Mapping current research trends on neuromuscular risk factors of non-contact ACL injury

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Abstract

The aim of this systematic review was (i) to identify neuromuscular markers that have been predictive of a primary non-contact ACL injury, (ii) to assess whether proposed risk factors have been supported or refuted in the literature from cohort and case-control studies, and (iii) to reflect on the body of research that aims at developing field based tools to assess risk through an association with these risk factors. Electronic searches were undertaken, of PubMed, SCOPUS, Web of Science, CINAHL and SPORTDiscus examining neuromuscular risk factors associated with ACL injury published between January 1990 and July 2015. The evidence supporting neuromuscular risk factors of ACL injury is limited where only 4 prospective cohort studies were found. Three of which looked into muscular capacity and one looked into muscular activation patterns but none of the studies found strong evidence of how muscular capacity or muscular activation deficits are a risk factor for a primary non-contact ACL injury. A number of factors associated to neural control and muscular capacity have been suggested to be related to non-contact ACL injury risk but the level of evidence supporting these risk factors remains often elusive, leaving researchers and practitioners uncertain when developing evidence-based injury prevention programs.

1 Introduction

Anterior cruciate ligament (ACL) injury is one of the most prevalent injuries associated with athletes in dynamic sport settings (Department of Orthopaedic Surgeries, 2009). In most cases the injury derives from a non-contact situation (Boden, Dean, Feagin, & Garrett, 2000; McNair, Marshall, & Matheson, 1990) with a high socio-economic burden as these injuries are also associated with long-term complications. One complication in particular is early onset of osteoarthritis of the knee, affecting 59 percent to 70 percent of the injured populations (American Academy of Orthopaedic Surgeons, 2007). Reported injury rates has been as high as 2.8 and 3.2 injuries per 10,000 hours exposure in women’s collegiate basketball and soccer, respectively with an estimation of 80,000 to 250,000 ACL injuries occur each year (Smith, et al., 2012). This has led to a growing number of studies trying to advance our understanding of who is at increased risk of sustaining a non-contact ACL injury. Such understanding is important to support the development of preventative programs.

Generally, prospective cohort studies provide the strongest evidence to support the development of intervention and prevention programs, as outlined in the Translating Research into Injury Prevention Framework, (Finch, 2006) where the success of the programs are based on modifying known risks associated with incurring the injury. The high costs associated with running prospective cohort studies tends to limit the amount of direct evidence on risk, particularly when experimental observations are time consuming or only possible in a lab environment, such as is often the case in the investigation of neuromuscular factors.

To date, a number of factors associated to neural control and muscular capacity have been suggested to be related to non-contact ACL injury risk. The level of evidence supporting the suggested risk factors remains to our knowledge often elusive, leaving researchers and practitioners uncertain when developing evidence-based injury prevention programs. Therefore the aim of this systematic review of the literature was (i) to identify those neuromuscular markers that have been predictive of a primary non-contact ACL injury, (ii) to assess whether the identified risk factors have seen supportive evidence from cohort and case-control studies, and (iii) to reflect on the body of research that aims at developing field based tools to assess risk through an association with these risk factors.

2 Method

The Cochrane Handbook (Higgins & Green, 2009) and the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) (Liberati, Altman, & Tetzlaff) guidelines were used in conducting this systematic review.

2.1 Electronic Literature search

The literature selection process consisted of exploring electronic databases from PubMed, Scopus, Web of Science, CINAHL and SPORTDiscus between January 1990 and July 2015. The search terms were constructed and tested prior to the initial search so that the key terms cover as much as possible the existing literature of neuromuscular risk factors for non-contact ACL injury. In addition, a hand search was done on the reference lists of included articles. The search terms were divided into four groups. Between groups, the search terms were connected with AND, and within groups the search terms were connected with OR. Depending on the search database, the appropriate search term notation technique was applied. The result of this search strategy is described in Table 1.

2.2 Literature Selection

From the titles and abstracts (first stage), two authors (R.S. and M.R.) independently identified potentially relevant papers for full review to avoid bias. If there were any disagreements between the two reviewers, consensus was sought through discussion between them. If no consensus was reached, a moderator (J.V.) was consulted to reach a final consensus. Selection based on full text assessment (second stage) was done by two other reviewers (R.R. and J.V.) and if there were any disagreements between the two reviewers, consensus was sought through discussion between them. If no consensus was reached, a moderator (M.R.) was consulted to reach a final consensus. For these titles, categorization as well as inclusion and exclusion criteria were implemented in a study classification system using EndNote® (version X7.0.1, Thomson Reuters) to select the relevant titles. Inclusion criteria across studies were as follows: (i) studies that measure neuromuscular variables (e.g.: isokinetic dynamometry, isometric strength, electromyography or EMG); and (ii) studies measuring other variables (e.g.: biomechanical or physiological variables) but still containing neuromuscular assessments. Classification of included studies is described in Table 2. Exclusion criteria were (i) studies without abstracts; (ii) invited reviews or systematic reviews; (iii) studies that focused on the effect and impact of treatment/training; (iv) studies that only looked into orthopaedic and rehabilitative aspects of ACL reconstruction; (v) in-vitro studies; (vi) studies on non-team sports (such as golf, walking, etc); (vii) technical studies and (viii) studies that were not in English.

2.3 Data Extraction

The first author (R.R.) extracted data from each included article based on their respective study designs. For prospective cohort studies, data supporting the strength of the prospective evidence (e.g.; number of subjects, monitoring/follow-up period and injury rate) and the neuromuscular variables measured were extracted. For retrospective and case-control studies the assessed task, neuromuscular variable measured, and findings were extracted. For associative studies (see Table 2), data that were extracted provided an insight to enable reflection on the amount of ongoing research that takes prospectively identified ACL injury risk factors as a foundation for their experimental research paradigm(s).

2.4 Methodological Quality Assessment

The first author (R.R.) assessed the methodological quality of the studies based on the Risk of Bias Tool by the Cochrane Bias Methods Group (Group) for prospective cohort, case-control studies, evaluating criteria associated to several factors (e.g., cohort selection, exposure assessment; see full list at bottom of table 3). For each item, one point could be scored and the total score of the methodological quality ranged between 0 – 7 (prospective cohort) and 0 – 6 (case-control studies). If an item was not present, not reported or insufficient information was given, 0 points were scored. Some items were not applicable, depending on the study design of the included studies, and then these items were excluded from calculation of the quality scores.

3 Results

3.1 Search Findings

Table 1 shows the overall process and outcome of keyword searches. The initial search retrieved a total number of 2,260 studies: PubMed (696), Scopus (99), Web of Science (712), CINAHL (409) and SPORTDiscus (344) (see Figure 1). Removing duplicates between database searches resulted in a total of 2,204 titles. From the title and abstract assessment (1st stage), 269 studies were retrieved and eligible for full text assessment. From full text review (2nd stage), a further 221 papers were excluded retaining 4 prospective studies, 14 case-control studies and 30 associative studies. The mean methodological quality score for prospective studies was 5.75 (range 4 to 7) and for case-control studies was 3.21 (range 2 to 5).

3.2 Prospective Studies

Of the 4 prospective studies observing the neuromuscular markers of ACL injury, 3 evaluated muscular capacity (comprising of isokinetic knee strength and H/Q ratio) as risk factor of non-contact ACL injury (Myer, et al., 2009; Söderman, Alfredson, Pietilä, & Werner, 2001; Uhorchak, et al., 2003), and 1 study evaluated muscular activation patterns (Mette K. Zebis, Andersen, Bencke, Kjær, & Aagaard, 2009) (see Table 4).

3.2.1 Muscular Capacity

Myer et al. (Myer, et al., 2009) found that females who went on to suffer an ACL injury had decreased hamstring strength compared to male controls whereas matched female healthy controls who did not suffer from ACL injury had decreased quadriceps strength compared to male controls. Soderman et al. (Söderman, et al., 2001) found that an imbalance of the hamstrings to quadriceps ratio (H/Q ratio) between legs in female athletes was predictive of players who suffered an ACL injury, with a lower H/Q ratio on the side that would become injured (Söderman, et al., 2001). On the contrary, Uhorchak et al. (Uhorchak, et al., 2003) did not find differences in H/Q ratios for males and females who go on to suffer ACL injury.

3.2.2 Muscular Activation Pattern

Zebis et al., 2009 (Mette K. Zebis, et al., 2009) focused on muscle co-activation patterns during side cutting in elite female athletes and found that reduced pre-activity of the semitendinosus (ST) combined with increased pre-activity of the vastus lateralis (VL) indicates an increased risk of future non-contact ACL injury.

3.3 Case-Control studies.

Fourteen studies were included in the review to assess the consistency of findings of the identified neuromuscular risk factors associated with non-contact ACL injury from the prospective studies. In this section studies were further separated based on whether the study observed differences between participants with ACL deficiency (ACL-D) and healthy controls, or differences between ACL reconstructed participants (ACL-R) and healthy controls.

3.3.1 Muscular Capacity

Five case-control studies analyzed deficits in muscular capacity in ACL-D subjects compared to healthy controls (Hsiao, Chou, Hsu, & Lue, 2014; Konishi, et al., 2011; Swanik, Lephart, Swanik, Stone, & Fu, 2004; Tsepis, Vagenas, Giakas, & Georgoulis, 2004; Urbach, Nebelung, Becker, & Awiszus, 2001). ACL-D subjects showed a deficit of the peak quadriceps torque in both isometric testing in males (Urbach, et al., 2001) and isokinetic testing (Konishi, et al., 2011; Tsepis, et al., 2004) in males and females. Another study found quadriceps and hamstring deficits for isometric and isokinetic tests in male and females (Hsiao, et al., 2014). In contrast, one study found greater isokinetic hamstring strength in ACL-D females (Swanik, et al., 2004). Finally, one study found no difference in quadriceps strength between ACL-D and healthy controls.

Five case-control studies investigated muscular capacity deficits of ACL-R compared to healthy controls (Drechsler, Cramp, & Scott, 2006; Holsgaard-Larsen, Jensen, Mortensen, & Aagaard, 2013; Hsiao, et al., 2014; Urbach, et al., 2001; Xergia, Pappas, Zampeli, Georgiou, & Georgoulis, 2013). Two studies demonstrated weaknesses in quadriceps strength that were still present at both 1 and 3 months after injury in males and females during isometric and isokinetic contraction (Drechsler, et al., 2006; Hsiao, et al., 2014). Another study also found a decrement of isokinetic strength in the quadriceps in males (Xergia, et al., 2013). One study that found a deficit in peak quadriceps torque in isometric contraction in males after ACL-R went on to observe that this deficit had disappeared two years after reconstruction (Urbach, et al., 2001). Another study also found a reduced function of the operated leg, 2 years post ACL-reconstruction, for hamstring isometric contraction where asymmetry in hamstring strength was greater after ACL-R (Holsgaard-Larsen, et al., 2013).

3.3.2 Muscular Activation Patterns

Five case-control studies examined deficits in muscular activation pattern between ACL-D and healthy controls (Aalbersberg, Kingma, & van Dieën, 2009; DeMont, Lephart, Giraldo, Swanik, & Fu, 1999; Steele & Brown, 1999; Swanik, Lephart, Giraldo, DeMont, & Fu, 1999; Swanik, et al., 2004). One study found that the hamstrings were activated more in ACL-D subjects and this increased activation was more apparent in extended than in flexed knee angles (Aalbersberg, et al., 2009). Another study focusing on a deceleration task found delayed biceps femoris (BF) and semimembranosus (SM) activation (Steele & Brown, 1999). Further studies observed muscle activations in ACL-D females (DeMont, et al., 1999; Swanik, et al., 1999; Swanik, et al., 2004). Muscle pre-activity strategies appeared to be different depending on the task being done with vastus lateralis (VL) activation being higher during hopping and vastus medialis obliquus (VMO) activation being lower during downhill walking (DeMont, et al., 1999). Reactive muscle activity (after ground contact) during running was seen to be greater when observing peak activity in the BF and vastus medialis (VM), but smaller when observing overall EMG activity (Swanik, et al., 1999). During landing, the ACL-D group demonstrated significantly less overall activity in the vastus lateralis (VL) (Swanik, et al., 1999). ACL-D females had significantly increased preparatory muscle activity in the BF before landing, but no differences in reactive muscle activity during landing or reflex latency after joint perturbations were observed (Swanik, et al., 2004).

Two case-control studies described differences in muscular activation patterns between ACL-R and healthy controls (Ortiz, et al., 2008; Ortiz, Olson, Trudelle-Jackson, Rosario, & Venegas, 2011). One study demonstrated co-contraction ratios between normalised hamstring and quadriceps activations that were significantly closer to 1 in the ACL-R group during drop jumps, and greater gluteus maximus (Gmax) and rectus femoris (RF) activations (Ortiz, et al., 2008). Another study from the same research group showed that neuromuscular recruitment strategies during two side hopping tasks in ACL-R females did not differ from healthy controls (Ortiz, et al., 2011).

3.4 Associative studies

Thirty associative studies were retained (see Table 6). Out of these studies, 11 studies investigated associations with muscular capacity as a risk factor. Five of the studies assessed isokinetic and isometric peak torques where 4 of the studies observed deficits in quadriceps and hamstring strength and 1 study focused on increments of isokinetic strength from an intervention to prevent ACL injury. The other 6 studies assessed H:Q ratios in a variety of ways.

Twenty studies investigated associations between muscular activation patterns as risk of ACL injury. Five of the 20 studies looked into an intervention to improve on quadriceps and hamstring activation or co-activation, 3 studies focused on pre-activation of the lower limbs in different tasks, 1 study investigated detraining effects on lower extremity EMG, 1 study assessed lower extremity neuromechanics relative to leg dominance during an unanticipated sidestep cutting task, with differing states of fatigue and training, 6 studies investigated the differences in muscle synergy strategy between gender, 2 studies observed the relationship between muscle co-contraction and knee flexion angle 1 study identified the phases of sidestep cutting that may place athletes at a greater risk for ACL injuries and 1 study investigated the effect of muscle fatigue on neuromuscular strategy during a functional side cutting movement.

4 Discussion

4.1 Prospective evidence

The evidence supporting risk factors of ACL injury associated with muscular capacity or muscular activation patterns is limited. This systematic review found only four prospective studies of which three studies looked into muscular capacity (Myer, et al., 2009; Söderman, et al., 2001; Uhorchak, et al., 2003) and only one study into muscular activation patterns (Mette K. Zebis, et al., 2009). From the studied cohorts, there were only a small number of individuals who incurred an injury with injury rates ranging from 1.3% to 9.0%. The small percentages of injuries in the prospective cohorts were due to infrequent of acquiring a non-contact ACL injury, even though there is a high case rate for ACL injury. In prospective risk factor studies, the power of the study is determined by (i) the association strength of the risk factor and injury risk (the stronger the association, the fewer cases are needed), (ii) the rate of injury (the more frequent the injury, the fewer cases are needed), and (iii) the chosen significance level (Bahr & Holme, 2003). With low rates of injury, suggestions for future work have been that risk of ACL injury would need to be studied in substantially larger cohorts than typically done but the cost associated to that is simply too high. The relatively higher incidence of injury in females has led to most cohort studies only involving females (Myer, et al., 2009; Söderman, et al., 2001; Mette K. Zebis, et al., 2009). Considering the knowledge that injury mechanisms in females are different than in males and other risk factors such as laxity and hormonal factors may also differ between males and females (Smith, et al., 2012), this makes translating the risk factors to male populations highly ambiguous. Differences between injured and non-injured individuals were small, providing relatively low sensitivity and specificity of the measure to predict injury (Myer, et al., 2009; Söderman, et al., 2001; Uhorchak, et al., 2003; Mette K. Zebis, et al., 2009). The value of the risk factors for targeted screening with a focus on differentiating interventions based on risk is therefore limited. Particularly, good research practice would require proposed risk factors to be confirmed in an independent study with an independent cohort, yet no risk factors have been independently confirmed to date. Altogether, whilst one may advise future research to involve greater cohorts, for example through multi-centre studies, such efforts should probably focus on multi-factorial risk. Particularly concerning neuromuscular factors, the link between muscular activation patterns and muscles' capacity to generate torque is often referred to when interpreting findings of one or the other (Myer, et al., 2009; Söderman, et al., 2001; Uhorchak, et al., 2003; Mette K. Zebis, et al., 2009), but whether this link holds true in the context of ACL injury risk remains unknown. Also, muscular capacity as well as muscular activation patterns at the knee are related to capacity and activation patterns at the ankle and probably at hip and abdominal musculature (S. J. Shultz, et al., 2012; Zazulak, et al., 2005; Zeller, McCrory, Kibler, & Uhl, 2003). No papers on this topic fit our inclusion and exclusion criteria, but the focus on knee musculature based on the premise that this is the closest evidence to predicting ACL injury may well not hold true. Another approach may still be suggested based on a recent systematic literature review on the effectiveness of prevention programmes (Grimm, Jacobs, Kim, Denney, & Shea, 2015). This review revealed that the prevention of ACL injury has until now mostly been ineffective, yet the prevention of knee injuries in general has seen more success. Considering some suggestions that non-contact lower limb injuries can have similar causality, a potentially viable approach to making prospective studies more cost-effective may be to explore risk factors of any knee injury rather than only ACL injury.

4.2 Post-injury case-control evidence

Whilst one may focus on the fact that sample characteristics of the various studies were diffuse, the overarching message concerning post-injury supportive evidence to risk factors is that the effect of injury is greater than any remaining person-specific effects of risk prior to the injury. Clear and often long-term reductions in muscular capacity were found for quadriceps muscles in ACL-D (Hsiao, et al., 2014; Konishi, et al., 2011; Tsepis, et al., 2004; Urbach, et al., 2001) and ACL-R (Drechsler, et al., 2006; Hsiao, et al., 2014; Xergia, et al., 2013) patients compared to healthy controls suggesting substantial consequences of post-injury inactivity, detrimental effects of kinesiofobia (Drechsler, et al., 2006), autograft repair (Hiemstra, Webber, MacDonald, & Kriellaars, 2004), and potentially lack of rehabilitation compliance. These considerable changes in muscular capacity and likely alterations in muscular activation patterns altogether suggest that risk of re-injury is based on very different factors than risk of primary injury. Rather than hamstring weakness combined with high quadriceps strength (low H/Q ratios), re-injury risk may need to be explored through the consequences of quadriceps weakness and/or lack of quadriceps activation in the injured leg, particularly in the context of compensation mechanisms in the contralateral leg where re-injury is most prevalent (Wright, Magnussen, Dunn, & Spindler, 2011). Hamstring weakness was in most post-injury case-control studies not an indication of risk, with hamstring strength being the same between injured and non-injured limb, and between injured and healthy controls (Drechsler, et al., 2006; Swanik, et al., 2004; Tsepis, et al., 2004; Xergia, et al., 2013). This may reflect the effectiveness of many ACL rehabilitation protocols that focus on strengthening the hamstrings as an ACL protective measure. The evidence on hamstring weakness as a risk factor for primary ACL injury remains poor, and is confounded by many other factors, including the fact that hamstring inadequacy may well be joint-angle and joint-angular velocity specific, or as mentioned above, that muscular capacity may well be dissociated from risk inducing activation patterns. In muscular activation pattern assessment, only two case-control studies (Swanik, et al., 1999; Swanik, et al., 2004) found reduced activation of the semitendinosus combined with increased activation of the vastus lateralis during dynamic tasks as was found through prospective work (Mette K. Zebis, et al., 2009). These observations again suggest discrepancies between risk factors of a primary injury versus re-injury. Changes observed in muscular activation patterns post ACL injury likely also result from adaptations associated with protective behaviour when performing selected tasks and/or as a result of rehabilitation focus.

4.3 Reflection on associative studies

The last decade has seen a substantial increase in studies that aim at translating evidence on risk into field-based screening tools through associating observations that are easy to assess in a clinical or field context with previously identified risk factors. For muscular capacity, 11 studies have looked into its association with sustaining a non-contact ACL injury (Ahmad, et al., 2006; Bee-Oh, et al., 2009; Bowerman, Smith, Carlson, & King, 2006; Grygorowicz, Kubacki, Pilis, Gieremek, & Rzepka, 2010; Hiemstra, Webber, MacDonald, & Kriellaars, 2007; Holcomb, Rubley, Lee, & Guadagnoli, 2007; Hosokawa, et al., 2011; Mattacola, et al., 2002; Roberts, Ageberg, Andersson, & Fridén, 2007; Wilkerson, et al., 2004; M. K. Zebis, et al., 2011). These studies have associated muscular capacity with risks of acquiring ACL injury, validating ACL screening tools to be used in intervention programs to prevent ACL injury. Considering that the 3 prospective studies (Myer, et al., 2009; Söderman, et al., 2001; Uhorchak, et al., 2003) did not find strong evidence of how muscular capacity deficits are a potential risk factor for non-contact ACL injury, the actual predictive value of screening tools with a moderately strong association to the actual risk factor is potentially very weak. The same case applies to screening for muscular activation deficits. There were 20 studies in the last 5 years that addressed an association with motion pattern deficits, seeking opportunities to observe risk from motion analysis (Begalle, Distefano, Blackburn, & Padua, 2012; Bencke & Zebis, 2011; Dai, Sorensen, Derrick, & Gillette, 2012; Elias, Hammill, & Mizner, 2015; Greska, 2012; Hannah, Folland, Smith, & Minshull, 2015; Hughes & Daily, 2015; Kipp, et al., 2014; Landry, McKean, Hubley-Kozey, Stanish, & Deluzio, 2009; Lategan, 2012; Liebensteiner, Platzer, Burtscher, Hanser, & Raschner, 2012; McLean, Borotikar, & Lucey, 2010; Nagano, Ida, Akai, & Fukubayashi, 2011; Palmieri-Smith, McLean, Ashton-Miller, & Wojtys, 2009; Podraza & White, 2010; R. Shultz, Silder, Malone, Braun, & Dragoo, 2015; Walsh, Boling, McGrath, Blackburn, & Padua, 2012; Wilderman, Ross, & Padua, 2009; Xie, Urabe, Ochiai, Kobayashi, & Maeda, 2013; M. K. Zebis, et al., 2011). Whilst there is value in understanding how motion patterns relate to the underlying activation of muscles, it is important to keep in mind that the proposed risk due to imbalance in activation between medial hamstring and lateral quadriceps muscles was based on a limited sample (5 injuries), one particular task (side cut), and a very small window of pre-activity observation (10 ms before touchdown) (Mette K. Zebis, et al., 2009), and that this has until now not been confirmed independently. With none of the associative studies strictly adhering to these criteria when measuring muscle activation patterns, any subsequent suggestions made around risk of ACL injury through a screening tool that is based on associations with the suggested muscle activation deficit should be interpreted with great care.

5 Limitations

This review was bound by the chosen search terms and may still not have captured all studies identifying neuromuscular risk factors associated with non-contact ACL injury. We undertook careful hand-searching to detect masquerading articles (articles that were not properly indexed) in an attempt to ensure that all relevant studies were included. Also, the neuromuscular risk factors observed in this systematic review were solely based on attributes of muscular capacity and muscular activation patterns, whereas the term ‘neuromuscular’ has in the past been used to cover a broader grouping of observations, for example including kinematic (motion) and kinetic (force) observations. Our review was based on published and accessible work only (articles that may have been relevant but were not available for access were excluded from the study), whereas we are aware of more recent unpublished prospective work. To our knowledge, none of that unpublished work seems to direct towards any convincing evidence for neuromuscular risk factors of primary ACL injury.

The sample demographics in the prospective studies varied across studies with respect to age, sex, playing level and type of sport, therefore different risk factors may apply to different subject characteristics as been observed in the ACL prognostic literature.

6 Conclusion

To date, (i) the neuromuscular markers that have been predictive of a primary non-contact ACL injury from prospective evidence are weak, (ii) post-injury case-control studies cannot be used as support for pre-injury risk and (iii) despite a substantial body of research that has studied various neuromuscular risk factors for ACL injury, current evidence is contradictory and ongoing efforts are limited largely to case-control and associative investigations. This means that the evidence-base for the development of field-based and/or large scale screening, as well as the development of prevention programmes, is currently weak. With high costs involved in prospective cohort studies, a change in approach to create stronger evidence may well be necessary.

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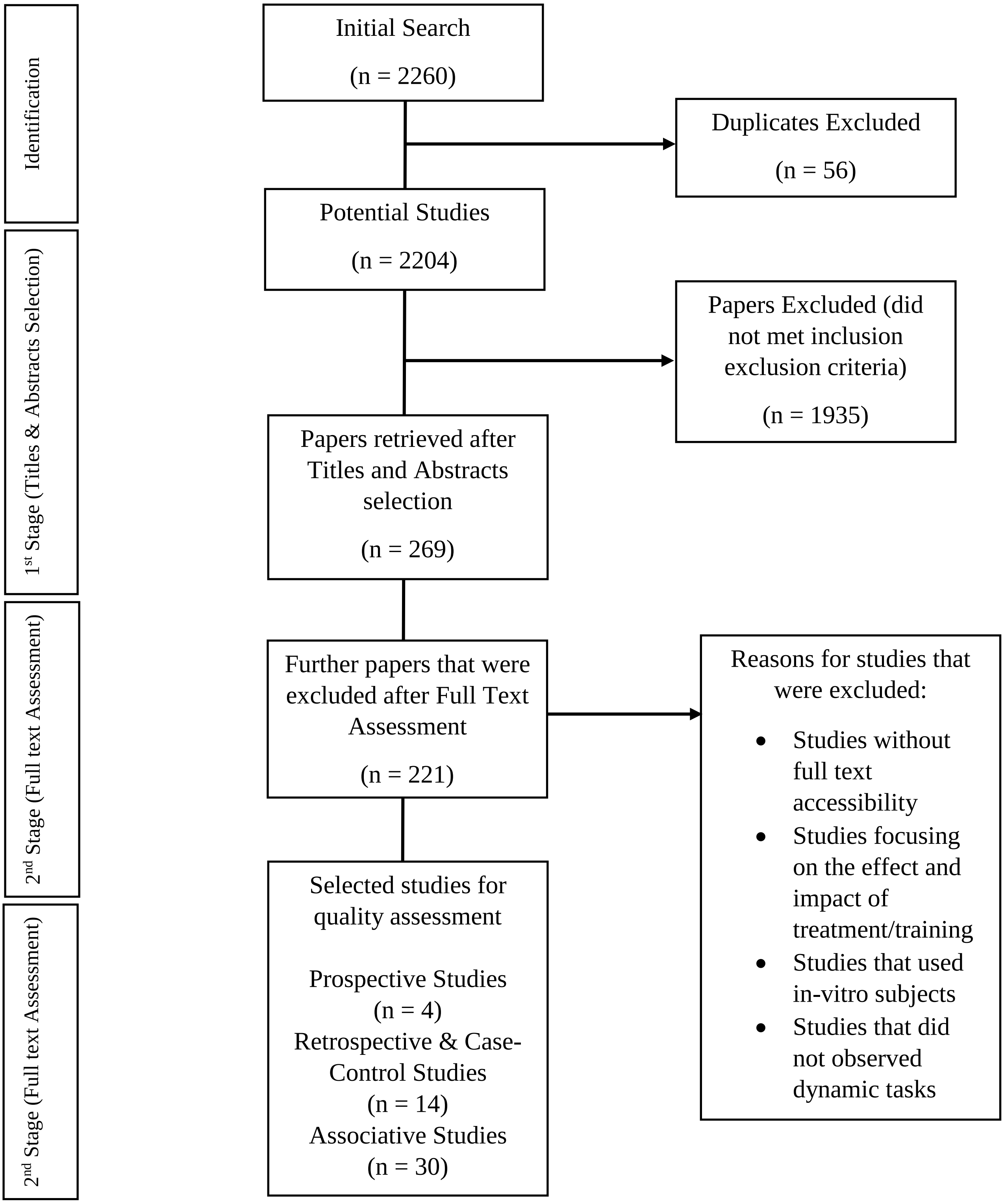

Figure 1 Flow diagram of the overall selection and exclusion process

Table 1 Search Strategy

Step	Strategy	PubMed	Scopus	Web of Science	CINAHL	SPORTDiscus
#1	Search "ACL injur*" OR "anterior cruciate ligament injur*"	9,626	4,159	22,358	4,632	2,022
#2	Search neuromuscular OR musc* OR timing OR activation OR isokinetic dynam* OR EMG OR electromyography	1,406,853	167,905	17,061,970	145,331	112,873
#3	Search #1 AND #2	1,809	383	9,703	1,165	733
#4	Search jump* OR land* OR run* OR sprint* OR side* OR cut* OR crossover OR hop* OR one-leg* OR one leg* OR single-leg OR single leg OR isokinetic OR isometric OR isotonic OR flexion OR extension OR contraction*	1,336,769	78,845	6,538,119	171,728	223,533
#5	Search #3 AND #4	1,171	130	2,658	695	463
#6	Search risk OR prevent* OR predict* OR screening OR associat* OR sensitivity OR specificity OR reproducibility OR reliability OR validity	8,354,639	11,308,360	23,799,549	1,322,386	354,238
#7	Search #5 AND #6	696	99	712	409	344

Table 2 Classification of studies for risk factor studies

Classification	Description
Prospective Cohort Studies	Study designs in which neuromuscular characteristics of one or more samples (called cohorts) are assessed and the occurrence of a non-contact ACL injury is followed prospectively to determine which initial participants' characteristics (risk factors) are associated with increased risk of incurring an ACL injury.
Case-Control Studies	Study designs that compared people who have suffered a non-contact ACL injury ('cases') with people from the same source population but without significant knee injury ('healthy controls'), to examine changes in neuromuscular characteristics after injury. Whilst these changes may reflect person-specific differences prior to injury, they also reflect post-injury adaptations due to prolonged deficiency (ACL-D) or reconstruction (ACL-R).
Associative Studies	Study designs that used previously suggested risk factors in their work to establish associations with (a combination of) other characteristics of that population sample, typically to detect surrogate observations that are easier/cheaper when screening for non-contact ACL injury risk on a large scale or in the field.

Table 3 Methodological quality of studies

	Study	Quality Score	A	B	C	D	E	F	G	H	I
Prospective Cohort	Myer et al. [10]	6/7	Y	Y	Y	N/A	N/A	N	Y	Y	Y
	Söderman et al. [11]	6/7	Y	Y	Y	N/A	N/A	Y	N	Y	Y
	Uhorchak et al. [12]	7/7	Y	Y	Y	N/A	N/A	Y	Y	Y	Y
	Zebis et al. [13]	4/7	Y	NR	Y	N/A	N/A	Y	N	N	Y
Case-control Studies	Hsiao et al. [14]	3/6	N/A	N	Y	Y	N	Y	N	N/A	N/A
	Konishi et al. [15]	2/6	N/A	N	N	Y	N	Y	N	N/A	N/A
	Swanik et al. [16]	5/6	N/A	Y	Y	Y	Y	Y	N	N/A	N/A
	Tsepis et al. [17]	4/6	N/A	Y	N	Y	Y	Y	N	N/A	N/A
	Urbach et al. [18]	5/6	N/A	Y	Y	Y	Y	Y	N	N/A	N/A
	Holsgaard-Larsen et al. [19]	3/6	N/A	Y	N	Y	N	Y	N	N/A	N/A
	Xergia et al. [20]	5/6	N/A	Y	Y	Y	Y	Y	N	N/A	N/A
	Drechsler et al. [21]	2/6	N/A	N	N	Y	N	Y	N	N/A	N/A
	Aalbersberg et al. [22]	3/6	N/A	Y	Y	N	N	Y	N	N/A	N/A
	DeMont et al. [23]	3/6	N/A	Y	N	Y	N	Y	N	N/A	N/A
	Steele et al. [24]	3/6	N/A	Y	N	N	Y	Y	N	N/A	N/A
	Swanik et al. [25]	3/6	N/A	Y	Y	Y	N	N	N	N/A	N/A
	Ortiz et al. [26]	2/6	N/A	N	N	N	Y	Y	N	N/A	N/A
	Ortiz et al. [27]	2/6	N/A	N	N	N	Y	Y	N	N/A	N/A

NA not applicable, N no or insufficient information, NR not reported, Y yes

a Was selection of the prospective cohorts drawn from the same population

b Can we be confident in the assessment of activity exposure in subjects

c Can we be confident that any injury was not present at start of the study (prospective) or had suffered from ACL injury and controls had not (case-control)

d Were the cases (those who acquired ACL injury) appropriately selected

e Were the controls appropriately selected

f Did the study match injured and uninjured subjects (prospective) or cases and controls (case-control) for all variables that are associated with the potential risk factor or did the statistical analysis adjust for these prognostic variables

g Was the nature/cause of the ACL injury well defined

h Can we be confident in the assessment of the ACL injury

i Was the follow up of cohorts adequate

Table 4 Study characteristics and outcomes (Prospective Studies)

Author	Subjects Characteristics	Monitoring/Follow up period	Neuromuscular Measurement	Injury Rate (%)	Objective	Results/Findings
(Myer, et al., 2009)	Females = 1692 19 Postpubertal and 3 pubertal (only on injured subjects) High school and collegiate soccer and basketball players	5 years	Isokinetic Knee Strength	22 non-contact ACL injuries (1.3%)	To determine the association of quadriceps and hamstrings strength to anterior cruciate ligament (ACL) injury risk in female atheltes.	Female ACL subjects had decreased hamstrings strength compared to MC (15%; 95% CI, 1 to 27%; P = 0.04). FC were not different from MC in hamstrings strength. Conversely, Female ACL subjects did not differ compared to the MC in quadriceps strength, and the FC demonstrated decreased quadriceps strength relative to MC (10%; 95% CI, 3 to 18%; P = 0.01).
(Söderman, et al., 2001)	Female = 221 146 (75 dropouts) 20.6 ± 4.7 years Soccer players from 13 teams of 2nd and 3rd Swedish division	6 months (1 out-door season)	Isokinetic Knee Strength	5 ACL injuries- did not mentioned contact or non-contact (2.3%)	To study possible risk factors for leg injuries in female soccer players.	Multivariate logistic regression showed hyperextension of the knee joint, a low postural sway, reduced H/Q ratio during concentric action, and a higher exposure to soccer to significantly increase the risk of traumatic leg injury. All five players who suffered an anterior cruciate ligament injury during the study period had a lower hamstring to quadriceps ratio during concentric action on the injured side than on their non-injured side. Three of them had a H/Q ratio lower than 50%, and the other two had a H/Q ratio of 52% and 53% on the injured side.
(Uhorchak, et al., 2003)	1198 Male = 1021 Female = 177 18.4 years (ranged from 17 to 23) Military cadets playing in competitive club and varsity sports	4 years	Isokinetic Knee Strength	24 non-contact ACL injuries (16 Males with 1.56% and 8 Females, with 4.52%)	To prospectively evaluate risk factors for noncontact anterior cruciate ligament injuries in a large population of young athletic people.	Men - Knee extensor and flexor strength ratios, including the eccentric hamstring muscles to concentric quadriceps muscles and end-range of motion ratios (P = 0.353 to 0.961) were not significantly different between the groups. Women - The strength ratios evaluating relationships between the quadriceps and hamstring muscle groups as well as strength in the end-range of motion (P = 0.424 to 0.700) were not significantly different between groups.
(Mette K. Zebis, et al., 2009)	Female = 55 24 ± 5 years Elite female handball and soccer athletes	2 years (2 subsequent season)	Muscle Activation (vastus lateralis & medialis, rectus femoris, semitendinosus and bicep femoris) during side cutting.	5 non-contact ACL injuries- did not mentioned contact or non-contact (9.0%)	To identify risk factors that have high clinical relevance in the prevention of ACL rupture.	In the present study, currently non-injured female athletes with reduced EMG pre-activity of the ST and increased EMG pre-activity of the VL during side cutting were at increased risk of future noncontact ACL rupture. The study's data indicate that a high-risk zone can be used to identify non-injured players at high risk of future ACL rupture. Consequently, individual preventive efforts can be introduced in time. However, large prospective studies are needed to confirm this finding before definitive clinical recommendations can be made.

Table 5 Study characteristics and outcomes (Retrospective and Case-Control Studies)

Author/Year	Subjects Characteristics	Methodology of Data Collection	Dependent variable – test procedure	Results/Findings
(Hsiao, et al., 2014)	12 ACL-D to ACL-R subjects (9 Males & 3 Females) 25.7 ± 9.3 years Non-active participants except for 3 subjects 15 Healthy Controls (11 Males & 4 Females) 23.0 ± 3.3 years Did not report control subjects sports participation	KIN-COM Isokinetic Dynamometer	Isometric knee strength - a series of contractions over a knee range between 10 and 90 of flexion, at 20° decrement (10°, 30°, 50°, 70°, and 90° of knee flexion) in random order. After a practice trial, 3 attempts of 5-second MVCs from quadriceps and hamstrings were allowed in each joint position with a 15-second rest in between and the highest force of contraction among 3 attempts was measured. Isokinetic knee strength - a series of contractions of the quadriceps and hamstrings over a knee joint range between 10 and 90° of flexion, in the form of 3 reciprocal concentric-concentric cycles with a 15-second rest in between. Contractions were performed in a random order at angular velocities of 50, 100, 150, 200, and 250°.s^{-1}. In each case, the highest force of contraction among 3 attempts was measured.	***Before Reconstruction*** Both quadriceps and hamstrings of the uninjured knees showed similar isometric performance to the control subjects; there was no significant difference between the uninjured and control groups at all testing knee angles in isometric MVCs. Compared with the uninjured knees, the injured knees showed significant weakness in both quadriceps and hamstrings ($p < 0.05$) across the whole range of knee angles tested. Before the reconstruction, there was no significant difference in the isokinetic force production in uninjured knees when comparing with the control group in all testing velocities for both quadriceps and hamstrings. The isokinetic MVCs from both quadriceps and hamstrings of the injured knees before reconstruction showed significant weakness at all movement velocities ($p < 0.05$) ***After Reconstruction*** There was no significant difference among the isometric MVCs produced by the uninjured knees preoperatively, 3 and 6 months after the ACL reconstruction, for both quadriceps and hamstrings. The isokinetic performance of the quadriceps and hamstrings also showed no significant change throughout the follow-up period at all testing movement velocities. Compared with the preoperative stage, isometric MVCs of the quadriceps at the 3-month follow-up was significantly weaker especially at positions that were more flexed ($p < 0.005$ at 90 and 70° of knee flexion). Unlike the quadriceps, there were no significant changes in isometric hamstrings MVCs of the injured knee at the 3 or 6-month follow-up. Quadriceps showed a more profound weakness during isokinetic contractions at the 3-month follow-up, with a diminished pattern of force: velocity relationship. There was a slight return of force and pattern of force production at 6-month follow-up when compared with that in the preoperative stage. Hamstrings showed slight though non-significant improvement in the isokinetic force production continuing through- out the 6-month follow-up period
(Konishi, et al., 2011)	22 ACLD (11 Males & 11 Women) 24.7 ± 5.3 years 10 competitive, 10 recreational and 2 occasional sports participation) 22 Healthy Controls (13 Males & 9 Women) 24.3 ± 5.7 years Various levels of sports activity were reported	Biodex 3 Isokinetic Dynamometer	Isokinetic knee strength - All subjects performed maximum concentric knee extensions ranging from 90-degree knee flexion to full extension. Isokinetic knee extension torque at preset angle velocities of 60 and 180°/s and were performed 5 times by each subject for each velocity. Patients with ACL injury were measured starting from the uninjured side and then continued on the injured side. Each trial was separated by a rest period of 2 min.	The mean torque values for knee extension of the injured and uninjured sides analyzed using a paired t-test indicated that mean torque values of the injured side at both 60 and 180°/s were significantly lower than those of the uninjured side ($p < 0.01$ at 60°/s, $p <0.01$ at 180°/s). Peak torque for the groups at 60°/s and 180°/s were, injured side (134 ± 45, 97 ± 33), uninjured side (171 ± 46, 113 ± 28) and Control group (182 ± 46, 125 ± 42) respectively.

Table 5 Continued

Author/Year	Subjects Characteristics	Methodology of Data Collection	Dependent variable – test procedure	Results/Findings
(Swanik, et al., 2004)	12 ACLD 25.2 ± 7.3 years 17 Healthy Controls 22.7 ± 4.0 years Tegner activity score with an average of 5.4 All Females	Surface EMG (Noraxon) were placed on the VM, VL, Medial Hamstrings & Lateral Hamstrings. Biodex 2 Isokinetic Dynamometer	Muscular activation - The subject stood on a 20-cm step, balanced momentarily on the test limb, and hopped to a target (x) placed 30 cm horizontally. The subject did 2 practice attempts followed by 3 test trials and the ensemble peak was used for amplitude normalization. EMG preparatory muscle activity was represented by a 150-ms period before landing and reactive muscle activity was described by a 250-ms period after ground contact. Isokinetic knee strength - a standardized knee position was assumed and testing was done at speeds of 60°/second with torque values automatically adjusted for gravity. Warm-up procedures consisted of two submaximal (50% and 75%), and one maximal repetition followed by data collection during five reciprocal maximum repetitions.	Females with anterior cruciate ligament deficiencies had significantly increased preparatory muscle activity in the lateral hamstring before landing, but no differences in reactive muscle activity during landing or reflex latency after joint perturbation. Female ACLD also had greater peak torque and torque development for knee flexion.
(Tsepis, et al., 2004)	32 ACLD (3 groups of knee function High, Intermediate and Low) 27.7 ± 7.3 years 12 Healthy Control 22.1 ± 2.9 Amateur soccer players All Males	Biodex 3 Isokinetic Dynamometer	Isokinetic knee strength - A warm up on the dynamometer consisted of five repetitions of incremental intensity from 50% to 100% of each subject's estimated maximal effort. After one minute of complete rest, 5 maximal repetitions of concentric extensions and flexions were performed at 60°/s. The testing order of the knees was randomized.	The average peak torque (APT) of the quadriceps of the injured knee was significantly lower than the APT of the intact knee in all-experimental groups (lowest F= 6.8; *P*<0.001). Regarding the hamstrings, the APT in the injured knee was significantly lower than the APT of the intact knee in the low knee function (L3) group only (F= 11.08, *P*<0.001).
(Urbach, et al., 2001)	12 ACL-D to ACL-R subjects 26.9 years (ranged from 14.9 to 43.5) 12 Healthy Controls 26.4 years (ranged from 15.3 to 42.3) Tegner activity score with an average of 7.9 only on injured subjects were reported All Males	Purpose-built Chair (Urbach et al., 2001)	Isometric knee strength - Patients were seated in an upright position on a purpose-built chair. For electrical stimulation of the muscle aluminium-plate electrodes were strapped to the quadriceps and a constant current was applied (Dantec Counterpoint K II, Skovlunde, Denmark). The subjects were instructed to extend their knee fully for 5 seconds to determine the force at maximum voluntary contraction (MVC) measured as extension torque and for maximal potentiation of the twitch response. Immediately after twitch potentiation, the subjects performed isometric contractions with 90%, 75%, 50% and 100% of their MVC force by matching the visualized torque level on the monitor with the desired torque. When the torque was stable three single stimuli were applied to the muscle.	Before operation we found a deficit of voluntary activation of the quadriceps on both the injured (mean ± SEM 74.9 ± 3.5%) and the uninjured side (74.6 ± 3.0%) in comparison with the control group (91 ± 0.9%). Two years after reconstruction of the ACL the voluntary activation of the quadriceps improved significantly on both sides but remained less than that of the controls.

Table 5 Continued

Author/Year	Subjects Characteristics	Methodology of Data Collection	Dependent variable – test procedure	Results/Findings
(Holsgaard-Larsen, et al., 2013)	23 ACL-R 27.2 ± 7.5 years 25 Healthy Controls 27.2 ± 5.4 years MET score with an average of 36 All Males	Stabilized Dynamometry (Jensen et al., 2011)	Isometric knee strength & H:Q ratio - For each muscle group, 3 trials of approximately 4-s duration were performed and the trial with highest isometric strength (joint moment) was selected for further analysis. All contractions were performed in the sitting position with 90° of knee flexion. Pauses between successive contractions were 20–30 s. To stabilize the body, subjects were secured with a waist strap positioned across the proximal part of the thigh and participants were allowed to hold on to the construction for further support.	Maximal hamstring voluntary contraction was reduced by 0.22 Nm kg^{-1} in the operated versus non-operated limb in patients, resulting in a greater (p b 0.001) asymmetry in ACL-patients (77.4%) than controls (101.3%). In contrast, no limb-to-limb asymmetry was detected for maximal quadriceps strength. An 11.1% reduction in H/Q-ratio was observed in the ACL-patients on the operated side while no difference (0.5%) between legs was observed in controls, leading to greater ($p < 0.001$) asymmetry in ACL-patients (85.7% vs. 103.4%).
(Xergia, et al., 2013)	22 ACL-R 28.8 ± 11.2 years 22 Healthy Controls 24.8 ± 9.1 years Tegner activity score with an average of 6.5 All Males	Biodex 3 Isokinetic Dynamometer	Isokinetic knee strength - The range of motion was set from 90° of flexion to full extension (0°) and was performed at 120°/s, 180°/s, and 300°/s. All tests were first performed on the intact lower extremity, followed by the involved lower extremity. For the control group, the dominant lower extremity was tested first. The test consists of 5 repetitions with a 1-minute rest period in between.	Compared to the control group, the ACLR group had greater isokinetic knee extension torque deficits at all speeds ($P<0.001$) When averaged across speeds, the ACLR group had a lower Limb Symmetry Index (LSI) compared to the control group (76.9% versus 98.2%).
(Drechsler, et al., 2006)	31 ACLR (25 Males & 6 Females) 30.0 ± 8.0 years 20 Inactive Healthy Controls - RC (10 Males & 10 Females) 24.0 ± 4.0 years 5 Active Healthy Controls - SC (2 Males & 3 Females) 28.0 ± 3.0 High performance sporting activities	Purpose Built Chair (refer to Drechsler et al., 2006) Surface EMG were placed on the RF. Digitizer DS7 current stimulator	Isometric knee strength and muscular activation - Subjects performed 3 or more MVCs (5-s duration) of quadriceps femoris, with a 2 min rest period between each MVC. The first 2 MVCs acted as trial attempts and were undertaken without stimulation. On the third occasion, the stimulator delivered 1 Hz stimuli for 5-s to the relaxed muscle. If the subject was unable to activate fully (i.e. the twitch augmented the MVC by more than 5%), MVC testing with twitch superimposition was repeated up to two additional times.	There were no significant differences in mean isometric MVC of the quadriceps femoris of uninjured limbs of the ACLR group, one month after surgery and of the RC and SC groups. In contrast the mean isometric MVC of quadriceps of the injured limbs of the ACLR group was significantly less ($P = 0.0001$) than that of the uninjured limb at both 1 and 3 months after surgery despite increases of I/U% from 1 to 3 months of 23 ± 3% and 16 ± 4% for male and female subjects, respectively.

Table 5 Continued

Author/Year	Subjects Characteristics	Methodology of Data Collection	Dependent variable – test procedure	Results/Findings
(Aalbersberg, et al., 2009)	11 ACL-D (4 Males & 7 Females) 35.0 years (ranged from 20.0 to 46.0) 15 Healthy Controls (10 Males & 5 Females) 23.0 years (ranged from 18.0 to 51.0) Did not report subjects sport participation	Custom-build seat (Aalbersberg et al., 2009) Kistler Force Plate Surface EMG were placed on the VM, RF, VL, SM, ST, BF & MG muscles.	Muscular activation - Subjects performed 3 maximum voluntary isometric contractions (MVIC) for both the quadriceps and the hamstrings at 90° of knee flexion in 3 positions (knee behind, over and in front of the ankle). Another series of 3 MVIC was performed for the GM muscle at 90° of ankle flexion.	No significance in muscle activation variables nor the moments between ACL-deficient and control subjects during knee behind the ankle position In postures with the knee in front of the ankle, ACL-deficient subjects showed, averaged over three force levels and three knee angles, a median activation level of 6.6% MVC (range 3.2–12.3) hamstrings activation, against 4.2% (range 1.8–17.4) in control subjects. In postures with the knee over the ankle hamstrings activation were 9.1% MVC (range 2.0–29.0) for ACL-deficient and 4.0% MVC (range 2.2–35.7) for control subjects. The differences between ACL-deficient and control subjects (2.4% MVC for postures with the knee in front of the ankle and 5.1% MVC for postures with the knee over the ankle) were significant.
(DeMont, et al., 1999)	6 ACL-D 12 ACL-R 6 Healthy Controls 29.4 ± 10.4 years (all subjects) Tegner activity score with an average of 6.8 ± 1.5 (All Females)	Integrated EMG on the VMO, VL, MH, LH, MG and LG.	Muscular activation- Subjects performed 4 dynamic activities for IEMG assessment of downhill walking at 0.92 m/s, running at 2.08 m/s, 10 step hopping task and jump-landing task from a 20.3 cm step.	Side-side differences. Landing – ACLD shows side-to-side differences between the LG (involved 36.4% ±19.7% and uninvolved 60.1% ±23.6%, P < 0.05).], Running – ACLD shows side differences in the VMO (involved 11.4% ±3.8%, uninvolved 7.2% ±3.1%, P < 0.05) and VL (involved 13.3% ±2.7%, uninvolved 8.9% ±1.9%, P < 0.05) and Downhill Walking – ACL shows side differences between the VMO (involved 9.2% ±4.2%, uninvolved 19.5% ±7.3%, P < 0.05). Mean amplitude of IEMG. Running – ACLD differences between the VMO (involved 78.2% ±23.2%, uninvolved 45.8% ±18.9%, P < 0.05), Downhill Walking – ACLD shows differences between the LG (involved 79.7% ±30.3% and uninvolved 122.3% ±34.9%, P < 0.05) and Hopping – ACLR shows a side-to-side differences on the LG Landing – ACLD shows differences between the LG (involved 74.7% ±40.0% and uninvolved 52.8% ±14.3%, P < 0.05). ANOVA revealed group differences on the involved VL during hop and the VMO when walking downhill. ACLD had significantly higher IEMG area than controls in VL (ACLD 12.9% ±5.8% and Controls 7.1% ±3.9%, P < 0.05) but lower in VMO (ACLD 9.2% ±4.2% and Controls 15.7% ±3.6%, P < 0.05). The side-to-side differences of the ACLD and ACLR groups, as well as the group differences between ACL-D and control, suggest that different muscle activation strategies are used by females when performing different dynamic activities. Therefore, muscle unit differentiation may be the cause of our results. These changes appear to be reversed through surgery or the associated postoperative rehabilitation.
(Steele & Brown, 1999)	11 ACL-D (8 Males & 3 Females) 31.6 ± 7.6 years 11 Healthy Controls (8 Males & 3 Females) 30.4 ± 8.3 years Did not report subjects sport participation	Surface EMG (Noraxon) were placed on the VM, RF, VL, SM, BF & MG muscles.	Muscular activation - Subjects performed 5 trials of a dynamic and abrupt deceleration task in which they accelerated forward for three steps to receive a chest level pass, landed on the test limb in single-limb stance, and stabilized their position without raising the landing foot.	Peak BF & SM activity displayed by the control subjects' involved limbs occurred earlier than that for their non-involved limbs while the ACLD subjects displayed the reverse trend.

Table 5 Continued

Author/Year	Subjects Characteristics	Methodology of Data Collection	Dependent variable – test procedure	Results/Findings
(Swanik, et al., 1999)	6 ACL-D 12 ACL-R 6 Healthy Controls 29.4 ± 10.4 years (all subjects) Tegner activity score with an average of 6.8 ± 1.5 (All Females)	Intergrated EMG (Noraxon) were placed on the VM, VL, Medial Hamstrings & Lateral Hamstrings.	Muscular activation- Subjects performed 4 dynamic activities for IEMG assessment of downhill walking at 0.92 m/s, running at 2.08 m/s, 10 step hopping task and jump-landing task from a 20.3 cm step.	During running, the ACLD group demonstrated significantly greater area and peak IEMG activity in the MH in comparison with the ACLR group (30.3 ± 5.7, P<0.05, CI =19.1 to 41.5 and 365.4 ± 123.3, P<0.05, CI =123.7 to 607.1 respectively) and greater peak activity in the LH when compared with the control group (379.5 ± 105.5, P<0.05, CI =172.7 to 586.3). The ACLD group also demonstrated greater peak activity in the VM (428.2 ± 110.2, P<0.05, CI =212.2 to 644.2) and less area of IEMG activity in the LH than the control group (30.1 ± 6.9, P<0.05, CI =16.57 to 43.6) during running. During landing, the ACLD group demonstrated significantly less area of IEMG activity in the VL when compared with the control group (109.7 ± 50.3, P<0.05, CI =11.1 to 208.3)
(Ortiz, et al., 2008)	13 ACL-R 25.4 ± 3.1 years 15 Healthy Controls 24.6 ± 2.6 years Recreational fitness activities (All Females)	Surface EMG were placed on GMax, RF, LH and MH (Cram et al., 1998).	Muscular activation - 5 trials of a 40-cm single-legged drop jump and a 20-cm up down hop task. These tasks were randomly ordered. Each participant was allowed to rest as much as she wanted to prevent fatigue. No participant was allowed to rest less than 1 minute between trials.	Multivariate analysis for EMG variables showed statistically significant differences between groups ($F_{4,23}$ = 6.47, P = .001; ES = 0.53, β = 0.97) during drop jumps. Follow-up analyses of variance on each EMG variable showed significantly greater co-contraction ratios ($F_{1,26}$ = 8.83, P = .006; ES = 0.25, β = 0.82), greater gluteus maximus full-wave rectified normalized EMG (F1,26 = 10.64, P = .003; ES = 0.29, β = 0.88), and greater rectus femoris full-wave rectified normalized EMG (F1,26 = 14.73, P = .001; ES = 0.36, β = 0.96) in the group with ACL reconstruction .
(Ortiz, et al., 2011)	14 ACL-R 25.4 ± 3.1 years 15 Healthy Controls 24.6 ± 2.6 years Recreational fitness activities (All Females)	Surface EMG were placed on GMax, RF, LH and MH (Cram et al., 1998).	Muscular activation - The participant stood on the force plate of her preference and started jumping single-legged from one force plate to another for 10 consecutive times across the marked lines. One jump was defined as jumping away and back to the same force plate. A side-hopping maneuver was defined as the direction of movement to the opposite side of the weight- bearing leg whereas a crossover hop was defined as the direction of movement toward the same side of the weight-bearing leg	In neither group did group × maneuver interaction ($F_{4,22}$ = 1.05; *P* = 0.402; effect size: 0.16; power: 0.28), group main effect ($F_{4,22}$ = 2.05; *P* = 0.12; effect size: 0.27; power: 0.52), or maneuver main effect ($F_{4,22}$ = 2.20; *P* = 0.10; effect size: 0.29; power: 0.55) in the gluteus, rectus femoris, and hamstrings muscles or the co-contraction ratios reach statistical significance. Electromyographic data revealed no statistically significantly differences between the groups.

VL vastus lateralis ***VM*** vastus medialis ***VMO*** vastus medialis obliquus ***RF*** rectus femoris ***LH*** lateral hamstring ***MH*** medial hamstring ***BF*** biceps femoris ***ST*** semitendinosus ***LG*** lateral gastrocnemius ***MG*** medial gastrocnemius ***Gmax*** gluteus maximus ***ACLD*** anterior cruciate ligament deficiency ***ACLR*** anterior cruciate ligament reconstructed ***MVC*** maximum voluntary contraction ***MVIC*** maximum voluntary isometric contraction ***RC*** inactive controls ***SC*** active controls ***H/Q*** hamstring/quadriceps ***EMG*** electromyography ***IEMG*** integrated electromyography

Table 6 Associative studies

Neuromuscular Risk Factor	Papers	Variables Observed
Muscular Capacity	(Hiemstra, et al., 2007; Mattacola, et al., 2002; Roberts, et al., 2007; Wilkerson, et al., 2004; M. K. Zebis, et al., 2011)	Isokinetic and isometric peak torques
	(Ahmad, et al., 2006; Bee-Oh, et al., 2009; Bowerman, et al., 2006; Grygorowicz, et al., 2010; Holcomb, et al., 2007; Hosokawa, et al., 2011).	H:Q ratio
Muscular Activation	(Begalle, et al., 2012; Elias, et al., 2015; Nagano, et al., 2011; R. Shultz, et al., 2015; Wilderman, et al., 2009)	Intervention to improve on quadriceps and hamstring activation or co-activation
	(Bencke & Zebis, 2011; Hannah, et al., 2015; McLean, et al., 2010)	Pre-activation of the lower limbs in different tasks
	(Dai, et al., 2012)	Detraining effects on lower extremity EMG
	(Greska, 2012)	Lower extremity neuromechanics relative to leg dominance during an unanticipated sidestep cutting task, with differing states of fatigue and training
	(Hughes & Daily, 2015; Kipp, et al., 2014; Landry, et al., 2009; Lategan, 2012; Liebensteiner, et al., 2012; Palmieri-Smith, et al., 2009)	Differences in muscle synergy strategy between gender
	(Podraza & White, 2010; Walsh, et al., 2012)	Relationship between muscle co-contraction and knee flexion angle
	(Xie, et al., 2013)	Phases of sidestep cutting that may place athletes at a greater risk for ACL injuries
	(M. K. Zebis, et al., 2011).	Muscle fatigue on neuromuscular strategy during a functional side cutting movement