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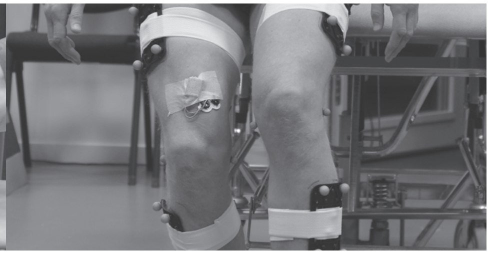

Kissing knees – factors behind the attraction

Knee abduction in individuals with anterior cruciate ligament injury

ANNA CRONSTRÖM

MUSCULOSKELETAL FUNCTION | DEPARTMENT OF HEALTH SCIENCES | LUND UNIVERSITY

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Individuals with anterior cruciate ligament (ACL) injury often exhibit poor movement quality, in the form of increased knee abduction during activity, which may affect function and increase the risk of re-injury. The results from this thesis indicate that sensorimotor function, such as proprioception and muscle activation patterns should be considered when designing training regimes, aiming at reducing knee abduction to possibly prevent further injuries in this population. Given that healthy women perform weight-bearing activities with increased knee abduction compared to men, there may need to be a greater focus on this movement pattern during prevention and rehabilitation training in women, whereas other factors may be more relevant in men.

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DOCTORAL DISSERTATION
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Title and subtitle

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Abstract

Anterior cruciate ligament (ACL) injury and patellofemoral pain (PFP) are common sports-related knee injuries. Their consequences include compromised health of the effected individual and substantial financial costs for society. Increased knee abduction or a knee medial to foot position (KMFP), so called “kissing knees”, during weight-bearing activities is reported to be more common in patients with ACL injury or PFP than in non-injured individuals and is also reported to be associated with greater pain and worse function in these patients. Furthermore, increased knee abduction during activity is suggested to increase the risk of sustaining both primary and subsequent ACL injuries. However, the contributing factors for this altered movement pattern are not well understood. Therefore, the primary aim of this thesis was to investigate the association between sensorimotor factors, modifiable by training, and knee abduction in patients with ACL injury.

Two systematic reviews with meta-analyses were conducted (papers I and II). These included patients with ACL injury or PFP and healthy individuals and investigated the association between sex, muscle strength, muscle activation, sensory function and joint range of motion (ROM), respectively, and knee abduction. The association between sensory function (n=51, 23 women), muscle strength and muscle activation (n=29, 11 women), respectively, and a knee abduction/KMFP in patients with ACL injury were investigated in three cross-sectional studies (papers III – V).

This thesis shows that non-injured women and those with PFP perform weight-bearing activities with greater knee abduction compared to their male counterparts. In healthy individuals, lower trunk lateral flexion strength, lower gluteus maximus activation, increased hip external rotation ROM and reduced ankle dorsi-flexion range of motion were associated with increased knee abduction/KMFP. In individuals with ACL injury, reduced sensory function was associated with a KMFP, and lower vastus medialis (VM) activation and iliocostalis activation on the non-injured side but higher semitendinosus (ST) activation and ST/VM ratio were associated with increased 3D knee abduction during weight-bearing activities. Hip and knee strength was not, or only weakly, associated with knee abduction in healthy individuals and in those with knee injury.

The result from this thesis indicates that sensorimotor function, such as proprioception and muscle activation patterns should be considered in the rehabilitation after ACL injury. Given that healthy women perform weight-bearing activities with increased knee abduction compared to men, there may need to be a greater focus on this movement pattern during prevention and rehabilitation training in women, whereas other factors may be more relevant in men. Further investigations are needed to confirm these results and to establish the factors, both structural and neuromuscular, that contribute to knee abduction in men and women with ACL injury.

Key words ACL injury, sensorimotor function, postural orientation, knee abduction

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To my family

Content

Abstract

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Populärvetenskaplig sammanfattning

Främre korsbandsskada i knäet och främre knäsmärta är två vanligt förekommande idrottsrelaterade skador som medför stora konsekvenser för den drabbade individen och höga kostnader för samhället. En korsbandsskada resulterar ofta i knäinstabilitet och funktionsnedsättning med försämrad livskvalité som följd. Dessutom innebär en korsbandsskada ofta sjukskrivning och att den drabbade måste undvika fysisk aktivitet helt eller delvis under en längre tid. Omkring hälften går aldrig tillbaka till den aktivitetsnivå de hade innan skadan.

Funktionella test utgör en viktig del i bedömningen av patientens funktion. Det är främst kvantitativa tester som används i kliniken där man mäter t.ex. muskelstyrka eller hoppförmåga. Senare forskning har visat att även kvalitéten på rörelsen har betydelse. När det gäller knäet är det framförallt knäets position i förhållande till foten som utvärderas. Större knäabduktion eller en knäposition där knäet är medialt om foten under aktivitet, så kallade ”kissing knees” är vanligare hos patienter med korsbandsskada eller främre knäsmärta än hos individer utan knäskada och samvarierar även med sämre funktion och mer smärta hos dessa patienter. Större knäabduktion samvarierar också med högre risk att drabbas av en korsbandsskada och högre risk för efterföljande korsbandsskada i antingen samma knä eller i andra knäet. Det är inte klarlagt vilka faktorer som ligger bakom detta rörelsemönster. Syftet med denna avhandling var därför att undersöka sambandet mellan olika sensomotoriska faktorer, som kan påverkas med träning, och knäabduktion under funktionella test hos individer med korsbandsskada.

Två systematiska litteraturgranskningar med meta-analys genomfördes (studie I och II), där vi undersökte betydelsen av kön, muskelstyrka, muskelaktivering, sensorisk funktion och rörelseomfång för knäabduktion. Dessa studier inkluderade patienter med främre korsbandsskada eller främre knäsmärta samt friska individer. I tre tvärsnittsstudier (studie III-V) undersöktes sambandet mellan sensorisk funktion (n=51, 23 kvinnor), muskelstyrka och muskelaktivering (n=29, 11 kvinnor) och knäabduktion/medial knäposition för patienter med främre korsbandsskada.

Avhandlingen visar att hos personer utan knäskada och hos de med främre knäsmärta har kvinnor större knäabduktion än män när de utför funktionella test. Hos friska individer samvarierade lägre sidobålstyrka, lägre gluteus maximus aktivering, sämre rörelseomfång i fotleden och ökat rörelseomgång i utåtrotationen i höften med ökad knäabduktion under funktionella test. Hos individer med främre korsbandsskada var sämre sensorisk funktion relaterat till en medial knäposition mätt visuellt. Lägre vastus medialis (VM) aktivitet och iliocostalis aktivitet för den icke skadade sidan men högre semitendinosus (ST) aktivitet och ST/VM ratio samvarierade med ökad 3D knäabduktion under aktivitet. Det fanns inget samband eller endast ett svagt samband mellan styrka i höft- och knämuskler och knäabduktion för individer utan knäskada och för de med främre korsbandsskada.

Avhandlingens resultat tyder på att sensorisk funktion, som t.ex. proprioception (ledsinne) och muskelaktivering är faktorer att ta hänsyn till i rehabilitering efter korsbandsskada. Eftersom kvinnor verkar vara mer benägna att utföra rörelser med större knäabduktion än män, kan det vara viktigt att lägga mer fokus på detta rörelsemönster under skadeförebyggande träning och rehabilitering efter skada medan andra faktorer kan vara mer relevanta för män. Fortsatta studier behövs för att bekräfta dessa resultat och för att fastställa vilka faktorer, både strukturella och neuromuskulära, som har betydelse för knäabduktion hos män och kvinnor med korsbandsskada.

List of studies

I. Cronström A, Creaby MW, Nae J, Ageberg E. Gender differences in knee abduction during weight-bearing activities: A systematic review and meta-analysis. Gait Posture. 2016;49:315-28.

II. Cronström A, Creaby MW, Nae J, Ageberg E. Modifiable factors associated with knee abduction during weight-bearing activities: A systematic review and meta-analysis. Sports Med. 2016;46(11):1647-62.

III. Cronström A, Ageberg E. Association between sensory function and medio-lateral knee position during dynamic tasks in patients with anterior cruciate ligament injury. BMC Musculoskelet Disord. 2014;15(1):430.

IV. Cronström A, Creaby MW, Blackmore T, Nae J, Ageberg E. Is trunk and lower extremity strength associated with knee abduction angle during weight-bearing activities in patients with anterior cruciate ligament reconstruction? In manuscript.

V. Cronström A, Creaby MW, Franettovich Smith MM, Blackmore T, Nae J, Ageberg E. Alterations in trunk and lower extremity muscle activation are associated with knee abduction during weight-bearing activities in patients with anterior cruciate ligament injury. In manuscript

Definitions and Abbreviations

Definitions

Sensorimotor function

In this thesis, sensorimotor function is defined as the processing of the afferent sensory input, signal integration in the CNS and the activation of efferent motor signals that contribute to control functional joint stability, by modulation of, for example, muscle activation and force production.

Postural orientation

In this thesis defined as the ability to stabilize the body segments in relation to each other, the environment and gravity during static and dynamic tasks.

Neuro muscular control

In this thesis defined as the ability to produce controlled movement through coordinated muscle activity to maintain joint stability.

Proprioception

In this thesis defined as the afferent information arising from mechanoreceptors in the knee joint that contribute to postural control and joint stability.

Abbreviations

ACL	anterior cruciate ligament
ACLD	anterior cruciate ligament deficiency
ACLR	anterior cruciate ligament reconstruction
ADL	activity of daily living
CNS	central nervous system
EMG	electromyography
Gmax	gluteus maximus
Gmed	gluteus medius
IC	iliocostalis
JPS	joint position sense
KMFP	knee medial to foot position
MF	medial femoral condyle
MGc	medial gastrocnemius
MM	medial malleolus
MTP 1	metatarsophalangeal joint 1
MVC	maximum voluntary contraction
N	force in newton
Nm	newton meter
OA	osteoarthritis
PFP	patellofemoral pain
ROM	range of motion
SDM	standard difference in mean
SLHD	single-leg hop for distance
SLS	single-leg squat
ST	semitendinousus
TDPM	threshold to detection of passive motion

Introduction

Anterior cruciate ligament injury

The anterior cruciate ligament (ACL) is an intraarticular ligament situated in the knee joint with the main purpose of providing mechanical stability to the knee during movements by preventing anterior tibial translation and rotational load [1, 2]. The ACL originates at the posteromedial corner of the lateral femoral condyle and then attaches to the anterior intercondylar fossa on the tibia. The ligament consists of two bundles, the anteromedial and the posterolateral bundles, with different functions on the knee joint. When the knee is in an extended position, it is mainly the posterolateral bundle that contributes to knee stability by passive tension of this part of the ligament, whereas the anteromedial bundle is lax. On the contrary, when the knee is flexed, the anteromedial bundle tautens whereas the posterolateral bundle is lax. Hence, the ACL is able to provide stability to the knee during the whole motion path [1].

Injury to the ACL is a common sports-related injury with major consequences for the individual and with individual life time costs up to 88,000 US dollars for society [3]. In Sweden, the incidence has been estimated to approximately 8.1 in 10,000 individuals [4]. Most injuries occur during sports-related non-contact episodes [5], typically around 50 milliseconds after foot contact, with the foot planted on the surface with a nearly extended knee together with increased trunk lean and increased knee abduction [6, 7]. A non-contact ACL injury has a multi-factorial etiology with several potential risk factors. Extrinsic risk factors that have been suggested include dry and warm weather, playing on artificial grass, on a hard surface or indoors as well as the type of shoes used [8, 9]. Intrinsic risk factors may include female sex, increased knee joint laxity, subtalar joint pronation, reduced hip range of motion (ROM), lower extremity asymmetries, joint stiffness, increased knee abduction moment, high ground reaction force, worse core stability, lower hamstring to quadriceps ratio, female hormones, previous knee injury and heredity [7, 10–17]. There is, however, conflicting evidence regarding the role of knee abduction [14, 18–20] and lower extremity strength [12, 17, 21, 22] for ACL injury.

Consequences of an ACL injury

Common consequences after injury are functional limitations such as mechanical instability [23], impaired balance [24], reduced lower extremity strength [25], altered muscle activation patterns [26–28] and impaired proprioception [29]. However, the main symptom after ACL injury is perceived instability during weight-bearing activities, so called “giving way” [30]. Furthermore, these individuals are at an increased risk of developing tibiofemoral and patellofemoral osteoarthritis (OA) when they are only 35 to 40 years old [31, 32]. Reduced self-reported quality of life, both in the short and in the long term is also commonly reported after ACL injury [33, 34]. Also, almost 50% of these patients suffer from depressive symptoms prior to the ACL surgery which has shown to be associated with worse self-reported function one year later [35]. Previous studies report changes in the central nervous system (CNS) after knee injury, in terms of higher frontal theta power [36, 37] and lower activation in sensory cortical areas, but higher activation in motor areas and visual-motor areas [38–40] during activity. This indicates that neuroplasticity allows the brain to compensate for the loss of sensory information from the anterior cruciate ligament when this ligament is ruptured.

Treatment of an ACL injury

An ACL injury is treated with rehabilitation with or without reconstructive surgery. However, previous studies report that surgery does not improve objective or self-reported function [34, 41–43] nor does it prevent the development of early knee osteoarthritis [44] compared to rehabilitation alone. Rehabilitation after ACL injury typically includes trunk and lower extremity strength training, range of motion training and neuromuscular training including coordination, balance and proprioceptive exercises [7, 23], modification of landing techniques and lower extremity alignment during functional activities (the knee in line with the hip and ankle) [5, 7]. Despite thorough rehabilitation, it takes approximately two years for these patients to regain pre-injury function [45]. There are, however, still functional impairments present, and many patients do not return to their pre-injury activity level; this is especially true of women [46]. Only 39% to 55% of the individuals who sustain an ACL injury return to competitive sports after reconstruction and finalized rehabilitation [47, 48]. In addition to physical function such as strength and hop performance, several psychological factors including fear of re-injury, motivation and self-esteem seem to be important for the athletes’ decision whether to return to sport [47, 49–51].

Risk of re-injury

After return to sport there is also a substantial risk of subsequent injuries to the knee. The incidence of either a re-injury to the same knee or a contralateral ACL injury is reported to be approximately 20%, with higher rates in young individuals [52]. Female sex, higher body mass index, early reconstruction, early return to high level sport, decreased postural control, asymmetrical quadriceps strength and walking with lower knee flexion force seem to increase the risk of re-injury [7, 53–55]. In a recent study, Grooms et al. also proposed that neuroplastic changes and re-organization in the CNS after the primary injury may pre-dispose the individual to subsequent injuries [40].

Sensorimotor function and functional knee joint stability

Sensorimotor function involves the processing of the afferent sensory input, signal integration in CNS and the activation of efferent motor signals that contribute to control functional joint stability, by modulation of, for example, muscle activation and force production.

Functional joint stability is traditionally defined as the ability of the joints to remain stable during weight-bearing activities and perturbations, sometimes called neuromuscular control [56]. At the knee, passive joint stability is provided by several structures such as the meniscus, the geometry of the joint, the joint capsule and knee joint ligaments, whereas functional joint stability depends on loads from gravity and muscles acting on the knee joint. Components involved in functional joint stability include sensory function, range of motion, muscle strength, muscle activation and endurance, all factors that can be modified by training [57]. While interaction of all these factors is significant for joint stability, force produced by the surrounding knee muscles is suggested to be one of the most important factors contributing to functional knee joint stability [56, 58].

Sensory function

Proprioceptive information arises from mechanoreceptors situated in the muscles, joints, ligament- and cutaneous tissues. Together with the visual and vestibular system, they all contribute to the ability of defining the position of the body in space and the position of the joints in relation to each other. Proprioceptive acuity is important for the performance of daily tasks, i.e. walking or maintaining balance, and plays an essential role in joint stability [56, 59]. Mechanoreceptors such as the fast adapting Pancinian corpuscles, slow adapting Ruffini endings, Golgi receptors and free nerve endings are situated in the ACL, collateral ligaments and joint capsule and provide the CNS with important information regarding joint angles, load and movements. Muscle spindles located in the extrafusal muscle fibres provide the nervous system with information about muscle length and contraction velocity, and contribute to the ability to distinguish joint movement (kinesthesia) and joints position sense (JPS) [56].

In animal studies, afferent signals from the receptors situated in the ACL are shown to be important for the gamma-muscle spindle regulation and control of muscle stiffness during movements by providing the muscle spindles with proprioceptive information. The muscle spindles are thereby subconsciously contributing to joint stability by preparatory muscle stiffness regulation via the ACL-reflex hamstring arc [59]. Dyhre-Poulsen et al. and Tsuda et al. verified the existence of this ACL-reflex hamstring arc by electronic stimulation of the ACL in humans [60, 61]. A delayed reflex-hamstring response was also evident in the injured leg compared to the uninjured leg and to non-injured controls in individuals suffering from ACL injury, and this delay was further related to an increased number of give-way symptoms [62]. Furthermore, reflex transmitted co-contraction of the hamstring and quadriceps muscles has been shown to be important for stabilizing the knee joint in response to a perturbation [63].

Individuals with ACL injury have an impaired proprioception sense as assessed with kinesthesia or JPS [64], which may persist even after a return to sport [65]. This deficiency has been reported to be associated with worse hop performance [66], worse balance [67], give-way episodes [68] and worse self-reported knee function [69], indicating that adequate proprioceptive acuity plays an important role for function in these patients.

Another aspect of sensory function that has been proposed to be closely connected to proprioception is vibration sense [70]. Tactile sense, like vibration sense, arises from receptors partly shared with those responsible for proprioception, such as, the Pancinian corpuscles, but also originates from other receptors, i.e. Meissner's corpuscles, Merkel's disks and Ruffini endings, situated in the deeper layer of the skin, between the muscles, and in the periosteum. Afferent information regarding vibration sense then travels along the same pathway as proprioception sense to the cerebral cortex [71]. Vibration sense is known to be impaired in patients with hip or knee OA [72, 73]. Reduced vibration sense was also reported to be related to OA severity [74] and to be associated with a higher knee joint loading during gait, an indicator of OA progression [75]. Furthermore, in a group of individuals with or at high risk of knee OA, poor vibration sense was found to be related to the occurrence of self-reported knee instability episodes [76]. In patients with meniscectomy, poorer vibration sense at the knee was found to be related to worse performance of the number of knee bends in 30 seconds [77]. Vibration sense is poorly investigated in patients with ACL injury [69, 78]. Thorlund et al. found no difference in vibration sense between a group consisting of patients with ACL injury or meniscectomy and a healthy control group [78]. However, in a recent study from our research group, we reported an association between poorer vibration sense and worse self-reported function as assessed by the Knee Injury and Osteoarthritis Outcome Score [69], indicating some relevance of vibration sense for function in these patients.

Muscle strength and muscle activation

Muscle strength is an important factor in functional ability, and is commonly measured as peak torque. The magnitude of muscle torque is calculated as the product of the force applied and the lever arm length, which can be influenced by several different factors, i.e. muscle activation level, limb weight, movement velocity and the angle between the force vector and the lever arm. Hence, since most of these factors vary when the limb is moved by muscular activation, the muscle may produce different torque values, even though the muscle activation level is the same. Muscle activation on the other hand is a product of both the reflex transmitted signals from mechanoreceptors and the descending alpha motor neuron signals [79]. Co-activation of agonist and antagonist joint muscles is believed to contribute to functional joint stability by increasing muscle stiffness, i.e. the muscles' resistance to lengthening, and thereby the stiffness of the joint [58]. Specifically, co-contraction of the hamstring and quadriceps muscles are reported to be important for frontal plane knee stability [80]. Recent research also indicates that the level (%maximal voluntary contraction (MVC)) to which the muscle is activated is more important for knee stability than the actual force it produces [81].

Individuals suffering from ACL injury have decreased hip and knee torque, compared to a non-injured population [25], that often persists even 20 year after the injury was sustained [82]. In addition, these patients commonly exhibit altered muscle activation pattern, such as decreased voluntary quadriceps activation [26] and delayed muscle activation onset of the quadriceps, hamstrings, gluteus maximus (Gmax), gluteus medius (Gmed) and gastrocnemius muscles [27, 83, 84]. An increased average activation amplitude of the hamstring muscles [28, 85-88], Gmax [86, 88] and gastrocnemius muscles [86] during functional performance compared to non-injured individuals is also reported after ACL injury. Moreover, hamstring stiffness has been found to be greater in the ACL-injured leg compared to the uninjured leg and to healthy controls [89]. Decreased hamstring stiffness was also related to worse perceived functional performance, assessed with the Noyes rating scale, after ACL injury [90].

Given that both the hamstring and gastrocnemius muscles act as ACL agonists and thereby resist anterior tibial translation [91, 92], it has been suggested that these alterations in muscular activity are compensatory mechanisms intended to maintain neuromuscular control after the loss of the ACL [91, 92]. In patients with ACL reconstruction (ACLR), greater knee laxity has been associated with reduced hamstring voluntary activity, [93] and delayed gastrocnemius onset during perturbation [84], respectively. Taken together, this implies that appropriate activation of these muscles is important for functional knee stability in the ACL injured population.

Postural orientation and knee abduction

One aspect of sensorimotor function is postural orientation. Postural orientation is defined as the ability to stabilize the body segments in relation to each other, the environment and gravity; e.g. to keep the trunk, hip, knee and ankle aligned during dynamic activities [94]. Worse postural orientation during weight-bearing activities has been reported in individuals with ACL injury compared to the non-injured leg and to individuals without injury [95, 96]. This altered movement pattern was also associated with worse knee confidence [97], worse self-reported function [96, 98] and reduced hop performance [96] in these patients.

Postural orientation at the knee is commonly evaluated by the position of the knee in relation to the foot. A position where the knee is positioned medial to the foot is considered poor postural orientation, whereas a position where the knee is aligned over the foot is considered good postural orientation. This idea of "good and poor" movement pattern has been founded on anecdotal rather than scientific evidence. However, recent studies show that a knee medial to foot position (KMFP) or increased knee abduction is more common in individuals with ACL injury or patellofemoral pain (PFP) than in uninjured controls [94, 100–102] and is still observed 20 years after injury [81].

Increased knee abduction is also consistently reported to be part of the mechanism of non-contact ACL injury [11, 103–105], and is associated with greater strain on the ACL [106–110]. With respect to PFP, greater knee abduction has been demonstrated to increase contact forces within the lateral patellofemoral joint [111]. Thus, knee abduction has been suggested to be a risk factor in sustaining both PFP and ACL injury [112] as well as subsequent knee injuries [17, 113].

The gold standard to evaluate this movement pattern is by assessing knee abduction in degrees (frontal plane angle between the thigh and shank) with 2D or 3D movement analysis systems [98]. However, a more clinically feasible method is to evaluate medio-lateral knee position by visual observation, which is a reliable method that recently showed good validity against both 2D and 3D analysis [99].

The contributing factors for increased knee abduction are not well established. Several mechanisms have been suggested to be associated with this movement pattern in healthy individuals, such as static alignment, reduced muscle strength, altered muscle activation and decreased foot and ankle mobility [99–104]. Furthermore, women are believed to exhibit greater knee abduction during activity compared to men, which has been suggested to be a contributing factor for the increased knee injury risk observed in women [19]. However, the results of these studies are inconsistent [105–108] and studies on the corresponding factors in patients with knee injury is poorly investigated [109, 110].

Overall aim and goal of the thesis

The overall aim of this thesis was to investigate the association between sensorimotor factors and knee abduction in patients with ACL injury. The goal was to identify factors that are modifiable by training and exercise therapy. This knowledge may be helpful in designing rehabilitation protocols aimed at reducing knee abduction and preventing subsequent knee injuries in this population.

Specific aims

Specific aims were to:

1. Systematically review possible gender differences in knee abduction (I) and the association between modifiable sensorimotor factors and knee abduction (II) during weight-bearing activities in individuals with ACL injury, with PFP and in a healthy population.

2. Investigate the association between sensory function (kinesthesia and vibration sense) and knee abduction assessed by visual observation during weight-bearing activity in individuals with ACL injury and in addition, investigate any gender differences in the presence of knee abduction and/or in the contribution of sensory function for knee abduction (III).

3. Investigate the association between muscle strength (IV) and muscle activation (V), respectively, and knee abduction (3D) during weight-bearing activities in individuals with ACL injury.

Methods (I–V)

Participants (I–V)

The two first studies in this thesis were systematic reviews with meta-analysis with the intention of investigating what was already known about which factors contribute to knee abduction. Thus, in addition to individuals with ACL injury, we also included in these two reviews individuals with PFP and healthy individuals. Study I included 58 articles with in total 114 participants with ACL injury, 116 with PFP and 2,465 healthy individuals. Study II Included 33 articles with in total 67 participants with ACL injury, 35 with PFP and 1,005 healthy individuals (Figures 1 and 2). In study III, the cohort constituted a sample of convenience, including 28 men and 23 women with arthroscopic or MRI-verified ACL deficiency (ACLD), or ACLR, recruited from physiotherapy clinics in Skåne, Sweden. The results in studies IV and V were based on one cohort (18 men and 11 women with ACL reconstruction), where the participants were mainly recruited from the Department of Orthopedics, Skåne University Hospital, Sweden. All patients that had undergone an ACL reconstruction between June 1st and December 8th, 2015 (n=106) were invited to participate (Figure 3). Exclusion criteria common to studies III–V were: age <18 or >39, usage of external devices to assist with weight-bearing, no longer participating in formal rehabilitation and/or suffering from other injuries or diseases that affected function. The participants included had a mean pre-injury activity level [111] of 9 (III) and 8 (IV and V), respectively. We included participants both with and without associated injuries to the knee. In study III, 64% had associated injuries and in studies IV and V, 76% had associated injuries, with meniscus injury being the most commonly associated injury in both cohorts, see Table 1 for characteristics.

The three original studies were approved by the Advisory Committee for Research Ethics in Health Education at the Faculty of Medicine of Lund University (VEN 48–12) (III) or the Regional Ethical Review Board in Lund, Sweden (2015/581) (IV and V).

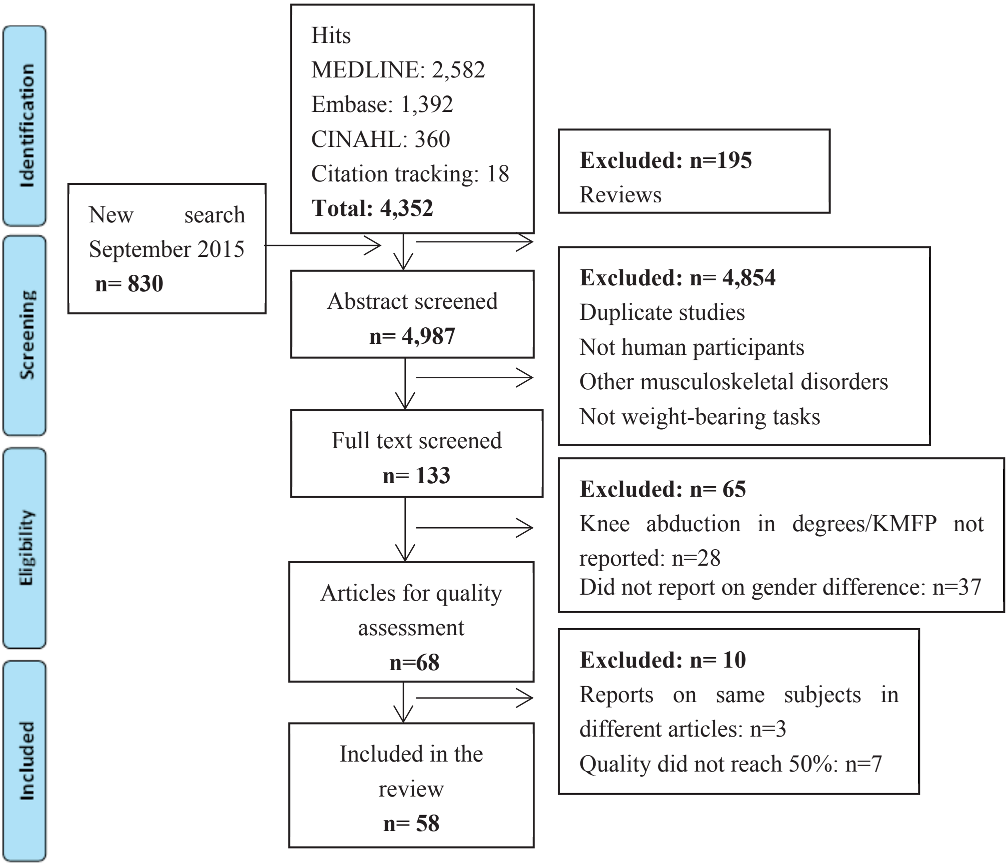


Fig 1. Flow chart of the inclusion process. KMFP knee medial to foot position (I)

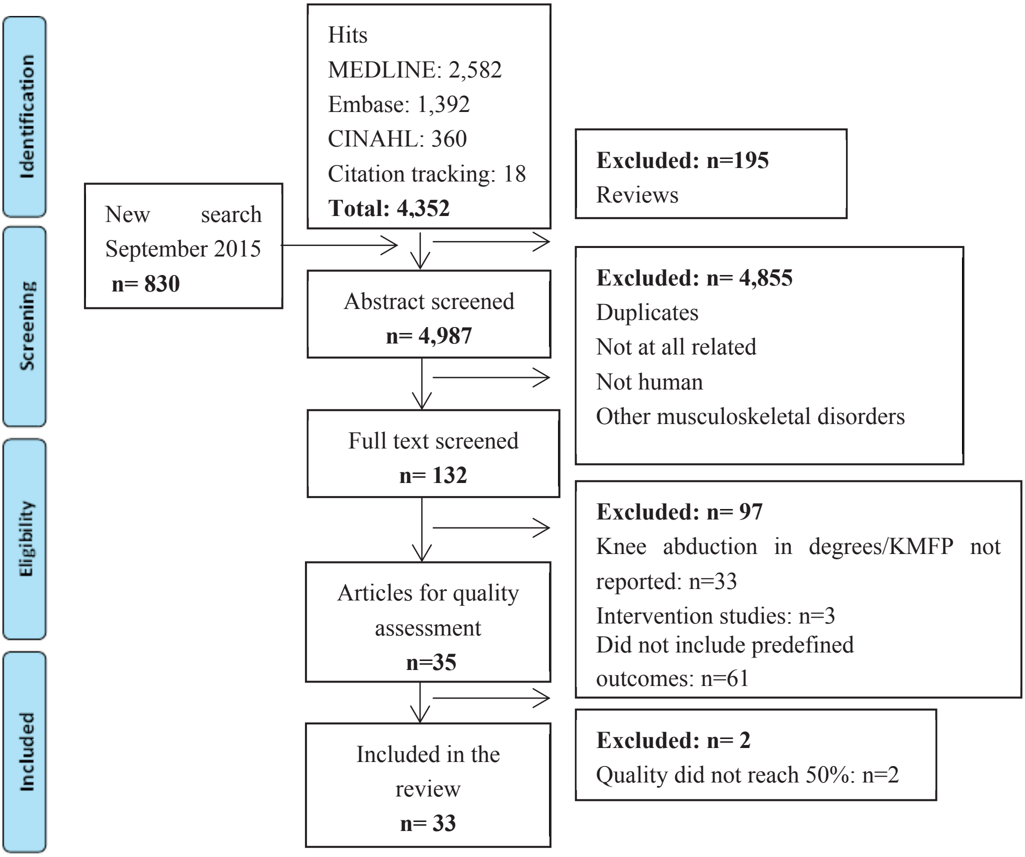


Fig 2. Flow chart of the inclusion process. KMFP knee medial to foot position (II)

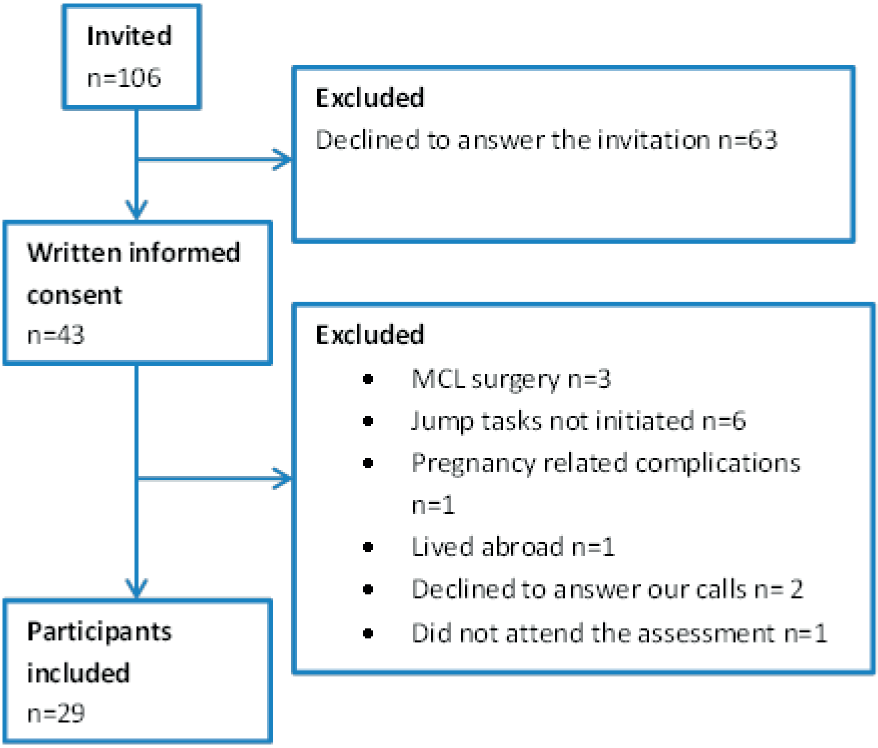


Fig 3. Flow chart of the inclusion process (IV and V)

Table 1. Characteristic of the participants included in study III-V

Characteristics	Study III		Study IV and V
	Women (n = 23)	Men (n = 28)	n=29 (11 women, 18 men)
Women, n (%)	NA	NA	11 (38)
Age (years)¤	23 (4.0)	26 (6.1)	27 (5.6)
BMI¤	22.5 (2.21)	24.7 (2.85)	25.9 (3.6)
Tegner activity score pre injury #	9 (8–9)	9 (8–9)	8 (7-9)
Tegner activity score at assessment #	3 (2–6)	4 (3–7)	3 (2-4)
Injured right knee, n (%)	11 (48)	20 (71)	12 (41)
Time since injury, non-reconstruction (weeks)¤	45 (42.1)	66 (57.9)	NA
Reconstruction, n (%)	19 (83)	19 (68)	29 (100)
Time since reconstruction (weeks)¤	36 (40.7)	47 (52.5)	29 (6.4)
Associated injuries, n (%)	13 (57)	20 (71)	22 (76)
Collateral ligament, n (%)	5 (22)	8 (28.6)	8 (28)
Meniscal, n (%)	9 (39)	16 (57)	19 (65)
Cartilage, n (%)	8 (35)	7 (25)	7 (24)

¤ = mean (SD), # = median (quartiles), BMI= body mass index, NA=not applicable

Systematic reviews (I and II)

Studies I and II were both systematic reviews. In the beginning these were meant to be one review, investigating modifiable factors and gender as contributing factors for knee abduction, with the purpose of guiding the content in my subsequent studies. However, after the initial search was performed, we realized that the number of studies and amount of data available were much more substantial than we had initially believed and, therefore, we decided to divide the results into two reviews: (I) gender differences in knee abduction, and (II) modifiable factors associated with knee abduction. These systematic reviews were conducted according to the PRISMA guidelines and the protocol was pre-registered in the International Prospective Register of Systematic reviews (PROSPERO) (2013: CRD42013005415). The initial systematic search conducted in August 2013 included the databases Medline (PubMed), CINAHL and EMBASE. The same search strategy was applied to both reviews, including the following terms;

(healthy[Title/Abstract]) OR non-injured[Title/Ab-stract]) OR ACL reconstruct*[Title/Abstract]) OR ACL injur*[Title/ Abstract]) OR anterior cruciate ligament injur*[Title/Abstract]) OR anterior cruciate ligament reconstruct*[Title/Abstract]) OR patellofemoral pain[Title/Abstract]) OR “Anterior Cruciate Ligament”[Mesh]) OR “Anterior Cruciate Ligament Reconstruction”[Mesh]) OR “Patellofemoral Pain Syndrome”[Mesh])) OR uninjured[Title/ Abstract])) AND (“joint position sense”[Title/Ab-stract]) OR propriocept*[Title/Abstract]) OR kinesthesia[Title/ Abstract]) OR proprioception[MeSH Terms]) OR Muscle activation[Title/Abstract]) OR Muscle strength[Title/Abstract]) OR muscle strength[MeSH Terms]) OR muscle strength dynamometer [MeSH Terms]) OR range of motion[Title/Abstract]) OR ROM[Title/ Abstract]) OR range of motion, articular[MeSH Terms]) OR gender [Title/Abstract]) OR sex[Title/Abstract])OR females[Title/Ab-stract]) OR males[Title/Abstract]) OR sex characteristic[MeSH Terms])OR“Sex Factors”[Mesh]))AND (biomechanic*[Title/ Abstract]) OR kinematic*[Title/Abstract]) OR valgus[Title/Ab- stract]) OR “postural orientation”[Title/Abstract]) OR alignment [Title/Abstract]) OR “movement quality”[Title/Abstract]). This search was then updated in September 2015.

We intended to include all original studies that investigated any of the following factors: gender, muscle strength, muscle activation, proprioception and/or joint range of motion (ROM) as a contributing factor in knee abduction (assessed by visual observation or 2D or 3D motion analysis) during any kind of weight-bearing activity in patients with ACL injury or PFP or in healthy individuals. Two reviewers (AC and JN) independently screened abstracts and full-text articles against the inclusion-exclusion criteria. The same reviewers then assessed all articles that met the inclusion criteria for methodological quality by using a checklist previously developed for quality assessment of observational studies [112]. A quality score of at least 50% was required to be included in the reviews, as the result in low quality studies may be affected by bias due to poor methodology.

Sensory function (III)

The aim of study III was to investigate the importance of adequate sensory function, as measured by kinesthesia and vibration sense, for the ability to control frontal plane knee movement during weight-bearing activities. We chose kinesthesia over JPS, since kinesthesia has been proven to be a more reliable and valid test of proprioception, with lower measurement errors [113]. Kinesthesia was measured by the threshold of detection of passive motion (TDPM) with a device specially built for this purpose. For a full description of the assessment procedure, see Ageberg et al., [114]. The device consists of a platform mounted on a steel frame with an electrical motor at one end. The subject lies on the platform in a lateral position with their shank in a plaster brace. The brace is connected to the electrical motor with a wire and, by pushing a button on a remote control, the tester can make the brace move the knee in either flexion or extension at an angular speed of 1 degree per second. An analogue scale at the end of the platform registers movements in increments of 0.25°. In order to prevent any false experience of movements derived from the sound when the measuring device was started, all participants wore headphones and listened to a recording of the sound that was produced by the electric motor. The subjects were told to close their eyes and indicate by raising their hand when any movement in the knee was felt. TDPM was measured towards extension and flexion from a 20-degree (knee flexion) starting position. This starting position was chosen because with this device higher reliability and sensitivity have been reported closer to the end point of range of motion compared to the middle part of range of motion [114]. The median value from three measurements of the extension and flexion assessments respectively were determined, and the sum of these measures was then used in the statistical analysis. A higher value indicates poorer TDPM.

To gain a broader understanding of sensory function in patients with ACL injury, we also included vibration sense as another measure of sensory function. Vibration sense is assessed by the vibration perception threshold (VPT) with a biothesiometer, which is a reliable [72] and commonly used measure of sensory function in patients with OA [72, 73] or injury to the lower extremity [78, 115, 116]. During the assessments, the participant was in a supine position on a treatment bench. Before the trials, the biothesiometer was tested on the processus styloideus ulna in order to familiarize the participant with the procedure. The head of the biothesiometer was then held to the participants' most prominent point of the metatarsophalangeal joint 1 (MTP1), the medial malleolus (MM), and the medial femoral condyle (MF) with a standard pressure. These locations were chosen due to the results of previous studies where generalized deficiencies in vibration sense but better vibration sense at more distal body parts compared to more proximal body parts in patients with OA were reported [72, 73]. The participants were told to close their eyes and indicate by raising their hand when any sense of vibration was felt. The amplitude was increased by 1 volt per second, and the voltage when the subject first felt any sensation of vibration was noted as the VPT. A higher value indicated worse VPT.

Muscle strength (IV)

The aim of study IV was to investigate the relation between trunk and lower extremity strength and knee abduction. Therefore, we assessed the isometric peak force (N) of the hip external rotators, hip abductors, hip extensors, knee flexors, knee extensors, trunk extensors, and trunk lateral flexors (side-bridge test) with a hand-held dynamometer (Commander Echo, JTECH Medical, Salt Lake City, Utah, USA) according to previously described methods [100, 117–121]. During all assessments, a belt was used to fixate the dynamometer, and the participant was encouraged to push their leg/trunk against the dynamometer as forcefully as they could, see Figure 4 a-g and [122] for a full description of testing positions. Prior to the strength assessments, the distance between the dynamometer location and the rotation axis of the joint for each muscle group was assessed with a tape measure and noted as the lever arm. The peak value of three trials was then calculated in Newton metres (Nm) by multiplying the peak force value with the corresponding lever arm for all tests except for the side-bridge test, which was multiplied with the distance between acromion and the lateral malleolus. These values were then normalized to body mass (Nm/kg). The participant held each contraction for 5 seconds with 15 seconds of rest in between. Before the data included in this study were collected, a pilot study including 9 healthy individuals was performed. The reasons for this pilot study were partly for me to learn the method properly, but also to determine test-retest reliability for all strength measures. All strength assessments showed moderate to excellent test-retest reliability; hip external rotators (ICC=0.88), hip abductors (ICC=0.77), hip extensors (ICC=0.80), knee flexors (ICC=0.95), knee extensors (ICC=0.80), trunk extensors (ICC=0.73) and trunk lateral flexors (ICC=0.62). I then collected all the strength measure data in the original study.

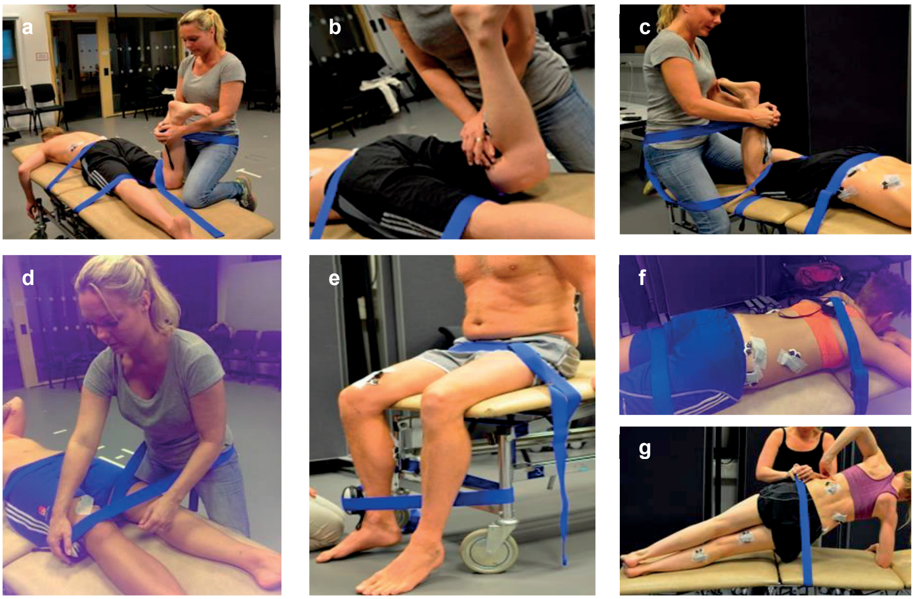


Figure 4 a-g. Strength assessment positions (IV)

Electromyography (V)

In study V, I aimed to investigate the possible association between muscle activation of the trunk and lower extremity muscles and knee abduction. Average muscle activation patterns of the Gmax, gluteus medius (Gmed), semitendinosus (ST), vastus medialis (VM) medial gastrocnemius (MGc) and Iliocostalis (IC) muscles for the ACLR leg (both sides for IC) were, therefore, synchronously collected with the kinematic data. For this purpose, surface electromyography (EMG) electrodes with a wireless EMG system (Desktop DTS, Noraxon U.S.A. Inc, Scottdale, Arizona, USA) with a sampling frequency of 1500Hz and a lowpass filter of 500Hz was used. Prior to the placement of the electrodes, the skin was shaved and lightly abraded with a medical abrasion gel (Nuprep, Weaver and company, Aurora, Colorado, USA). Disposable self-adhesive dual EMG electrodes (Noraxon, USA. Inc, Scottdale, Arizona, USA) with an inter-electrode distance of 17.5 mm were used. The electrodes were placed parallel to the muscle fibres for all muscles (except for VM which was placed perpendicular to the line between the landmarks) and at locations according to the Surface Electromyography for Non-Invasive Assessment of Muscles (SENIAM) guidelines [123].

MVC data for each muscle was collected synchronously with the muscle strength data used in study IV. The participants were encouraged to push their leg/trunk against a manual resistance as much as they could and hold for 5 seconds. The MVCs were calculated from the maximum value of three repetitions with 15 seconds of rest in between.

All EMG data was collected during the flexion phase for the single-leg squat (SLS) and the single-leg hop for distance (SLHD), respectively. The raw EMG data were then ECG-reduced, high-pass filtered at 20Hz, full-wave rectified and smoothed by a root mean square algorithm over 50ms windows (MyoRESEARCH Biomechanical Analysis, Noraxon, version 3.6). All processed EMG signals for each muscle were then normalized to the maximum value from the respective MVC. Collection of corresponding EMG data was also included in the pilot study on 9 healthy individuals, mentioned in the method section of the muscle strength assessment, in order for me to become familiarized with the method before the original data collection. Moderate to excellent reliability has been reported for surface EMG measurements of the lower extremity and trunk during weight-bearing activities [124].

Functional tasks included in studies III–V

In this thesis, we wanted to investigate contributory factors for increased knee abduction during weight-bearing functional activities with different degrees of difficulty. Thus, in study III we included functional tasks commonly used for assessing postural orientation in the clinical setting, reflecting both activities of daily living (ADL) (SLS, stair descending) and more strenuous sport-related activities (forward lunge, drop jump). However, in the consecutive studies, we only included one task reflecting ADL activity (SLS) and one task reflecting sporting activity (SLHD). In studies IV and V, we chose to replace the drop jump task with the SLHD, since the drop jump has recently been reported to be a poor screening task for predicting future knee injuries [18] and for discriminating between men and women [125]. The participants wore shorts, sports bra (women) and their own personal trainers (when needed) during the tasks. The ADL activities were repeated 5 times, whereas the sporting activities were repeated only 3 times due the risk of fatigue in these tasks. Up to 3 practice trials were allowed to familiarize participants with the tests.

Single-leg squat (III–V)

The single-leg squat (SLS) was performed according to Ageberg et al. [126], but without allowing fingertip support for maintaining balance. The participant was standing on one leg with the second toe placed on a marked longitudinal line with the contralateral leg lifted from the floor. They were then instructed to flex the injured knee until they could not see their toes (approximately 50°) (study III), or until they touched a treatment bench placed behind them with their bottom (60°) (studies IV and V), and then return to extension. The squat was repeated five times at a speed of 3 seconds per squat. The participant performed the task barefoot (study III) or with shoes (studies IV and V) (Figure 5a).

Stair descending (III)

This task was performed according to Pfeifer et al [127], but modified to use a step board 27 centimetres high. The participant stood with both feet (hip-width apart) on the step board. They were then instructed to step down onto the floor with their non-injured leg and then return to the starting position. The injured leg, which is in contact with the step board throughout the entire movement, was evaluated. The task was repeated 5 times. The participant performed the task barefoot.

Forward lunge (III)

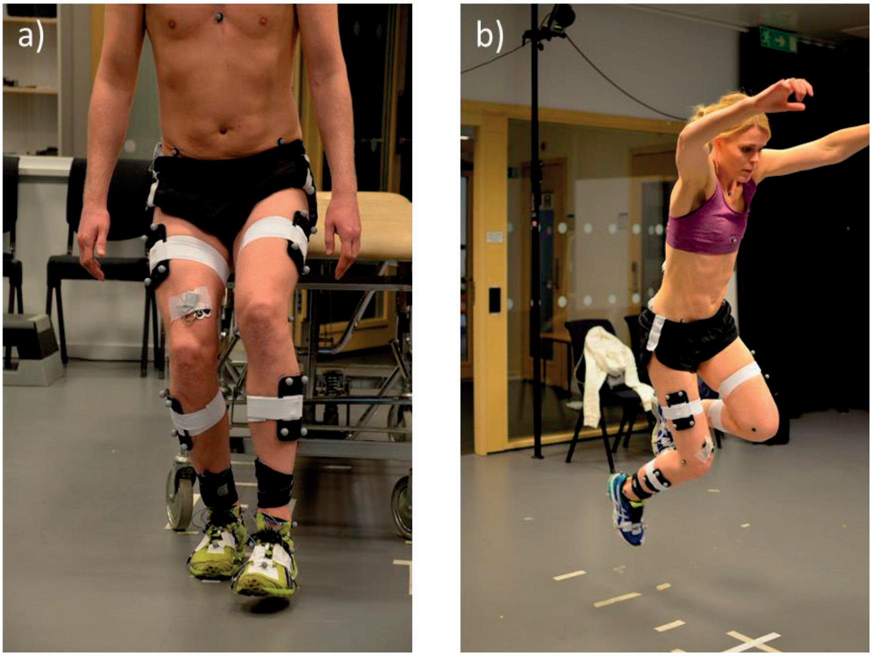
The forward lunge was performed according to Alkjaer et al [128]. The participant was standing with their feet hip-width apart on the floor. They were then instructed to take a long stride forward, about 1 m, with the injured leg and to flex the knee to approximately 90°, and then push back to the starting position by extending the front leg. This task was repeated 3 times. The participant performed the task with shoes.

Drop jump (III)

The drop jump was performed according to Hewett et al., [19] but modified to use the second landing in the analysis instead of the first landing that is more commonly used. This approach was chosen because the second landing may better represent a situation when an ACL injury occurs [129]. The participant stood on a step board (27 cm high) with their feet hip-width apart. They were then instructed to drop from the step board and directly perform a maximal vertical jump. Arm swing was allowed during the jump. The task was repeated 3 times. The participant performed the task with shoes.

Single-leg hop for distance (IV and IV)

Performed according to Zätterström et al.[130] to allow arm swing during the jump to enable a more functional execution of the task. The participant stood on their ACLR leg with the toes behind a marked line, and with the other leg lifted from the floor by flexing the knee. The participant was then told to jump forwards as far as possible, taking off and landing on the same foot, and to maintain balance on landing for 3–5 seconds. The distance in centimetres from toe at take-off to heel in landing was then measured. If there was more than 30 cm between the longest and shortest jump, additional jumps were performed until less than 30 cm was achieved. This approach was chosen so as to reduce the risk of too many repeated jumps on the individual's injured leg. The task was repeated 3 times. The participant performed the task with shoes (Figure 5 b).



Figures 5a-b. The single-leg squat (a) and the single-leg hop for distance (b) (IV and V)

Assessment of knee abduction (III–V)

Visual observation and scoring (III)

In study III, we used visual observation and scoring of the position of the knee in relation to the foot as a measure of knee abduction. Visual observation is an easy of handling and a clinically feasible way of assessing postural orientation of the knee, and has been reported to be valid in both 2D and 3D [131]. Two experienced raters independently scored the position of the knee in relation to the foot on video recordings of each trial. The raters were able to watch the video in slow motion and to review the movie as many times as needed. The knee position relative to the foot during the participant's performance of each task was assessed on an ordinal scale from 0 to 2. If the mid-point of the patella was in line with or lateral to the second toe, a score of 0 = "good" was given for the postural orientation. If the mid-point of the patella was medial to the second toe, a score of 1 = "fair" was given. Finally, if the mid-point of the patella was clearly placed medial to the first toe, a score of 2 = "poor" was given (Figure 6). A consensus score from the two raters was then used in the analysis. These assessments of postural orientation showed good to excellent agreement (ICC = 0.710–0.939).

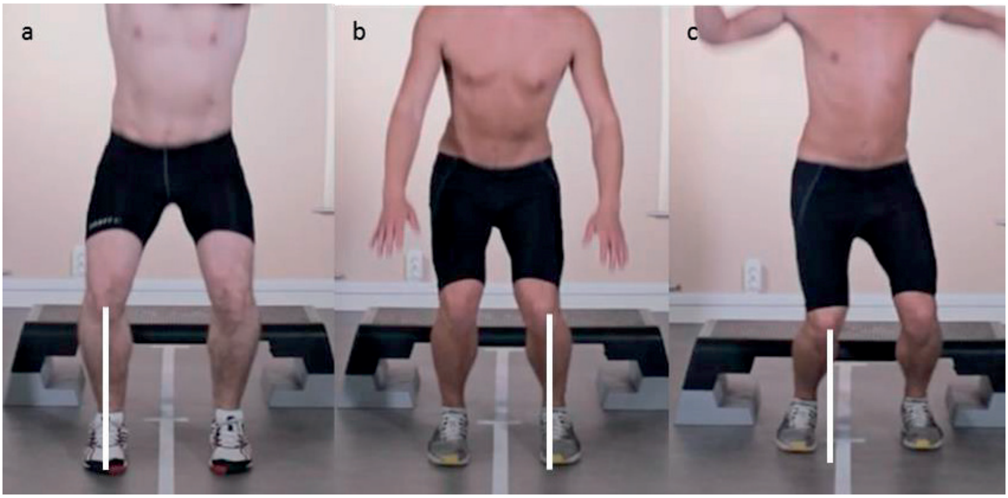


Figure 6 a-c. The position of the knee in relation to the foot a) A score of 0, b) A score of 1, c) A score of 2 (III)

3D movement analysis (IV and V)

In studies IV and V, we used three-dimensional (3D) motion analysis equipment for assessing knee abduction. A combination of individual reflective markers and marker clusters were attached to the trunk and the participants' injured leg so as to track their kinematics. An eight-camera motion analysis system (Qualisys motion capture system, Gothenburg, Sweden) (150 Hz) was then used for collection of 3D knee abduction data during the flexion phase of the SLS and SLHD. For the SLS, the flexion phase was defined as the time frame from when the knee flexion angle increased by more than 2 degrees from full extension at the commencement of the squat to when the knee flexion angle reached 2 degrees less than the angle achieved at full flexion (the bottom of the squat). An adaptation of the methods of Fellin et al. [132] was used to define foot contact in the SLHD as the time at which lowest height of the distal heel or toe marker occurred (whichever occurred first). The flexion phase for the SLHD was defined as the time frame from foot contact to when the knee flexion angle reached 2 degrees less than the peak knee flexion angle achieved during the landing. From these data, peak knee abduction angle and knee abduction excursion (the change in angle from foot contact to peak knee abduction) during the flexion phase of the two tasks were calculated.

The 3D data was reconstructed and labelled in Qualisys Track Manager (version 2.12). All further processing was carried out in Visual 3-D (version 5.02, C-motion, Germantown, MD, USA). Marker trajectories were filtered with a 12Hz, 4th order, low pass Butterworth filter [133]. Knee kinematics (flexion-extension, abduction-adduction and internal-external rotation) in all movement trials were calculated using a joint coordinate system approach [134]. The mean value of the five squats, and the three jumps, respectively, were then included in the analyses

Statistical analysis

(I and II)

In studies I and II, the results were based on meta-analyses. Comprehensive Meta-Analysis software (version 2.2.064, Biostat, Englewood, USA) was used for this purpose. The effect size with 95% CI was calculated on standardized mean difference (SDM) in knee abduction between men and women (I) and as Pearson's correlation coefficient for the association between the assessed factor and knee abduction (II). If appropriate data was not provided, the relevant effect size was calculated from the p-value and sample size [135]. When only group comparison studies were included in the analysis, the effect size was calculated on SDM in knee abduction between the two groups also in study II. If studies reported data for more than one leg (I and II) or more than one strength measure (II), right and dominant legs and the strength measure (isometric, eccentric, concentric) represented in most studies in that specific analysis were included. To deal with the problem of including multiple interventions, so called double counting, from one study in meta-analyses, we chose to divide the sample size with the number of tasks to create smaller comparator groups if a study reported data for more than one functional task. Each task was then treated as an independent study. This is one of a few approaches suggested by Cochrane [136] to resolve this problem. A random effect model was used in both reviews (I and II) due to expected heterogeneity between studies, such as the use of different functional tasks and different outcomes, i.e. visual observation, 2D or 3D analysis. Between-studies, heterogeneity in effect size was calculated with the Q-test and expressed as I2-statistics. Where possible, subgroup analyses for specific tasks or gender were performed. Meta-analyses were performed separately for healthy individuals, individuals with ACL injury and individuals with PFP. Since there may be methodological differences in assessing knee abduction with motion analysis or by visual observation, separate analysis was conducted also for all data assessed with motion analysis equipment and visual observation. Publication bias was evaluated using Funnel plots with trim and fill imputations [137].

(III–IV)

The calculations for studies III–V were performed with SPSS (version 20, IBM Corporation, New York, USA) (I) and version 21 (IV and V). All data was checked for normality by visual inspection of histogram, Q-Q plots and the Kolmogorov-Smirnov test (III–V). In studies IV and V, the residuals were also checked for normality. Pearson's correlation coefficient, Spearman's rank correlation coefficient, and the independent T-test were used as appropriate to investigate any possible association between participant demographics and knee abduction in all three studies. Since postural orientation was visually scored on an ordinal scale in study III, Spearman's rank correlation coefficient was used to determine the association between the sensory measures and knee position. In this study, the knee position scores were also dichotomized for each test; one group included subjects who were given a score of "0" (good), and one group included subjects who had been given a score of either "1" or "2" (poor). These values were then used to evaluate any differences in the sensory measures between subjects with good and poor postural orientation using the independent t-test. In studies IV and V, Pearson's correlation coefficient (normally distributed data) or Spearman's rank correlation coefficient (data not normally distributed) were used for evaluating the association between each muscle torque and each muscle activation variable, respectively, and knee abduction. Each statistically significant factor (IV) or all variables that correlated with knee abduction (r/rs-value ≥0.3, p-value≤0.1) (V) were then included in separate linear regression models (normally distributed data) or in a partial correlation model (data not normally distributed), adjusting for sex and BMI to evaluate the contribution of each measure for the dependent knee abduction variables (peak and excursion). To investigate any possible gender differences in the association between sensory function and knee abduction, men and women were analysed separately in study III. In this study, the Mann–Whitney U-test was also used to detect any differences in knee abduction between men and women.

RESULTS

Gender differences in knee abduction during weight-bearing activity (I and III)

The meta-analyses in study I showed that women with PFP exhibit greater peak knee abduction during weight-bearing activities (SDM; -1.34, 95%CI; -1.83 to -0.84) compared to men with PFP. Non-injured women were found to perform the tasks with increased knee abduction during the entire movement (initial contact, peak abduction, excursion) (SDM; -0.68 to -0.79, 95%CI; -1.04 to -0.37) compared to their male counterparts (Figure 7). Most tasks discriminated between men and women, e.g., walking, running, jump landings and cutting, whereas vertical drop jump did not.

We found no gender difference in knee position score, assessed by visual observation in individuals with ACLD or ACLR during the SLS, stair descending, forward lunge or drop jump (p>0.116) (study III).

Study name	Task	Std diff in means	Lower limit	Upper limit
Gehring 2009	BL drop	-4,37	-5,78	-2,95
Kernozek 2005	BL drop	-3,14	-4,20	-2,07
Hughes 2008	BL jump	-0,96	-2,16	0,23
Medina Mckeon 2010	BL jump	-0,58	-1,39	0,24
Beaulieu 2009	Cutting	-0,99	-1,75	-0,23
Fedie 2010	Cutting	-0,42	-1,08	0,23
Ford 2005	Cutting	-1,33	-1,72	-0,94
Malinzak 2001	Cutting	-1,76	-2,80	-0,72
Malinzak 2001	Running	-1,76	-2,80	-0,72
Mclean 2004	Cutting	-0,43	-1,42	0,56
Mclean 2005	Cutting	-1,70	-2,72	-0,68
Nagano 2011	Cutting	0,60	-0,30	1,49
Pollard 2004	Cutting	-0,16	-0,96	0,64
Russel 2006	Cutting	-1,47	-2,26	-0,69
Sigward 2012	Cutting	-0,54	-0,86	-0,22
Tanikawa 2013	Cutting	-0,17	-1,05	0,71
Wallace 2007	Cutting	0,81	0,03	1,60
Cortes 2007	Drop jump	0,59	0,02	1,15
Earl 2007	Drop jump	-1,23	-2,21	-0,25
Earl 2007	Step down	-1,20	-2,18	-0,22
Ford 2010 post	Drop jump	-1,20	-1,79	-0,61
Ford 2010 pub	Drop jump	0,08	-0,28	0,44
Herrington 2010	Drop jump	-1,03	-1,62	-0,44
Herrington 2010	SL drop	-0,63	-1,20	-0,07
Mclean 2007	Drop jump	-0,55	-1,44	0,35
Brophy 2010	kick	0,50	-0,29	1,30
Weltin 2015	L jump	-1,82	-2,77	-0,87
Ford 2006	L drop	-1,61	-2,92	-0,31
Ford 2006	M drop	-1,21	-2,44	0,02
Dwyer 2010	Lunge	0,05	-1,00	1,10
Dwyer 2010	SL squat	0,19	-0,86	1,24
Dwyer 2010	SuO	0,09	-0,96	1,14
Ferber 2003	Running	-0,81	-1,45	-0,17
Kernozek 2008	SL drop	-0,68	-1,42	0,06
Kiriyama 2009	SL drop	-0,24	-0,54	0,06
Orishimo 2009	SL drop	-0,16	-0,87	0,55
Orishimo 2014	SL drop	-0,90	-1,55	-0,25
Pappas 2007	SL drop	-0,99	-1,72	-0,25
Benjaminse 2008	SL jump	-1,29	-2,08	-0,50
Hart 2008	SL jump	-1,30	-2,37	-0,22
Jacobs 2005	SL jump	-0,63	-1,58	0,32
Claiborne 2006	SL squat	-0,17	-0,89	0,54
Graci 2012	SL squat	-1,86	-2,94	-0,78
Silva 2014	SL squat	-1,55	-2,22	-0,87
Baldon 2013	Step down	-0,73	-1,47	0,01
Cho 2004	Walking	-3,12	-3,71	-2,53
		-0,86	-1,11	-0,61

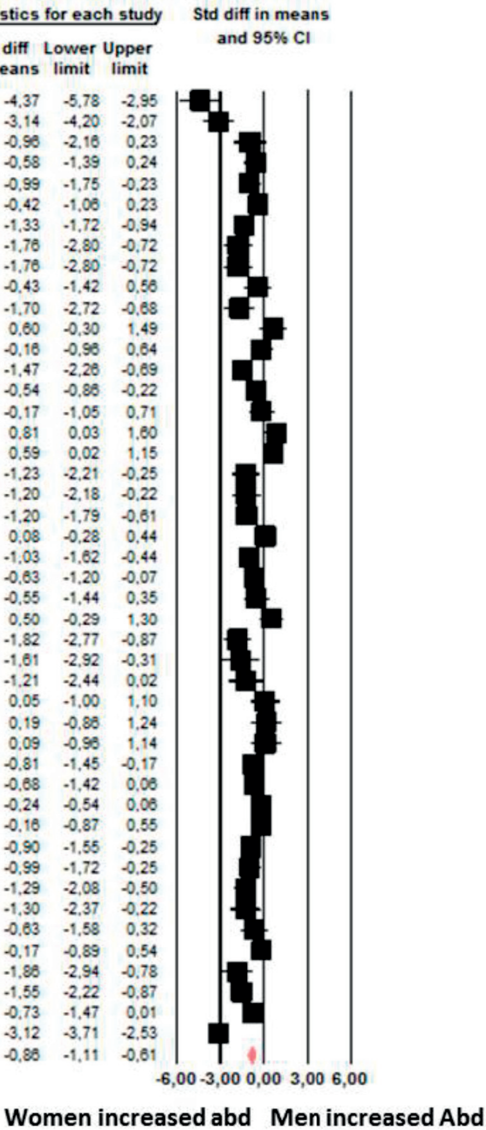


Figure 7. Gender difference in peak knee abduction during functional tasks in healthy individuals (I).

Association between sensory function and medio-lateral knee position (III)

Sixteen of the 51 subjects were not able to perform all tasks (due to being too close to surgery/injury or fear of performing the jumping tasks), leaving between 13 and 28 individuals in the gender-stratified analysis. We found that worse kinesthesia was associated with a KMFP during the drop jump in both men (rs = 0.423, p = 0.044) and women (rs = 0.469, p = 0.106). In women, worse vibration sense at MTP1 (rs = 0.453, p = 0.034) and MM (rs = 0.626, p = 0.002) was associated with a KMFP during stair descending. Worse vibration sense at MM was also associated with a KMFP during the forward lunge (rs = 0.544, p = 0.016). Consistent with the correlation analyses, there were significant differences in sensory function between those with good and poor postural orientation, i.e., women with a KMFP during stair descending had worse vibration sense at MTP 1 and MM and women with a KMFP during forward lunge had worse vibration sense at the MM compared to those with a knee over foot position (KOFP) (Figure 8).

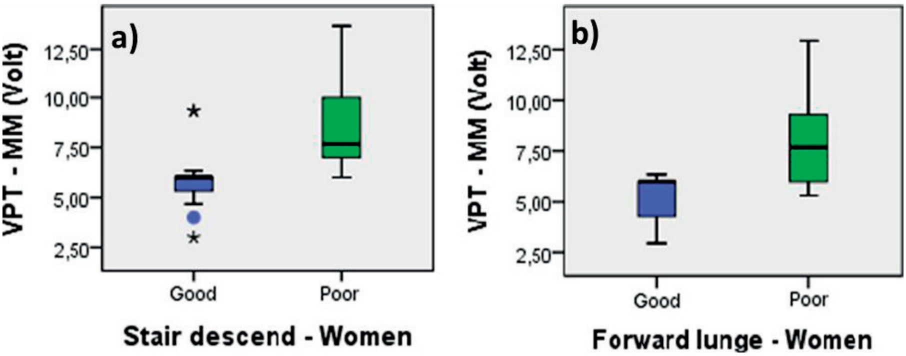


Figure 8. Differences in vibration sense between women (ACLD/ACLR) with good and poor postural orientation during stair descending (a) and the forward lunge (b) (III). VPT=vibration perception threshold, MM=medial malleolus

Association between joint ROM and knee abduction during weight-bearing activities (II)

The meta-analyses on healthy individuals in study II showed that reduced passive ankle dorsi-flexion ROM (knee extended) (SDM: -0.40; 95 % CI -0.85 to 0.05) but increased hip external rotation ROM (SDM: 0.50; 95 % CI 0.09 to 0.91) were associated with a KMFP during bilateral squatting in a group consisting of both men and women. No relation was found between ankle dorsi-flexion with the knee flexed, hip internal rotation or hip abduction ROM and knee abduction.

Association between muscle strength and knee abduction during weight-bearing activities (II and IV)

In study II, the meta-analyses showed no or only weak associations between lower extremity strength and knee abduction in healthy individuals when tasks were pooled ($r \leq 0.21$, $p = 0.013–0.426$) (Figure 9). However, in a sub group analysis of the single-leg squat, lower hip external rotator torque was associated with greater peak knee abduction (r -0.38; 95 % CI -0.53 to –0.21). No associations were found between hip abductor, hip extension or hip external rotation strength and knee abduction during the tasks in a subgroups analysis consisting of women only ($r \leq -0.25$; 95% CI -0.48 to 0.16). However, lower trunk lateral flexion torque, assessed with the side-bridge test, was associated with greater peak knee abduction during a SLS (r -0.39; 95 % CI -0.54 to -0.22) in a group consisting of both men and women.

In study IV, lower BMI was associated with both greater strength and greater knee abduction and was thus included as a covariate together with sex in the regression models. Consistent with the results in study II, we found mainly no associations between lower extremity peak torque and knee abduction during the SLS or the SLHD in individuals with ACLR after adjusting for sex and BMI. However, higher knee flexion peak torque was associated with increased knee abduction excursion during the SLHD. In this study including individuals with ACLR, we found no relation between the side-bridge test and knee abduction during the two tasks (Table 2).

Study	Factor	Sex	Strength	Task	Correlation	Lower limit	Upper limit
Homan et al.	Abd	B	Iso	DJ	-0.10	-0.36	0.18
Heinert et al.	Abd	F	Iso	Run	-0.39	-0.64	-0.06
Jacobs and Mattacola.	Abd	F	Ecc	SLJ	-0.61	-0.90	0.03
Willson et al.	Abd	B	Iso	SLS	0.23	-0.07	0.49
Claiborne et al.	Abd	F	Ecc	SLS	-0.30	-0.59	0.07
Stickler et al.	Abd	F	Iso	SLS	-0.46	-0.68	-0.18
Hollman et al.	Abd	F	Iso	SD	0.46	0.02	0.75
Hollman et al.	Abd	F	Iso	SLS	-0.17	-0.45	0.15
Norcross et al.	Abd	B	Iso	SD	0.37	0.09	0.60
					-0.10	-0.33	0.15
Claiborne et al.	Ext	F	Iso	SLS	-0.12	-0.46	0.25
Stickler et al.	Ext	F	Iso	SLS	-0.40	-0.63	-0.10
Hollman et al.	Ext	B	Iso	SLS	-0.22	-0.49	0.10
Hollman et al.	Ext	F	Iso	SLS	-0.01	-0.32	0.30
					-0.19	-0.35	-0.02
Homan et al.	Extrot	B	Ecc	DJ	-0.27	-0.50	-0.01
Lawrence et al.	Extrot	F	Iso	SLDL	0.11	-0.23	0.42
Willson et al.	Extrot	B	Iso	SLS	-0.40	-0.62	-0.12
Claiborne et al.	Extrot	F	Iso	SLS	-0.22	-0.54	0.15
Stickler et al.	Extrot	F	Iso	SLS	-0.46	-0.68	-0.18
Hollman et al.	Extrot	F	Iso	SD	0.12	-0.34	0.54
Norcross et al.	Extrot	B	Iso	SD	0.05	-0.25	0.34
					-0.18	-0.35	0.01

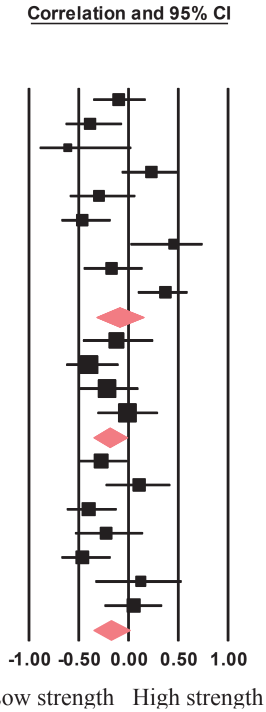


Figure 9. Association between hip abductor, hip extensor and hip external rotator strength and peak knee abduction during functional tasks in healthy individuals (II).

Association between average muscle activation amplitude and knee abduction during weight-bearing activities (II and V)

In study II, we found that lower Gmax activation was associated with greater 3D peak knee abduction during functional tasks in healthy females (r -0.34; 95 % CI -0.51 to -0.15), whereas there was no relation between Gmed or MGc and knee abduction (SDM ≤0.26; 95 % CI -0.87 to 1.39).

In individuals with ACLR (V), higher ST activation was associated with greater knee abduction excursion during the SLS after adjusting for sex and BMI in the regression models. Lower VM activation and lower IC activation on the non-injured side were associated with greater peak knee abduction during the SLHD (Table 2). The partial correlations showed that greater ST/VM ratio was associated with greater peak knee abduction during the SLS and greater peak knee abduction and excursion during the SLHD (r_{sp}=0.415 – 0.583, p≤0.012).

Table 2. Linear regression (β) of the contribution of each muscle peak torque and each muscle activation variable, adjusted for sex and BMI for the knee abduction variables (peak, excursion) during the single-leg squat (SLS) and single-leg hop for distance (SLHD) (IV and V).

	SLS								SLHD							
	Knee abduction (degrees)								Knee abduction (degrees)							
	Peak				Excursion				Peak				**Excursion**			
Peak torque (Nm/kg)	β	SE	95% CI	p-value	β	SE	95% CI	p-value	β	SE	95% CI	p-value	β	SE	95% CI	p-value
Hip abduction	-	-	-	-	-	-	-	-	4.62	3.91	-3.43;12.67	0.249	-	-	-	-
Knee flexion	6.78	4.43	-2.34;15.9	0.138	6.26	3.32	-0.58;13.09	0.071	8.66	6.06	-3.84;21.14	0.166	7.85	3.59	0.449;15.25	**0.039**
Trunk extension	4.38	3.31	-2.43;11.20	0.197	-	-	-	-	5.86	4.51	-3.43;15.16	0.206	-	-	-	-
Side-bridge	0.80	0.52	-0.27;1.86	0.137	-	-	-	-	1.17	0.70	-0.28;2.61	0.109	-	-	-	-
Average muscle activation (% MVC)																
Gmed	-0.11	0.07	-0.25;0.03	0.104	-	-	-	-	-	-	-	-	-	-	-	-
ST	0.26	0.13	-0.01;0.52	0.055	0.20	0.10	0.00; 0.40	**0.048**	-	-	-	-	**-**	**-**	**-**	**-**
VM	-	-	-	-	-	-	-	-	-0.10	0.02	-0.13;-0.03	**0.004**	**-**	**-**	**-**	**-**
IC injured	-0.39	0.22	-0.84;5.06	0.080	-	-	-	-	-	-	-	-	**-**	**-**	**-**	**-**
IC non-injured	-	-	-	-	-	-	-	-	-0.07	0.03	-0.13;-0.01	**0.028**	**-**	**-**	**-**	**-**

SE=standard error, CI=confidence interval, - indicate variables not included in the regression model, bold characters indicate significant correlation ($p<0.05$).

Discussion

The aim of this thesis was to determine which factors contribute to altered movement patterns in terms of increased knee abduction during weight-bearing activities, with special emphasis to individuals with ACLR. For that purpose, two systematic reviews with meta-analysis and three original studies were conducted. The meta-analyses revealed that female sex, reduced trunk lateral flexion strength, lower Gmax activation, increased hip external rotation ROM and reduced ankle dorsi-flexion ROM were associated with increased knee abduction during activity in healthy individuals, whereas lower extremity strength had, at best, a weak association with knee abduction. In patients with ACL injury the results from this thesis show that impaired sensory function (as assessed by kinesthesia and vibration sense), and alterations in trunk and knee muscle activation may be predictive of knee abduction in these patients. Consistent with reports in healthy individuals, our study found no association between reduced lower extremity strength and knee abduction in individuals with ACLR.

Gender differences in knee abduction

Women are reported to be at a greater risk of sustaining both a primary and subsequent ACL injury compared to men [15, 53]. That women perform weight-bearing activities with greater knee abduction has been proposed to be one explanation for this gender difference [19]. Despite inconsistent evidence, the assumption that women are more prone to knee abduction than men have been widely accepted in research and in clinical sport settings [7]. At the start of the work of this thesis, numerous studies had been conducted aiming at establish this gender-difference but with inconsistent results [105-108]. In our systematic review with meta-analysis (I) including 58 articles, we could conclude that both healthy women and women with PFP performed weight-bearing tasks with greater knee abduction compared to their male counterparts throughout the whole movement cycle, at initial contact, peak abduction and abduction excursion. We did not find a sufficient number of studies in patients with ACL injury to be able to perform meta-analysis to establish if this was the case also after ACL injury. However, in a single study of patients with ACL injury (that we identified as part of the systematic review), Yamazaki et al., reported that women with ACLD exhibited greater 3D peak knee abduction than men with ACLD during a SLS [139], in line with the result in healthy individuals and in those with PFP.

In study III, we investigated possible gender differences in knee abduction by visual observation of the positon of the knee in relation to the foot, during several different functional tasks with increasing difficulty in a group consisting of patients with either ACLD or ACLR. We found no gender difference in frontal plane knee position during any of the tasks, i.e., SLS, stair descending, forward lunge or drop jump. The main differences between our study and the study by Yamasaki et al., [139] are that we included both males and females, both patients with ACLD and ACLR and perhaps most important we assessed knee abduction as a KMFP by visual observation. A KMFP (the frontal plane position of the knee relative to the foot) as assessed visually may not reflect the knee abduction angle (the rotation of the shank in the frontal plane of the thigh) assessed with 3D motion analysis. Previous studies suggest that a visually observed KMFP is in fact a product of adduction and internal rotation of the hip rather than true knee abduction [126, 140]. This discrepancy in how knee abduction was assessed may be one explanation for the lack of gender difference in frontal plane knee position in study III. However, a recent review with meta-analysis from our research group concluded that visual observation of frontal plane knee position is valid in both 2D and 3D, i.e., the individuals that had a KMFP during weight-bearing activity also had greater knee abduction in both 2D and 3D compared to those with a KOFP [131].

Although our research confirms the suggested gender difference in 3D knee abduction in healthy individuals, the underlying reasons for this discrepancy are unclear. Several different factors, both biomechanical and neuromuscular have been proposed to pre-dispose women to this altered movement pattern. These factors include greater pelvic width, femoral anteversion, greater static knee abduction, joint laxity, greater landing forces, lower hamstrings to quadriceps torque ratios and reduced Gmax activation in females compared to males [7]. Also, the mechanism for sustaining an ACL injury may differ between males and females in such ways that knee abduction load seems to be consistently involved in ACL injury in females whereas knee abduction does not appear to be related to the injury mechanism in males [141, 142]. Together with the results from our review, this indicates that different strategies for men and women should be considered in prevention and rehabilitation of ACL injury. Specifically, women may benefit from exercise therapy aiming at improving knee alignment whereas other factors may be considered in men to prevent primary and subsequent ACL injury.

Sensorimotor factors associated with knee abduction

In the second study, the meta-analysis showed that reduced trunk lateral flexion strength as assessed by the side-bridge test, lower Gmax activation, increased hip external rotation ROM and reduced ankle dorsi-flexion ROM were associated with increased knee abduction during activity in healthy individuals, whereas lower extremity muscle strength was not. The factors contributing to knee abduction in individuals with ACL injury were however poorly investigated (II). Thus, our next step was to investigate possible sensorimotor factors that may contribute to increased knee abduction in patients with ACL injury. Patients suffering from ACL injury are known to have decreased sensorimotor function such as impaired proprioception [29], reduced muscle strength [25] and altered muscle activation patterns [26, 83] compared to non-injured individuals. Thus, and because that these factors are all modifiable by training we chose to include sensory function and trunk and lower extremity muscle strength and muscle activation as potential contributors for knee abduction in the subsequent studies.

Sensory function

We found that in patients with ACLD or ACLR, worse kinesthesia was associated with a KMFP during the drop jump in both men and women whereas worse vibration sense was associated with a KMFP during stair descending and forward lunge in women only (III). As mentioned in the introduction part of this thesis, the ACL includes several different mechanoreceptors responsible for the perception of the orientation of the segments in relation to each other and to the environment [143]. When the ACL is ruptured, the afferent input from these proprioceptive receptors is lost and a re-organization of the CNS then likely occurs to compensate for this deterioration to be able to maintain join stability during activity [38-40]. Thus, it is plausible that impaired proprioception sense after ACL injury may affect the individual’s ability to control frontal plane knee motion during activity.

Poor vibration sense has recently been linked to worse self-reported function in patients with ACL injury [69]. We are however not aware of any studies on the relation between vibration sense and objective function in these patients. In this thesis, we found worse vibration sense to be related to a KMFP during activity in women but not in men (III). The underlying cause for this gender difference is not clear. One could speculate that women may rely more on sensory abilities for joint stability whereas muscle function may be more important in men. Further research is however needed to investigate the underlying cause of the gender difference.

Muscle activation

In healthy individuals, we found lower Gmax activation to be associated with increased 3D peak knee abduction during activity (II). We were not able to confirm this result in patients with ACLR (V). However, we did find that lower IC activation on the non-injured side, higher ST activation, lower VM activation as well as greater ST/VM ratio was associated with greater knee abduction during the SLS and SLHD (V). Adequate activation of the trunk and core muscles has been proposed to decrease the risk of knee injury [10, 11]. Specifically, greater ipsilateral trunk motion has been reported to be related to greater peak knee abduction [144], increased knee abduction moment [145, 146] and a higher risk of sustaining an ACL injury [10, 11] in healthy individuals. If IC activation on the contralateral side is reduced, the individual may not be able to prevent lateral trunk lean to the ipsilateral side [147-149] and may thereby also increase knee abduction. This could constitute an explanation for the association between lower IC activation on the non-injured side and increased knee abduction on the injured side observed in study V.

Patients with ACL injury are reported to have higher average activation of the hamstring muscles [85] and lower activation of the quadriceps muscles [26] compared to healthy individuals. Since the hamstring muscles are important ACL agonists and resists anterior tibial translation, whereas the quadriceps is an ACL antagonist, these alterations may be due to central modifications to compensate for the decrease in joint stability that often is present after the loss of the ACL [91, 92]. The ST muscle is involved in adduction of the hip and in medial rotation of the hip and knee [150], and may thus play a role in knee abduction, since hip adduction and internal rotation are known contributors for this movement pattern [151]. Given the above-mentioned function of the hamstring as a joint stabilizer and that most patients are reconstructed using a ST graft, these patients are likely to have a preference of activating this muscle to a relatively high extent during activity. However, this compensatory strategy may in fact contribute to alterations in movement pattern in the form of increased knee abduction that may predispose these individuals to further injuries to the knee. Further research is required to confirm these findings and to assess whether this strategy is a preventive factor or risk factor for further injury.

Muscle strength

Previously, there has been great attention on the role of muscle strength for knee abduction and especially the hip muscles are believed to contribute to knee abduction due to their role of resisting adduction and internal rotation of the hip during activity [152]. But also, the muscles acting at the knee joint has been proposed to influence knee abduction because of the capacity of the hamstring and quadriceps muscles to support knee abduction/adduction moments of the knee [80]. In this thesis, we did not find that lower extremity strength including hip extension, abduction, external rotation or knee flexion and extension peak torque were associated with knee abduction in healthy individuals (II) or in those with ACLR (IV). In support of this finding, several studies report no improvement in knee abduction during activity after participation in a lower extremity strength training program [153-156]. An association between reduced hip muscle strength and increased hip muscle activation has been reported [139, 157-160], suggesting a compensatory increase in muscle activation to maintain joint stability and lower extremity alignment during activity when muscle strength is impaired. This indicates that the level of activation of the lower extremity muscles may be more important for postural orientation of the knee during activity than the absolute strength of the muscle as assessed by peak torque.

Trunk lateral flexion strength as assessed by the side-bridge test was associated with increased 3D peak knee abduction during a SLS in healthy individuals (II). We found however no such association in patients with ACLR (IV). This could indicate that the factors contributing to knee abduction may differ between healthy individuals and those with knee injury. However, study IV only included 29 participants with ACLR compared to 109 participants in the meta-analysis on healthy individuals (II), which could suggest that we were underpowered to detect this relation in study IV. Further studies are therefore needed to confirm the results in patients with ACLR.

The role of Knee abduction for ACL injury risk

Despite the fact that increased knee abduction seems to be involved in the knee injury mechanism in women [11, 161–163], whether knee abduction is a risk factor for sustaining the ACL injury is still a subject of debate. In the meta-analysis in this thesis we found that non-injured women performed weight-bearing activities with significantly greater knee abduction compared to men. This finding may support the hypothesis that knee abduction is a contributing factor for the high ACL injury incidence in women. However, to this date, four studies have investigated the association between knee abduction at baseline and the risk of sustaining future primary ACL injury using a prospective study design [14, 18-20]. In the study by Hewett et al., 205 high school court sport female athletes were screened at baseline. The nine athletes that sustained an ACL injury during the season had significantly greater knee abduction at initial contact of a vertical drop jump landing compared to those that did not sustain and injury [19]. In contrast, in three other studies (screened athletes n=171-782, sustained ACL injuries n=5-42) there were no association between knee abduction during the drop jump task and the risk of sustaining a primary ACL injury [14, 18, 20]. It should however be noted that two of these latter studies were conducted in Norway in female adult elite team hand ball and soccer players [18, 20]. Norway is known for their rigorous injury prevention programs aiming at improve lower extremity alignment [164]. Consequently, these participants have most likely been participating in neuromuscular prevention training and may, therefore, be well trained to keep their knee over the foot during the assessment, which may have influenced the result of these studies. This is also reflected by the low amount of knee abduction observed during the drop jump in these studies (approximately 2 degrees) compared to the study by Hewett et al., where a mean knee abduction angle of 5 to 9 degrees was observed [18-20]. In a recent study, Fox et al., determined that normal knee abduction values during a vertical drop jump range from 5 to 17 degrees in females [165]. This implies that the participants in these studies were all in the normal range of knee abduction. Also, to date there is no consensus regarding the amount of knee abduction that is considered excessive enough to amplify the risk of injury. Taken together, the effect of knee abduction on knee injury risk in women is equivocal. Furthermore, the association between knee abduction and knee injury risk in men is unclear, since all available studies are conducted in women. That said, knee abduction may be relevant for knee injury in younger individuals, not playing on an elite level. Although the evidence for the role of knee abduction in primary ACL injury is not univocal, there seem to be an association between greater knee abduction during a drop jump at baseline and a second ACL injury in both men and women [18, 151]. However, further studies are still needed to establish the importance of lower extremity alignment during activity for the risk of sustaining both the primary and subsequent ACL injury.

Methodological considerations

General limitations (I-V)

This thesis includes some limitations. First, a knee injury may occur during several different movements, e.g., landings and cutting movements. Since increased knee abduction has been suggested to account for some of the gender-difference in knee injury incidence, we were in study I initially interested in investigating if women in general performed weight-bearing activities with increased knee abduction compared to men. The same applies for study II, where we wanted to elucidate the effect of the investigated factors on knee abduction during weight-bearing activities. Consequently, we included all available tasks in the meta-analyses. We are, however, aware that this approach may introduce some potential bias. It could not be ruled out that the different movement strategies used in each task may influence the magnitude of knee abduction differently or affect the contribution of each sensorimotor factor for knee abduction in a different manner and, thus, have an influence on the results. In an effort to deal with this problem, we performed separate analyses for each task that included two or more articles. Although this was an adequate approach, including separate analysis for most tasks in study I, it was not feasible in study II where only the association between hip strength and knee abduction during the SLS was eligible for separate analysis.

Second, in study III we included patients with ACLD and ACLR in the same analysis to reflect the population that typically presents clinically for rehabilitation post ACL injury. However, studies have shown that there may be differences both in proprioceptive acuity [64] and in the relation between sensory function and self-reported knee function [69] between individuals with ACLD and ACLR. Thus, it is possible that the result would have been different if we had analysed these groups separately. It is also for this reason we chose to only include participants with an ACLR in studies IV and V in an effort to have a more homogeneous population.

Third, no power calculations were performed in studies III-V. The sample in study III constituted a sample of convenience (n=51) and in studies IV and V all individuals that have performed an ACLR at Skåne University Hospital in Sweden between June and December, 2015 were invited to participate in the study (n=106). Out of the 106 that were invited, only 29 participants were finally included in the studies. The data was collected between February 16th and May 30th, 2016. Due to time constrains we were unfortunately not able to include additional participants within the time frame of this thesis. Thus, there is a possibility that the lack of associations between some variables and knee abduction are due to a lack of power. Consequently, the small sample also prevented us from performing separate analysis for men and women in study IV and V, which was our aim initially. Although we adjusted for sex in the regression models, the result may have been different if we were able to perform gender stratified analyses. Thus, a larger sample size is needed to determine our findings in studies IV and V.

Sensory measures

In study III we investigated the relation between proprioception (kinesthesia) and visually observed frontal plane knee positon. Assessment of kinesthesia (and all other measures of proprioception) depends on the individual's conscious perception of the movement and may thus be affected by cognitive abilities. Also, the assessment of "conscious" proprioception may not reflect the unconscious movement strategies that are suggested to play a role in joint stability. Furthermore, although great effort is being put on reducing sensory input from the skin and the equipment by padding and the use of socks, it is not possible to perform such assessment without affecting other sensory mechanoreceptors. For example, receptor in the skin will send information about movement to the CNS when the skin is stretched during flexion/extension of the knee, thus it is hard to distinguish the source/origin of the afferent signals that contribute to the conscious perception of the movement during the assessment [113]. Also, in our study, kinesthesia was assessed during passive movement. It has been proposed that this approach is not ecologically valid [113], since passive movement does not reflect a real-life situation [166]. Thus, more functional measures of proprioception, as used in other studies [167, 168], that includes weight-bearing and active movements may have provided other results.

Muscle activation

Traditionally there have been several methodological limitations associated with surface EMG data collection, such as the difference in EMG signal amplitude due to the size of the electrode, type of electrode fixation, inter-electrode distance and/or location of the reference electrode, which have made it hard to compare results between studies. These limitations are minimized with modern wireless EMG equipment with self-adhesive standard dual electrodes with a fixed inter-electrode distance [123]. However, other limitations that should be considered are the high risk of collecting cross-talks from adjacent muscles [123, 169] and the presence of baseline noise and movement artefacts [170] that may affect the EMG signal. Movement artefacts are a particularly problem during dynamic tasks such as the SLHD used in study V. In fact, we had to exclude 7 out of the 29 participants from the analysis on IC muscle activation on the injured side due to movement artefacts, which may have affected the statistical power of this analysis.

To be able to compare muscle activation amplitude between individuals, you must normalize the data. The most common normalization method is to divide the processed EMG amplitude for each muscle collected during the trial with the amplitude collected for that specific muscle during a MVC [171, 172]. A common problem with this method is however that you cannot be sure that the data collected during the MVCs really reflects the true MVC. This is especially problematic when, as in study V, the data of interest are collected during dynamic movements (SLS and SLHD) but are then normalized to data collected during isometric testing. This was not a general problem in our study (V), but for one muscle (VMO), 11 (38%) participants had a task data/MVC ratio of between 1 and 3. In other words, in these cases the participants activated their VMO up to three times more during the task than during the MVC test. This implies that the isometric MVC did not appear to represent the true MVC in these cases. The only method to ensure that a true MVC is collected is by a twitch interpolation technique [173]. This was not feasible in our study since this technique involves percutaneous electrical impulses that are both uncomfortable for the participants and require advanced equipment. However, in an effort to gain the maximal recruitment of the muscles, we used a standardized protocol, where the participants were given the same instructions on how to perform the task and were verbally encourage to produce maximum force during the task. In addition, a question about perceived pain during the performance of the task was asked to minimize pain related failure during the tasks.

3D motion analysis

Although 3D motion analysis is considered the “gold standard” to assess human movement, this method is not without limitations. Several factors affect the probability of obtaining accurate and reliable movement data from the motion analysis system. Systematic errors, associated with for example laboratory set-up and calibration of the cameras, and random errors originating from electronic noise are common instrument-related problems in 3D assessments [174]. The latter may, however, be minimized through certain filtering and smoothing techniques [133]. Another limitation associated with 3D assessment includes difficulties with accurate identification of the anatomical bone landmarks for marker placement and the centre of the joints which have substantial influence on the reliability of the data obtained [175]. Furthermore, soft tissues artefacts (STA) are an important factor that should be considered in 3D motion analysis. This is a particular problem during high impact movements such as the SLHD. STA is provoked by displacement of the skin were the markers are attached in relation to the subcutaneous bone structure and may be influenced by muscle contractions, type of activity and the location of the markers [176]. Previous studies have reported that the thigh is associated with the greatest error during functional tasks such as stair descending, cutting and SLHD [176-179]. Also, the use of skin markers showed poor reliability in frontal plane knee rotations with errors up to 70% between the assessed movement and the actual real joint movement [176]. To minimize the errors from STA, the marker model in our studies (IV and V) was designed according to the Visual 3D recommendations based on the work by Cappozzo et al [180]. Despite these limitations, 3D motion analysis is the closest we can get to identify the movement of the joints. 3D knee abduction has shown high inter and intra reliability during several tasks including different jumping tasks and the SLS [181-183] as well as high reliability between different laboratories and systems [184].

Clinical implications

Previous research proposes an association between increased knee abduction during activity and worse self-reported function [97, 98] and worse hop performance [96], respectively, in individuals with ACL injury. In addition, this movement pattern seems to increase the risk of subsequent ACL injury [18, 151]. Thus, exercises with the aim of decreasing knee abduction are today often incorporated in rehabilitation programs after knee injury [5]. Studies report that neuromuscular training including plyometric exercises, strength training, proprioception training and modification of landing techniques may reduce the risk of injury [185, 186] and improve biomechanical factors associated with knee injury such as knee abduction and lateral trunk lean [187]. However, the specific factors that should be targeted to reduce knee abduction have not been established.

In this thesis, we found that altered muscle activation rather than muscle strength seem to play a role in knee abduction in both healthy individuals (II) and in those with ACLR (IV and V). Previous research also found no improvement in frontal plane knee motion after strength training protocols in healthy individuals and in those with PFP [153-156]. This indicates that absolute strength may not be as important for knee abduction as previously believed and that incorporating exercises targeting the activation of the muscles instead of force may be more beneficial for improving this movement pattern. Zebis et al., reported that a 12-week neuromuscular exercise program improved knee muscle activation pattern commonly associated with knee injury risk [188].

Another factor that may be important in the prevention and rehabilitation of ACL injury is ankle dorsiflexion ROM. In study II, we found that those with a KMFP during activity had significantly reduced ankle-dorsi flexion ROM compared to those with a KOFP. Reduced ankle ROM is proposed to increase foot pronation and prevent knee flexion and may thereby introduce compensatory strategies at the knee such as increased knee abduction [189-191].

Proprioceptive training should also be considered when aiming at reducing knee abduction after ACL injury, since we found that individuals with a KMFP had decreased proprioception during a drop jump compared to those with a KOFP (III). In study I, we reported that women exhibit greater knee abduction during weight-bearing activity than men. This may suggest that exercise therapies aiming at reducing knee abduction would be more beneficial in women than in men. Other factors than knee abduction may therefore be considered in men to improve function and reduce the risk of subsequent knee injury.

The altered knee movement pattern observed after ACL rupture may also be elicited by neuroplastic changes and alterations to the CNS after injury which may be hard to target with conventional rehabilitation strategies. Electromyographic biofeedback, transcutaneous electrical nerve stimulation and neuromuscular electrical stimulation are methods that may be helpful in restoring neuromuscular alteration after knee injury by improving motor unit recruitment, reflex excitability and muscle inhibition as well as exaggerate voluntary muscle contraction [192]. Also, rehabilitation after ACL injury may be enhanced by integrating exercises with higher demands on the brain. Incorporating cognitive tasks that include visual-spatial-motor tasks and mental imagery may ameliorate neuromuscular control and joint stability by increasing muscular activation and improving coordination after ACL injury and thereby potentially decrease frontal plane knee motion [193, 194].

In this thesis, we investigated gender and sensorimotor factors modifiable by training as possible contributors to knee abduction. However, we found only moderate associations between the investigated factors and knee abduction, implying that there are other factors that also contribute to knee abduction. Several non-modifiable factors, such as greater tibial slope, pelvic width and static knee alignment have been proposed to influence frontal plane knee motion during activity [195, 196]. Also, the relative contribution of the different factors for knee abduction is not clear. Thus, future studies that include both structural and sensorimotor factors as potential contributors for knee abduction are warranted. Also, most studies on both knee injury risk and movement pattern alterations are conducted in women. Further studies are thus needed to evaluate which specific factors that is associated with knee abduction and knee injury risk in men.

Conclusions

The result from this thesis indicates that alterations in sensorimotor function play a role in knee abduction during weight-bearing activities. Specifically, lower trunk lateral flexion strength, reduced ankle dorsi-flexion ROM and lower Gmax activation are associated with greater knee abduction in healthy individuals. In patients with ACL injury, reduced sensory function and alterations in trunk and knee muscle activation may increase knee abduction, whereas lower extremity muscle strength does not seem to be important for knee abduction in individuals both with and without knee injury. Given that healthy women perform weight-bearing activities with increased knee abduction compared to men, there may need to be a greater focus on this movement pattern during prevention and rehabilitation training in women, whereas other factors may be more relevant in men. Further investigations are needed to confirm our results and to establish which factors, both structural and neuromuscular, that contributes to knee abduction in men and women with ACL injury.

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