under tension on strength gain – A systematic literature review. 2nd Cooperation Congress reha schweiz & Physioswiss online 06./07.05.2021 (poster presentation, peer-reviewed)

Glaettli, J., Reinhard, C., **Blasimann, A.** (2021). Strength tests after anterior cruciate ligament repair for return to sports – a systematic review. 2nd Cooperation Congress reha schweiz & Physioswiss online 06./07.05.2021 (poster presentation, peer-reviewed)

Hug, F., Muri, G., **Blasimann, A.** (2021). Assessments for psychological readiness for return to sports after anterior cruciate ligament injury. 2nd Cooperation Congress reha schweiz & Physioswiss online 06./07.05.2021 (poster presentation, peer-reviewed)

Hug F., Muri G., **Blasimann, A.** (2020). Assessments for psychological readiness for return to sports after an anterior cruciate ligament injury. Scandinavian Sports Medicine Congress in Copenhagen (DK) 30.01. – 01.02.2020 (poster presentation, peer-reviewed)

Blasimann, A., Glättli, J., Reinhard, C. (2019). Strength testing after anterior cruciate ligament repair for return to sports – A systematic literature review. World Conference for Physiotherapy in Geneva (CH), 10.-13.05.2019 (poster presentation, peer-reviewed).

Blasimann, A., Gisler, D., Schwammberger, H. (2018). Effect of activity trackers on weight reduction and movement behavior of overweight adults. A systematic literature review. 1st Swiss Sports Med & Sportfisio Conference in Bern (CH), 15./16.11.2018 (poster presentation, peer-reviewed).

Blasimann, A., Henle, P., Busch, A., Boesch, L., Baur, H. (2017). [Neuromuscular control of patient with an anterior cruciate ligament tear during stair walking.]. Nominated for the Swiss Olympic Science Award during the coaches' conference of Swiss Olympic in Magglingen (CH), 25.10.2017 (poster presentation, peer-reviewed). German.

Blasimann, A., Freiburghaus, S., Marolf, M., Busch, A., Boesch, L., Henle, P., Baur, H. (2017). Altered muscle activity in patients with ACL tear compared to healthy controls during stair descent. 1st Cooperation Congress „Rehabilitation in the future", Swiss Association for Physiotherapy, Davos (CH), 19./20.10.2017 (poster presentation, peer-reviewed)

Blasimann, A., Burgener, S., Taraschewski, K. (2017). [Effects of Pilates on physical symptoms in patients with multiple sclerosis: a systematic review.] 1st Cooperation Congress „Rehabilitation in the future", Swiss Association for Physiotherapy, Davos (CH), 19./20.10.2017 (poster presentation, peer-reviewed) German.

Blasimann, A., Busch, A., Boesch, L., Henle, P., Baur, H. (2017). Muscle activity in patients with ACL tear during stair descent. 2nd World Conference on Sports Physical Therapy in Belfast (IE), 10.2017 (poster presentation, peer-reviewed)

Blasimann, A., Gigon, M. (2016). [Efficacy of a home-based program only versus ambulatory physiotherapy in a 1:1-setting after total knee arthroplasty – a systematic review.] physiocongress 2016 (Swiss Association for Physiotherapy) in Basel (CH), 17./18.06.2016 (poster presentation, peer-reviewed). German.

Dietiker, H., Zürcher, **A., Blasimann, A.** (2016). [Scapular kinematics in patients with limited glenohumeral range of motion. A systematic review.] physiocongress 2016 (Swiss Association for Physiotherapy) in Basel (CH), 17./18.06.2016 (poster presentation, peer-reviewed). German.

Eberle, S., Scuderi, M.M., **Blasimann, A.** (2016). [Effect of Core Muscle Strengthening Exercises (Including Plank and Side Plank) on Injury Rate in Male Adult Soccer Players: A Systematic Review] physiocongress 2016 (Swiss Association for Physiotherapy) in Basel (CH), 17./18.06.2016 (poster presentation, peer-reviewed). German.

Dietiker, H., Zürcher, A., **Blasimann, A.** (2015). Scapular kinematics in patients with limited glenohumeral range of motion. A systematic review. Return to Play – 1st World Congress in Sports Physical Therapy in Bern (CH), 20./21. November 2015 (poster presentation, peer-reviewed)

Blasimann, A., Juchler, I., Baur, H., Radlinger, L. (2015). The effect of kinesiotape on neuromuscular activity of peroneus longus during downhill running. Return to Play - 1st World Congress in Sports Physical Therapy in Bern (CH), 20./21. November 2015 (poster presentation, peer-reviewed)

Blasimann, A., Heuberger, M., Hofer, N. (2015). Pain relief through elastic tape - a systematic review. Return to Play - 1st World Congress in Sports Physical Therapy in Bern (CH), 20./21. November 2015 (poster presentation, peer-reviewed)

Blasimann, A., Nötzli, A., Schaffner, L., Baur, H. (2015). Non-surgical treatment of pes planovalgus associated pain - a systematic review. World Conference for Physiotherapy in Singapore (SG), 05.2015 (poster presentation, peer-reviewed)

Blasimann, A., Heuberger, M.S., Hofer, N., Baur, H. (2014). [Pain relief through elastic tape – a systematic review.] physiocongress 2014 (Swiss Association for Physiotherapy) in Bern (CH), 13./14.06.2014 (poster presentation, peer-reviewed). German.

Blasimann, A., Nötzli, A., Schaffner, N., Baur, H. (2014). [Conservative interventions in patients with posterior tibial tendon dysfunction referring to the outcome pain.] physiocongress 2014 (Swiss Association for Physiotherapy) in Bern (CH), 13./14.06.2014 (poster presentation, peer-reviewed). German.

Blasimann, A., Diener, M., Mahnig, S., Radlinger, L. (2012). [Development and testing of the inter- and intrateter reliability of a measurement system for thoracic rotational capability.] physiocongress 2012 (Swiss Association for Physiotherapy) in Geneva (CH), 10./11.05.2012 (poster presentation, peer-reviewed). German.

Blasimann, A., Wood-Dauphinee, S., Staal, B. J. (2011). Translation, cross-cultural adaptation, reliability and validity of the German version of the Hip Osteoarthritis Outcome Score. World Conference for Physiotherapy in Amsterdam (NL), 20.-23.06.2011 (poster presentation, peer-reviewed)

Contributing author

Rogan, S., Luijckx, E., Zinzen, E., **Blasimann, A.** (2023). Evidence of multiple-choice questions in education for health professionals - a review of the literature. International Conference on Medical Education (ICME) 2023 in Baku (AZ) 09./10.10.2023 (oral presentation, peer-reviewed).

Köcker, S., **Blasimann, A.**, Busch, A., Francik-Boesch, L., Henle, P., Bruhn, S., Baur, H. (2022). [Hamstring reflex activity in healthy, conservatively and surgically treated subjects after ACL rupture.] 6th Physiotherapy Research Symposium in Freiburg i.Br. (DE) 30.09./01.10.2022 (poster presentation, peer-reviewed). German.

Baur, H., Busch, A., Boesch, L., Schmidt, A., Henle, P., **Blasimann, A.** (2022). [Changes in reflex activity of hamstring muscles during rehabilitation after rupture of the anterior cruciate ligament.] 37th Jahreskongress der GOTS in Berlin (DE) 19./20.05.2022 (poster presentation, peer-reviewed). German.

Köcker, S., **Blasimann, A.**, Busch, A., Boesch, L., Henle, P., Bruhn, S., Baur, H. (2022). [Hamstring reflex activity in healthy, conservatively and surgically treated subjects after ACL rupture.] 37th Annual Congress of GOTS in Berlin (DE) 19./20.05.2022 (oral presentation, peer-reviewed). German.

Luginbuehl, H., Koenig, I., Rogan, S., **Blasimann, A.**, Zuber, S. (2021). Transforming traditional physiotherapy hands-on skills teaching to technology enhanced learning during the Covid-19 pandemic. AMEE (An International Association for Medical Education) virtual conference 27. – 30.08.2021 (oral presentation, peer-reviewed).

Imhof, S., Hanusch, K.-U., Neuenschwander-Blaser, S., Baur, H., **Blasimann, A.** (2021). Validität des Testprotokolls für VKB-PatientInnen des Spitals Emmental. 36th Annual Congress of GOTS online, 01.-02.07.2021 (poster presentation, nominated for poster prize, peer-reviewed)

Wirth, S.U., Stucki, N., **Blasimann, A.** (2019). What effect do duration and speed of the foam roll have on mobility? - A systematic review. World Conference for Physiotherapy in Geneva (CH), 10.-13.05.2019 (oral presentation, peer-reviewed).

Busch, A., **Blasimann, A.**, Henle, P., Baur, H. (2019). Neuromuscular activity during stair descent in ACL reconstructed patients: a pilot study. World Conference for Physiotherapy in Geneva (CH), 10.-13.05.2019 (oral presentation "rapid five", peer-reviewed).

Schmidt A., **Blasimann, A.,** Boesch, L., Henle, P., Baur, H. (2018). Comparison of neuromuscular hamstring activity of people with acute anterior cruciate ligament rupture and at one-year follow-up - a pilot study. Poster presentation at the 1st Swiss Sports Med & Sportfisio Conference in Bern (CH), 15./16.11.2018 (poster presentation, peer-reviewed).

Busch, A., Henle, P., Boesch, L., **Blasimann, A.**, Baur, H. (2017). Neuromuscular control in patients with acute ACL injury during stair ascent - a pilot study. German Olympic Sports Medicine Congress 2018 in Hamburg (DE), 24.05.2018 (poster presentation, peer-reviewed).

Eichelberger P., **Blasimann, A.,** Woodtly, S.I., McEvoy J.C., Bohnenblust, M., Kaufmann, E., Krause, F., Baur, H. (2017). Coupling of navicular mobility and foot length change during walking. 1st cooperation congress „Rehabilitation in the future", Swiss Association for Physiotherapy, Davos (CH), 19./20.10.2017 (poster presentation, peer-reviewed)

König, I., **Blasimann, A.**, Hauswirth, A., Eichelberger, P., Baeyens, J.P., Radlinger, L. (2017). Wavelet analysis of muscle activity of lower extremities and pelvic floor muscles in women while walking or running: a systematic review. 1st cooperation congress „Rehabilitation in the future", Swiss Association for Physiotherapy, Davos (CH), 19./20.10.2017 (oral platform presentation, peer-reviewed)

Eichelberger P., **Blasimann, A.,** Woodtly S.I., McEvoy J.C., Bohnenblust M., Kaufmann E., Krause F., Baur H. (2017). Coupling of navicular mobility and foot length change during walking. World Conference for Physiotherapy in Cape Town (ZA), 02.-04.07.2017 (poster presentation, peer-reviewed)

Koenig I., **Blasimann, A.,** Hauswirth A., Eichelberger P., Baeyens J.-P., Radlinger L. (2017). Wavelet analysis of muscle activity of lower extremities and pelvic floor muscles in women while walking or running: A systematic review. World Conference for Physiotherapy in Cape Town (ZA), 02.- 04.07.2017 (oral platform presentation, peer-reviewed)

Baur, H., Boesch, L., **Blasimann, A.**, Bruhn, S., Henle, P. (2016). [Sensorimotor control of the knee of people with and without torn anterior cruciate ligament.] Research symposium for Physiotherapy in Bochum (DE), 17./18.11.2016 (oral platform presentation, peer-reviewed). German.

König, I., **Blasimann, A.**, Hauswirth, A., Eichelberger, P., Radlinger, L. (2016). Wavelet analysis of muscle activity of lower extremities while walking or running and pelvic floor muscles in women: A systematic Review. International Continence Society (ICS) Congress 2016 in Tokyo (JP), 13.-16.09.2016 (oral podium presentation, peer-reviewed)

Eichelberger, P., Lutz, N., **Blasimann, A.,** Krause, F., Baur, H. (2016). A marker set for clinically focused 3D dynamic foot function assessment. International Foot and Ankle Congress (i-FAB) 2016 in Berlin (DE), 23.-25.06.2016 (poster presentation, peer-reviewed)

Eichelberger, P., Lutz, N., **Blasimann, A.**, Krause, F., Baur, H. (2016). Reliability of a new foot model for dynamic navicular drop measurement. physiocongress 2016 (Swiss Association for Physiotherapy) in Basel (CH), 17./18.06.2016 (oral platform presentation, peer-reviewed)

Eberle, S., Scuderi, M.M., **Blasimann, A.** (2015). Effect of core muscle strengthening for injury prevention in male adult soccer players: a systematic review. Return to Play – 1st World Congress in Sports Physical Therapy in Bern (CH), 20./21. November 2015 (winner of the Young Research Award of the Swiss Sports Physical Therapy Association; poster & short oral podium presentation, peer-reviewed). German/English.

Leitner, M., **Blasimann, A.**, Dubach, B., Baur, H. (2014). Effects of whole-body vibration on musculoskeletal complaints of surgery staff. AHFE International (5th International Conference on Applied Human Factors and Ergonomics, 3rd International Conference on Human Factors and Ergonomics in Health Care) in Krakow (PL), 19.-23.07.2014 (oral podium presentation, peer-reviewed)

Eichelberger, P., Baur, H., Ferraro, M., Minder, U., **Blasimann, A.**, Denton, T. (2014). Analysis of measurement performance in optical motion capturing. 13th International Symposium on 3D Analysis of Human Movement 2014 in Lausanne (CH), 14.-17.07.2014 poster presentation, peer-reviewed)

Leitner, M., **Blasimann, A.**, Baur, H. (2014). [Effect of stochastic whole body vibration on musculoskeletal complaints in surgery nurses.] physiocongress 2014 (Swiss Association for Physiotherapy) in Bern (CH), 13./14.06.2014 (poster presentation, peer-reviewed). German.

Eichelberger, P., Baur, H., Ferraro, M., Minder, U., **Blasimann, A.**, Denton, T. (2014). [Optical 3D-measurements of small movements in the foot.] physiocongress 2014 (Swiss Association for Physiotherapy) in Bern (CH), 13./14.06.2014 (poster presentation, peer-reviewed). German.

SCIENTIFIC RELATED ACTIVITIES

Congress visits

2023	38th Annual Congress of GOTS in Luxembourg (LU) Scandinavian Sports Medicine Congress (SportsKongres) in Copenhagen (DK)
2022	Annual sportfisio Symposium in Bern (CH) - Swiss Sports Physiotherapy Association, topic «Best Practice" 4th IFSPT World Congress for Sports Physical Therapy in Nyborg (DK) – International Federation for Sports Physical Therapy 37th Annual Congress of the Society for Orthopedics and Traumatology in Sports Medicine GOTS hosted by GOTS Germany, Berlin (DE)
2021	IOC World Conference "Prevention of injury and illness in Sport" in Monte Carlo (MC) 36th Annual Congress of the Society for Orthopedics and Traumatology in Sports Medicine GOTS hosted by GOTS Switzerland, online 2nd Cooperation Congress physioswiss & reha Switzerland, online 1st virtual summit of the Isokinetic Conference Voyage: "The ongoing ACL dilemma", online World Conference for Physical Therapy (WCPT), online
2020	3rd Sports Medical Performance Day (Altius Clinic) in Rheinfelden (CH) Annual sportfisio Symposium (in Bern (CH) - Swiss Sports Physiotherapy Association, topic "knee", online Scandinavian Sports Medicine Congress (SportsKongres) in Copenhagen (DK)

2019
Annual sportfisio Symposium in Bern (CH) -
Swiss Sports Physiotherapy Association, topic "Shoulder and Sports"
GOTS Switzerland Winter Congress in Basel (CH)
World Conference for Physical Therapy (WCPT) in Geneva (CH)
zfass – Zurich Forum for Applied Sports Sciences in Zurich (CH)
thiemekongress West, Sports Physiotherapy Day in Essen (DE)
2nd Sports Performance Day, altius Sports Clinic in Rheinfelden (CH)

2018
1st Swiss sportfisio & Sportsmedicine Conference in Bern (CH)
GOTS Switzerland Winter Congress in Basel (CH)

2017
2nd IFSPT World Congress for Sports Physiotherapy –
International Federation for Sports Physical Therapy (IFSPT) in Belfast (IE)
Annual sportfisio Symposium in Bern (CH) -
Swiss Sports Physiotherapy Association
1st Cooperation Congress physioswiss & reha Switzerland, Davos (CH)
3rd Bioelettronica Day EMG State of the Art – Bioelettronica, Torino (IT)
GOTS Switzerland Winter Congress in Basel (CH)

2016
11th Clinical Research Forum in Zurich (CH) – Physiotherapy Sciences Foundation
Annual sportfisio Symposium in Bern (CH) - Swiss Sports Physiotherapy Association
zfass – Zurich Forum for Applied Sports Sciences in Zurich (CH)
Biannual Congress for Physiotherapy in Basel (CH) -
Swiss Association for Physiotherapy (Physioswiss)

2015
1st World Congress for Sports Physiotherapy in Bern (CH) –
International Federation for Sports Physical Therapy (IFSPT)
Annual sportfisio Symposium in Bern (CH) - Swiss Sports Physiotherapy Association
zfass – Zurich Forum for Applied Sports Sciences in Zurich (CH)

2014
Annual sportfisio Symposium in Bern (CH) -
Swiss Sports Physiotherapy Association
Biannual Congress for Physiotherapy in Bern (CH) -
Swiss Association for Physiotherapy (Physioswiss)
zfass – Zurich Forum for Applied Sports Sciences in Zurich (CH)

2013
Annual sportfisio Symposium in Bern (CH) -
Swiss Sports Physiotherapy Association

2012
Annual sportfisio Symposium in Bern (CH) -
Swiss Sports Physiotherapy Association
Biannual Congress for Physiotherapy in Geneva (CH) -
Swiss Association for Physiotherapy (Physioswiss)

2011
Symposium SwissDRG – University Hospital, Inselspital, Bern (CH)
World Conference for Physical Therapy (WCPT) in Amsterdam (NL)
zfass – Zurich Forum for Applied Sports Sciences in Zurich (CH)

2010
Biannual Congress for Physiotherapy -
Swiss Association for Physiotherapy (Physioswiss) in Basel (CH)
Congress "Function and Gait" – University Children's Hospital of Basel (CH)

2009
4th Clinical Research Forum – FIDOS Physiotherapy Database/
Zurich University of Applied Sciences, Winterthur (CH)
Annual sportfisio Symposium in Bern (CH) - Swiss Sports Physiotherapy Association
Sportmed Conference in Bern (CH) – Swiss Olympic Association
3rd Interdisciplinary Sports Symposium – Sport Medical Base, Kerenzerberg Zurich (CH)
4th International Football Medicine Congress – IFOMEC, Basel (CH)

2008
Annual sportfisio Symposium in Bern (CH) - Swiss Sports Physiotherapy Association
2nd Interdisciplinary Sports Symposium – Sport Medical Base, Kerenzerberg (CH)
Current aspects in orthopedic surgery – Schulthess Clinic, Zurich (CH)

2006
Current aspects in orthopedic surgery – Schulthess Clinic, Zurich (CH)

2005
SART congress "Stop and Go – Rehabilitation after sports injuries" – SART, Basel (CH)
Update treatment guidelines after orthopedic interventions – Schulthess Clinic, Zurich (CH)

2002
Biannual Congress for Physiotherapy - Swiss Association for
Physiotherapy (Physioswiss) in Lucerne (CH)

Review activity for journals, associations, and conferences:

- Journal for Disability and Rehabilitation
- Journal for Health-Related Quality of Life Outcomes
- Journal of Orthopedic and Sports Physical Therapy
- World Conference of Physical Therapy (abstracts, posters)
- Royal Dutch Society for Physiotherapy (research grant)
- Physiotherapy UK Conference (abstracts)
- Congress of the Swiss Association for Physiotherapy (abstracts for biannual congress)

Memberships:

- physioswiss – Swiss Association for Physiotherapy
- sportfisio – Swiss Association for Sports Physiotherapy SASP
- SART - Swiss Working Group for Rehabilitation and Training
- SSSS - Swiss Society for Sports Sciences

EDUCATIONAL ACTIVITIES

Coaching and supervising activities

Supervisor of Master thesis in Physiotherapy (Bern University of Applied Sciences)

2023 – 2024

Philipp Koch: [Evaluation of the most relevant stressors and coping strategies among students in Bachelor of Science in Physiotherapy] German, co-supervision together with I. Koenig

Gabi Bähler: [Entrustable Professional Activities (EPA) – Validation of EPA prototypes in physiotherapy] German, co-supervision together with I. Koenig

Marc-Joël Blaser: [Evaluation of a pilot project to implement Entrustable Professional Activities (EPA) in the BSc Physiotherapy program] German, co-supervision together with I. Koenig

2022 – 2023

Susanne Neuenschwander-Blaser: "Is there an association between force, function, and failure rate after isolated meniscal repair? A retrospective data analysis of a test protocol of a Swiss regional hospital"

Raphael Ritz: [Predictors of prospective students for admission to the Bachelor of Science in Physical Therapy program to be examined in the aptitude assessment] German, co-supervision together with I. Koenig

2021 – 2022

Jonas Engel: "Force measurement of Knee Extensor and Flexor Using a Fixed Handheld Dynamometer: A Reliability and Validity Study"

2020 – 2021

Martina Steiner: "Gender-specific differences in neuromuscular activation in the knee stabilizing muscles in adults"

2019 – 2020

Sabrina Imhof: "Return to sport after anterior cruciate ligament rupture - Validation study of the test protocol of a Swiss regional hospital"

Co-Supervisor of Master thesis in Psychology (University of Bern)

2015 – 2016

Nora Banz, Nathalie Buscher und Yannik Faes: [Stochastic whole-body vibration in a seated position] German, co-supervision together with Dr. P. Eichelberger (Bern University of Applied Sciences) and Prof. A. Elfering (University of Bern)

Supervisor of Bachelor thesis in Physiotherapy (Bern University of Applied Sciences)

2022 – 2023

Sarina Sommer & Sara Wüthrich: [Secondary Prevention for Athletes after ACL Injury - An Evidence Summary] German

Katja Wasser & Lea Widmer: [Does surgical reconstruction or conservative treatment of an anterior cruciate ligament rupture lead to a higher overall KOOS value? A retrospective data analysis] German

2021 – 2022

Lina Frank & Kim Jaeggi: [Pain-related fear of movement regarding performance of a familiar physical activity after anterior cruciate ligament reconstruction. Comparison of two surgical techniques] German

Simone Luethi & Sina Vogt: [Overview of objective clinical tests after rotator cuff injuries and their physiotherapeutic relevance. An Evidence Summary] German

Jan Rothenbuehler & Syra Schmid: [Influence of supplemental Pilates training in adolescents and young adults on jump height in volleyball and basketball. A systematic review with meta-analysis] German

2020 – 2021

Dominik Graf & Manuel Megert: [Review of the effectiveness of prevention programs to prevent ACL ruptures. An Umbrella Review] German

Melanie Bucher & Carina Hänni: [Pain and ADL questionnaires after rotator cuff injuries. A systematic literature review with practice recommendations] German

Noemi Riedi & Laura Tüscher: [The effectiveness of the FIFA 11+ prevention program on knee injuries in football and futsal. A systematic review] German

2019 – 2020

Anja Eschermann: [What is the impact of preventive training on the wobble board on the rupture rate of anterior cruciate ligament tears? A systematic review] German

Luca Marras & Jasmin Stoller: [Effects of open and closed chain strength training related to anterior stability in early rehabilitation after anterior cruciate ligament reconstruction] German

Sabrina Streit & Michal Weber: [Prevention of re-injury after supination trauma. A systematic review] German

2018 – 2019

d'Allens Lilianne & Melanie Gonseth: [Effects of stretching in warm-up on performance parameters in ice hockey - a systematic review] German

Fabienne Hug & Gina Muri: [Assessments to evaluate psychological readiness for return to sport after ACL rupture. Psychometric properties and applicability in practice] German

Giulia Jung & Leonie Ruch: [Comparison of surgical versus conservative follow-up of anterior cruciate ligament rupture with respect to active knee stability. A systematic review] German

2017 – 2018

Chantal Abgottspon & Charlotte Schwab: [Effect of muscle tension duration on muscle gain. A systematic review] German

Jasmin Glättli & Chantal Reinhard: [A review of strength tests to assess return to sport after anterior cruciate ligament reconstruction. A systematic review] German

Nina Stucki & Salome Wirth: [What is the effect of fascia roller application duration and speed on range of motion? A systematic review] German

2016 – 2017

Dominik Gisler & Helen Schwammberger: [The effect of activity trackers on weight loss and physical activity behavior in overweight adults. A systematic review] German

Cornelia Krummenacher & Carla Vogel: [Conservative follow-up after primary traumatic patellar dislocation in adolescents. A review of the current evidence] German

2015 – 2016

Marion Bohnenblust & Eveline Kaufmann: [The behavior of foot length change and the navicular bone during walking with consideration of the reliability of a 3D measurement system. A retrospective data analysis] German

Annique Hari & Céline Schmidlin: [Use of foot and hip strategies on unstable surfaces with different bases of support. A descriptive single-case study] German

Sabrina Burgener & Katharina Taraschewski: [Effect of Pilates on physical symptom outcomes in multiple sclerosis. A systematic review] German

2014 – 2015

Hannah Dietiker & Annina Zürcher: [Scapular kinematics in patients with glenohumeral movement restriction. A systematic review with practice recommendations.] German

Manuela Gigon: [Effectiveness of a home-based program alone in patients undergoing total knee arthroplasty. A systematic review] German

Simon Eberle & Manuel Scuderi: [Effect of trunk strength training on injury susceptibility in adult soccer players. A systematic review] German

2013 – 2014

Ramona Bachem & Patricia Metzler: [Influence of treatment by head orthosis on the course of head deformities in infants - a retrospective study] German

Seraina Dübendorfer & Sandra Füllemann: [How do physiotherapists deal with their own occupational musculoskeletal complaints?] German

2012 – 2013

Michaela Heuberger & Nina Hofer: [Pain relief with elastic tape - current state of the evidence. A systematic review] German

Annina Noetzli & Lisa Schaffner: [Conservative interventions for posterior tibialis muscle tendon dysfunction related to the outcome pain. Systematic review] German

Ramona Hilpert-Bärlocher & Nicole Etter: [Effect of strength and balance training on fear of falling in the elderly as measured by the FES-I. A systematic review] German, co-supervision together with J. Kessler

2011 – 2012

Alexander Baumgartner & Isabelle Juchler: [The influence of Kinesio Tape on neuromuscular activity of the peroneus longus muscle in functional instability] German

Ursula Fleuti & Meret Rufener: [Electromyographic activity of back muscles during stochastic whole-body vibration] German

2010 – 2011

Michelle Diener & Sara Mahnig: [Inter- and intrarater reliability of a measurement system for thoracic rotational capability] German

Rahel Klingler & Stefanie Leuenberger: [Change in general mobility over the course of the day. An observational study of young women] German

Vanessa Haenni & Daniela Michel: [Hip muscle activity three years after surgical hip dislocation during walking, stair climbing and cycling - a retrospective single case study] German

Teaching activities

Academic setting (Bern University of Applied Sciences, School of Health Professions)

- Lecturer “Change management in practice” (MSc programs in Physiotherapy, Nursing, Midwifery and Nutrition, interprofessional module “Leadership, project and change management”
- Lecturer “Performance of ice hockey game officials” (4th semester MSc Physiotherapy, specialization in sport, module “Performance”)
- Lecturer “Neuromuscular control and ACL injury” (4th semester MSc Physiotherapy, specialization in professional development, module “Anatomy and biomechanics”)
- Lecturer “Physiotherapy as scientific discipline” (MSc Nursing, module “Philosophy of science for health professions”)
- Lecturer “Gait analysis” (1st semester BSc Physiotherapy, module “Basics in examination”)

Further education (art of motion Switzerland)

- Senior Lecturer for Pilates Essentials matwork course/Pilates Anatomy/Experience Anatomy (further education)

National sport association (Swiss Ice Hockey Federation (SIHF))

- Lecturer “Relevance of core stability for game officials in ice hockey”
- Off-ice athletic coach for female referees and linespersons during SIHF Women Game Officials summer camp

Private and public services

- Substitution and vacation replacement Pilates mat courses – Fitness Center Bodyline, Langnau i.E. (CH)
- Substitution and vacation replacement Pilates mat courses – Fitness Center & Physiotherapy Aemmefit, locations Luetzelflueh & Burgdorf (CH)
- Various introductory courses for Pilates mat – Women's clubs, communities of Trub and Eggiwil (CH)
- Swimming teacher for schoolchildren during summer swimming week (familiarization with water and beginners) – community of Langnau i.E. (CH)

Further activities in education

- Organization internal "Research Colloquium", Bern University of Applied Sciences, Bern (CH)
- Guidance internships of Master students (MSc Physiotherapy) – Bern University of Applied Sciences, School for Health Professions, Bern (CH)
- External expert for Bachelor theses (BSc Physiotherapy) – University of Applied Sciences of Western Switzerland (HES-SO), Leukerbad (CH)
- Practice instructor for physiotherapy students, Bern University of Applied Sciences, School for Health Professions, FEUSI Physiotherapy School, Center for Education University Hospital, Inselspital, Bern, all in Bern (CH)
- Second assessor vocational baccalaureate, direction health and social work, subject biology, written final examinations, vocational baccalaureate schools, Canton of Bern (CH)
- Assessor for Pilates mat (further education) – art of motion Switzerland
- Expert for Diploma in Physiotherapy – Feusi Physiotherapy School, Bern (CH)
- Expert for Diploma in Physiotherapy – Center for Education, University Hospital, Inselspital, Bern (CH)

Didactic courses

2023

Further education „Resilience in Physiotherapy", physiobern, Bern (CH)

Symposium "Wellbeing in Medical Education – Yes, we care!", University of Bern, Bern (CH)

Workshop "Visualization Advanced – Digital Visualization", Bern University of Applied Sciences, Bern (CH)

Workshop "First steps with open educational resources", Bern University of Applied Sciences, Bern (CH)

2022

Workshop "Visualization Advanced - Human Beings", Bern University of Applied Sciences, Bern (CH)

Workshop "Psychology meets Physiotherapy" – Prof. Dr. Thorsten Weidich & Comb'in Private Physiotherapy Practice, Burgdorf (CH)

E-Learning Day "Future Skills", Bern University of Applied Sciences, Bern (CH)

Workshop "Visualization Basics 2", Bern University of Applied Sciences, Bern (CH)

Certificate for Higher Education and Didactics, Bern University of Applied Sciences, Bern (CH)

E-Learning Day "Student-centered higher education", Bern University of Applied Sciences, Bern (CH)

2020

Workshop "Visualization Basics 1", Bern University of Applied Sciences, Bern (CH)

Workshop "Activating methods - online and in presence", Bern University of Applied Sciences, Bern (CH)

Workshop "Gamification in teaching", Bern University of Applied Sciences, Bern (CH)

Workshop "Designing effective presentations", Bern University of Applied Sciences, Bern (CH)

2018

Late afternoon course "Coaching students in Master thesis and seminar papers", Bern University of Applied Sciences, Bern (CH)

2009

Professional course for practice supervisors, Bern University of Applied Sciences, Bern (CH)

2008

Workshop "Research & Bachelor theses", Bern University of Applied Sciences, Bern (CH)

Workshop "Clinical reasoning in physiotherapy, Bern University of Applied Sciences, Bern (CH)

Workshop for diploma assessors, Bern University of Applied Sciences, Bern (CH)

2007

Workshop "Introduction for practice supervisors", Bern University of Applied Sciences, Bern (CH)

2004

Workshop "Perceiving learning situations in the supervision of physiotherapy students", Center for Education, University Hospital, Inselspital, Bern (CH)

2003

Course "Educating Clinical Reasoning", FEUSI Physiotherapy School, Bern (CH)

Management courses

2022 - 2023

Internal education "Leadership at BFH", Bern University of Applied Sciences
Module 1: Development, reflexion and leadership,
Module 2: Empowerment and instruments for leadership

Individual and group coaching with facilitator
Daniel Osterwalder, visualdynamics GmbH, Bern (CH)

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PD Dr. Heiner Baur, Bern University of Applied Sciences

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