Lower limb strength and biomechanics after anterior cruciate ligament reconstruction

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STATEMENT OF SOURCES

This thesis contains no material that has been extracted in whole or in part from a thesis that I have submitted towards the award of any other degree or diploma in any other tertiary institution. No other person's work has been used without due acknowledgment in the main text of the thesis. All research procedures reported in the thesis received the approval of the relevant Ethics/Safety Committees.

[redacted]

Argell Joseph Tolentino San Jose

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Beyond Medyo. Para sa Diyos, sa pamilya, at sa bayan. Puso!

LIST OF PUBLICATIONS

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1. **San Jose AJ,** Maniar N, Timmins RG, Beerworth K, Hampel C, Tyson N, Williams MD, Opar DA. Explosive hamstrings strength asymmetry persists despite maximal hamstring strength recovery following anterior cruciate ligament reconstruction using hamstring tendon autografts. Knee Surg Sports Traumatol Arthrosc. 2022 Aug 23. doi: 10.1007/s00167-022-07096-y. Epub ahead of print. PMID: 35999280.

2. **San Jose AJ,** Maniar N, Whiteley R, Opar DA, Timmins, RG, Kotsifaki A. Lower patellofemoral joint contact force during side-step cutting following return to sport clearance after anterior cruciate ligament reconstruction. American Journal of Sports Medicine. OnlineFirst. May 15, 2023. https://doi.org/10.1177/03635465231166104

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3. **San Jose AJ,** Kotsifaki A, Whiteley R, Opar DA, Timmins, RG, Maniar N. Lower limb muscle contributions to sidestep cutting tasks at return to sport after anterior cruciate ligament reconstruction. British Journal of Sports Medicine. Under preparation.

LIST OF CONFERENCE PRESENTATIONS

1. **San Jose AJ,** Maniar N, Timmins RG, Beerworth K, Hampel C, Tyson N, Williams MD, Opar DA. Explosive hamstrings strength asymmetry persists despite maximal. hamstring strength recovery following anterior cruciate ligament reconstruction using hamstring tendon autografts. Sports Medicine Australia – Gold Coast, Australia. November 2022.

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LIST OF ABBREVIATIONS AND NOMENCLATURE

ACL – Anterior cruciate ligament

ACLR – Anterior cruciate ligament reconstruction

ACL-RSI – Anterior cruciate ligament return to sport index

BW – Bodyweight

BW.s – Bodyweight seconds of impulse

EMG – Electromyography

F_Q – Quadriceps force

F_P – Patella tendon force

GRF – Ground reaction force

HT – Hamstring tendon

H:Q – Hamstrings-to-quadriceps

I^2 – Percentage of variation across studies due to heterogeneity rather than chance

kg – kilogram of body mass

LSI – Limb symmetry index

LSD – Limb strength deficit

m – metres

ms - milliseconds

MD – Mean difference

MVC – Maximum voluntary contraction

N – Newtons of force

Nm – Newton metres of torque

Nm/kg – Newton metres of torque normalised to body mass

PFJ – Patellofemoral joint

PT – Patellar tendon

REML – Restricted maximum likelihood model

RFD – Rate of force development

RTD – Rate of torque development

RTS – Return to sport

SD – standard deviation

95% CI – 95% confidence interval

THESIS ABSTRACT

Rupture of the anterior cruciate ligament (ACL) is one of the most significant injuries to the knee joint, with the frequency of injury increasing over the last 10 years. Of these injuries, the increase in incidence among young female athletes (<18 years) has been especially significant. Direct and indirect management of ACL injuries range from $100 million in countries like Australia, to as much as $2 billion in the United States. The increasing rates of ALC injury and significant associated costs places significant pressure on the healthcare system.

The high economic cost of ACL injuries is typically associated with ACL reconstruction (ACLR) and the subsequent rehabilitation period. Restoration of lower limb muscle strength, function, and coordination, as well as a gradual return to activities like running, jumping, landing, and agility tasks are all components of a structured rehabilitation program and criteria for return to sports (RTS). Following the completion of rehabilitation, up to 80% of people are able to RTS of some level. Despite the high rate of RTS, a significant number of ACLR individuals will report poor subjective knee function (e.g., knee pain during activity), be subjected to a high risk of reinjury and be prone to early onset of knee osteoarthritis. There is evidence that these poor outcomes are worse in females than in males.

Lower limb strength (e.g., hamstrings and quadriceps) and biomechanical asymmetries are common after ACLR. These asymmetries have been associated with the poor outcomes previously mentioned. As a result, restoration of maximal hamstrings and quadriceps strength symmetry is a focus of rehabilitation and criteria for RTS clearance following ACLR. However, there is evidence that explosive quadriceps strength does not recover at the same rate as maximal quadriceps strength during the first year following ACLR. Whether this is also true in the hamstrings is still unknown and previous studies have only explored concurrent recovery of explosive and maximal strength in males.

Given their function in providing dynamic stability and loading on the knee joint, the hamstrings and quadriceps have received much attention during assessment, rehabilitation, and criteria for RTS following ACLR. However, dynamic tasks (e.g., sidestep cutting) commonly performed in team sports require complex activity and coordination of the different lower limb muscles. This has been previously investigated in healthy individuals but to date, it is still unknown how ACLR affects the function of the different lower limb muscles during sidestep cutting. Additionally, reductions in knee joint loading (e.g., contact force) have been reported from 3-9 months and up to 2 years following ACLR. Quadriceps strength deficits have been proposed to be a major factor influencing the reduced knee joint contact forces after ACLR. However, it is still unknown whether knee joint contact forces are reduced after the restoration of quadriceps strength at RTS.

The purpose of this doctoral thesis was two-part. Firstly, to investigate restoration of both explosive and maximal hamstrings and quadriceps strength during early and late rehabilitation following ACLR in males and females. Second, to explore lower limb biomechanics following the restoration of strength following rehabilitation. The knowledge derived from this program of research is aimed at identifying factors that are modifiable during the rehabilitation period after ACLR, information that should help to guide future clinical and research effort.

The first study of this program of research (Chapter 2) was a systematic review and meta-analysis that explored the time-course of hamstrings and quadriceps strength asymmetries during the preoperative period up to six and 12 months following ACLR between males and females. Initial database search retrieved 6,046 articles. After screening for eligibility, 31 studies were included in the systematic review while 13 articles had enough data for meta-analysis. The findings showed that limb symmetry in maximal hamstrings and quadriceps strength are the most commonly used measure of strength following ACLR. Strength asymmetries in the hamstrings and quadriceps were present from preoperative to six and 12 months after ACLR. Despite the proposed importance of explosive strength following ACLR, studies looking at its time-course of recovery are limited. Furthermore, while sex differences in patient outcomes have been previously reported, majority of the data collected were either not stratified and/or dominated by male participants (males = 62%; females = 30%, sex not reported = 8%).

To address gaps in the literature identified in Chapter 2, an observational cohort study was conducted for the second study of this thesis (Chapter 4). This study investigated the maximal and explosive strength recovery of the quadriceps and hamstrings following ACLR. In this study, participants were assessed during the early (3-6 months) and late (7-12 months) stage of rehabilitation following an ACLR with hamstring tendon (HT) autografts. There was a significant influence of time after ACLR on the limb-symmetry index (LSI) for maximal hamstrings (Early: 86 ± 14; Late 92 ± 13; $p = 0.005$) and quadriceps (Early, 73 ± 15; Late 91 ± 12; $p < 0.001$) strength. Additionally, explosive quadriceps strength LSI showed significant improvements over time (Early: 82 ± 30; Late: 92 ± 25; $p = 0.03$). However, despite the recovery of maximal hamstring strength there were still significant deficits in explosive hamstring measures later in rehabilitation (Early: 86 ± 46; Late: 83 ± 22; $p = 0.75$). Additionally, Chapter 4 also investigated whether there were differences in strength recovery between males and females following ACLR. While no differences were found in the rate of explosive and maximal strength recovery between sexes, females had greater quadriceps strength asymmetries (maximal and explosive) compared to males across ACLR rehabilitation.

The ability to perform dynamic tasks (e.g., sidestep cutting) is one of the major determinants of an ACLR individual's readiness to RTS. Sidestep cutting tasks, in particular, are common in change-of-direction sports. It is also during these tasks that ACL injuries frequently occur.

Previous studies found kinematic and kinetic impairments during sidestep cutting performance in ACLR individuals. However, these studies have been joint level analysis of lower limb biomechanics. Given the complex coordination of the different lower limb muscles during the performance of a sidestep cut, the third study of this thesis (Chapter 5) explored the lower limb muscle contributions to ground reaction forces during vertical support, deceleration, propulsion, and redirection of forces during a sidestep cut in ACLR limbs (who had a quadriceps strength LSI $\geq$ 90%) and compared them to healthy limbs. Chapter 5 found that muscle function during a sidestep cut is significantly different in the ACLR limb when compared to the contralateral and control limbs. There were less contributions to vertical support (contralateral mean difference = -0.040 BW.s, 95%CI = -0.049 to -0.031, $p < 0.001$; control mean difference = -0.042 BW.s, 95%CI = -0.061 to -0.022, $p < 0.001$), braking (contralateral mean difference = 0.020 BW.s, 95%CI = 0.014 to 0.027, $p < 0.001$; control mean difference = 0.029 BW.s, 95%CI = 0.017 to 0.041), and medial redirection (contralateral mean difference = -0.006 BW.s, 95%CI = -0.01 to -0.001, $p = 0.011$) GRFs from the quadriceps of the ACLR limb when compared to the contralateral uninjured limb. Alterations in gluteus maximus, gastrocnemius, soleus, hamstrings, and dorsiflexors muscle function were also found when comparing the ACLR and contralateral uninjured limbs. Despite resolution of quadriceps strength asymmetry following ACLR rehabilitation, the quadriceps' role in contributing forces for the execution of a sidestep cut is significantly impaired. Furthermore, muscle contributions from other major lower limb muscles are also altered following RTS.

Given the alterations in the ability of the quadriceps to modulate GRFs despite restoration of isokinetic strength symmetry, the final study of this thesis (Chapter 6) was conducted with the aims of investigating patellofemoral (PFJ) contact forces in the ACLR limb when compared to healthy limbs at time of RTS. Chapter 6 demonstrated that ACLR limbs have lower PFJ contact forces compared to the contralateral (mean difference = 5.89 BW, 95%CI = 4.7 to 7.1, p <

0.001) and control limbs (mean difference = 4.44 BW, SE = 2.1 to 6.8, $p = < 0.001$). Additionally, the ACLR limb possessed smaller knee flexion angles (contralateral mean difference = 4.88°, 95%CI = 3.0 to 6.7, $p < 0.001$; control mean difference = 6.01°, 95%CI = 2.0 to 10.0, $p < 0.002$) as well as lower knee extension moment and quadriceps force (contralateral mean difference = 4.14 BW, 95%CI = 3.4 to 4.9, $p < 0.001$; control mean difference = 2.83 BW, 95%CI = 1.4 to 4.3, $p < 0.001$). These findings suggest that PFJ loading can still be impaired despite the restoration of quadriceps strength symmetry which could have potential implications for PFJ osteoarthritis.

In conclusion, this program of research showed that explosive and maximal quadriceps strength asymmetries resolve during ACLR rehabilitation. Hamstrings maximal strength also restores during the same time; however, explosive hamstrings strength did not. While it was also found that sex does not influence strength recovery, females did have larger maximal and explosive quadriceps strength asymmetries compared to males following ACLR. Finally, impairments in lower limb biomechanics (less quadriceps muscle contributions to vertical support, deceleration, and medial redirection, lower PFJ contact force and quadriceps force, and smaller knee flexion angle) are still present in the ACLR limb compared to the healthy limbs during the performance of a sidestep cut. These deficits still exist, despite the recovery of maximal quadriceps strength following ACLR and provides evidence for the assessment of lower limb muscle function during dynamic movements as part of the RTS criteria.

1 INTRODUCTION AND OVERVIEW

Anterior cruciate ligament (ACL) rupture is a burdensome injury commonly seen during sports that require jumping, cutting, and pivoting [1, 2]. The incidence of ACL injuries has increased over the last two decades with prevalence highest in young, active male individuals [3, 4]. However, when adjusted for exposure, females have been reported to be at higher relative risk of ACL injuries compared to males [1, 3, 5]. Management of ACL injuries typically involves ACL reconstruction (ACLR) followed by a rehabilitation period of 12 months or longer. Annual medical and health care costs related to ACL injuries are estimated at more than A$100 million in Australia [4] and up to $1 billion in America [6], imposing a significant burden to the health care system.

Following rehabilitation, ~80% of individuals are able to return to some form of physical activity after ACLR [7]. However, only ~65% of people return to their previous level of activity and only half return to competitive sports [7]. Of those who return to sport (RTS), ~20% of ACLR individuals [8-15] will suffer from a second ACL injury. A quarter of these reinjuries is seen in young athletes (<18 years old) [10, 11, 14] with females reported to have a higher relative risk of reinjury compared to males [10, 16]. Beyond the high risk of recurrent ACL injuries, long-term complications related to degeneration of the knee joint is common [17, 18]. The ACLR limb is up to six times more likely to develop knee osteoarthritis compared to the contralateral/uninjured limb [19]. The onset of knee osteoarthritis is reported as early as 5 years after ACLR [20] update from PFJ paper and is associated with poor outcomes related to pain, function, and overall quality of life [21, 22]. Given the high rates of ACLR in the younger population (~18 years old) [3, 4], this could lead to what has been termed “young patients with old knees” – individuals who have knee osteoarthritis as early as their 20s [17]

Rehabilitation and clearance to RTS is typically guided by a set of criteria utilised to determine recovery following ACLR [23-25]. Time following ACLR has been the most common milestone for RTS [25]. Over the last decade, objective measures such as symmetry in lower limb strength (e.g., isokinetic hamstrings and quadriceps strength) and functional performance (e.g., hop test for distance) has changed the way RTS decision following ACLR is performed [23, 25]. There is a substantial evidence base showing hamstrings and/or quadriceps asymmetries are associated with poor patient reported outcomes related to knee pain [26], function [27-31], and return to activity [32]. These strength deficits have also been associated with the risk of knee reinjury [33, 34] as well as correlated with the early onset of knee osteoarthritis [35, 36]. As such, rehabilitation programs and RTS criteria has focused on restoration of hamstrings and quadriceps strength symmetry after ACLR [23, 37, 38].

Despite the focus on strength recovery, lower limb strength deficits are common following ACLR [39, 40]. Quadriceps strength deficits in patients with PT grafts are often noted, whereas hamstring weakness in those with HT grafts is more common [41]. Such strength deficits have been shown to persist for more than five years following ACLR [39, 40, 42-44] and are problematic as hamstrings and quadriceps function is essential after ACLR given their role in providing knee joint stability and loading during dynamic tasks [45-48]. There is some evidence that hamstrings and quadriceps strength deficits are greater in females compared to males following ACLR [49]. Given that females have poorer outcomes following ACLR with knee function, return to sport, and risk of reinjury, these strength deficits are important to address [REF]. Despite the influence of sex on key outcomes following ACLR, it is still unclear how strength recovery during rehabilitation differs between males and females.

Isokinetic hamstrings and quadriceps peak torque during maximal strength assessments has been the objective gold standard strength measure following ACLR for decades [50]. However, there has been growing evidence regarding the importance of explosive (rate of torque development (RTD)) strength as a measure of recovery in ACLR individuals [51, 52]. Given that most dynamic tasks (e.g., jumping/landing, change of direction) require the rapid production of force [53, 54], the measurement of explosive strength characteristics is important. Explosive (i.e. rate of force/torque development) hamstrings and/or quadriceps strength asymmetries has been reported from early (<6 months) [27, 51, 52, 55, 56] to late phase (>7-12 months) [51, 52, 55, 57, 58] of rehabilitation after ACLR. These asymmetries have been associated with poor knee function [27, 59] and impairment in lower limb kinetics [55, 57, 60]. However, unlike maximal strength, the time-course of explosive strength recovery is still not well understood. There is some evidence that shows the persistence of explosive quadriceps strength asymmetry despite restoration of maximal strength symmetry in male athletes [52, 56]. Whether this discrepancy in recovery is also true for explosive and maximal hamstrings strength is still unknown. Given the common use of hamstring tendon autografts [61] and the associated graft-related morbidities [40, 41], a better understanding of how explosive hamstrings and quadriceps strength recovers following ACLR is needed. The knowledge derived from this can help in the development of targeted rehabilitation programs while also informing patient readiness to RTS.

Rehabilitation programs are commonly designed to not only address hamstrings and quadriceps strength deficits but to restore the overall lower limb function of an individual after ACLR [23, 62-64]. This includes the ability to perform gait through to more demanding tasks such as running, jumping/landing, and cutting [62, 64, 65]. Hamstrings and quadriceps function are invaluable given their importance in modulating forces (e.g., deceleration and propulsion) during the execution of these tasks [46, 66-69]. However, lower limb function in general requires the optimal activity and contribution of other lower limb muscles as well [70]. For example, the gluteus maximus and plantar flexors are major contributors to support and propulsion forces during the abovementioned tasks in healthy individuals [46, 66-69]. It is still unknown how ACLR affects the function of different lower limb muscles. Identifying how the lower limb muscles function during dynamic activities following ACLR may help guide exercise selection during rehabilitation which could potentially improve short-term and long-term outcomes.

The risk of knee osteoarthritis following ACLR may be one of its most burdensome complications [17-20, 71, 72]. Quadriceps strength deficits and impairments in lower limb biomechanics have received much attention as factors that contribute to this risk [35, 73-76]. Asymmetries in lower limb kinematics (e.g., knee flexion, knee valgus, tibial rotation) and kinetics (e.g., vertical ground reaction forces, knee extension moment) are well documented during walking [73, 77, 78], running [79, 80], hopping, jumping/landing [81-85], and sidestep cutting [86-89] after ACLR. Emerging evidence has also shown lower knee joint (e.g., patellofemoral joint (PFJ)) contact forces during gait, running, and hopping in ACLR limbs compared to healthy knees [75, 83, 90]. Individuals who had lower PFJ contact forces in the ACLR limb were found to be more likely to develop PFJ osteoarthritis five years after surgery [76]. The presence of quadriceps strength deficits is a common explanation for the reduction in knee joint contact forces during the early and long-term period following ACLR [80, 85, 91, 92]. However, it is still unknown whether knee joint loading will normalize once quadriceps strength is restored. To date, no study has investigated if the restoration of lower limb strength also leads to a restoration of PFJ contact forces after ACLR.

1.1 THESIS OVERVIEW

The overall aims of this program of research are to 1) explore maximal and explosive hamstrings and quadriceps strength recovery during the rehabilitation period following ACLR in males and females and 2) investigate lower limb biomechanics (e.g., muscle function and knee joint loading) during dynamic tasks (e.g., sidestep cutting) following ACLR in males and females. While we were able to address the first aim, we were not able to fully explore Aim 2 due to the restrictions to participant recruitment and testing during the COVID-19 pandemic. As this became unfeasible due to the pandemic, we had to modify our aims with the data that was available. Hence, modifications were made where we explored lower limb biomechanics following restoration of quadriceps strength and subsequent clearance to RTS in males only.

Given this, we modified the overall aims of this program of research to 1) identify recovery of maximal and explosive hamstrings and quadriceps strength during the rehabilitation period following ACLR in males and females, 2) determine lower limb muscle contributions to sidestep cutting tasks following ACLR and 3) explore PFJ contact forces during the stance phase of a sidestep cut in ACLR limbs and compare these to control limbs. A systematic review and meta-analysis (Chapter 2) was conducted to synthesise the current literature on hamstrings and quadriceps strength asymmetry in males and females following ACLR. Based on the gaps identified in Chapter 2, an observational cohort study aimed at exploring maximal and explosive strength recovery of the hamstrings and quadriceps during early and late rehabilitation following ACLR was conducted (Chapter 4). Additionally, Chapter 4 also investigates the influence of sex on the recovery of maximal and explosive strength. The two subsequent studies of this thesis (Chapters 5 and 6) focused on lower limb biomechanics using musculoskeletal modelling techniques. Chapter 5 investigated the effect of ACLR on lower limb muscle contributions to support, deceleration/propulsion, and redirection forces during the execution of a sidestep cutting tasks after clearance to RTS. Finally, Chapter 6 focused on investigating PFJ contact forces during a sidestep cutting task following restoration of quadriceps strength asymmetry and clearance to RTS.

2 AGE AND SEX DIFFERENCES IN KNEE EXTENSOR AND FLEXOR STRENGTH RECOVERY AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTIVE SURGERY: A SYSTEMATIC REVIEW AND META-ANALYSIS

2.1 PUBLICATION STATEMENT

This chapter is comprised of the following paper, which has been submitted to several journals but is currently not under review.

San Jose AJ , Maniar N, Timmins RG , Pitcher C, Hickey JT, Opar DA

2.2 ABSTRACT

Knee extensor and flexor strength asymmetry is commonly reported following anterior cruciate ligament reconstruction (ACLR). Persistence of strength asymmetries even after rehabilitation and clearance to return-to-sport (RTS) after ACLR is associated with poor patient-reported outcomes, higher risks of revision ACLR, and early onset of knee osteoarthritis. Sex differences in knee extensor and flexor strength has been reported in uninjured individuals, however this is still inconclusive in individuals who had ACLR. The purpose of this review is to synthesise the current evidence on the time-course of knee extensor and flexor strength asymmetry 12-months following ACLR and to determine if differences exist based on age and sex. A systematic literature search was performed from inception to November 2018. Studies included were those with participants who had ACLR using primarily ipsilateral hamstring tendon (HT) and/or patellar tendon (PT) autografts, who had knee extensor and flexor strength of the injured and uninjured limb assessed preoperatively, and between 6 months and/or 12 months after surgery using isokinetic dynamometry. Meta-analysis of absolute mean differences (MD) and limb symmetry index (LSI) with 95% CI was performed for the knee extensors and flexors across different timepoints. Meta-regression analysis was performed to evaluate the effect of age and/or sex on strength outcomes (MD or LSI) at each time point evaluated. Thirty-one studies were included in the review. Age was not stratified for in any of the identified studies while only three studies directly examined the differences between males and females. Meta-analysis of strength, regardless of age and/or sex showed knee extensor and flexor strength asymmetry were often present preoperatively and at six months after ACLR, and inconsistently at 12 months. Whilst a meta-regression indicated no consistent differences in strength asymmetry based on age or sex, the current evidence mostly focuses on males between 25-30 years old. Knee extensor and flexor strength asymmetry is present

preoperatively and persists at six and 12 months after ACLR. Associations between age and sex and knee extensor and flexor strength asymmetry during rehabilitation is inconclusive.

2.3 INTRODUCTION

Anterior cruciate ligament (ACL) injury is commonly seen in sports that require jumping, cutting, and pivoting [1, 2]. The injury is increasingly seen in younger athletes (14-24 years) [3, 4] with females at a higher risk compared to males [3]. Direct and indirect financial costs of ACL reconstruction (ACLR) and rehabilitation [4, 6] as well as the early development of knee osteoarthritis (OA) makes ACL injuries burdensome to both the injured individual and the wider community [12, 17, 93]. Because of this, much work has been done to explain the occurrence of ACL injuries [45, 94-97] and subsequently to develop programs to reduce the likelihood of this injury. Furthermore, research has also focused on trying to identify the optimal return-to-sport (RTS) criteria after ACLR [24, 25, 33, 34, 98, 99].

About a third of young athletes will experience a recurrent ACL injury within 1-2 years after RTS [11, 14, 15]; with females up to six times more likely to have a recurrent ACL injury than males [16]. Of concern, having a second ACLR doubles the risk of developing knee OA compared to those with only one ACLR [100]. Given females are reported to have worse knee OA outcomes compared to males after ACLR [101] and that these complications are associated with poorer long-term quality of life [102], it is imperative to identify factors that may compound these outcomes for younger female athletes.

Lower limb muscle strength recovery, commonly measured using isokinetic dynamometry, is considered critical in meeting clinical discharge criteria before RTS after ACLR [34, 98]. Strength recovery is typically assessed and reported as a limb symmetry index (LSI), which is a measure of strength symmetry between the injured and uninjured limb [50]. Regaining strength symmetry appears to be crucial after ACLR with a recent review reporting a 3% reduction in re-injury rates for every percentage point increase in LSI of the knee extensors [33]. Furthermore, deficits in strength seem to also play a role in the long-term outcomes, with persistent knee extensor weakness associated with the accelerated onset of knee OA in an ACLR population [103].

Despite the evidence showing the importance of strength recovery after ACLR, a recent study reported that more than a third of young athletes did not meet the recommended knee extensor and flexor LSI strength criteria (≥90%) despite being cleared for RTS [32]. While previous studies have shown differences in muscle strength between healthy males and females [104-106] of different ages [105, 107], evidence looking at the time-course of strength asymmetry after ACLR between different age and sex groups is not often a focus in the literature. Therefore, the aim of this review is to synthesise and analyse current evidence on the time-course of knee extensor and flexor strength asymmetry for the first 12 months after ACLR to determine if differences exist in strength asymmetry based on age and sex. Exploring any potential differences in strength asymmetry between age and sex groups may provide information to tailor rehabilitation and potentially improve outcomes in different ACLR cohorts (i.e. young females vs older males).

2.4 MATERIALS AND METHODS

2.4.1 Search strategy

A systematic literature search was performed on MEDLINE, SPORTDiscus, CINAHL, and Web of Science from inception to November 2018. A combination of keywords (Table 2.1) was chosen to identify relevant articles aligned with the research aims. References were imported into EndNote X8 (Thomson Reuters, New York, USA) with initial review of titles and abstracts conducted after duplicate titles were deleted. Full texts were then collated for all articles that provisionally met the inclusion criteria. A reference list search was also performed to ensure all relevant articles were included. The systematic review protocol was not pre-registered.

Table 2.1. Keywords for search strategy

Definition of injury	Surgical management	Strength assessment	Muscle group
Anterior cruciate ligament *injury	*ACL reconstruction	Isokinetic dynamometer	*Knee joint#
ACL Injury	Reconstruct#	*Muscle strength	*Hamstring muscle
Injur#	Surgery	Strength	*Quadricep muscle
Rupture#		Force	Knee flexor#
Tear		Torque	Hamstring#
Torn		Exercise test	Knee extensor#
			Quadricep#

Boolean term OR was used within categories; AND was used between categories

* Mesh headings; # Truncation

2.4.2 Eligibility criteria

Selection criteria were developed prior to literature search to provide objective decision making for the inclusion of identified studies. Papers were included using the following criteria:

- Studies with participants who had ACL injury and reconstruction using ipsilateral grafts primarily from the hamstring tendon (HT) or patellar tendon (PT) sites;
- Measures of both knee extensor and knee flexor strength in both the injured and uninjured limbs before ACLR (preoperative), and either at 6 months and/or 12 months after surgery using isokinetic dynamometry in participants who have not yet returned to sport;
- Peer reviewed studies published in English (excluding review articles, conference abstracts, unpublished papers, case studies, and case reports)

Title and abstract screening for articles that were clearly inappropriate was performed by one of the authors. Full text copies for the remaining articles were then retrieved. Two authors then performed full text review and final screening of the studies using the inclusion criteria.

2.4.3 Assessing bias and methodological quality

Three independent examiners performed quality assessment on the studies that were included in the review. A modified Downs and Black checklist [108] was used to assess the bias of each study (Appendix A Table 2.1). This modified version was deemed suitable to the present review as these excluded questions related to the validity of methodological design related to interventions (items 4, 8, 13, 14, 15, 19, 22, 23, and 24) as were items 20 and 28 as these were not applicable to the present review. The checklist also included an amended version of questions 27 and the addition of item 29 as per a previous systematic review [109]. High methodological quality was given for a score ≥17 (≥81%), moderate quality for scores 14 to 16 (67-76%), and a score of ≤13 (≤62%) indicating low quality [77]. A maximum score of 21 was available for each study and was reported as a percentage. All results were cross-checked together by the three examiners after initial independent assessment. In cases of discrepancies in scoring, a fourth examiner was consulted for consensus.

2.4.4 Data extraction

Data extraction was performed by one of the authors. These data included sample size, sex distribution and age of participants, graft type used, type of isokinetic strength assessment, strength assessment time point, and strength data. The time from injury to ACLR, the type and aims of the studies and the rehabilitation utilized, if available, were also extracted. The corresponding authors, for five studies with insufficient data from the published article or the accompanying supplementary material, were contacted through email to attempt to obtain additional or missing data.

2.4.5 Statistical analysis

Data were stratified and analysed according to the mode of contraction (concentric, eccentric, isometric), velocity of contraction, strength measure (torque, force, limb symmetry measures), and timepoint of strength assessment (preoperative, six and/or 12 months postoperative). Limb symmetry measures were expressed as either an absolute mean difference (MD), as an LSI (percentage strength of injured limb against the uninjured limb):

$$LSI = \frac{\text{injured limb strength}}{\text{uninjured limb strength}} \; x\; 100\%$$

or as a limb strength deficit (LSD) which expresses the percentage difference between the injured and the uninjured limb:

$$LSD = \frac{\text{uninjured limb strength} - \text{injured limb strength}}{\text{uninjured limb strength}}\ x\ 100\%$$

Subgroup analysis of the graft used to perform ACLR (grouped as either HT or PT autografts) was also performed. A meta-analysis of the studies that had sufficient data was also conducted. To be included in the meta-analysis, studies were required to report the mean and random variability (standard deviation or suitable alternative) of their findings together with the number of participants in the study. A descriptive approach was used to report the results of the studies that were not included in the meta-analysis.

Meta-analysis was conducted in R (R Development Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing, 2010) using the "meta" package [110] and the "metafor" package [111]. For all outcomes assessed, a restricted maximum likelihood (REML) method was used to estimate variance and a random effects model was used to pool data. Absolute MD and 95% confidence intervals were computed for studies that reported magnitude (e.g. concentric peak torque) of muscle strength between injured and uninjured limb. For studies that reported strength ratio (e.g. concentric peak torque LSI/LSD), all strength data were standardized to LSI for meta-analysis (LSD were converted to LSI). An LSI with an upper 95% confidence interval of ≤90% was considered to indicate the presence of a strength deficits for any given timepoint. This cutoff was used as it is widely considered as the clinical threshold for safe RTS [33, 98, 112]. The pooled LSI mean and 95% confidence intervals were computed using an inverse variance method. Visual inspection of funnel plots for asymmetry was performed to assess for publication bias. Heterogeneity of pooled data was defined using the I^2 statistic using the following thresholds [113]:

- 0-40%: might not be important
- 30-60%: may represent moderate heterogeneity
- 50-90%: may represent substantial heterogeneity
- 75-100%: considerable heterogeneity

A meta-regression analysis was performed to evaluate the effect of age and/or sex on strength outcomes (MD or LSI) at each time point evaluated. To perform meta-regression for age, we used the mean age of each study's cohort. For sex, we used the distribution of females (0-100%) of each study's cohort in order to obtain a continuous variable suitable for meta-regression analysis. Bubble plots were also generated to visually inspect the meta-regression analysis. For the absolute mean difference (between injured and uninjured limb) and meta-regression analysis, significance was set at $P < 0.05$.

2.5 RESULTS

A summary of the search strategy can be seen in Figure 2.1. A summary of the study design and characteristics of the included studies is shown on Appendix A Table 2.2.

2.5.1 Risk-of-bias assessment

The risk-of-bias assessment of each study included is shown in Table 2.2. Included studies ranged from a score of 10 to 18 (48-86%) with an average score of 14 (67%). Seven studies were of high quality, 11 were moderate, and 13 were assessed as low quality. The most common items not addressed by the studies included were; distribution of principal confounders (item 5), characteristics of participants lost to follow-up (item 9), reporting of participant recruitment, representation, and distribution (items 11, 12, and 21), adjustment for confounding in the analyses (item 25), and calculation and meeting study power (item 27).

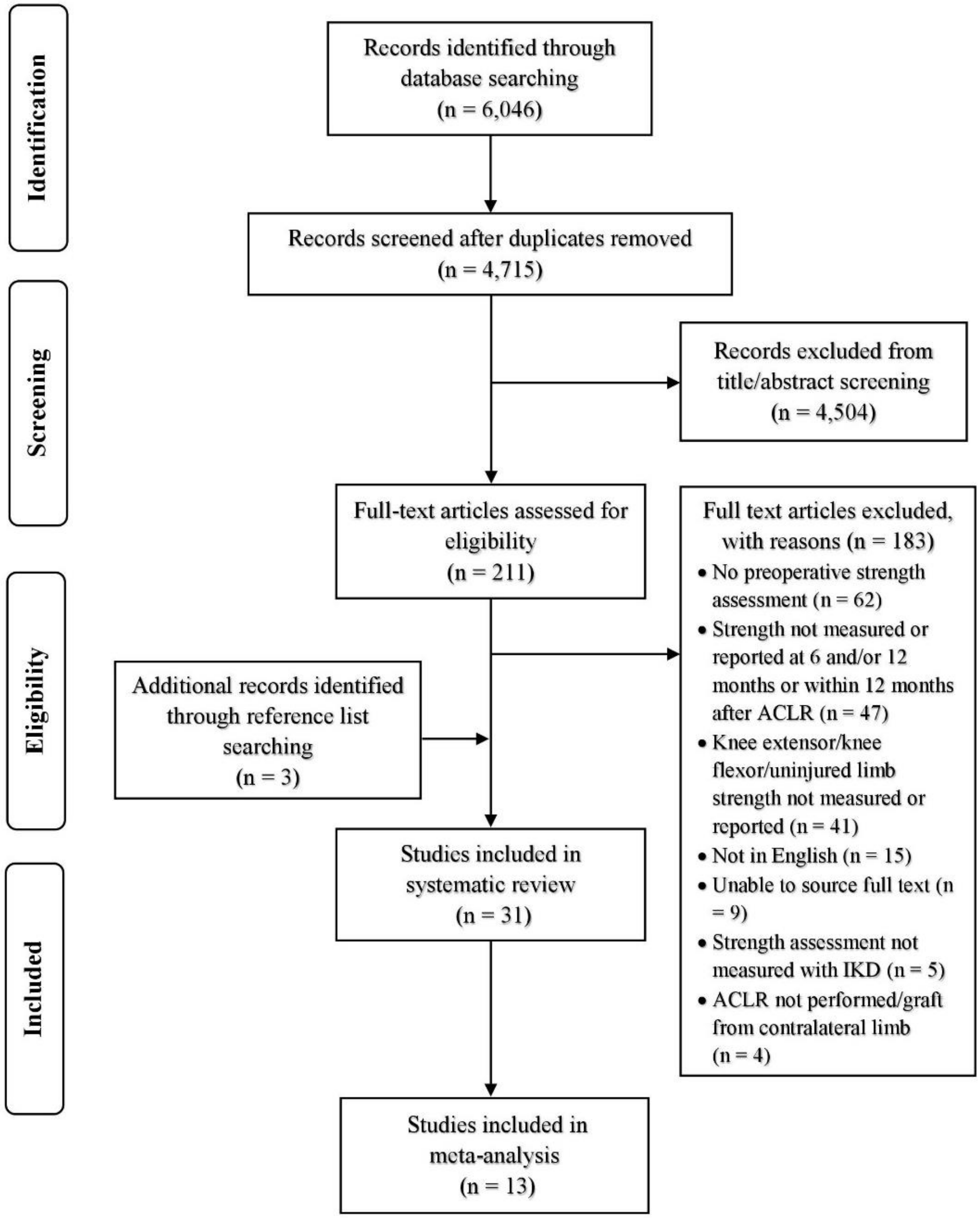

Figure 2.1. PRISMA flowchart outlining study selection process. Isokinetic dynamometer (IKD); Anterior cruciate ligament reconstruction (ACLR)

2.5.2 Description of studies

2.5.2.1 Participants

A summary of the demographics of the participants is shown in Appendix A Table 2.2. A total of 1,988 participants (n=1,249 male, n=595 female, n=144 sex not reported; age range, 12-63 years) were assessed across the included studies. A total of 23 studies had both male and female participants [114-136], five studies had males only [56, 137-140], one study examined females only [141], and two studies did not report the sex of the participants [142, 143]. Of the 23 studies that had both male and female participants, only three studies [115, 120, 131] reported strength results separately for sex. No study stratified reporting of strength results based on age of participants.

2.5.2.2 Graft types

A summary of the graft types used in the studies is shown in Appendix A Table 2.2. A total of 15 studies used HT autografts [116, 118, 119, 121-123, 126, 128-130, 134, 135, 137, 139, 141], eight studies assessed participants who had PT autografts [56, 117, 120, 125, 127, 132, 133, 138], while five studies had both graft types included in their cohort [114, 115, 136, 142, 143]. In addition, two studies had participants who were treated with HT, PT, or “other grafts” [131, 140], while one study [124] assessed participants who had a PT, quadriceps, or Achilles grafts. As outlined with the inclusion criteria, the three studies with either quadriceps, Achilles, and/or “other grafts” still had HT and/or PT autografts as primary grafts used.

Table 2.2. Itemised scoring of study quality using a modified Downs and Black checklist (see Appendix A Table 2.1)

Study	1	2	3	5	6	7	9	1	1	1	1	1	1	2	2	2	2	2	Scor	%	Quality
Knezevic et al.. 2014[a]	1	1	1	2	1	1	0	1	0	1	1	1	1	1	2	1	1	1	18	86	High
Knezevic et al., 2014[b]	1	1	1	2	1	1	0	1	0	1	1	1	1	1	2	1	1	1	18	86	High
Anderson et al., 2002	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	17	81	High
Fu et al., 2013	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	17	81	High
Risberg et al., 2009	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	17	81	High
Tanaka et al., 2010	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	17	81	High
Ueda et al., 2017	1	1	1	2	1	1	1	1	1	0	1	1	1	1	2	0	1	0	17	81	High
Seo et al., 2017	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	0	1	16	76	Moderate
Setuain et al., 2017	1	1	1	1	1	1	0	1	1	0	1	1	1	1	1	0	1	1	15	71	Moderate
Yasuda et al., 1995	1	1	1	1	1	1	1	1	1	0	1	1	1	0	1	1	0	1	15	71	Moderate
Beard et al., 2001	1	1	1	1	1	1	0	0	0	1	1	1	1	0	1	1	1	1	14	67	Moderate
de Jong., 2007	1	1	1	1	1	1	0	1	1	0	1	1	1	0	1	1	0	1	14	67	Moderate
Hsu et Al., 2018	1	1	1	1	1	1	1	1	0	0	1	1	1	1	0	1	0	1	14	67	Moderate
Lee et al., 2015	1	1	1	1	1	1	0	1	1	1	1	1	1	0	0	1	1	0	14	67	Moderate
Ogrodzka-	1	1	1	0	1	1	0	1	1	1	1	1	1	1	0	1	0	1	14	67	Moderate
Tashiro et al., 2003	1	1	1	2	0	0	1	0	1	1	1	1	1	0	1	1	0	1	14	67	Moderate
Teitsma et al., 2014	1	1	1	1	1	1	0	1	1	0	1	1	1	1	1	1	0	0	14	67	Moderate
Thomas et al., 2013	1	1	1	1	0	0	1	1	1	1	1	1	1	0	0	1	1	1	14	67	Moderate
Jansson et al., 2003	1	1	0	1	1	0	1	1	0	0	1	1	1	0	1	1	1	1	13	62	Low
Radziunas et al., 2012	1	1	1	1	1	0	1	0	0	0	1	1	1	1	1	1	0	1	13	62	Low
Witvrouw et al., 2001	1	1	0	1	1	1	1	1	0	0	1	1	1	0	1	1	0	1	13	62	Low
Janssen et al., 2013	1	1	1	0	1	1	0	1	0	0	1	1	1	0	0	1	1	1	12	57	Low
Keays et al., 2000	1	1	1	1	1	1	0	1	1	0	1	1	1	0	0	0	0	1	12	57	Low
Keays et al., 2001	1	1	1	1	1	1	0	1	1	0	1	1	1	0	0	0	0	1	12	57	Low
Keays et al., 2003	1	1	1	1	1	1	0	1	1	0	1	1	1	0	0	0	0	1	12	57	Low
Soon et al., 2004	1	1	1	0	1	0	0	0	1	1	1	1	1	1	0	1	0	1	12	57	Low
Tyler et al., 2004	1	1	0	1	0	0	0	1	0	1	1	1	1	1	0	1	1	1	12	57	Low
Hsiao et al., 2014	1	1	1	0	1	1	0	1	0	1	1	1	1	1	0	0	0	0	11	52	Low
Melikoglu et al., 2008	1	1	1	1	1	1	0	0	0	0	1	1	1	1	0	0	0	1	11	52	Low
Mittlmeier et al., 1999	1	1	1	0	0	1	1	1	0	0	1	1	1	0	0	1	0	1	11	52	Low
Domingues et al.,	1	1	1	0	1	1	0	1	0	0	1	1	1	1	0	0	0	0	10	48	Low

Risk-of -bias assessment score of >81% indicated high quality study, 67-76% as moderate quality study, and low quality study ≤62%.

2.5.2.3 Concomitant injuries/Treatment

The presence of concomitant injuries (posterior cruciate ligament, medial collateral ligament, cartilage, chondral, and meniscal injuries) was used to exclude participants for recruitment in seven studies [117, 119, 123, 126, 139, 142, 143]. Injury to the meniscus [115, 116, 118, 120-122, 127-129, 135, 140, 143] with subsequent repair/treatment [115, 116, 128, 143] or meniscectomy [120-122, 127-129, 135, 143] were the most commonly reported secondary injury and treatments. Chondral [115, 135, 143], medial collateral ligament [143], and cartilage injuries [127] were also reported without any description of treatment performed. Additionally, 12 studies did not report the presence of concomitant injuries [56, 114, 124, 125, 130-134, 137, 138, 141]. A summary of concomitant injuries and treatment of the participants is shown in Appendix A Table 2.2.

2.5.2.4 Rehabilitation

Patients underwent a controlled rehabilitation program in 27 studies [56, 114-116, 118-122, 124-130, 132-136, 138-143] while the remaining 4 studies [117, 123, 131, 137] did not control or report their rehabilitation program. A summary of the rehabilitation program utilised by the researchers can be found in Appendix A Table 2.2.

2.5.2.5 Outcomes

A summary of the different strength outcome measures is shown in Appendix A Table 2.3. Knee extensor and flexor concentric strength measured at velocities of 60°/sec [114-116, 118-125, 127, 129-138, 140-143] and 180°/sec [115, 116, 119, 123, 125, 126, 128, 130, 131, 133, 138] were the most commonly reported. Isometric strength was reported for the knee flexors in one study [130], while five studies [56, 117, 135, 138, 139] measured both knee extensors and flexors isometric strength. Isometric strength was assessed at different knee flexion angles across studies (10°, 30°, 50°, 70°, 90° [117]; 45° [56, 138]; 60° and 90° [135]; 70° and 90° [130]; and 90° [139]). Knee extensor and flexor eccentric strength was tested in only one study at a velocity of 60°/sec [114].

The majority of the measures were reported as peak torque [115, 116, 118-126, 128-141, 143], while five studies reported total work [119, 123, 124, 127, 128] and two studies reported peak force [56, 117] and mean torque [114, 142]. Peak force or peak torque normalized [118, 132, 139] to or as a percentage [117, 141] of body weight of the participant were also reported. One study each reported knee extensor and flexor isometric rate of force development (RFD) at 45° of knee flexion [56], mean power [133], and endurance ratio and mean difference between limbs [124]. Strength ratios were reported as knee extensor and flexor LSI [56, 116-118, 122, 123, 127, 129, 130, 134-136, 138, 140, 141, 143] or LSD [115, 120-122, 125, 131, 133] in 21 studies, and Hamstrings-to-quadriceps (H:Q) ratio [123, 138, 141] in 3 studies. Data for concentric hamstrings and quadriceps strength (peak torque) had sufficient data and were included in the meta-analysis. Additionally, values for LSD were converted to LSI for pooling and were also included in the meta-analysis.

2.5.3 Meta-analysis of concentric knee extensor and knee flexor strength

2.5.3.1 Preoperative – absolute mean difference

Significantly lower knee extensor (Figure 2.2A) and flexor (Figure 2.3A) concentric strength was found in the injured limb compared to the uninjured limb at 60°/sec. A significantly lower knee extensor strength at 120°/sec was also observed in the injured limb compared to the uninjured limb (Figure 2.4A). However, there was no difference in knee flexor strength (Figure 2.5A) at this velocity. Significantly lower strength in the injured limb compared to the uninjured limb was also seen with both the knee extensors (Figure 2.6A) and flexors (Figure 2.7A) at 180°/s.

2.5.3.2 Preoperative – Limb symmetry index

Strength asymmetry (LSI >90%) was found with the knee extensors at 60°/sec (Figure 2.8A) and 180°/sec (Figure 2.10A) and the knee flexors at 60°/s (Fig. 9A) but not at 180°/s (Figure 2.11A).

2.5.3.3 6 month – absolute mean difference

Knee extensor strength of the injured limb was lower compared to the uninjured limb at 60°/s (Figure 2.2B), 120°/s (Figure 2.4B), and 180°/s (Figure 2.6B). Injured limb knee flexor strength was also found to be lower compared to the uninjured limb at 60°/s (Figure 2.3B) and 180°/s (Figure 2.7B) but not at 120°/s (Figure 2.5B).

2.5.3.4 6 months – Limb symmetry index

Knee extensor LSI at 60°/sec (Figure 2.8B) and at 180°/sec (Figure 2.10B) showed significant asymmetries (LSI <80%) between the injured and uninjured limb 6 months after ACLR. Knee flexor LSI at 60°/sec (Figure 2.9B) and at 180°/sec (Figure 2.11B) were within and above the clinical threshold for strength symmetry respectively (LSI ≥90%).

2.5.3.5 12 months – absolute mean difference

Differences in strength between injured and uninjured limb were still present for both the knee extensors (Figure 2.2C) and knee flexors (Figure 2.3C) at 60°/s 12 months post-operatively. Meta-analysis for absolute MD in knee extensor and knee flexor strength at 120°/s and 180°/s at 12 months post-ACLR was not performed due to insufficient data.

2.5.3.6 12 months – Limb symmetry index

Asymmetry between the injured limb and the uninjured limb was still present for knee extensor strength at 60°/s (LSI <90%, Figure 2.8C) but not at 180°/sec (LSI ≥90%, Figure 2.10C). Knee flexor LSI at 60°/s (Figure 2.9C) and at 180°/sec (Figure 2.11C) were above the threshold for strength symmetry (LSI >90%).

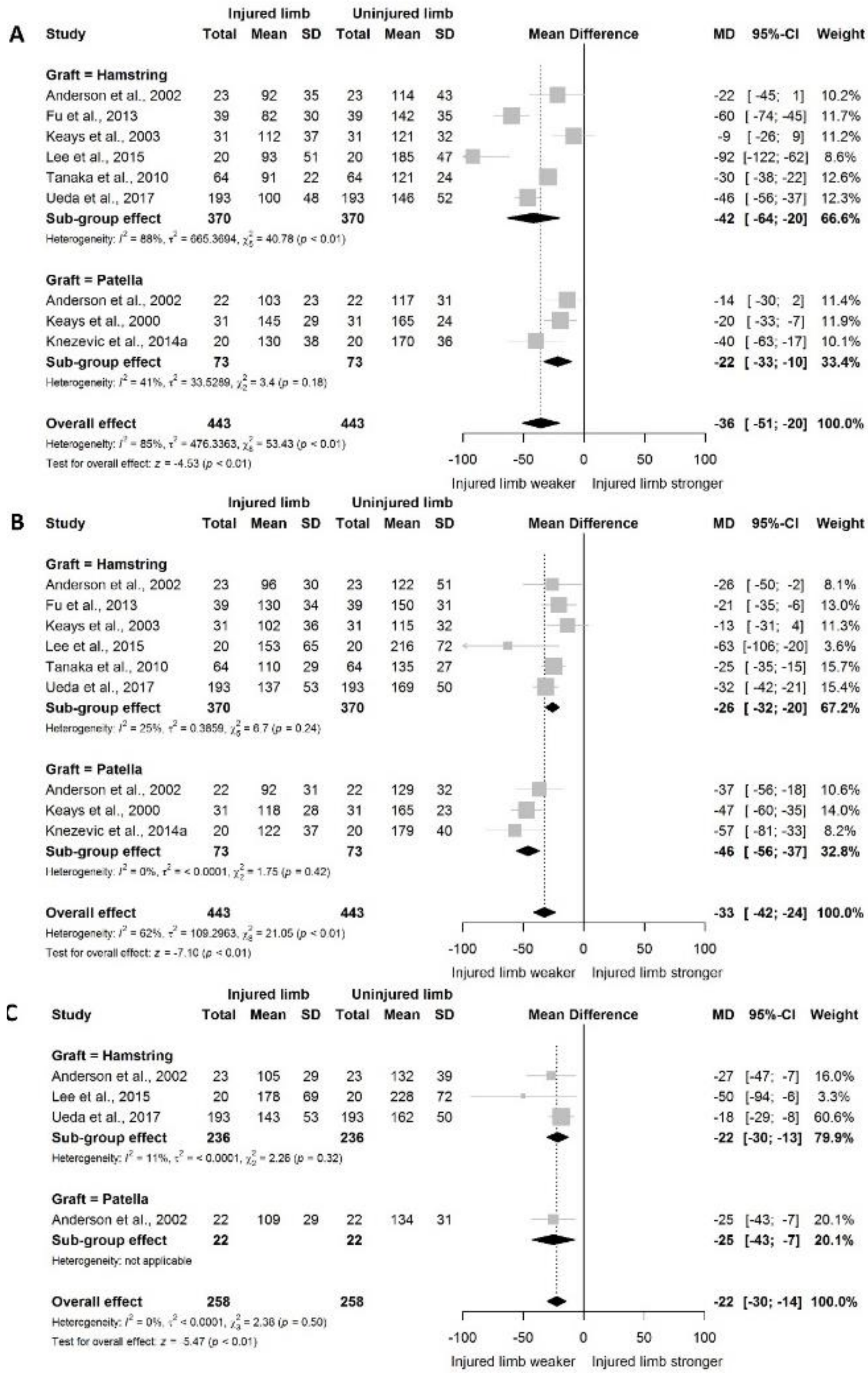

Figure 2.2. Forest plot of concentric knee extensor peak torque absolute mean difference at 60°/sec between injured and uninjured limbs at (A) preoperative, (B) 6-months postoperative, and (C) 12-months postoperative

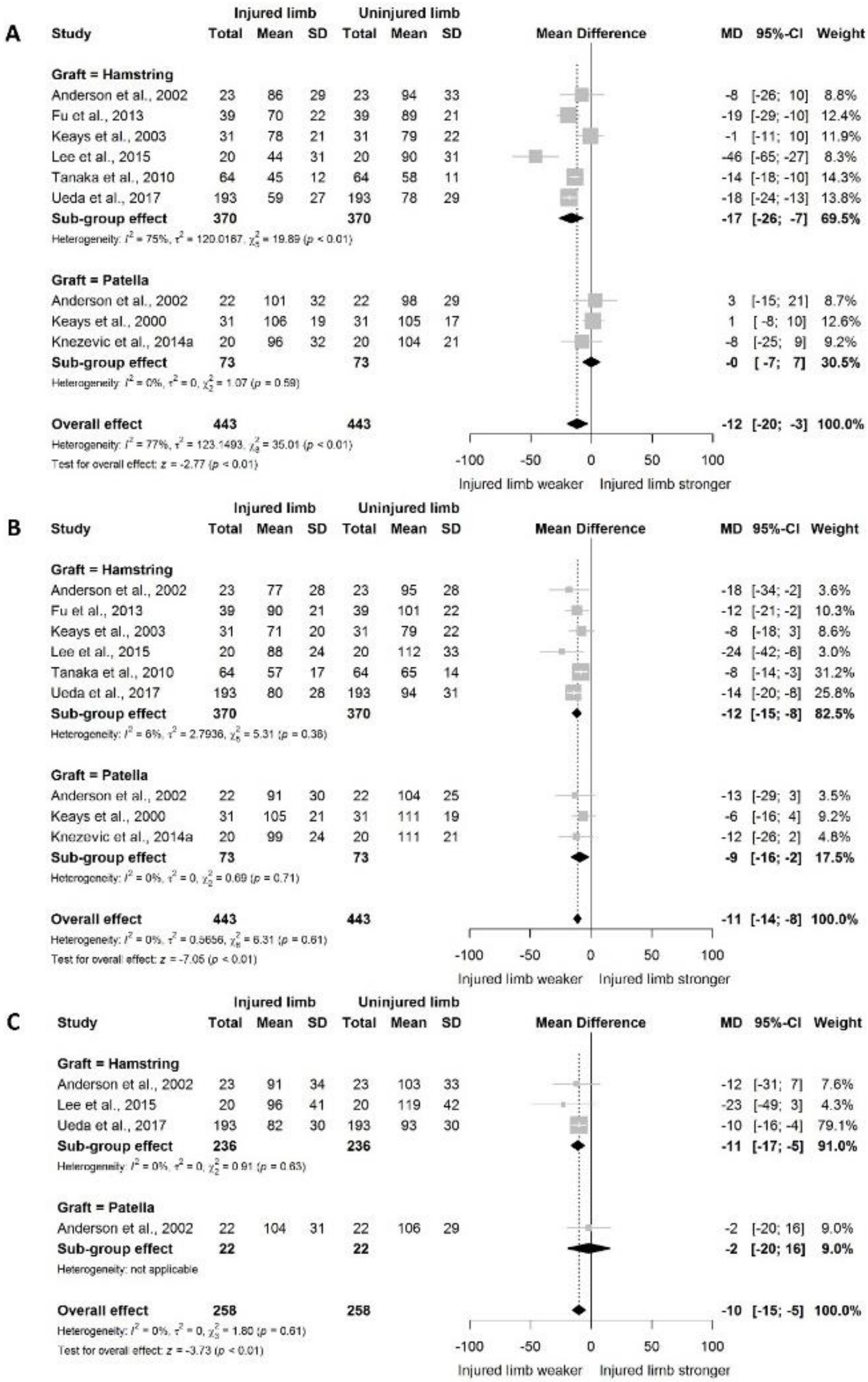

Figure 2.3. Forest plot of concentric knee flexor peak torque absolute mean difference at 60°/sec between injured and uninjured limbs at (A) preoperative, (B) 6-months postoperative, and (C) 12-months postoperative

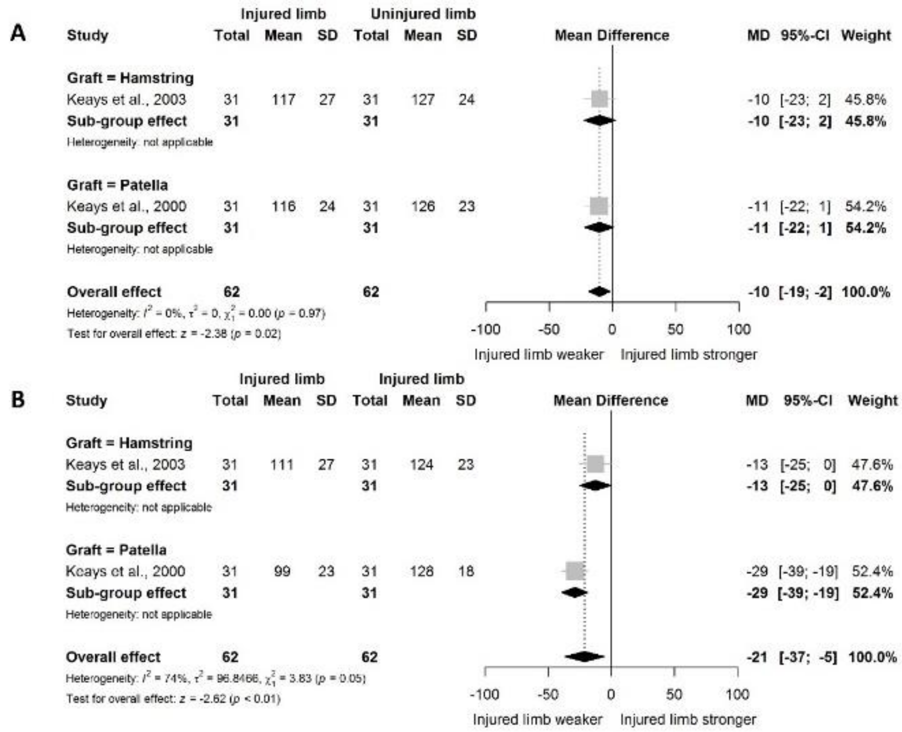

Figure 2.4. Forest plot of concentric knee extensor peak torque absolute mean difference at 120°/sec between injured and uninjured limbs at (A) preoperative, and (B) 6-months postoperative

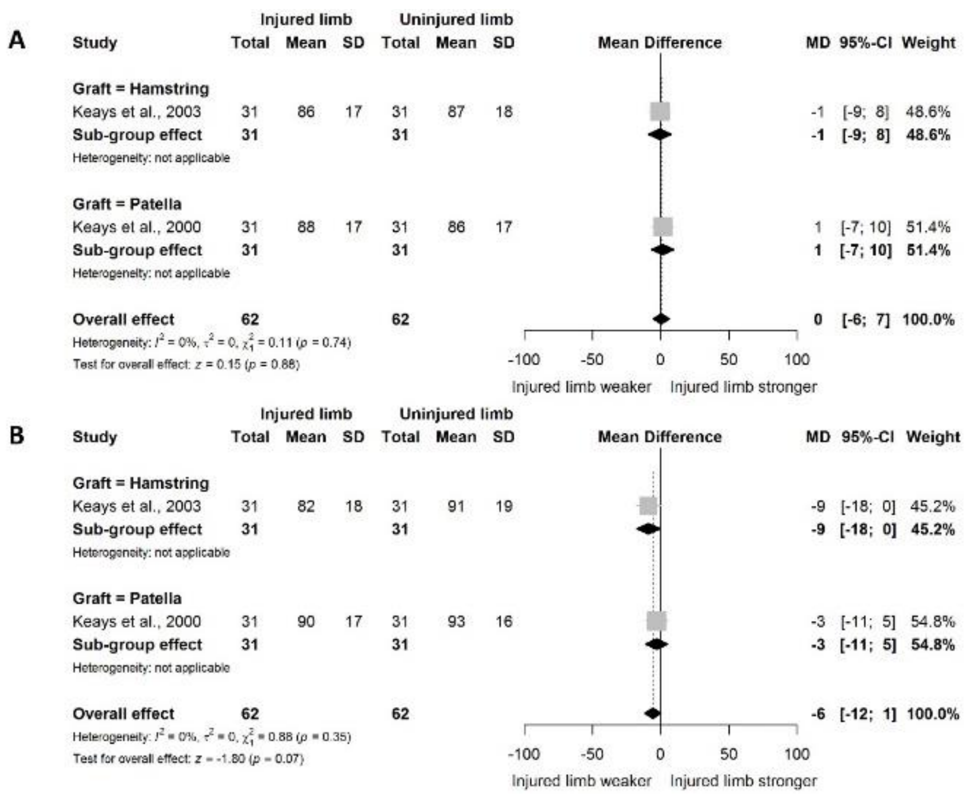

Figure 2.5. Forest plot of concentric knee flexor peak torque absolute mean difference at 120°/sec between injured and uninjured limbs at (A) preoperative and (B) 6-months postoperative

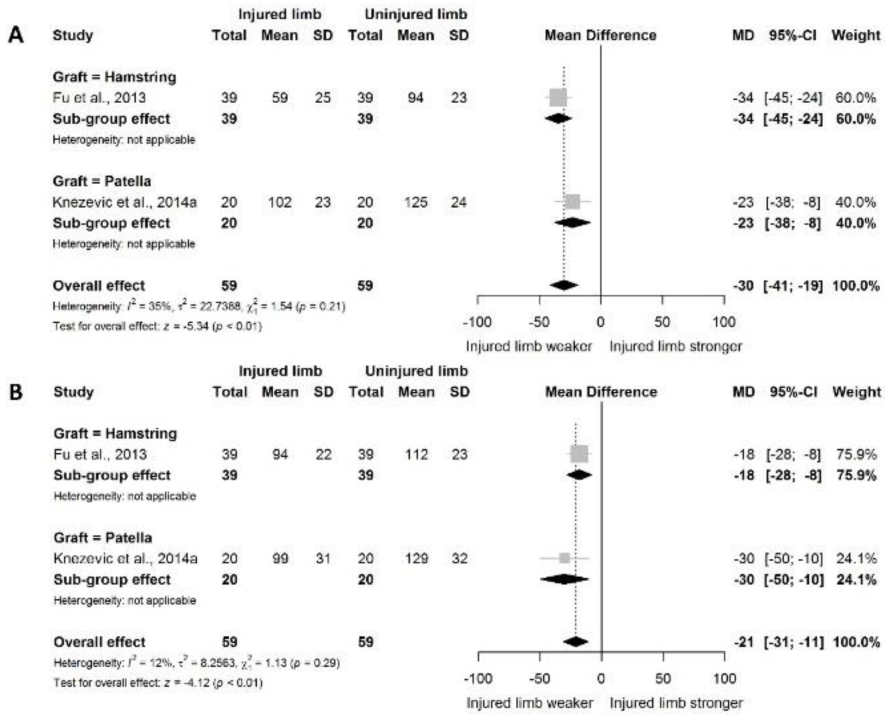

Figure 2.6. Forest plot of concentric knee extensor peak torque absolute mean difference at 180°/sec between injured and uninjured limb at (A) preoperative and (B) 6-months postoperative

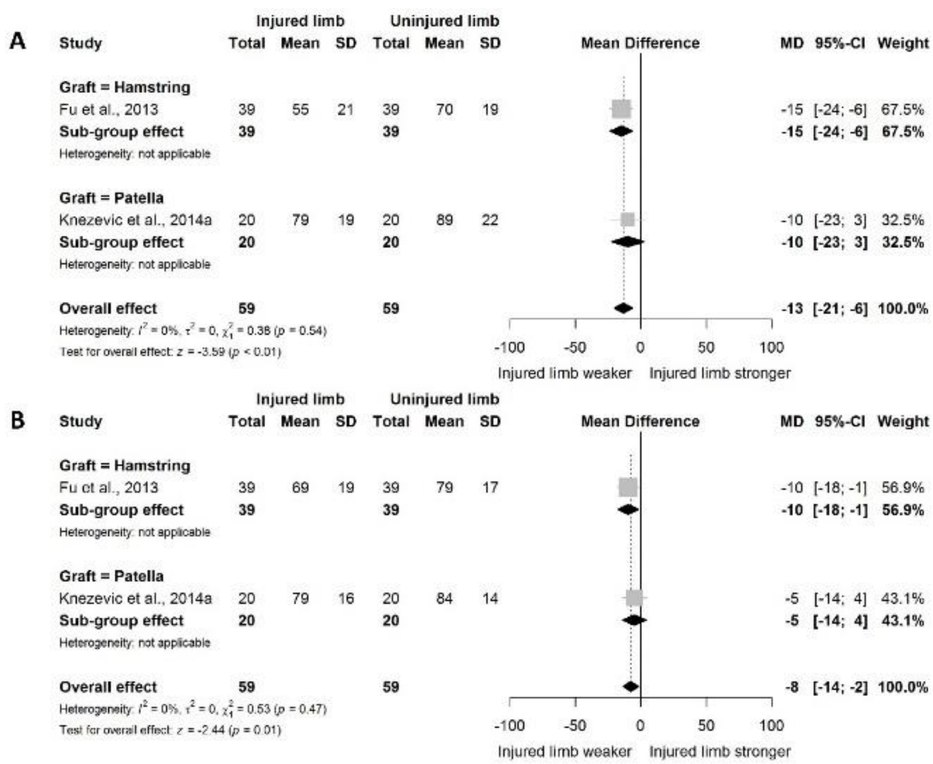

Figure 2.7. Forest plot of concentric knee flexor peak torque absolute mean difference at 180°/sec between injured and uninjured limbs at (A) preoperative and (B) 6-months postoperative.

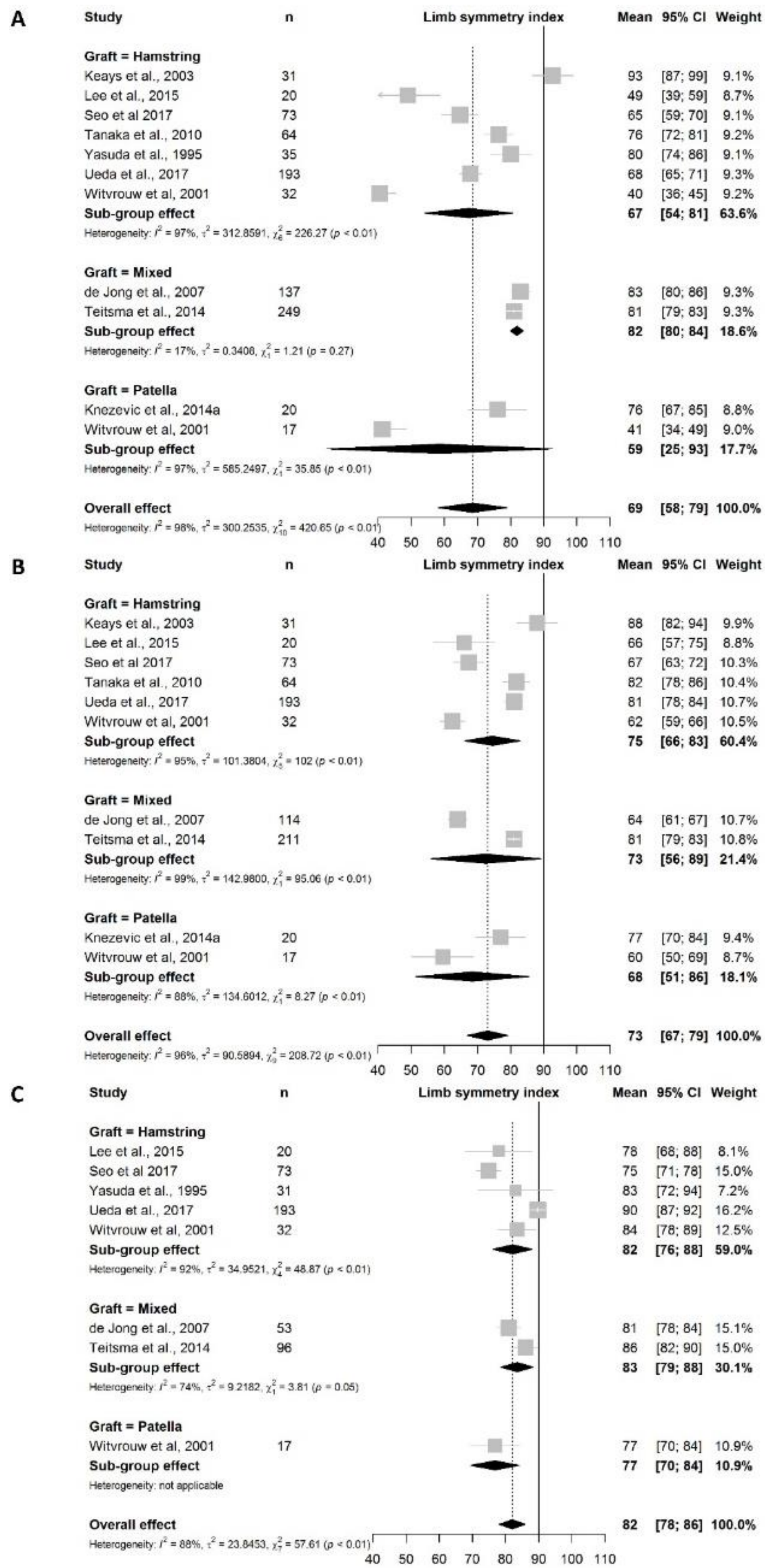

Figure 2.8. Forest plot of concentric knee extensor peak torque limb symmetry index (LSI) at 60°/sec between injured and uninjured limbs at (A) preoperative and (B) 6-months postoperative, and (C) 12-months postoperative

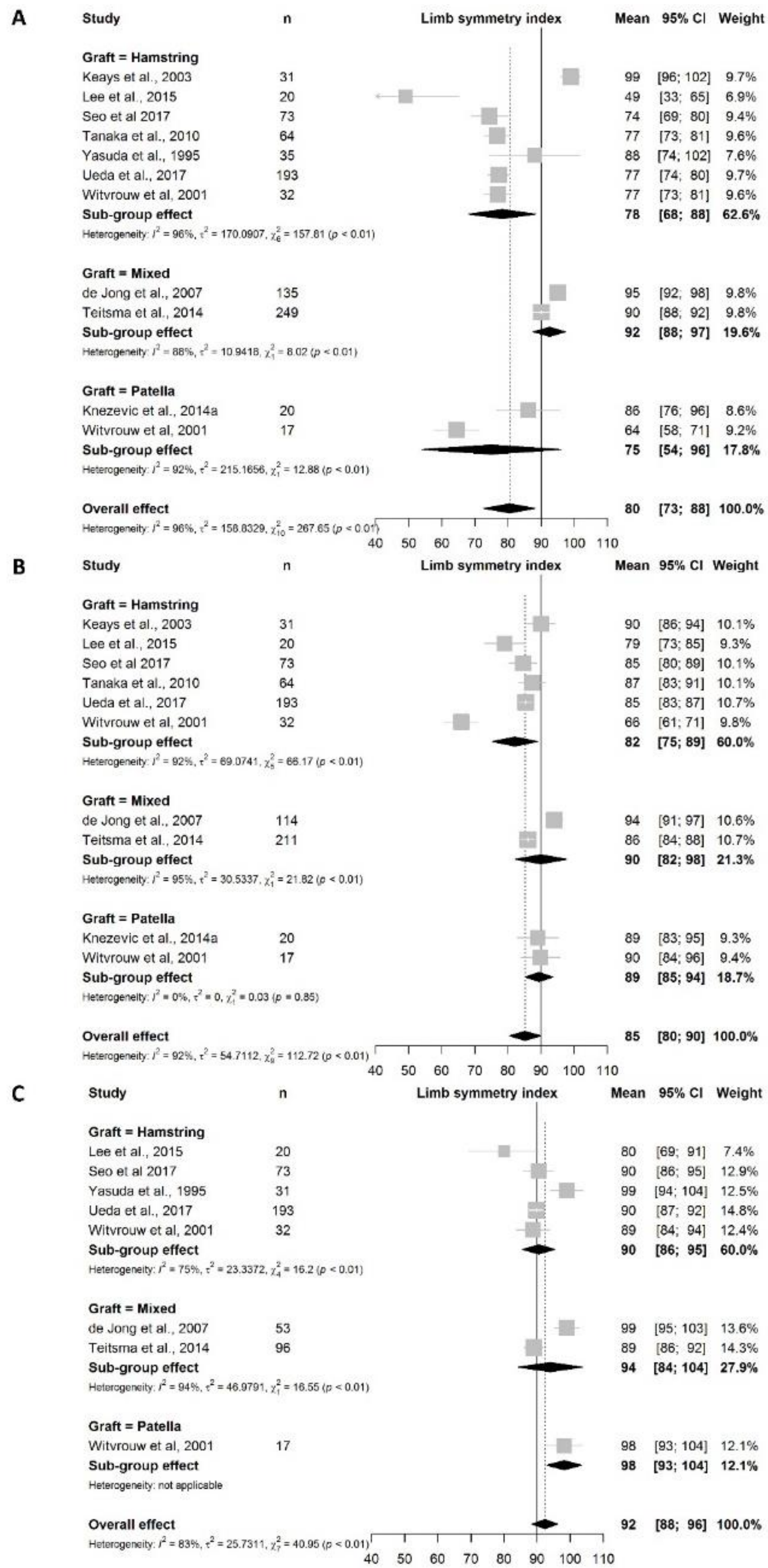

Figure 2.9. Forest plot of concentric knee flexor peak torque limb symmetry index (LSI) at 60°/sec between injured and uninjured limbs at (A) preoperative and (B) 6-months postoperative, and (C) 12-months postoperative

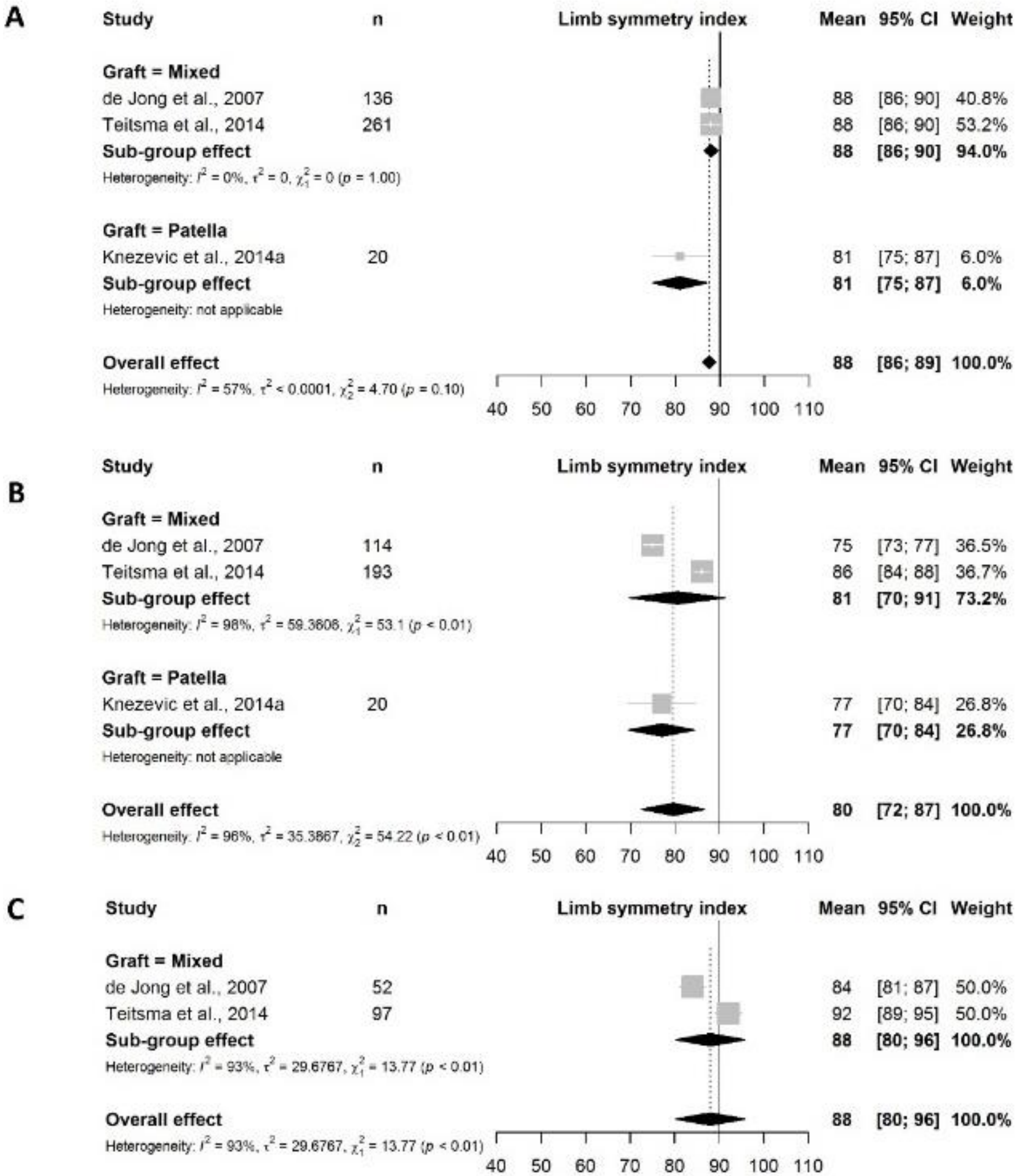

Figure 2.10. Forest plot of concentric knee extensor limb symmetry index (LSI) at 180°/sec between injured and uninjured limbs at (A) preoperative and (B) 6-months postoperative, and (C) 12-months postoperative

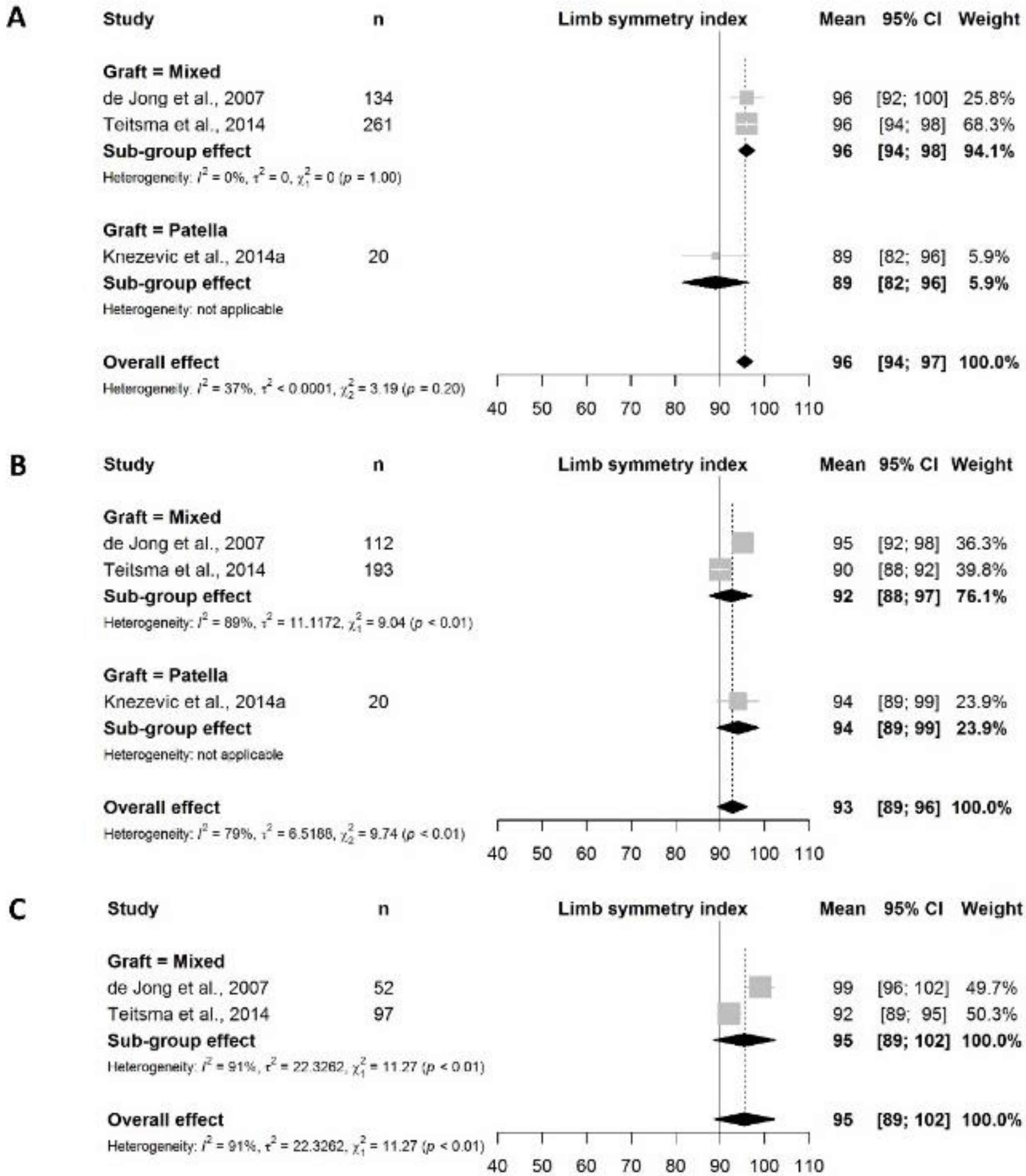

Figure 2.11. Forest plot of concentric knee flexor peak torque limb symmetry index (LSI) at 180°/sec between injured and uninjured limbs at (A) preoperative and (B) 6-months postoperative, and (C) 12-months postoperative

2.5.4 Results from studies not included in meta-analysis

The primary reason for studies not to be included in the meta-analysis was 1) that there was insufficient data provided in the manuscript (i.e. no reporting of standard deviations or suitable alternatives) and this data could not be obtained by contacting the corresponding author or 2) the amount of available data was too limited to include in meta-analysis.

2.5.4.1 Preoperative - Limb symmetry index

Soon et al. [129], Beard et al. [142], and Jansson et al. [143] reported lower concentric knee extensor strength at 60°/sec in the injured limb compared to the limb (LSI range: 67-85%). Concentric asymmetry in the knee flexors of the injured limb at 60°/sec (86% LSI) were also reported by Soon et al. [129]. In contrast, Beard et al. [142] found knee flexor LSI to be above 90% at 60°/sec.

Isometric strength asymmetries were also reported in the knee extensors (LSI range: 72-85%) and flexors of the injured limb (LSI range: 71-89% LSI) [117, 138]. However, these measures were taken at different angles of knee flexion. Hsiao et al [117] specified measurement at 10°, 30°, 50°, 70°, and 90° of knee flexion, whereas Knezevic et al [138] measured at 45° of knee flexion.

2.5.4.2 6 months - Limb symmetry index

Soon et al. [129] reported knee extensor and flexor concentric strength LSI at 60°/sec to be 92% and 89%, respectively.

Isometric strength LSI for the knee extensors and flexors was reported to range from 51-79% and 65-79% LSI, respectively [117].

2.5.4.3 12 months - Limb symmetry index

One year after ACLR, Beard et al. [142], and Jansson et al. [143] reported that the injured limb knee extensors were still weaker than the uninjured limb (LSI range: 79-85%) at 60°/sec.

2.5.4.4 Eccentric strength

Only a single paper reported on eccentric knee extensor and flexor strength differences preoperatively, as well as 6- and 12-months postoperatively [114]. At these time points an absolute MD of -18Nm (95%CI, -44 to 8), -40Nm (95%CI, -67 to -13) and -14Nm (95%CI, -42 to 14) for the knee extensors and -3Nm (95%CI, -24 to 18), -22Nm (95%CI, -47 to 3) and -15Nm (95%CI, -41 to 11) for the knee flexors in those with a BPTB graft was reported. For those with a HT graft, knee extensor absolute mean difference was -29Nm (95%CI, -60 to 2), -32Nm (95%CI, -59 to -5) and -24Nm (95%CI, -57 to 9) and knee flexor mean differences were -10Nm (95%CI, -34 to 14), -22Nm (95%CI, -43 to -1) and -8Nm (95%CI, -32 to 16), respectively.

2.5.5 Meta-regression: age, and sex and strength asymmetry

Age was not stratified for in any of the included studies, while three studies stratified for sex [115, 120, 131]. While the main aim of this review was to perform subgroup analysis on the effect of age and/or sex on strength recovery, this was not undertaken due to either differences in measures used to report strength or lack of a measure of random variability. Instead, we performed a meta-regression analysis using the mean age and the distribution of sex from each of the studies in the meta-analysis. This was then used to identify any association between age and sex on knee extensor and flexor strength asymmetry from preoperative to 6- and 12-months postoperatively (Figures 2.12 and 2.13). Meta-regression analysis did not show any effect of age in strength recovery for both knee extensors and flexors (Figure 2.12). Sex tends to influence knee extensor strength at 12 months post-ACLR, with males showing larger strength asymmetries than females (Figure 2.13C). There were no differences found in knee flexor strength between sex across the different timepoints (2.13D-F). It should be noted that the 12-month datapoints were predominantly male participants (Figure 2.13).

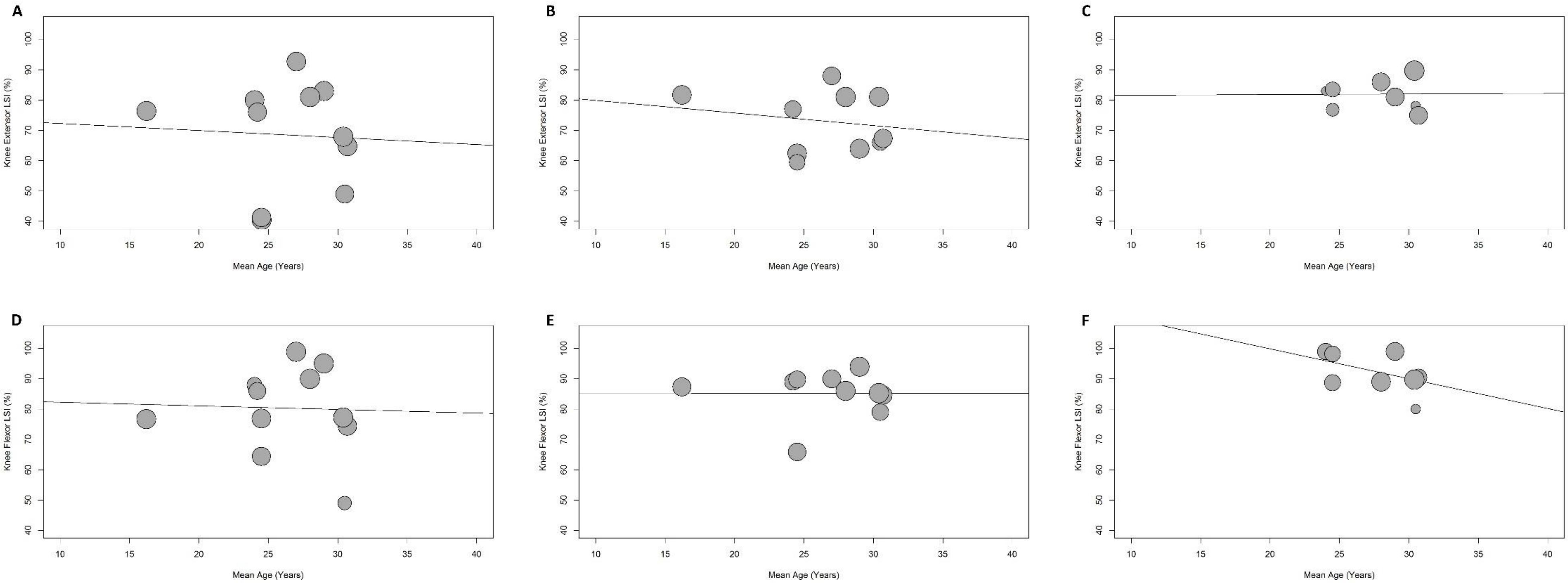

Figure 2.12. Meta-regression plots assessing the effect of age on concentric peak torque limb symmetry index (LSI) at 60°/sec. Knee extensor LSI at (A) preoperative ***p=0.87***, (B) 6-months postoperative ***p=0.59***, and (C) 12-months postoperative ***p=0.98***. Knee flexor LSI at (D) preoperative ***p=0.91***, (E) 6-months postoperative ***p=0.99***, and (F) 12-months postoperative ***p=0.17***

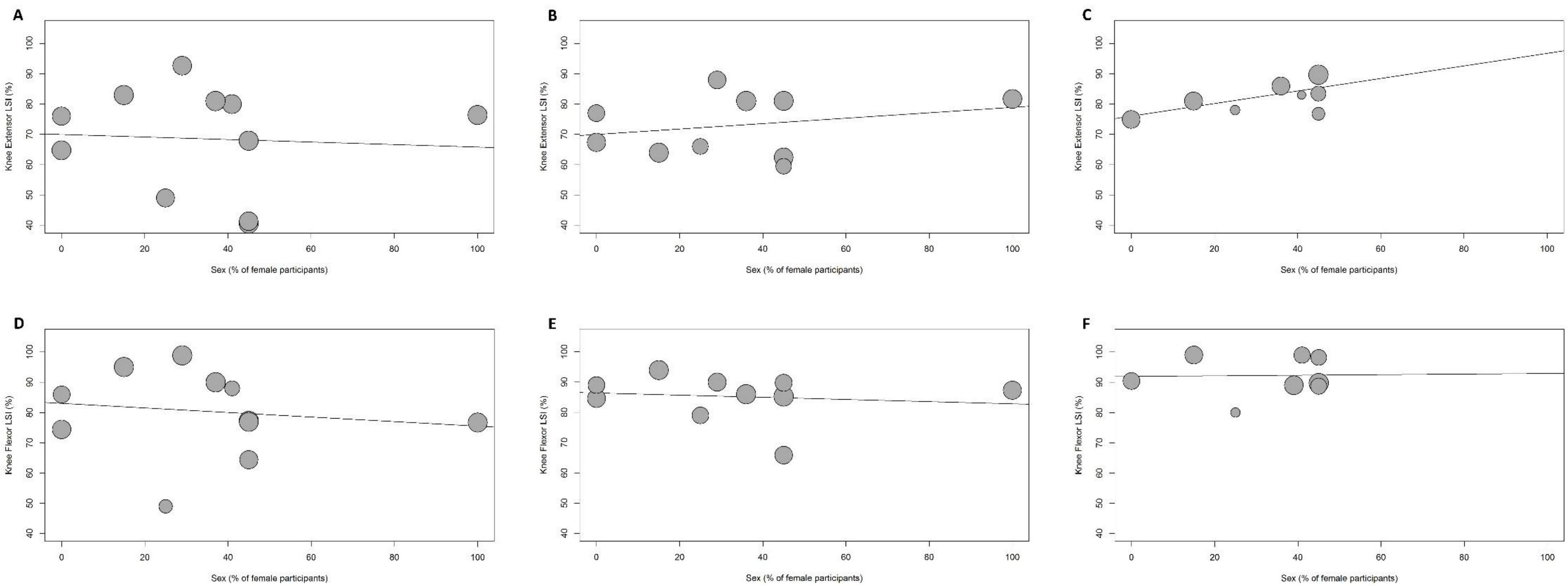

Figure 2.13. Meta-regression plots assessing the effect of distribution of sex concentric peak torque limb symmetry index (LSI) at 60°/sec. Knee extensor LSI at (A) preoperative ***p=0.84***, (B) 6-months postoperative ***p=0.43***, and (C) 12-months postoperative ***p=0.02***. Knee flexor LSI at (D) preoperative ***p=0.63***, (E) 6-months postoperative ***p=0.71***, and (F) 12-months postoperative ***p=0.95***. Sex distribution is presented as the percentage distribution of females (a female only cohort indicated as 100%) compared to males (a male only cohort indicated as 0%)

2.6 DISCUSSION

The main findings of this review showed the presence of knee extensor strength asymmetries from preoperative to 12 months following ACLR. Knee flexor strength asymmetries were also present preoperatively and at six months but were within clinical threshold for symmetry at 12 months. The initial aims of this review were to explore age and sex differences in strength after ACLR, however, our results indicate that studies rarely stratify for age and/or sex when reporting knee extensor and flexor strength measures preoperatively and up to 12 months after ACLR. Consequently, there is limited data available in the literature to analyse differences in the time course of strength asymmetry between age and sex groups following ACLR. Given the increased incidence of ACLR in youth and adolescent populations [3, 4] and the elevated risk of reinjury in females [10, 16] this is a critical gap in the literature that needs to be addressed.

A meta-regression of the available data showed age had no significant effect on knee extensor or flexor strength asymmetry pre-operatively or at 6- or 12-months post-operatively (Figure 2.12). However, these results should be taken with caution. Visual inspection of the distribution of the mean participant age shows these are mostly clustered between 25 to 30 years in the majority of studies in this review (Figure 2.12). Given the high incidence of primary and recurrent ACL injuries among adolescents [4, 11, 15, 97], the results of our meta-regression analysis do not fully represent the age spectrum of ACLR individuals. The meta-regression demonstrated a significant effect for sex as males had lower knee extensor strength symmetry at 12 months following ACLR (Figure 2.13C). This is inconsistent with two previous studies that show females to be weaker and/or more asymmetrical as males at 12 months [49, 115] after ACLR.

Meta-analysis of the time-course of asymmetry regardless of age and sex, shows presence of knee extensor (Figures 2.2A-B, 2.4A-B, 2.6A-B, 2.8A-B, 2.10A-B) and flexor (Figures 2.3A-B, 2.7A-B, 2.9A) strength asymmetry preoperatively up until six months after ACLR. While, generally, symmetry improved as time from ACLR increased, knee extensor (Figures 2.2C and 2.8C) and flexor (Figure 2.3C) strength asymmetries were still present 12 months after ACLR for selected variables when assessed at 60°/sec. A previous review showed that underlying strength deficits might be hidden when using faster velocities (>60°/sec) as torque output decreases with an increase in velocity [50]. The finding of this review further shows the importance of performing strength assessment at slower velocities (0-60°/sec) to reduce the likelihood of masking strength deficits following ACLR.

The presence of preoperative knee extensor strength asymmetry has been associated with persistent weakness and poor functional scores during rehabilitation [115] and at two-year follow-up [144]. This suggests that preoperative assessment and rehabilitation, which has been shown to improve preoperative strength [145, 146] and functional outcomes [126] after ACLR, should be strongly considered. Furthermore, the strength deficits found at six and 12 months after ACLR in this review are critical, as this is when most athletes are returning to running, jumping, and cutting activities [37, 63, 126, 147] as well as being cleared to RTS [32-34, 58]. Not being able to resolve strength asymmetry at these timepoints could partially explain why a large percentage of ACLR individuals are still weak at RTS [32, 58]; potentially contributing to the poor short- and long-term outcomes [33, 34].

The deficits found in this review appear to be larger and more persistent in the knee extensors compared to the knee flexors. The enduring presence of knee extensor weakness can have significant consequences for the individual. Knee extensor strength deficits post-ACLR have been associated with lower patient reported outcomes (International Knee Documentation Committee and Knee Injury and Osteoarthritis Outcome Score) [28], poor functional performance (hopping, jumping, and cutting) [30, 122, 148], and alterations in biomechanics [30, 82, 149]. In combination, the latter two could potentially increase the risk of a recurrent ACL injury [82] and alterations in biomechanics have been proposed to increase the risk of knee OA in ACLR populations [150].

The results of this review appear less conclusive for knee flexor strength. Absolute mean difference between injured and uninjured limbs shows significant strength asymmetry is present in the injured limb at all timepoints, when assessed at 60°/sec (Figure 2.3). However, meta-analysis of knee flexor LSI only showed clinically relevant asymmetries (<90%) pre-operatively at 60°/sec (Figure 2.9A). One of the possible explanations for this could be that the meta-analysis of strength asymmetry was measured during concentric actions. It should be noted that the summary of isometric strength asymmetry from the included studies that were not part of the meta-analysis, show deficits for both the knee extensors and flexors [117, 129]. Previous studies have also shown the persistence of knee flexor weakness during isometric (at different knee angles) [151] and eccentric [152] actions from one year up to 10 years after ACLR. As most research in strength asymmetry has focused on knee extensor strength during concentric actions [40], the actual extent of knee flexor strength asymmetry during eccentric or isometric actions at differing angles is underreported. Future work in this area should consider comparing strength recovery across different contraction modes for both the knee extensors and flexors across a diverse range of age and sex populations.

Limitations

There were some limitations with the current work. The inadequate number of studies that stratified for knee extensor and flexor strength asymmetry between age and sex groups preoperatively, 6- and 12-month after ACLR limited the ability of this review to make conclusions related to any associations between these factors. As the majority of the participants' age (25-30 years) and the distribution of sex (>50% males) do not fully reflect those who are at most risk of ACL injury and reinjury, future studies looking at strength recovery after ACLR should consider stratifying their results based on these factors. Results of the meta-analysis of the postoperative period also did not include all studies from the preoperative period as several studies did not measure at six months or at 12 months. These could have influenced results, as "missing" studies either from not being reported or published can affect the effect sizes of meta-analysis [153, 154]. To determine whether this affected our results, visual inspections for asymmetry of funnel plots were performed. While our results suggest publication bias, it should be noted that the low number of studies (n <13) in our meta-analysis limited the ability of our funnel plots to detect bias. The overall results of the meta-analysis should also be interpreted with caution. Significant heterogeneity, noted from the I^2 statistic, can be observed across different timepoints in the meta-analysis (see Fig 2-11). However, this could be attributed to the limited number of studies in the meta-analysis. Additionally, factors such as the type and duration of rehabilitation given to the study participants could have also influenced heterogeneity of our meta-analysis. As this review did not perform analysis on the different rehabilitation protocols used by the included studies, future studies could focus on possible differences of rehabilitation protocols and strength asymmetry after ACLR. Whilst the meta-analysis was performed with sub-group analysis for different graft types, as well as reporting an overall effect, exploration of the effect of graft type was not an aim of this review. The data is presented as sub-groups in the meta-analysis is for the benefit of the reader, however, the authors do not interpret this data, in line with the aim of the review. Lastly, while the main outcome measure reported in this review was concentric peak torque (as either absolute mean difference and LSI), previous studies have reported that strength deficits are angle-specific for the knee extensors [155, 156] and knee flexors [130]. However, given the limited number of studies and the large variations in the assessment and reporting of strength measures, analysis of strength deficits using angle-specific torque was not possible for this review.

2.7 Conclusion

To date, few studies have sought to identify differences in knee extensor and flexor asymmetry across different age and sex ranges for the 12 months following ACLR. Future studies should stratify for these variables given the increasing incidence of ACLR in younger populations and the high risk of recurrence in females. Meta-analysis of strength asymmetry, regardless of age and sex, showed the presence of knee extensor and knee flexor strength asymmetry from preoperative to 6-months post-ACLR. While these deficits improved across each timepoint, some deficits were still present at 12 months after ACLR.

3 METHODOLOGY AND DESIGN

Note: This chapter has been included to fulfil the University's Higher Degree Research Regulations. The methodology for each study has also been outlined in the corresponding chapters.

3.1 SYSTEMATIC REVIEW AND META-ANALYSIS

3.1.1 Search strategy

A systematic literature search was performed on MEDLINE, SPORTDiscus, CINAHL, and Web of Science from inception to November 2018. A combination of keywords (Table 2.1) was chosen to identify relevant articles aligned with the research aims. References were imported into EndNote X8 (Thomson Reuters, New York, USA) with initial review of titles and abstracts conducted after duplicate titles were deleted. Full texts were then collated for all articles that provisionally met the inclusion criteria. A reference list search was also performed to ensure all relevant articles were included. The systematic review protocol was not pre-registered.

3.1.2 Eligibility criteria

Selection criteria were developed prior to literature search to provide objective decision making for the inclusion of identified studies. Papers were included using the following criteria:

- Studies with participants who had ACL injury and reconstruction using ipsilateral grafts primarily from the hamstring tendon (HT) or patellar tendon (PT) sites;

- Measures of both knee extensor and knee flexor strength in both the injured and uninjured limbs before ACLR (preoperative), and either at 6 months and/or 12 months after surgery using isokinetic dynamometry in participants who have not yet returned to sport;
- Peer reviewed studies published in English (excluding review articles, conference abstracts, unpublished papers, case studies, and case reports)

Title and abstract screening for articles that were clearly inappropriate was performed by one of the authors. Full text copies for the remaining articles were then retrieved. Two authors then performed full text review and final screening of the studies using the inclusion criteria.

3.1.3 Assessing bias and methodological quality

Three independent examiners performed quality assessment on the studies that were included in the review. A modified Downs and Black checklist [108] was used to assess the bias of each study (Appendix A Table 2.1). This modified version was deemed suitable to the present review as these excluded questions related to the validity of methodological design related to interventions (items 4, 8, 13, 14, 15, 19, 22, 23, and 24) as were items 20 and 28 as these were not applicable to the present review. The checklist also included an amended version of questions 27 and the addition of item 29 as per a previous systematic review [109]. High methodological quality was given for a score ≥17 (≥81%), moderate quality for scores 14 to 16 (67-76%), and a score of ≤13 (≤62%) indicating low quality [77]. A maximum score of 21 was available for each study and was reported as a percentage. All results were cross-checked together by the three examiners after initial independent assessment. In cases of discrepancies in scoring, a fourth examiner was consulted for consensus.

3.1.4 Data extraction

Data extraction was performed by one of the authors. These data included sample size, sex distribution and age of participants, graft type used, type of isokinetic strength assessment, strength assessment time point, and strength data. The time from injury to ACLR, the type and aims of the studies and the rehabilitation utilized, if available, were also extracted. The corresponding authors, for five studies with insufficient data from the published article or the accompanying supplementary material, were contacted through email to attempt to obtain additional or missing data.

3.1.5 Statistical analysis

Data were stratified and analysed according to the mode of contraction (concentric, eccentric, isometric), velocity of contraction, strength measure (torque, force, limb symmetry measures), and timepoint of strength assessment (preoperative, six and/or 12 months postoperative). Limb symmetry measures were expressed as either an absolute mean difference (MD), as an LSI (percentage strength of injured limb against the uninjured limb):

$$LSI = \frac{\text{injured limb strength}}{\text{uninjured limb strength}} \ x \ 100\%$$

or as a limb strength deficit (LSD) which expresses the percentage difference between the injured and the uninjured limb:

$$LSD = \frac{\text{uninjured limb strength} - \text{injured limb strength}}{\text{uninjured limb strength}} \ x \ 100\%$$

Subgroup analysis of the graft used to perform ACLR (grouped as either HT or PT autografts) was also performed. A meta-analysis of the studies that had sufficient data was also conducted. To be included in the meta-analysis, studies were required to report the mean and random variability (standard deviation or suitable alternative) of their findings together with the number of participants in the study. A descriptive approach was used to report the results of the studies that were not included in the meta-analysis.

Meta-analysis was conducted in R (R Development Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing, 2010) using the "meta" package [110] and the "metafor" package [111]. For all outcomes assessed, a restricted maximum likelihood (REML) method was used to estimate variance and a random effects model was used to pool data. Absolute MD and 95% confidence intervals were computed for studies that reported magnitude (e.g. concentric peak torque) of muscle strength between injured and uninjured limb. For studies that reported strength ratio (e.g. concentric peak torque LSI/LSD), all strength data were standardized to LSI for meta-analysis (LSD were converted to LSI). An LSI with an upper 95% confidence interval of ≤90% was considered to indicate the presence of a strength deficits for any given timepoint. This cutoff was used as it is widely considered as the clinical threshold for safe RTS [33, 98, 112]. The pooled LSI mean and 95% confidence intervals were computed using an inverse variance method. Visual inspection of funnel plots for asymmetry was performed to assess for publication bias. Heterogeneity of pooled data was defined using the I^2 statistic using the following thresholds [113]:

- 0-40%: might not be important
- 30-60%: may represent moderate heterogeneity

- 50-90%: may represent substantial heterogeneity

- 75-100%: considerable heterogeneity

A meta-regression analysis was performed to evaluate the effect of age and/or sex on strength outcomes (MD or LSI) at each time point evaluated. To perform meta-regression for age, we used the mean age of each study's cohort. For sex, we used the distribution of females (0-100%) of each study's cohort in order to obtain a continuous variable suitable for meta-regression analysis. Bubble plots were also generated to visually inspect the meta-regression analysis. For the absolute mean difference (between injured and uninjured limb) and meta-regression analysis, significance was set at $P < 0.05$.

3.2 HAMSTRINGS STRENGTH ASYMMETRY PERSISTS DESPITE MAXIMAL HAMSTRING STRENGTH RECOVERY FOLLOWING ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION USING HAMSTRING TENDON AUTOGRAFTS

3.2.1 Participants

This study was approved by the Australian Catholic University Human Research Ethics Committee (approval number:2017-17HC). The study utilised an observational cohort study design with data collected from a community-based clinic. Participants were recruited from a sports clinic between 2017 and 2018. These patients had suffered a primary ACL rupture and underwent a subsequent ACLR performed using either a semitendinosus tendon autograft (n = 47) or a semitendinosus with gracilis tendon autograft (n = 42) by 10 surgeons from the same clinic and one surgeon from another practice.

Recruited participants were assessed between 3-6 months (early rehabilitation period) and 7-12 months (late rehabilitation period) following their ACLR. These timepoints were utilised as six and 12 months are the most commonly used cut-off for return to sports participation (six months) [157] and full clearance to return to sports (12 months) [13]. There was a total of 89 patients assessed during the early rehabilitation phase and 42 were re-assessed during the late rehabilitation phase. Rehabilitation was designed and prescribed by physiotherapists both from, and external, to the clinic in consultation with the patient's surgeon. Of the 89 patients, 48 had their rehabilitation supervised at the clinic while the remaining 41 patients undertook supervised rehabilitation programs from physiotherapists external to the clinic, but guidance was provided to the external physiotherapists on the rehabilitation approached used by the clinic. The rehabilitation protocol from the clinic included primary outcome measures related to: management of swelling/effusion; early restoration of knee extension and flexion; early ambulation; and recovery of hamstrings and quadriceps strength through gradual and progressive overload using open- and close-chain kinetic exercises [34]. Participants were progressed to running, plyometric training, and sports specific activities based on their progression from the aforementioned outcome measures [34].

Inclusion criteria were (1) age 15-40 years; (2) primary ACL injury; (3) unilateral ACLR using hamstring tendon autograft (semitendinosus only or semitendinosus with gracilis) taken from the injured leg; (4) ACLR within the previous three to six months prior to first testing session. Patients who had a previous ACLR or any other major knee joint/ligament injury were excluded. All participants provided written informed consent (or for minors, consent was provided by their guardian and the minor provided assent) to be included in the study.

3.2.2 Data collection

Data collection was performed during the participant's routine physiotherapy consultation in the clinic. All subjective and clinical assessments of the knee joint were collected during these visits which occurred between 3-6 months and 7-12 months after ACLR. Upon arrival at the clinic, participants completed the International Knee Documentation Committee (IKDC) which have been previously reported to be a valid and reliable measure of the participants' perception of their knee function and activities of daily living [158]. The participants then performed a strength testing battery for the hamstrings and quadriceps using an isokinetic dynamometer followed by a single leg hop for distance test [159].

Maximal voluntary contractions (MVC) of the hamstrings and quadriceps during isometric and concentric contractions were collected during the trials. Prior to strength testing, participants were asked to perform a 5-minute warm-up on a cycle ergometer using low resistance. Participants were then seated on a Humac Isokinetic Dynamometer (CSMi, Stoughton, MA, USA) with hips maintained at 85° of flexion throughout the test and the lateral epicondyle of the femur aligned with the fulcrum of the dynamometer. Correction for limb weight was taken before the test [160]. All dynamometer strength tests were conducted on each leg, commencing with the uninjured leg. Verbal encouragement and visual feedback was provided by the tester on all tests to motivate the participant to perform maximally throughout all measurements [160].

Isometric hamstrings and quadriceps strength testing commenced with the participant's knee 45° from full knee extension. The participant was instructed to pull the leg down (hamstring assessment) as hard and as fast as possible for three seconds, rest for two seconds, and then push the lower leg up (quadriceps assessment) as hard and fast as possible for three seconds. This was performed for three repetitions per muscle group [160]. The participant then rested for two minutes while seating on the dynamometer. While resting, range of motion for concentric strength testing was set at 0-90° of knee flexion (0° = full extension). For the concentric strength test, participants performed five repetitions of knee extension and flexion at 180°/sec, followed by 60°/sec. Participants performed one set of five consecutive MVCs at each movement velocity with a minimum of 30 seconds of rest between sets. Isokinetic/isometric strength testing is the gold standard for strength assessment following ACLR [50] and has been previously shown to be reliable (ICC = 0.81-0.97) [161].

After isokinetic strength testing, participants were then asked to perform a single leg hop for distance [159]. The test was performed by the participants barefooted, starting from a stationary position in a single leg stance with their hands placed on their lower back. The participant then performed a single hop for maximum distance, landing on the same leg [159]. The participant was required to hold their final landing position without their contralateral limb and/or their upper limbs touching down on the floor for the test to be considered successful. This was performed three times on each leg with the best score from three trials recorded in centimetres by measuring the distance covered from the line of the great toe before and after the hop [159].

3.2.2.1 Data reduction

A custom-written software program was used to collect data (LabVIEW 2017 SP1; National Instruments, Austin, TX) from the isokinetic dynamometer with torque and time data captured at 1000 Hz. Once data was collected, another custom-written software package (LabVIEW 2017 SP1; National Instruments, Austin, TX) was used to individually process each set of data (isometric and concentric hamstring and quadricep repetitions) from each limb of each participant.

Peak isometric and concentric hamstring and quadriceps strength as well as isometric RTD were determined for each limb at each testing velocity as the highest torque recorded during all repetitions. Peak RTD was defined as the greatest increase in force (increase in resting force ≥ 4N from onset of contraction) within a rolling 200ms window (Figure 3.1), which has previously been shown to be more reliable than alternative methodologies [53, 162]. We decided to collect RTD from isometric contractions as this was deemed more reliable compared to RTD from isokinetic efforts [53]. The isometric repetition with the greatest RTD (Nm/s) for the hamstrings and quadriceps was used for further analysis [163].

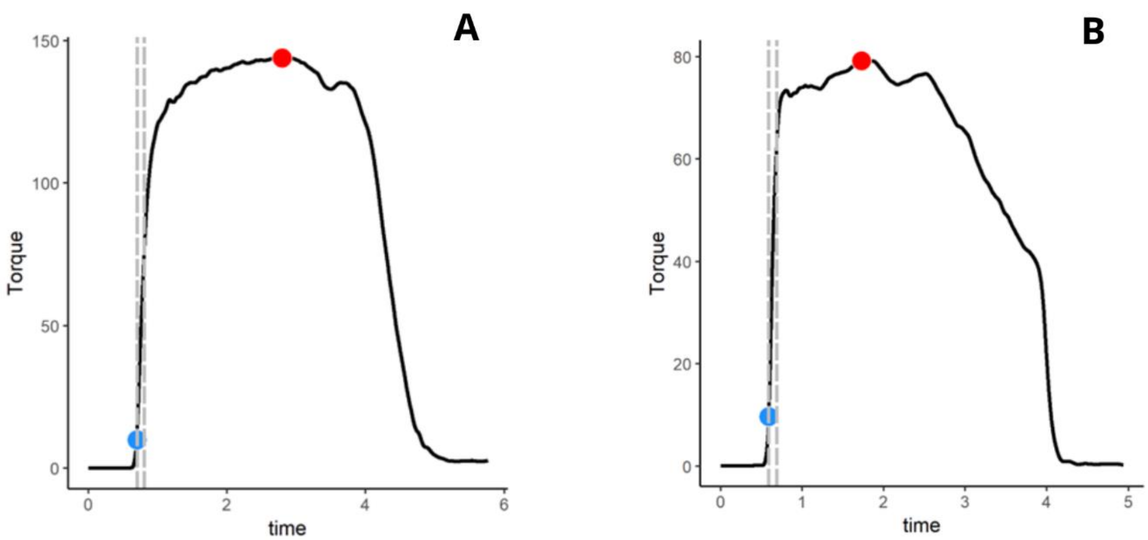

Figure 3.1. Torque-time trace of isometric quadriceps (A) and hamstrings (B) contraction. The red dot represents the peak isometric torque while the blue dot represents the greatest increase in torque over a 200-millisecond window (vertical broken lines).

Limb symmetry index was calculated as the percentage of the injured limb relative to the uninjured limb for all strength assessments (MVC and RTD) and single leg hop distance, per the equation below [33].

$$LSI = \frac{\text{injured limb score}}{\text{uninjured limb score}} \ x \ 100$$

3.2.3 Statistical Analysis

To compare LSI from hamstring and quadriceps MVCs, RTD and single leg hop distance data between sexes across the early (3 to 6 months post-operative) and late (7 to 12 months post-operative) phases of ACL rehabilitation, a linear mixed model fitted with restricted maximum likelihood method was utilised with fixed factors of time (early/late) and sex (male/female) as well as the random factor of participant identification number. Interactions between sex and time were explored when a main effect was identified for both fixed factors. Where main or interaction effects were detected a post-hoc Students t-test was used to identify the differences. Statistical analysis was performed using JMP statistical software (Version 14.2.0 2018; SAS Institute, Cary, NC) with significance set at $p = 0.05$. A convenience sample size was used for this study. Post-hoc power analyses determined that when comparing between the early (n=89) and late (n=42) rehabilitation groups with isometric hamstring MVC as the outcome measure (d = 0.53), the study had a power of 0.88.

3.3 MUSCULOSKELETAL MODELLING OF ANTICIPATED SIDESTEP CUTTING BETWEEN ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTED AND HEALTHY INDIVIDUALS

Chapters 5 and 6 of this program of research utilised musculoskeletal modelling to explore lower limb muscle function (e.g., muscle contributions to lower limb forces) and patellofemoral joint

(PFJ) contact forces following clearance to RTS in ACLR individuals. This section expounds on the methods also described in Chapters 5 and 6.

3.3.1 Study design

Data collection for this case-control comparative study was performed at the biomechanics laboratory of the Aspetar Orthopaedic and Sports Medicine Hospital. Participants were recruited between November 2018 and October 2019. Informed consent was obtained from all participants prior to participating in the study. This study is part of a larger body of work investigating return to sport criteria following ACLR rehabilitation [84]. Ethics approval for this study was granted (IRB F2017000227). The transfer and use of previously collected and non-identifiable data was approved by the Australian Catholic University Human Research Ethics Committee (Registration number: 2021-29N).

3.3.2 Participants

Forty-nine participants were recruited for studies Chapters 5 and 6 (Studies 3-4). This included 26 males who had ACLR and 23 healthy males (control group). Participants in the ACLR group were team sport athletes (pre-injury Tegner Activity scale score ≥7 [164]) between 18 and 35 years who had a unilateral ACLR either by a hamstring tendon – semitendinosus + gracilis (n = 10) or a bone-patellar tendon-bone (n=16) autograft from their ipsilateral limb. Choice of graft type was a shared clinical decision by the patient and the treating surgeon. Participants in the ACLR group was recruited after the completion of a supervised rehabilitation program and subsequent clearance to RTS at Aspetar Orthopaedic and Sports Medicine hospital. Criteria for RTS clearance were taken from previous literature which included (1) clearance from both their surgeon and physiotherapist, (2) completion of a sports-specific on-field rehabilitation program, (3) isokinetic quadriceps strength (LSI ≥ 90%), and (4) hop test for distance performance (LSI ≥ 90%) [34]. Exclusion criteria from the study included full thickness articular cartilage lesion and any other major lower extremity injury in both legs (e.g., concomitant grade III knee ligament injury other than ACL). A convenience sample from a pool of professional and high-level recreational athletes was used to recruit the control group. Inclusion criteria for the control group were age (between 18-35 years), Tegner score of ≥7, Level I or II sports participation (≥ 3 times/week), and no history of any lower limb injury in the last three months prior to testing. Patient reported outcomes related to pain, function, and psychological readiness was collected using the International Knee Documentation Committee (IKDC) [158] and Anterior Cruciate Ligament-Return to Sport after Injury (ACL-RSI) [165] questionnaires.

3.3.3 Equipment, participant preparation and marker set

Forty-three reflective markers (Figure 3.2) were attached to the participant's torso (xiphoid process, sternum, the tip of each acromion, the spinous process of the 7th cervical vertebrae, the spinous process of a mid-thoracic vertebrae), pelvis (anterior superior iliac spines, posterior superior iliac spines, sacrum), and lower limbs (medial and lateral femoral epicondyles, medial and lateral malleoli, 1st and 5th metatarsophalangeal joints, calcaneus) [166] as well as three marker clusters on the lateral thigh and shank [167]. A 14-camera Vicon motion capture system (250Hz, Vicon, Oxford, UK) together with five ground-embedded force plates (1000 Hz, Kistler, Switzerland) were used to collect three-dimensional marker trajectories and ground reaction forces, respectively. Marker trajectories and ground reaction force data were low pass filtered using a zero-lag, 4th order Butterworth filter at 10Hz.

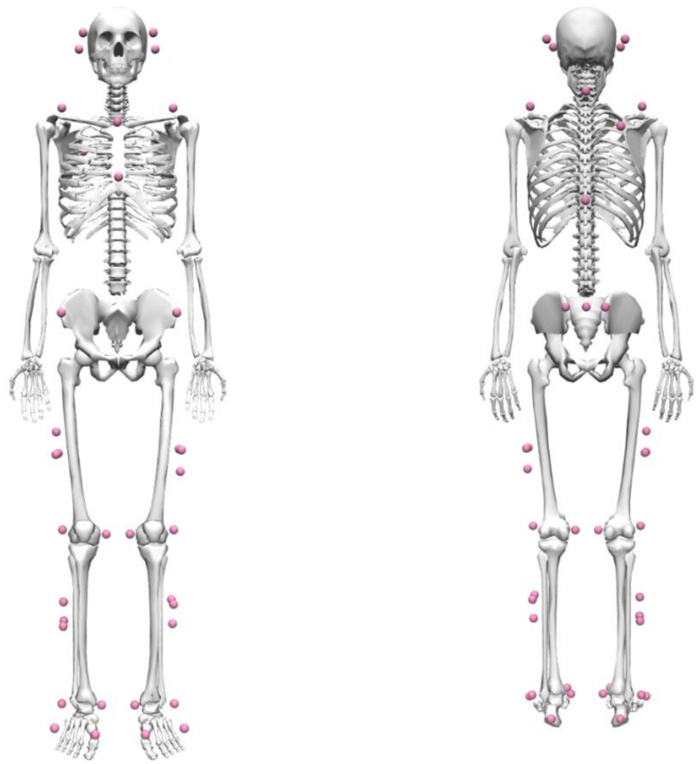

Figure 3.2. Anterior and posterior view of the experimental marker setup for three-dimensional motion capture.

3.3.4 Experimental procedure and testing

All participants were familiarised to the procedures and tasks prior to data collection methods. A 7-minute warm up consisting of running, side running, deep squats, and double leg jumps was performed prior to testing. All participants were wearing shorts and shoes during the performance of the tasks during the warmup and testing. For the sidestep cut task, participants were given instructions to accelerate with maximal effort towards the force plates from a standing position (6 metres away from the force plate) and perform three successful trials of an anticipated 45-degree sidestep cut. For a trial to be successful, a clear foot contact of the plant foot within the boundaries of the force plate was needed. Both limbs were tested, and coin toss was used to randomise the order of testing for each limb.

3.3.5 Musculoskeletal modelling

An overview of the overall approach to musculoskeletal modelling is shown below (Figure 3.3). In summary, a musculoskeletal model was scaled according to each of the participants' anthropometry (described in section 3.3.5.1). Inverse kinematics (described in section 3.3.5.2) and dynamics (described in section 3.3.5.3) were then performed to calculate joint angles and moments, while static optimization (see 3.3.5.4) was utilized to estimate muscle forces during the stance phase of an anticipated cutting task. To calculate the individual lower limb muscle contributions to GRFs produced during the performance of a sidestep cut, an induced acceleration analysis method was performed in Chapter 5 (described in section 3.3.5.5). Finally, a PFJ contact force model was used to determine PFJ contact forces during sidestep cutting in Chapter 6 (described in section 3.3.5.6).

Musculoskeletal modelling was performed using OpenSim v4.2 [168]. A generic musculoskeletal model with 29 degrees of freedom (DOF), 17 torque actuators (upper body), and 80 musculotendon actuators (lower body) was used to conduct the OpenSim simulations [169]. Each hip was modelled as a 3-DOF ball and socket joint. A 1-DOF hinge joint was used to represent the knees. Each ankle (talocrural joint) weas modelled as a 1-DOF pin joint while the subtalar and metatarsophalangeal joints were locked. A single rigid segment was applied to the head and trunk, articulating with the pelvis through a 3-DOF ball and socket joint.

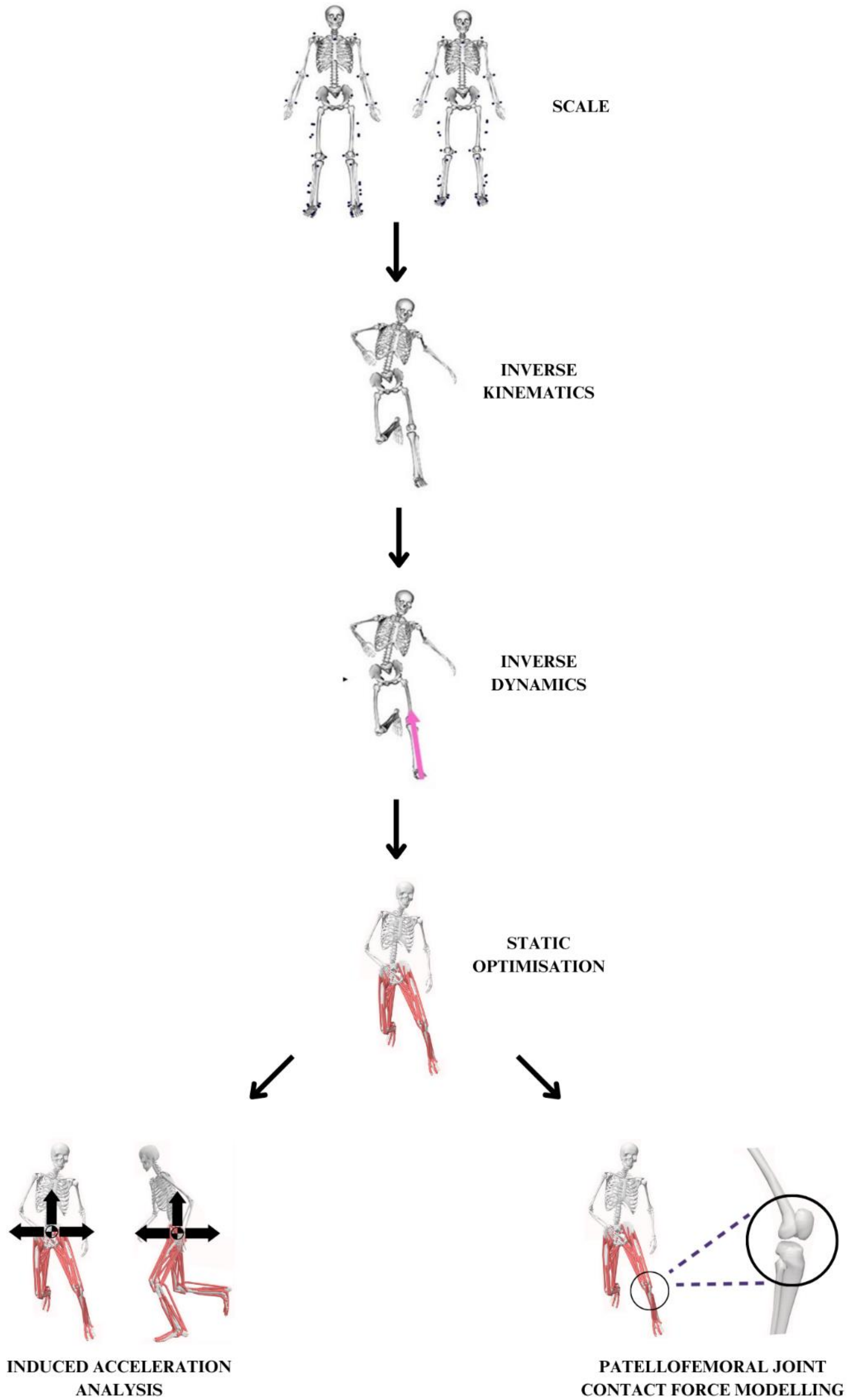

Figure 3.3. Overview of the musculoskeletal modelling pipeline to estimate muscle contributions using induced acceleration analysis (Chapter 5) and patellofemoral joint contact forces using contact force modelling (Chapter 6) during the stance phase of an anticipated sidestep cutting task

3.3.5.1 Scaling

The generic musculoskeletal model used in Chapters 5 and 6 were developed from 21 cadaveric data and magnetic resonance image from 21 healthy individuals [170]. To account for individual anthropometry of the study participants, a scaling process was performed in OpenSim [171]. Using experimental marker position from a static standing trial (from each participant), a scale factor was determined for each segment based on the relative distance between the experimental and virtual marker pairs from the model. This process then updates the anthropometry, dimensions, mass, inertial properties, and joint frame locations of the generic model to that of the participant. Additionally, muscle attachment points and length-dependent muscle parameters (i.e., optimal fibre length, tendon slack length) of the generic model were also modified based on the scaling procedure.

3.3.5.2 Inverse kinematics

Calculation of joint angles during the task was performed using inverse kinematics. This process was used to calculate joint angles by means of a least-squares global optimisation that minimises the difference between model and experimental marker positions during the sidestep cutting trials [172]. Through this process, inverse kinematics calculates a set of joint angles for each timepoint of recorded motion data. From this, the scaled model is configured as close as possible to the experimental kinematics of the participant. This method has been shown to reduce the error brought by soft tissue artefacts from the movement of the skin relative to the underlying bone [172].

3.3.5.3 Inverse dynamics

Inverse dynamics was utilized to compute the generalised forces and moments that are responsible for a given movement at each joint. This method uses the known motion (positions, velocities and accelerations) to solve the classical equation of motion to determine the unknown generalized forces and moments. However, inverse dynamics is prone to error (data noise) due to the double differentiation of joint angle positions to obtain joint accelerations [171]. To address this and improve the accuracy of calculations, GRF data is added to the equation. This is done as GRF data is sampled at a higher rate and is less prone to errors compared to joint angles. Still, one of the issues with this approach is the creation of residual forces and moments from kinematic (3D marker accelerations) and kinetic (GRF) data inconsistency. To address this in the present study, force and torque actuators were applied to the pelvis to enforce dynamic consistency [171]. Using the motion of the model (obtained from inverse kinematics), GRFs are applied to the feet of the model and the equations of motion are iteratively solved, starting from the distal foot segment and working upward. The net moment computed at each joint thus represents the net internal rotational force that produces the observed motion and is used in subsequently described muscle force estimation and muscle function techniques [68, 173, 174].

3.3.5.4 Static optimization

Static optimisation was used to decompose net joint moments into individual lower-limb muscle forces by minimising a cost function (sum of muscle activations squared) while considering the force-length-velocity properties of the musculotendinous units [175]. This method is not without limitations and there are other methods that can be used to estimate muscle forces [176]. However, static optimization was chosen based on its computational efficiency and previous use in musculoskeletal modelling studies on sidestep cutting tasks [177-179]. Muscle forces cannot be directly validated non-invasively, but a qualitative comparison of the joint angles and moments, as well as muscle forces with that of previous literature and experimental electromyography (EMG) can be assessed (described in section 3.3.7) as indirect validation [180]. Furthermore, estimated muscle forces from static optimisation are also relatively robust mass/inertial property uncertainties compared to other methods like computed muscle control [181], while also showing no significant differences in results when compared to forward dynamics [182].

3.3.5.5 Induced acceleration analysis

For Chapter 5, we explored lower limb muscle function by calculating individual muscle contributions to the superior/inferior (vertical support), anterior/posterior (propulsion/braking), and medial/lateral (redirection) ground reaction forces (GRFs) during sidestep cutting task using an induced acceleration analysis [46, 66, 183-185]. To do this, a universal "rolling on ground" constraint (foot-ground interaction model) or a single point model was utilized as per previous methods [46, 66, 183-185]. Other foot models have been previously utilised, and may have inherent advantages and limitations [185]. Two important factors were considered in the decision making for the model used in Chapter 5 – the number of foot-ground contact points and the type of kinematic constraint at each contact point. Previous studies in sagittal plane-dominant tasks like walking and running have shown no differences in vertical, propulsion, and deceleration GRFs when using single point or multipoint models [186, 187]. Conversely, mediolateral GRFs appear to be sensitive to the model used [185] which is critical given the task assessed in Chapter 5 (i.e., sidestep cutting) involves redirection of GRFs in the mediolateral direction. Because of this, the "rolling on ground" model was chosen given that it qualitatively described the foot-ground interaction during sidestep cutting and has previously been shown to reproduce experimental GRFs in similar high impact tasks [46, 184].

3.3.5.6 Patellofemoral joint contact force modelling

To calculate PFJ contact force, we used a separate empirically based model as described by Fok et al [188].

$$F_{PFJ} = \sqrt{F_Q^2 + F_P^2 + 2F_Q F_P \cos\beta}$$

Where FPFJ is the PFJ contact force, F_Q is the quadriceps force, F_P is the patella tendon force, and β is the patellar mechanism angle (angle between quadriceps muscle and patellar tendon). Calculation for F_P and β were based on data from an in-vitro study [189]. From these calculations, equations for F_P and β as a function of the knee flexion angle was established. Finally, knee flexion angle and F_Q calculated from the model were then applied together with F_P and β to calculate FPFJ.

The current modelling approach and focus on the sagittal plane was chosen consistent with previous literature [80, 85]. While other methods with more complex geometry of knee contact model between the patella and femur, which consider cartilage and ligament properties, are available (e.g., Concurrent Optimization of Muscle Activations and Kinematics (COMAK)), it has only been used in slow movements (e.g., walking and slow running). As the optimisation problem in COMAK minimises secondary tibiofemoral and patellofemoral accelerations, results for high impact movements (e.g., sidestep cutting) need validation prior to their implementation in clinical research. However, it is acknowledged that the frontal and transverse planes could contribute to the net PFJ contact force and future work is needed to understand how these could affect PFJ biomechanics.

3.3.6 Outcome variables

For Chapter 5, muscle contributions to GRFs (expressed using the global reference frame) were first normalized to bodyweight (BW) and subsequently integrated with respect to time to determine the net impulse during stance phase (BW.sec). Due to the large number of musculotendinous actuators in the model, we focused on muscle groups previously shown to contribute to GRFs during weightbearing tasks [48, 66, 67]: quadriceps (sum of rectus femoris and vastus intermedius, medialis and lateralis), soleus, gastrocnemius (sum of medial and lateral gastrocnemius), gluteus maximus, gluteus medius, hamstrings (sum of biceps femoris long head, semimembranosus, semitendinosus), and ankle dorsi-flexors (sum of tibialis anterior, extensor hallucis longus, extensor digitorum longus) of the stance leg.

For Chapter 6, peak PFJ contact force was extracted during the stance phase (defined as the raw ground reaction force exceeding 20N). Since the primary determinants of the PFJ force is the knee flexion angle and quadriceps force [188], we also calculated the knee flexion angle and quadriceps force at the time of peak PFJ contact force.

3.3.7 Validation and verification

One of the main limitations of the musculoskeletal modelling techniques utilised in this program of research is that these cannot be directly validated in-vivo using non-invasive methods. To maximise the credibility of our model predictions, validation and verification was conducted in accordance with best practice guidelines [180]. Qualitative comparisons between the temporal characteristics of predicted muscle forces with that of EMG data from previous work were performed [190] throughout the stance phase of the sidestep cut (Figure 3.3). Our results show general agreement between model-based predictions and EMG data for most muscles, once accounting for EMG-to-force physiological delays (~100ms) as per recommendations [180]. More notable qualitative differences in activation patterns were observed from some muscles, such as the adductor magnus, rectus femoris, and semitendinosus (Figure 3.3). These differences could be explained by their bi-articular nature (rectus femoris and semitendinosus) or complexity of attachment sites and muscle fiber orientation (adductor magnus). Qualitative verification of the temporal-varying characteristics of experimental joint angles (Appendix A. Figure 6.1) and moments (Appendix A. Figure 6.2) were also comparable to previous work on sidestep cutting in healthy individuals [47]. Finally, qualitative verification of the foot-ground interaction model via superposition shows agreement between the experimental and simulated GRFs (Figure 3.4).

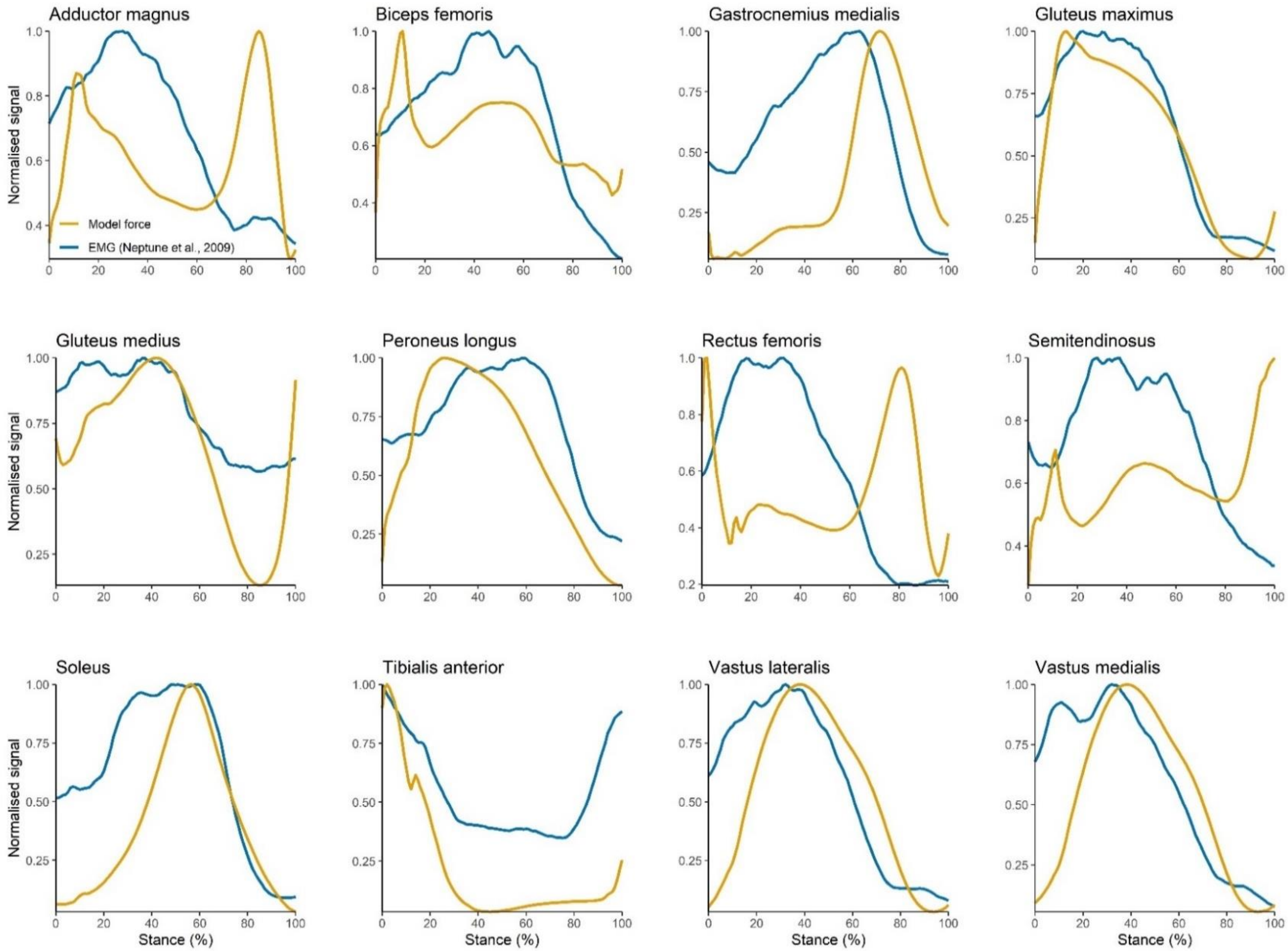

Figure 3.4. Comparison of predicted model force (yellow line) from the stance phase of the anticipated sidestep cut with the activations from electromyograph data from Neptune et al., 1999 [190]

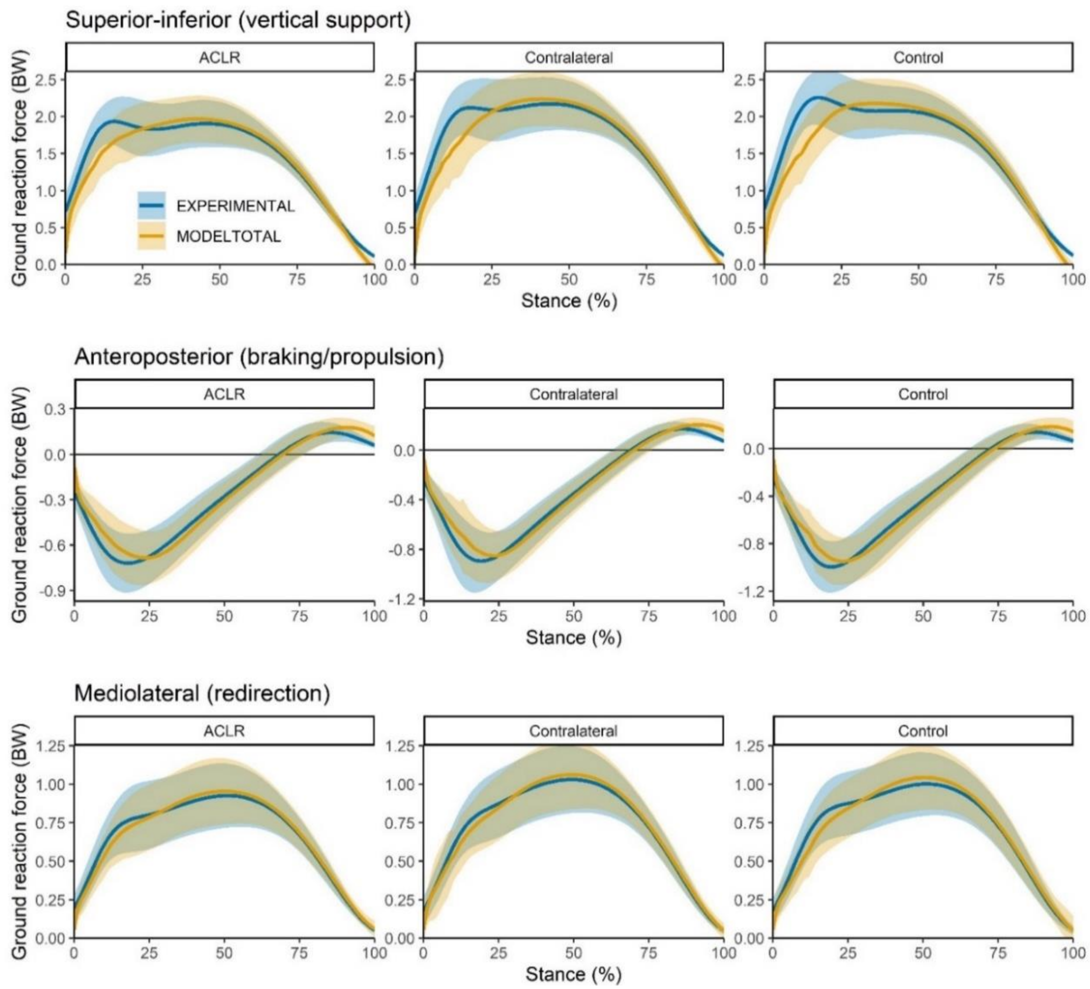

Figure 3.5. Contributions of all muscle forces to the superior-inferior (top row), antero-posterior (middle row), and mediolateral components of the ground reactions forces generated by the ACLR (1st column), Contralateral (2nd column), and control (3rd column) limbs during the anticipated sidestep cut from the experimental data (blue line) and model data (yellow line). Forces are averaged across all participants and are expressed in units of BW. *ACLR*, anterior cruciate ligament reconstruction; *BW*, body weight

3.3.8 Statistical analysis

Descriptive statistics was used to summarise participant characteristics. Shapiro-Wilk test was used to check for normality of distribution of the demographic data of the participants [191]. An independent sample t-test was used ($p < 0.05$) to determine between group comparisons in participant demographics. A linear mixed effects models [192] was used to determine if differences existed in the vertical support, braking and propulsion, and redirection GRFs for each muscle listed previously (see section 3.3.6) or PFJ outcomes previously described (see section 3.3.6). For each linear mixed model, limb (ACLR, contralateral, healthy control) was modelled as a fixed effect and participant ID as a random effect, whilst adjusting for approach velocity. Adjustment for approach velocity was performed as any variation between groups or trials (e.g., participants may run slower when cutting on their ACLR leg compared to healthy-leg cuts) could confound analysis if unaccounted for. Where significant effects were found for limb, we conducted post-hoc pairwise comparisons using Tukey's method [193]. Data assumptions (e.g., distributions) were verified via the visual inspection of qqplots and residual plots. For all analysis, statistical significance was set at $p < 0.05$.

4 EXPLOSIVE HAMSTRINGS STRENGTH ASYMMETRY PERSISTS DESPITE MAXIMAL HAMSTRING STRENGTH RECOVERY FOLLOWING ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION USING HAMSTRING TENDON AUTOGRAFTS

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San Jose AJ, Maniar N, Timmins RG, Beerworth K, Hampel C, Tyson N, Williams MD, Opar DA. Explosive hamstrings strength asymmetry persists despite maximal hamstring strength recovery following anterior cruciate ligament reconstruction using hamstring tendon autografts. Knee Surg Sports Traumatol Arthrosc. 2022 Aug 23. doi: 10.1007/s00167-022-07096-y. Epub ahead of print. PMID: 35999280.

4.1 LINKING PARAGRAPH

Chapter 2 highlights the most common measures used for strength assessment following ACLR. Isokinetic maximal (peak torque) hamstrings and quadriceps strength have been the gold standard of determining strength recovery in ACLR individuals. A growing body of evidence suggests that explosive strength (rate of force/torque development (RFD or RTD)) could be important with some studies showing differences in rate of recovery between explosive and maximal quadriceps strength. Chapter 2 also highlights the lack of reporting of strength measures between males and females even after evidence of poorer outcomes in the females after ACLR. Therefore, the aim of this study is to investigate explosive and maximal hamstrings and quadriceps strength recovery between males and females following ACLR.

4.2 ABSTRACT

Females have a higher risk of second anterior cruciate ligament (ACL) injuries than males. Hamstrings and quadriceps strength asymmetry are associated with an increased risk of a second ACL injury and emerging evidence have also shown the presence of rate of torque development (RTD) asymmetry and its potential implications to function after ACL reconstruction (ACLR). However, potential sex differences in quadriceps and hamstring strength and RTD throughout rehabilitation has not been previously studied. Therefore, this study was conducted to investigate the differences in maximal (isometric and concentric peak torque) and explosive (rate of torque development (RTD)) hamstring and quadriceps strength symmetry between males and females during early- and late-phase rehabilitation after anterior cruciate ligament reconstruction (ACLR) using hamstring tendon (HT) autografts and to determine the interaction of time and sex on maximal and explosive strength symmetry.

A total of 38 female and 51 male participants were assessed during early (3-6 months post-operative) and late (7-12 months post-operative) phases of rehabilitation following ACLR. Maximal (concentric and isometric peak torque) and explosive (isometric RTD) hamstring and quadriceps strength were assessed and presented as limb symmetry index (LSI).

Maximal concentric hamstrings asymmetry (Early: 86 ± 14; Late 92 ± 13; $p = 0.005$) as well as maximal concentric (Early, 73 ± 15; Late 91 ± 12; $p < 0.001$) and explosive (Early: 82 ± 30; Late: 92 ± 25; $p = 0.03$) quadriceps asymmetry decreased from early to late rehabilitation. However, there were no significant changes in maximal isometric quadriceps strength and explosive isometric hamstring strength in the same time period. Females had a larger asymmetry in maximal concentric (Females: 75 ± 17; Males: 81 ± 15; $p = 0.001$) and explosive (Females: 81 ± 32; Males:

89 ± 25; $p = 0.01$) quadriceps strength than males throughout rehabilitation. There were no sex differences in maximal and explosive hamstring strength. There were no sex by time interactions for any variables.

Explosive hamstring strength asymmetry did not improve despite recovery of maximal hamstring strength during rehabilitation following ACLR with HT autografts. While sex did not influence strength recovery, females had larger maximal and explosive quadriceps strength asymmetry compared to males throughout rehabilitation following ACLR.

4.3 INTRODUCTION

Anterior cruciate ligament (ACL) ruptures are traumatic injuries that commonly occur during jumping, cutting, and pivoting sports [1]. There is an increase in ACL injury rates in the last 15 years [4], with females reported to be at higher relative risks when compared to males [1]. Surgical management with ACL reconstruction (ACLR), a protracted rehabilitation period (6-12+ months), and financial costs between $100 million [4] to $2 billion annually [6] makes ACL injuries burdensome. However, despite ACLR and rehabilitation, poor outcomes related to return to sports [194], recurrent ACL injury [15], and knee osteoarthritis following the injury [20] are commonly reported. These poor outcomes have been reported to be worse in females than males [10, 195], suggesting a potential sex influence in outcomes following ACLR.

Hamstrings and quadriceps strength asymmetry are common after ACLR and have been previously reported to be graft-related (e.g., hamstring strength asymmetries more common with hamstring tendon graft use) [41]. These asymmetries are critical given the role of the hamstrings and quadriceps to knee joint stability [48]. Hamstring and quadriceps strength is commonly measured during maximal isometric or isokinetic contractions to assess strength recovery [50]. This is typically reported as between-limb strength or limb symmetry index (LSI) [33]. Greater levels of between leg asymmetry in hamstring and/or quadriceps strength is associated with poorer patient reported outcomes [196] and alterations in function and performance [196, 197]. Greater between leg quadriceps asymmetry has also been linked to an increased risk of re-injury [33]. Consequently, one of the main foci of rehabilitation and subsequent return to sports following ACLR is the recovery of hamstrings and quadriceps strength symmetry.

Recent body of evidence have shown that rate of torque development (RTD) or explosive strength might be an important criterion to assess strength recovery after ACLR [51]. Explosive strength is associated with knee function [59] and lower limb kinetics [55] following ACLR. Like maximal strength, explosive strength asymmetries are also found during the early (<6 months) [51, 55] and late phase (>7-12 months) [51] of rehabilitation following ACLR. However, there is some evidence that explosive quadriceps strength does not recover at the same rate as maximal quadriceps strength [52]. It is still inconclusive whether the same pattern of recovery exists in maximal and explosive hamstring strength. Given the common use of hamstring grafts, investigating explosive hamstring strength recovery in patients who had ACLR using hamstring tendon grafts is important to inform exercise selection during rehabilitation.

There is some evidence that maximal hamstring and quadriceps strength asymmetry following ACLR is more pronounced in females [59]. Kuenze et al [59] found that females have larger explosive quadriceps strength asymmetries compared to males. However, it is still not known whether females also have significant asymmetries in explosive hamstrings strength following ACLR. Additionally, whether recovery of maximal and explosive hamstrings and quadriceps strength differs between males and females is still unknown. Given the poorer outcomes in females and the potential implications of both maximal and explosive strength to these outcomes, understanding how males and females may recover differently during rehabilitation is an important first step in advancing the knowledge base in this area.

Therefore, the aims of this observational cohort study are 1) to investigate the effect of time on maximal and explosive hamstring and quadriceps strength asymmetry during the early and late phase of rehabilitation following ACLR using HT autografts, and 2) to explore the effect of sex on these asymmetries.

4.4 MATERIALS AND METHODS

4.4.1 Participants

This study was approved by the Australian Catholic University Human Research Ethics Committee (approval number:2017-17HC). The study utilised an observational cohort study design with data collected from a community-based clinic. Participants were recruited from a sports clinic between 2017 and 2018. These patients had suffered a primary ACL rupture and underwent a subsequent ACLR performed using either a semitendinosus tendon autograft (n = 47) or a semitendinosus with gracilis tendon autograft (n = 42) by 10 surgeons from the same clinic and one surgeon from another practice.

Recruited participants were assessed between 3-6 months (early rehabilitation period) and 7-12 months (late rehabilitation period) following their ACLR. These timepoints were utilised as six and 12 months are the most commonly used cut-off for return to sports participation (six months)

[157] and full clearance to return to sports (12 months) [13]. There was a total of 89 patients assessed during the early rehabilitation phase and 42 were re-assessed during the late rehabilitation phase. Rehabilitation was designed and prescribed by physiotherapists both from and external to the clinic in consultation with the patient's surgeon. Of the 89 patients, 48 had their rehabilitation supervised at the clinic while the remaining 41 patients undertook supervised rehabilitation programs from physiotherapists external to the clinic, but guidance was provided to the external physiotherapists on the rehabilitation approached used by the clinic. The rehabilitation protocol from the clinic included primary outcome measures related to: management of swelling/effusion; early restoration of knee extension and flexion; early ambulation; and recovery of hamstrings and quadriceps strength through gradual and progressive overload using open- and close-chain kinetic exercises [34]. Participants were progressed to running, plyometric training, and sports specific activities based on their progression from the aforementioned outcome measures [34].

Inclusion criteria were (1) age 15-40 years; (2) primary ACL injury; (3) unilateral ACLR using hamstring tendon autograft (semitendinosus only or semitendinosus with gracilis) taken from the injured leg; (4) ACLR within the previous three to six months prior to first testing session. Patients who had a previous ACLR or any other major knee joint/ligament injury were excluded. All participants provided written informed consent (or for minors, consent was provided by their guardian and the minor provided assent) to be included in the study.

4.4.2 Procedures

Data collection was performed during the participant's routine physiotherapy consultation in the clinic. All subjective and clinical assessments of the knee joint were collected during these visits which occurred between 3-6 months and 7-12 months after ACLR. Upon arrival at the clinic, participants completed the International Knee Documentation Committee (IKDC) which have been previously reported to be a valid and reliable measure of the participants' perception of their knee function and activities of daily living [158]. The participants then performed a strength testing battery for the hamstrings and quadriceps using an isokinetic dynamometer followed by a single leg hop for distance test [159].

Maximal voluntary contractions (MVC) of the hamstrings and quadriceps during isometric and concentric contractions were collected during the trials. Prior to strength testing, participants were asked to perform a 5-minute warm-up on a cycle ergometer using low resistance. Participants were then seated on a Humac Isokinetic Dynamometer (CSMi, Stoughton, MA, USA) with hips maintained at 85° of flexion throughout the test and the lateral epicondyle of the femur aligned with the fulcrum of the dynamometer. Correction for limb weight was taken before the test [160]. All dynamometer strength tests were conducted on each leg, commencing with the uninjured leg. Verbal encouragement and visual feedback was provided by the tester on all tests to motivate the participant to perform maximally throughout all measurements [160].

Isometric hamstrings and quadriceps strength testing commenced with the participant's knee 45° from full knee extension. The participant was instructed to pull the leg down (hamstring assessment) as hard and as fast as possible for three seconds, rest for two seconds, and then push the lower leg up (quadriceps assessment) as hard and fast as possible for three seconds. This was performed for three repetitions per muscle group [160]. The participant then rested for two minutes while seated on the dynamometer. While resting, range of motion for concentric strength testing was set at 0-90° of knee flexion (0° = full extension). For the concentric strength test, participants performed five repetitions of knee extension and flexion at 180°/sec, followed by 60°/sec. Participants performed one set of five consecutive MVCs at each movement velocity with a minimum of 30 seconds of rest between sets. Isokinetic/isometric strength testing is the gold standard for strength assessment following ACLR [50] and has been previously shown to be reliable (ICC = 0.81-0.97) [161].

After isokinetic strength testing, participants were then asked to perform a single leg hop for distance [159]. The test was performed by the participants barefooted, starting from a stationary position in a single leg stance with their hands placed on their lower back. The participant then performed a single hop for maximum distance, landing on the same leg [159]. The participant was required to hold their final landing position without their contralateral limb and/or their upper limbs touching down on the floor for the test to be considered successful. This was performed three times on each leg with the best score from three trials recorded in centimetres by measuring the distance covered from the line of the great toe before and after the hop [159].

4.4.3 Data Analysis

4.4.3.1 Data reduction

A custom-written software program was used to collect data (LabVIEW 2017 SP1; National Instruments, Austin, TX) from the isokinetic dynamometer with torque and time data captured at 1000 Hz. Once data was collected, another custom-written software package (LabVIEW 2017 SP1; National Instruments, Austin, TX) was used to individually process each set of data (isometric and concentric hamstring and quadricep repetitions) from each limb of each participant.

4.4.3.2 Maximal torque and rate of torque development (RTD)

Peak isometric and concentric hamstring and quadriceps strength as well as isometric RTD were determined for each limb at each testing velocity as the highest torque recorded during all repetitions. Peak RTD was defined as the greatest increase in force (increase in resting force ≥ 4N from onset of contraction) within a rolling 200ms window, which has previously been shown to be more reliable than alternative methodologies [53, 162]. We decided to collect RTD from isometric contractions as this was deemed more reliable compared to RTD from isokinetic efforts [53]. The isometric repetition with the greatest RTD (Nm/s) for the hamstrings and quadriceps was use for further analysis [163].

4.4.3.3 Limb symmetry index (LSI)

Limb symmetry index was calculated as the percentage of the injured limb relative to the uninjured limb for all strength assessments (MVC and RTD) and single leg hop distance, per the equation below [33].

$$LSI = \frac{\text{injured limb score}}{\text{uninjured limb score}}\ x\ 100$$

4.4.4 Statistical Analysis

To compare LSI from hamstring and quadriceps MVCs, RTD and single leg hop distance data between sexes across the early (3 to 6 months post-operative) and late (7 to 12 months post-operative) phases of ACL rehabilitation, a linear mixed model fitted with restricted maximum likelihood method was utilised with fixed factors of time (early/late) and sex (male/female) as well as the random factor of participant identification number. Interactions between sex and time were explored when a main effect was identified for both fixed factors. Where main or interaction effects were detected a post-hoc Students t-test was used to identify the differences. Statistical analysis was performed using JMP statistical software (Version 14.2.0 2018; SAS Institute, Cary, NC) with significance set at $p < 0.05$. A convenient sample size was used for this study. Post-hoc power analyses determined that when comparing between the early (n=89) and late (n=42) rehabilitation groups with isometric hamstring MVC as the outcome measure (d = 0.53), the study had a power of 0.88.

4.5 RESULTS

Participant demographic data, patient reported outcomes, and single leg hop for distance data can be found in Table 4.1 (early and late phases of rehabilitation) and Table 4.2 (between males and females).

Table 4.1. Summary of participant demographics, patient reported outcome questionnaires, and single leg hop for distance for all participants during the early and late phases of rehabilitation.

	Early Rehabilitation (n=89)	Late Rehabilitation (n=42)	*p value*
Age (years)	21 (18 to 25)	20 (18 to 25)	
Height (cm)	168 ± 6	175 ± 10	
Body mass (kg)	76 (66 to 86)	72 (66 to 84)	
Time from ACLR (months)	4 (4 to 5)	10 (9 to 11)	
IKDC	64 (59 to 70)	89 (83 to 95)	<0.001*
Single-leg hop (LSI)	77 ± 18	94 ± 11	<0.001*

Data presented as mean ± standard deviation for parametric data or median (interquartile range) for non-parametric data; *ACLR* anterior cruciate ligament reconstruction, *IKDC* International Knee Documentation Committee questionnaire, *LSI* limb symmetry index. *$p < 0.05$

Table 4.2. Summary of participant demographics, patient reported outcome questionnaires, and single leg hop for distance between males and females during the first assessment.

	Females (n=38)	Males (n=51)	*P value*
Age (years)	23 (20 to 29)	21 (18 to 25)	n.s.
Height (cm)	168 ± 6	182 ± 7	<0.001*
Body mass (kg)	66 (60 to 76)	82 (76 to 91)	<0.001*
Time from ACLR (months)	5 (4 to 5)	4 (3 to 5)	n.s.
IKDC	63 (59 to 69)	64 (60 to 75)	n.s.
Single leg hop for distance (LSI)	85 ± 18	86 ± 16	n.s.

Data presented as mean ± standard deviation for parametric data or median (interquartile range) for non-parametric data; *ACLR* anterior cruciate ligament reconstruction, *IKDC* International Knee Documentation Committee questionnaire, *LSI* limb symmetry index, *n.s.* not significant. *$p < 0.05$

4.5.1 Effect of time

Concentric hamstring MVC and isometric MVC LSI improved as a function of time, but isometric RTD LSI did not (Table 3). In addition, both concentric quadriceps MVC and isometric RTD LSI improved with time, but no change was observed for isometric MVC LSI (Table 4.3).

4.5.2 Effect of sex

No sex differences were found for any hamstring strength LSI measure (Table 4.4). Females had greater concentric quadriceps MVC and isometric RTD asymmetry, but no differences between groups were found for isometric MVC LSI (Table 4.4).

4.5.3 Sex by time interaction

No sex by time interactions were observed for any variables (Figures 4.1 and 4.2, Appendix A Table 4.1).

Table 4.3. Quadriceps and hamstring strength data in early and late-stage rehabilitation after anterior cruciate ligament reconstruction collapsed across males and females.

Strength measure	LSI (%)		Main effect
	Early rehabilitation	Late rehabilitation	Time
Concentric hamstring MVC (60°/sec)	86 ± 14	92 ± 13	0.005*
Concentric hamstring MVC (180°/sec)	88 ± 12	91 ± 13	0.023*
Isometric hamstring MVC	76 ± 17	84 ± 13	0.003*
Isometric hamstring RTD	86 ± 46	83 ± 22	n.s.
Concentric quadriceps MVC (60°/sec)	73 ± 15	91 ± 12	<0.001*
Concentric quadriceps MVC (180°/sec)	76 ± 14	87 ± 11	<0.001*
Isometric quadriceps MVC	87 ± 20	93 ± 20	n.s.
Isometric quadriceps RTD	82 ± 30	92 ± 25	0.033*

Data presented as mean ± standard deviation; *LSI* limb symmetry index, *MVC* maximum voluntary contractions, *RTD* rate of torque development, *n.s.* not significant. *$p < 0.05$

Table 4.4. Quadriceps and hamstring strength data for males and females collapsed across early and late rehabilitation after anterior cruciate ligament reconstruction.

Strength measure	LSI (%)		Main effect
	Females	Males	Sex
Concentric hamstring MVC (60°/sec)	88 ± 12	87 ± 15	n.s.
Concentric hamstring MVC (180°/sec)	90 ± 10	88 ± 14	n.s.
Isometric hamstring MVC	79 ± 17	78 ± 15	n.s.
Isometric hamstring RTD	85 ± 24	85 ± 49	n.s.
Concentric quadriceps MVC (60°/sec)	75 ± 17	81 ± 15	0.001*
Concentric quadriceps MVC (180°/sec)	76 ± 14	83 ± 13	<0.001*
Isometric quadriceps MVC	86 ± 20	92 ± 19	n.s.
Isometric quadriceps RTD	81 ± 32	89 ± 25	0.017*

Data presented as mean ± standard deviation; *LSI* limb symmetry index, *MVC* maximum voluntary contractions, *RTD* rate of torque development, *n.s.* not significant. *$p < 0.05$

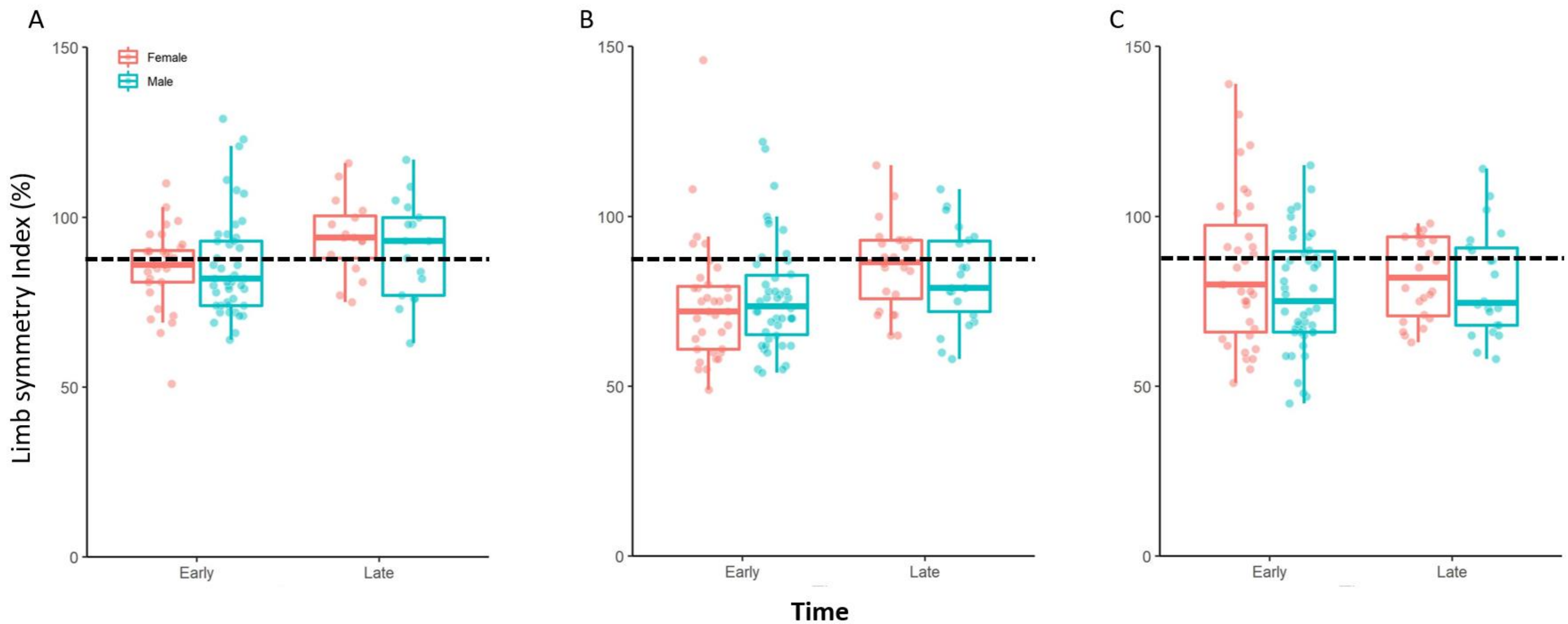

Figure 4.1. Hamstrings strength limb symmetry index (LSI) during maximal concentric strength at 60°/sec (A), maximal isometric strength (B) and explosive isometric strength (C) for males and females during early and late rehabilitation after anterior cruciate ligament reconstruction. Horizontal broken line within each panel in the figure represents 90% LSI. Note: There are 2 early datapoints from male participants (LSI scores: 180 and 444) and 1 late datapoint from a female participant (LSI score: 195) that are not visible in panel C due to the scale of the axis.

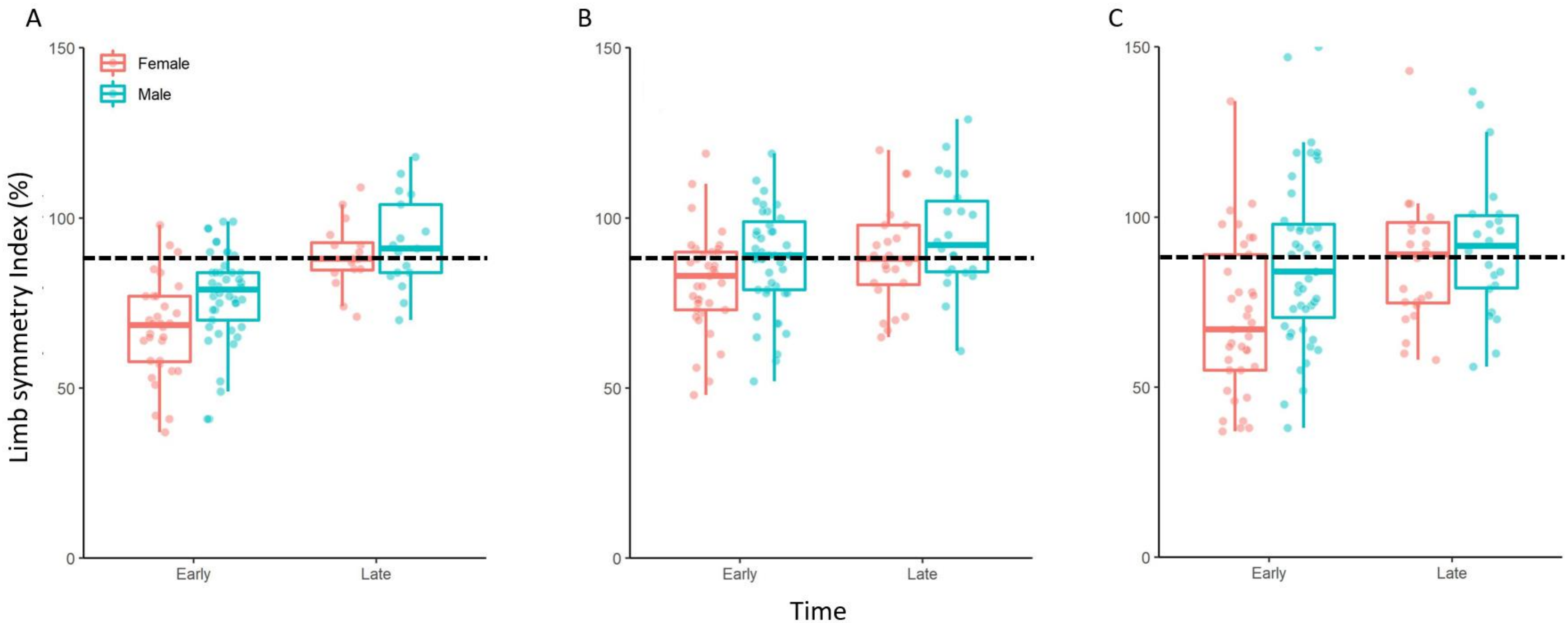

Figure 4.2. Quadriceps strength limb symmetry index (LSI) during maximal concentric strength at 60°/sec (A), maximal isometric strength (B) and explosive isometric strength (C) for males and females during early and late rehabilitation after anterior cruciate ligament reconstruction. Horizontal broken line within each panel in the figure represents 90% LSI. Note: There is 1 early male (LSI score: 160) and 1 late female (LSI score: 177) datapoint that are not visible in panel B due to the scale of the Y axis. Panel C has 2 females (LSI scores: 204 and 154) and 1 male (LSI score: 165) early datapoints and 1 females (LSI score: 177) late datapoint that are not visible due to the scale of the Y axis.

4.6 DISCUSSION

The most important finding of this study was that maximal hamstrings strength, but not explosive hamstrings strength improved over time following ACLR using HT autografts. Additionally, analysis of the effect of sex on strength following ACLR shows that females, when compared to males, typically had larger asymmetries in measures of maximal and explosive quadriceps strength but not for hamstring strength. The results of this study shows the importance of assessing explosive hamstring strength and incorporating exercises [54] that will address these qualities following ACLR with HT grafts. Additionally, even with the use of HT grafts, maximal quadriceps strength asymmetries are more prominent in females and should be one of the main aims of rehabilitation for females after ACLR.

Based on the results of this study, patients who had ACLR with HT autografts would show maximal hamstrings strength recovery (≥90% LSI) during late rehabilitation period even while still having significant explosive hamstring strength asymmetry. Previous studies have also found explosive hamstring strength deficits between 3-9 months [198] and 9-12 months [58] following ACLR. However, these results were taken from only one assessment timepoint. This is the first study to investigate explosive hamstring strength at different timepoints after ACLR. It has been previously proposed that RTD is an important neuromuscular quality, especially during jumping, landing, and change-of-direction tasks [53] and is related to sports performance that require rapid movements and muscle contractions [54]. As such, explosive hamstring strength asymmetry at the time of return to sport could potentially contribute to the risk of re-injury as ACL injuries typically occurs around 50 milliseconds after ground contact [199, 200]. However, this is speculative and future studies should determine if there is an association between explosive strength (i.e., RTD) after ACLR and subsequent rate of reinjury.

Potential changes to hamstring function following the tendon harvest may be a contributing factor to explain the persistence of asymmetry in explosive hamstring strength found in this study [201]. Regeneration of the hamstring tendon graft likely takes somewhere between 12 and 24 months [201, 202] which could affect force-transmitting capabilities [203]. Additionally, explosive muscle strength has been correlated with muscle morphology and fibre type distribution [53] which could have been altered due to graft-site morbidity [152, 204]. The persistence of explosive hamstring strength asymmetry could also be due to the choice of exercises performed during the rehabilitation period [51]. The recovery of maximal concentric and explosive quadriceps strength with persistence of explosive hamstring strength asymmetry in this study suggest that rehabilitation might have been sufficient to address quadriceps strength but not adequate to elicit a stimulus for explosive hamstring strength recovery after ACLR with hamstring autografts [38, 51].

Analysis of the effects of sex on maximal and explosive strength following ACLR showed that males and females are typically affected similarly in the hamstrings but not in the quadriceps. This is in contrast to the results by Nielsen et al. [198] who found significant effects of sex (female more impacted than males) in maximal and explosive hamstrings strength between 3-9 months following ACLR. An explanation for these differences could be the larger sample size, longer duration and the frequency and timing of testing throughout ACL rehabilitation (comparing early and late rehabilitation) in this study compared to their study. On the other hand, the larger maximal and explosive quadriceps strength asymmetries found in females compared to males are in agreement with the findings of Kuenze et al. [59], who also found similar results. One thing to note however, is that different graft types were used with their study population. In the present study, HT autografts were the graft of choice, which made the results somewhat unexpected given graft-related strength deficits are common after ACLR [41].

The exact mechanisms for the quadriceps strength differences between sex following ACLR is still inconclusive. One possible explanation could be the contribution of the inherent quadriceps morphological differences between males and females [205]. Quadriceps muscle atrophy is widely reported after ACLR and is proposed to result in quadriceps weakness [206]. Given that females tend to have smaller quadriceps muscle and Type II muscle fibre CSA compared to males [205], further atrophy from the injury could potentially exacerbate these leading to greater asymmetries in quadriceps strength. This may also be considered in the hamstrings where there are differences between sexes in muscle size [207], however as reported in this study we found no disparity in hamstring strength or RTD between males and females. Based on these findings, maximal and explosive quadriceps strength asymmetries can be expected in females following ACLR even when using HT autografts, however, the exact mechanism behind these changes are still to be determined. Overall, despite the recovery of maximal hamstrings strength throughout early and late rehabilitation, explosive hamstrings strength asymmetries tend to persist for both males and females. Sex did not influence recovery of any strength variable in this study. While females had larger quadriceps strength asymmetries overall, the rate at which this recover compared to males were similar.

The results of this study should be taken within the context of its limitations. First, the participants in this study were recruited from a single sports medicine clinic which received referrals from a small number of surgeons which ultimately reduced the heterogeneity of surgical approach. Because of this, we were unable to assess the effect that different graft types may have on the ability to restore hamstrings and quadriceps strength symmetry across ACL rehabilitation and the subsequent interaction with sex. Secondly, there were less participants who completed late rehabilitation assessments compared to early rehabilitation assessments. This was controlled for by including participant identification number as a random factor in our statistical approach, but this approach is not infallible. To provide further information, a post-hoc sensitivity analysis was conducted which included only participants (n = 42) who had early and late rehabilitation time points (Appendix A. Supplementary Table 4.2 and 4.3), noting that this approach has reduced statistical power compared to the main analysis. Thirdly, a dichotomised time-based definition (early and late rehabilitation) was utilised to determine the improvement in outcomes rather than grouping based on successfully meeting pre-determined criteria to progress from the early to the late-stage rehabilitation group. However, this approach was preferred as this is more relevant for clinicians in terms of what to expect from their patients at certain periods of their rehabilitation. Furthermore, whilst treating time from surgery as a continuous variable (as opposed to the dichotomised early and late rehabilitation) may appear appealing, this approach is confounded by limited available data at specific time points. Lastly, participants were not matched with a healthy control group. This would have helped in identifying whether the significant asymmetries found in this study were because of the interaction of ACLR and sex over time or were simply a normal physiologic difference in strength symmetry between males and females.

4.7 CONCLUSION

Following ACLR using HT autografts, explosive hamstring strength asymmetries persist despite recovery of maximal hamstring strength. These findings suggest that during rehabilitation from an ACLR, hamstring explosive strength does not recover to the same extent that maximal concentric and isometric hamstring strength does in patients who have had HT autografts. Additionally, even with previous findings of graft-related strength deficits, females who had ACLR with HT autografts are expected to have larger quadriceps strength asymmetries compared to males.

5 LOWER LIMB MUSCLE CONTRIBUTIONS TO SIDESTEP CUTTING TASKS AT RETURN TO SPORT AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

Note: This chapter is comprised of the following paper currently under preparation for submission at the *British Journal of Sports Medicine.*

San Jose AJ, Kotsifaki A, Whiteley R, Opar DA, Timmins, RG, Maniar N. Lower limb muscle contributions to sidestep cutting tasks at return to sport after anterior cruciate ligament reconstruction. British Journal of Sports Medicine. Under preparation.

5.1 LINKING PARAGRAPH

Chapter 4 shows the persistence of hamstring and quadriceps strength asymmetries throughout rehabilitation following anterior cruciate ligament reconstruction (ACLR). Assessment of lower limb function after ACLR is commonly directed at the hamstrings and quadriceps due to their role in lower limb biomechanics during dynamic tasks like sidestep cutting. However, this approach does not consider the potential contribution of other muscles to lower limb function during dynamic tasks. Alterations in lower limb biomechanics is associated with poor outcomes related to return to sport, reinjury and knee osteoarthritis following ACLR. Identifying the role and function of the different lower limb muscles may have implications in exercise selection during rehabilitation, which can help improve outcomes for ACLR individuals. Therefore, the aim of this study is to determine the differences in muscle contributions to vertical support, braking/propulsion, and redirection forces between the ACLR and healthy limbs during sidestep cutting tasks at return to sports (RTS) after ACLR.

5.2 ABSTRACT

The aim of this study was to explore lower limb muscle function (e.g., muscle contribution to ground reaction forces (GRFs)) during anticipated sidestep cutting following anterior cruciate ligament reconstruction (ACLR) and clearance to RTS. Differences between the ACLR, contralateral and healthy control limbs were evaluated. Three-dimensional motion capture and force plate data were collected in 49 male athletes (26 ACLR and 23 control) during an anticipated sidestep cutting task. Musculoskeletal modelling using static optimisation and induced acceleration analysis was performed to calculate individual lower limb muscle contributions to superior-inferior (vertical support), antero-posterior (braking-propulsion), and medio-lateral (redirection) GRFs during the stance phase of an anticipated sidestep cut. Between limb differences comparing the ACLR, contralateral, and control limbs were assessed using a linear mixed model analysis. Muscle contributions were lower in the quadriceps of the ACLR limb compared to the contralateral and control limbs during vertical support (contralateral mean difference = -0.040 BW.s, 95%CI = -0.049 to -0.031, $p < 0.001$; control mean difference = -0.042 BW.s, 95%CI = -0.061 to -0.022, $p < 0.001$) and braking (contralateral mean difference = 0.020 BW.s, 95%CI = 0.014 to 0.027, $p < 0.001$; control mean difference = 0.029 BW.s, 95%CI = 0.017 to 0.041) GRFs. The quadriceps of the ACLR limb also contributed less to medial redirection (contralateral mean difference = -0.006 BW.s, 95%CI = -0.01 to -0.001, $p = 0.011$) GRFs compared to the contralateral limb. There were also less muscle contributions to vertical support from the gluteus maximus, braking from the dorsi-flexors, and propulsion from the plantar flexors of the ACLR limb compared to the contralateral limb. Despite clearance for RTS, lower limb muscle function, especially in the quadriceps, is still altered during sidestep cutting task among male athletes following ACLR.

5.3 INTRODUCTION

Anterior cruciate ligament (ACL) rupture is a common injury to the knee [3] which is commonly managed through ACL reconstruction (ACLR) and subsequent rehabilitation (typically lasting up to 12 months) [13, 208]. Direct and indirect costs of ALCR management places a burden on the health care system with annual costs from $100 million and up to $2 billion in Australia and the United States respectively [4, 6]. Despite ACLR and rehabilitation, the rate of return to previous level of competition and performance is poor among ACLR individuals. Compounding this further, recurrent ACL injury [9], and development of knee osteoarthritis [20] is common following the initial injury. Much work is still required to identify factors that can improve patient outcomes following ACLR.

A fundamental goal of rehabilitation following ACLR is to progress the patient's ability to complete weight-bearing activities [209]. This includes the progression from walking to more high demand tasks which are commonly seen in team sports, such as running and sidestep cutting [210, 211]. The ability to perform sidestep cutting tasks is particularly important as it is not only a task frequently seen during many sports [210, 211] it is also a common mechanism of ACL injury [212, 213]. Previous studies on the biomechanics of the sidestep cut after ACLR have shown differences (e.g., less knee flexion angle, lower knee extension moment) in the ACLR limb compared to the contralateral limb [86, 88, 90, 214]. However, the majority of these studies explored lower limb biomechanics at a joint level [86, 214]. While useful, this does not take into account the complex role of the different lower limb muscles during the performance of a dynamic task [215]. A recent study by Maniar et al [67] explored lower limb muscle contributions to superior-inferior (vertical support), antero-posterior (propulsion and braking), and medio-lateral (redirection) ground reaction forces (GRF) during sidestep cutting in healthy individuals. This study reported that the quadriceps, gluteus maximus and medius, the hamstrings, and the plantar flexors were found to be major contributors to the GRFs needed to execute a sidestep task [67]. Given the common deficits in lower limb muscle function reported following ACLR [39, 51, 57, 83, 197, 203] and the importance of the proper execution of a sidestep cut task after return to sport (RTS) [211], understanding how ACLR might effect lower limb muscle contributions to a sidestep cut is needed. Understanding how ACLR effects lower limb muscle function during a sidestep cut could be beneficial in understanding the effect of the injury and inform more targeted rehabilitation to improve outcomes.

Therefore, the aim of this study was to investigate lower limb muscle contributions to vertical support, braking, propulsion, and redirection forces during sidestep cutting tasks at RTS after ACLR. Specifically, this study will compare vertical support, braking, propulsion, and redirection forces between the injured and uninjured limbs of individuals who have had an ACLR as well as comparisons to healthy controls.

5.4 METHODS

5.4.1 Study design

This case-control study is part of a larger body of work investigating RTS criteria following ACLR rehabilitation [84]. Data collection was performed at the biomechanics laboratory of the Aspetar Orthopaedic and Sports Medicine Hospital. Participants recruitment was performed between 2018 and 2019. Informed consent was obtained from all participants prior to participating in the study. Ethics approval was granted for this study (IRB F2017000227) while approval for the transfer and use of previously collected and non-identifiable data was given by the Australian Catholic University Human Research Ethics Committee (Registration number: 2021-29N).

5.4.2 Participants, inclusion, and exclusion criteria

Forty-nine participants took part in this study, 26 males in the ACLR group and 23 healthy males in the control group. Participants in the ACLR group were athletes (pre-injury Tegner Activity scale score ≥7) between 18 and 35 years who had a unilateral ACLR either by a hamstring tendon (semitendinosus + gracilis) or a bone-patellar tendon-bone autograft from their ispsilateral limb. Recruitment of the ACLR group was performed after the completion of a supervised rehabilitation program and subsequent clearance to RTS at Aspetar Orthopaedic and Sports Medicine hospital. Criteria for RTS clearance included (1) clearance from both their surgeon and physiotherapist, (2) completion of a sports-specific on-field rehabilitation program, (3) quadriceps strength (LSI ≥ 90%), and (4) hop test performance (LSI ≥ 90%) [34]. Participants with full thickness articular cartilage lesion and any other major lower extremity injury in both limbs were excluded from the study (e.g., concomitant grade III ligament injury other than ACL). The control group was recruited through referrals from other professionals and sports performance centres. Inclusion criteria for the control group were age (between 18-35 years), Tegner score of ≥7, Level I or II sports participation (≥ 3 times/week), and no history of any lower limb injury (i.e., muscle strains) in the last three months prior to testing.

5.4.3 Equipment, participant preparation and marker setup

Forty-three reflective markers were attached to the participant based on a full-body Plug-in Gait marker system together with additional markers to the sacrum, medial knee and ankle [166] as well as three marker clusters on the lateral thigh and shank [167]. A 14-camera Vicon motion capture system (250Hz, Vicon, Oxford, UK) together with five ground-embedded force plates

(1000 Hz, Kistler, Switzerland) were used to collect three-dimensional marker trajectories and ground reaction forces, respectively.

5.4.4 Experimental procedure and testing

All participants were familiarised to the procedures and tasks before data collection. A 7-minute warm up consisting of running, side running, deep squats, and double leg jumps was performed prior to testing. All participants were wearing shorts and shoes during the performance of the tasks during the warmup and testing. For the sidestep cut task, participants started in a standing position, six metres away from the force plates. They were then given instructions to accelerate maximally towards the force plates, performing three trials of an anticipated 45-degree sidestep cut to the left and to the right. For a trial to be successful, a clear foot contact of the plant foot on the force plate was needed. Both limbs were tested, and coin toss was used to randomise the order of testing for each limb.

5.4.5 Musculoskeletal modelling

Data analysis was performed using previous methods as described by Maniar et al. [47, 67, 216]. A semi-automated analysis via a custom R code (R core team, 2020) interfaced with OpenSim v4.2 [168] was performed to analyse data. A generic musculoskeletal model was scaled to the individual anthropometry of the participant based on a static trial [170]. To calculate joint angles during the task, an inverse kinematics algorithm was used by means of a weighted least-squares optimisation that minimises the difference between model and experimental marker positions during the static and dynamic trials [172]. Generalised forces and moments for these movements were then obtained via inverse dynamics. Static optimisation was then used to transform these joint moments into individual lower-limb muscle forces. To provide an estimate of muscle contributions to the deceleration (braking), acceleration (propulsion), vertical support, and redirection of the centre of mass during the tasks, an induced acceleration analysis was then performed [183, 184]. For this, a universal “rolling on ground” constraint (foot-ground interaction model) was utilized as per previous methods [46, 66].

5.4.6 Data processing

Muscle contributions to GRFs (expressed using the global reference frame) were first normalized to bodyweight (BW) and subsequently integrated with respect to time to determine the net impulse during stance phase (BW.sec). Due to the large number of musculotendinous actuators in the model, we focused on muscle groups previously shown to contribute to GRFs during weightbearing tasks [48, 66, 67]: quadriceps (sum of rectus femoris and vastus intermedius, medialis and lateralis), soleus, gastrocnemius (sum of medial and lateral gastrocnemius), gluteus maximus, gluteus medius, hamstrings (sum of biceps femoris long head, semimembranosus, semitendinosus), and ankle dorsi-flexors (sum of tibialis anterior, extensor hallucis longus, extensor digitorum longus) of the stance leg. Determination of the direction of muscle GRFs were performed to classify their contribution to vertical support (superior or inferior direction), braking (posterior direction) and propulsion (anterior directed), as well as redirection (medial or lateral direction).

5.4.7 Statistical analysis

Descriptive statistics were used to summarise participant characteristics. Shapiro-Wilk test was used to check for normality of distribution of the demographic data of the participants [187]. A Student t-test was used ($p < 0.05$) to determine between group comparisons of the participants’ demographic data. Linear mixed effects models [192] was used to determine if differences existed in the vertical support, braking and propulsion, and redirection GRFs for each muscle listed above. For ease of understanding, muscle contribution to – vertical support refers to its role in accelerating the center-of-mass upward; braking and propulsion refers to decelerating and accelerating the body's centre-of-mass, respectively; and redirection refers to whether the muscle is contributing to directing the body medially (to the direction of the cut) or in the opposite direction. For each linear mixed model, limb (ACLR, contralateral, healthy control) was modelled as a fixed effect and participant ID as a random effect. Mixed models were also adjusted for approach velocity by taking the average centre-of-mass forward velocity, 50ms prior to foot contact. This was performed to address any potential confounder as a result of any variations between groups or trials (e.g., participants may have slower approach in the ACLR limb compared to the contralateral and control limbs). For any significant limb effects, a post-hoc pairwise comparison using Tukey's method was performed [193]. Visual inspection of qqplots and residual plots were performed to verify data assumptions (e.g., distributions). A significance of $p < 0.05$ was set for all analysis.

5.5 RESULTS

Participant demographic and results of RTS testing can be found in Table 5.1. Mean approach velocity during the tasks were 3.7 ± 0.6 m/s for the ACLR leg, 3.9 ± 0.5 m/s for the contralateral leg, and 4.4 ± 0.6 m/s for the healthy control leg.

5.5.1 Vertical support (Superior-inferior forces)

Contribution to vertical support from the quadriceps was lower in the ACLR limb compared to the contralateral (mean difference = -0.040 BW.s, 95%CI = -0.049 to -0.031, $p < 0.001$, Figure 2-b) and control limbs (mean difference = -0.042 BW.s, 95%CI = -0.061 to -0.022, $p < 0.001$, Figure 2-b). Muscle contributions to vertical support was also lower in the gluteus maximus of the ACLR limb compared to the contralateral limb (mean difference = -0.005 BW.s, 95%CI = -0.009 to -0.001, $p < 0.001$, Figure 2-d).

Table 5.1. Participant demographics, patient reported outcome measures, quadriceps strength, and single leg hop for distance performance used as criteria for clearance to RTS

	ACLR group (n=26)	Control group (n=23)	*p value*
Age (years)	23.2±3.4	28.3±4.4	<0.001*
Body mass (kg)	71.4±12.1	76.1±7.4	0.10
Height (cm)	173 (166 to 182)	178.2±6.9	0.18
Body mass index ($kg.m^{-2}$)	23.3±2.3	23.9±1.6	0.24
Tegner score pre-injury	9 (9 to 9)	7 (7 to 9)	<0.001
IKDC	94.9±7.0	100	0.002
ACL-RSI	92.0±10.6	NA	NA
Quadriceps strength LSI %	94±6	NA	NA
SLHD LSI %	97±4	100±5	0.01*
Return to sport (months)	9.5±2.7	NA	NA
ACL hamstrings autograft, n (%)	10 (38)	NA	NA
Isolated ACL injury, n	15	NA	NA
Meniscal injury, n	11	NA	NA
Cartilage lesion, n	2	NA	NA

Values are presented as mean ± standard deviation for normally distributed data and median (interquartile range) for not normally distributed data, unless otherwise stated. ACLR, anterior cruciate ligament reconstruction; ACL-RSI, Anterior Cruciate Ligament-Return to Sport; IKDC, International Knee Documentation Subjective Knee questionnaire; LSI, Limb Symmetry Index; NA, not available; RTS, return to sports; SLHD, single leg hop for distance. *$p < 0.05$

5.5.2 Braking and propulsion (Antero-posterior forces)

Braking or propulsive forces were represented by posteriorly directed (negative direction) or anteriorly directed (positive direction) GRFs respectively (Figure 1 and 2, a-g). Muscle contributions to braking forces were less in the quadriceps of the ACLR limb compared to the contralateral (mean difference = 0.020 BW.s, 95%CI = 0.014 to 0.027, $p < 0.001$, Figure 1-b) and control (mean difference = 0.029 BW.s, 95%CI = 0.017 to 0.041, $p < 0.001$, Figure 2-b) limbs. Braking forces from the dorsi-flexors were also lower in the ACLR limb compared to the contralateral (mean difference = 0.015 BW.s, 95%CI = 0.010 to 0.019, $p < 0.001$, Figure 1-g) and control (mean difference = 0.011 BW.s, 95%CI = 0.003 to 0.020, $p = 0.006$, Figure 2-g) limbs. Additionally, contributions to propulsion from the gastrocnemius (mean difference = -0.007 BW.s, 95%CI = -0.009 to -0.004, $p < 0.001$, Figure 2-c) and soleus (mean difference = -0.009 BW.s, 95%CI = -0.012 to -0.006, $p < 0.001$, Figure 2-a) were less in the ACLR limb compared to the contralateral limb.

5.5.3 Redirection (mediolateral forces)

There were less muscle contributions to the medial GRF (i.e., toward the intended direction of the cut) from the quadriceps of the ACLR compared to the contralateral limb (mean difference = -0.006 BW.s, 95%CI = -0.01 to -0.001, $p = 0.001$, Figure 2-b). In contrast, greater contributions to medial forces from the hamstrings (mean difference = 0.001 BW.s, 95%CI = 0.0004 to 0.002, $p = 0.001$, Figure 2-f), gastrocnemius (mean difference = 0.004 BW.s, 95%CI = 0.0009 to 0.006, $p = 0.006$, Figure 2-c), and soleus (mean difference = 0.007 BW.s, 95%CI = 0.003 to 0.011, $p < 0.001$, Figure 2-a) were found in the ACLR compared to the contralateral limb. Lateral forces were also produced during the sidestep cut and was directed in the negative direction (away from the direction of the cut). The gluteus maximus (mean difference = -0.002 BW.s, 95%CI = -0.003 to -0.0004, $p = 0.006$, Figure 2-d) and dorsi-flexors (mean difference = -0.004 BW.s, 95%CI = -0.006 to -0.001, $p < 0.001$, Figure 2-g) of the ACLR limb contributed more to the lateral forces compared to the contralateral limb

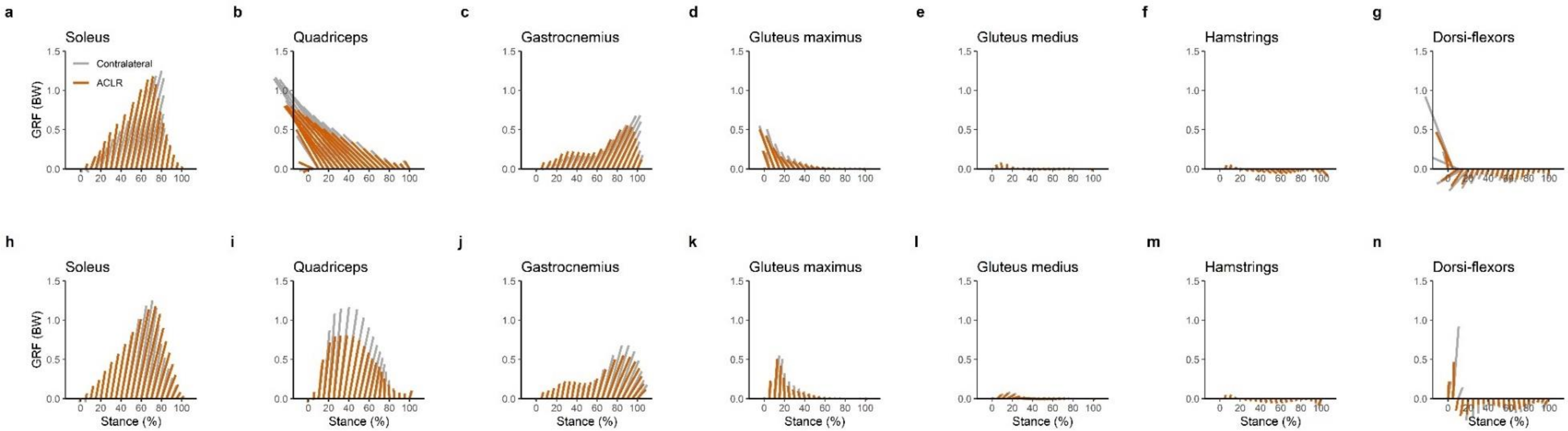

Figure 5.1. Individual lower limb muscle contributions to the ground reaction force (GRF) expressed relative to bodyweight (BW) in the sagittal (top row; a-g) and frontal plane (bottom row; h-n) between the ACLR limb (orange vector) and contralateral limb (grey vector) during the stance phase of an anticipated 45-degree sidestep cut. Note that the top row contains upward or downward vectors that represents superior or inferior GRF, respectively, while the rightward or leftward vectors represent either anterior or posterior GRFs, respectively. The bottom row contains upward or downward vectors that represents superior or inferior GRF, respectively, while rightward or leftward vectors represent either medial (toward the intended direction of the cut) or lateral GRFs, respectively. ACLR, anterior cruciate ligament reconstruction; BW, bodyweight; GRF, ground reaction force.

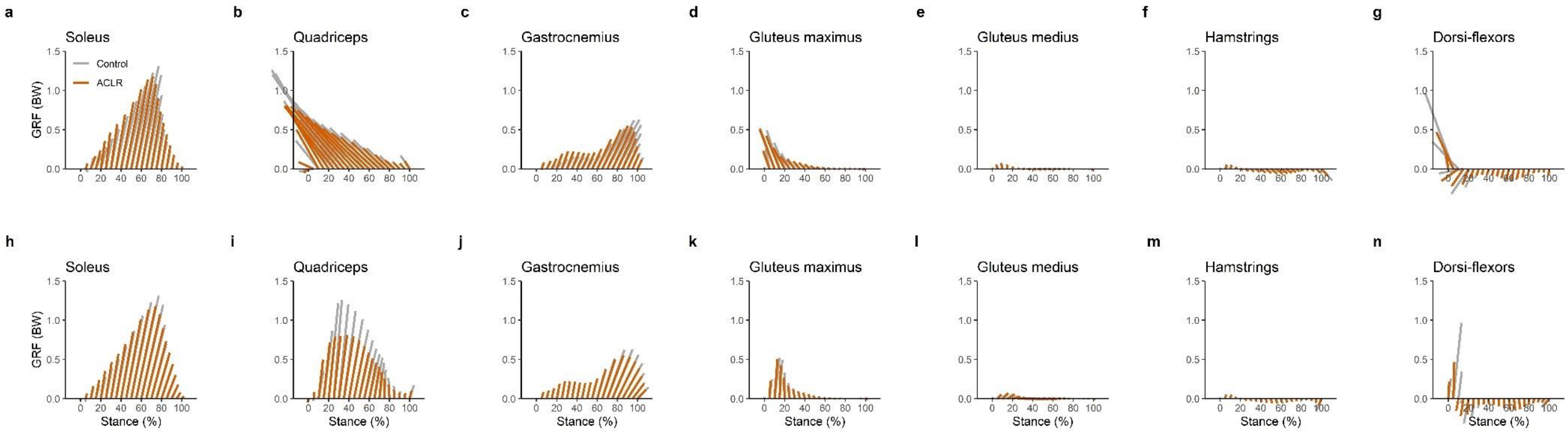

Figure 5.2. Individual lower limb muscle contributions to the ground reaction force (GRF) expressed to the bodyweight (BW) in the sagittal (top row; a-g) and frontal plane (bottom row; h-n) between the ACLR limb (orange vector) and control limb (grey vector) during the stance phase of an anticipated 45-degree sidestep cut. Note that the top row contains upward or downward vectors that represent superior or inferior GRF, respectively, while the rightward or leftward vectors represent either anterior or posterior GRFs, respectively. The bottom row contains upward or downward vectors that represents superior or inferior GRF, respectively, while rightward or leftward vectors represent either medial (toward the direction of the intended cut) or lateral GRFs, respectively. ACLR, anterior cruciate ligament reconstruction; BW, bodyweight; GRF, ground reaction force.

5.6 DISCUSSION

The primary aim of this study was to identify differences in muscle contributions to vertical support, braking/propulsion, and redirection forces between the ACLR, contralateral, and control limbs during a sidestep cut. The most pertinent findings were the lower contributions from the quadriceps of the ACLR limb to vertical support, braking, and medial redirection GRFs compared to the contralateral and control limbs during sidestep cutting tasks. Reductions in muscle contributions to vertical support (gluteus maximus), braking (dorsiflexors), and propulsion forces (gastrocnemius, soleus) from the ACLR limb were also found. Finally, compared to the contralateral limb, the gluteus maximus and the dorsi-flexors, contributed more to lateral directed GRF, while the gastrocnemius, soleus, and hamstrings had larger contributions to medial redirection forces in the ACLR limb compared to the contralateral limb.

To our knowledge, this is the first study to explore differences in muscle contributions to sidestep cutting between ACLR, contralateral, and control limbs. Similar to previous studies on sidestep cutting [67] walking [68], running [66, 183], single-leg forward and backward acceleration [217], and landing [46], the quadriceps were the major contributor to vertical support, braking, and medial redirection forces in this study (Figures 5.1b, 5.1i, 5.2b, 5.2i). However, our findings show that these contributions were significantly lower in the ACLR limb compared to the contralateral (Figure 5.1b, Figure 5.1i) and control limbs (Figure 5.2b, Figure 5.2i). Rehabilitation programs have focused on quadriceps strength recovery given the common alterations in quadriceps strength, activation [35], volume and size [206], rate of torque development [51], and force production [91] seen after ACLR. Based on our findings, it appears that rehabilitation might be sufficient to restore maximal quadriceps strength but not fully restore the quadriceps' contribution to a sidestep cut.

Compared to previous work previous work on sidestep cutting in uninjured individuals [67], we also found that the gluteus maximus, dorsi-flexors, and plantar flexors (gastrocnemius and soleus) were major contributors to vertical support, braking, and propulsion forces during the stance phase of a sidestep cut. However, these contributions were all lower in the ACLR limb compared to the contralateral limb in this study (Figures 1a-g and Figure 2a-g). that the majority of the literature has focused on muscle function and strength recovery of the quadriceps and hamstrings following ACLR [23, 25, 38, 218]. Our findings show that other muscles of the lower limb, which are important for the execution of a sidestep cut are also affected after ACLR. The reason for these impairments are still unknown. Much of the work done to explore these muscles (gluteus maximus, dorsi-flexors, and plantar-flexors) have been on their joint level function (e.g., hip extensors, plantar-flexors) and strength [39, 132, 219-223]. Muscle coordination and dynamic coupling in movement tasks is important during activities of daily living and execution of dynamic tasks (e.g., jumping/landing, sidestep cutting) [70, 190, 215, 224]. The presence of impairments in the gluteus maximus, dorsi-flexors, and plantarflexors could contribute to the persistence of alterations in movement mechanics even after RTS seen in this study and in the literature.

The hamstrings and plantar flexors all had larger contributions to forces towards the direction of the cut (medial redirection) in the ACLR limb compared to the contralateral limb (Figure 5.1f). Similarly, the gluteus maximus (Figure 5.1d) and dorsi-flexors (Figure 5.1e) also had greater contributions but towards the opposite direction of the cut (lateral redirection). There is evidence that muscle strength and kinematic impairments follow a different time-course of recovery after ACLR [224, 225]. As such, the presence of strength asymmetry in the quadriceps and/or other lower limb muscles during rehabilitation could lead to changes in muscle coordination and task compensations that may persist even after restoration of strength [224, 225]. It could be that the reduction in the ability of the quadriceps to produce medial redirection forces necessitated an increase in hamstring and plantar flexor contribution.

The findings of this study provide several considerations for designing a rehabilitation program and assessing recovery of lower limb muscle function following ACLR. Despite restoration of isokinetic strength symmetry (LSI ≥ 90%) in this study, the quadriceps contribution to sidestep cutting appears still lower in ACLR limbs. Other muscles or muscle groups, like the gluteus maximus, dorsi-flexors, and plantarflexors of the ACLR limb also showed a reduction in their contributions to sidestep cutting performance. These reductions in muscle contributions to task performance in the ACLR limb, could have implications for the ability of an ACLR individual to fully compete in sports. Indeed, up to 50% ACLR individuals are not able to return to their previous performance despite ACLR and rehabilitation [7]. Current assessment of lower limb strength and function following ACLR is focused on the hamstrings and quadriceps. While it appears that strength assessment alone (at least in the quadriceps) does not highlight the underlying deficits in function, it should be noted that given the findings of this study, an emphasis on assessment and targeted interventions for other lower limb muscles (e.g., gluteus maximus and plantarflexors)should be considered in rehabilitation following ACLR.

The results of this study also suggest that the use of limb symmetry (typically ≥ 90% LSI) in isokinetic strength and hop test for distance may lack external validity in relation to the performance of dynamic tasks (e.g., jumping/landing, cutting). Commonly used functional tests such as hopping for distance performance [34, 98] may not directly relate to quadriceps function and can be compensated for with other lower limb muscles or movement mechanics [84, 226]. Biomechanical analysis during relevant tasks (e.g., running, jumping/landing, cutting) may be necessary to better understand recovery from ACLR and subsequent readiness to RTS [227, 228].

We acknowledge that there were limitations to the current study. Firstly, only male participants were included in the present study. Females have been reported to have different kinematic and kinetic profiles compared to males [229, 230], therefore the generalisability of our results should be taken with caution. Additionally, given the higher relative risk of ACL injuries/re-injuries in females compared to males [1, 10], future studies focusing or including females is warranted. Second, this study explored muscle contributions to anticipated sidestep cutting which could have influenced the technique taken by the participants. Previous studies have shown differences to kinematics and kinetics between anticipated and unanticipated sidestep cutting [231] thus exploring muscle contributions to unanticipated sidestep cutting tasks is needed to answer whether the change in planning alters the muscle contribution as well. We used static optimisation to calculate muscle forces in this study. While this allows for estimation of muscle forces, direct validation of in-vivo muscle forces through non-invasive techniques is not feasible [182]. However, static optimisation has been previously reported to be a valid method of estimating joint contact forces, at least in walking [232]. As joint contact forces are highly dependent on muscle forces, this serves as an indirect validation of the muscles forces in this study [68]. Lastly, the current study utilised a universal “rolling on ground” foot model to calculate individual muscle contributions. Muscle contributions to the mediolateral GRF, particularly from the plantar flexors, are reported to be sensitive to the type of foot model used for GRF decomposition which could have influenced our results [185]. However, this model is the most commonly used in prior research and was reproduces experimental GRFs (see Chapter 3, Figure 3.3).

5.7 CONCLUSION

In conclusion, lower muscle contributions to vertical support, braking, propulsion, and redirection were found in the quadriceps of ACLR limbs compared to their contralateral and to control limbs. In addition, lower muscle contributions from the dorsiflexors (braking), plantar flexors (propulsion), and gluteus maximus (vertical support) were also found in the ACLR limb compared to the control limb. Lastly, compared to the contralateral limb, the hamstrings and plantar flexors as well as the gluteus maximus and dorsiflexors of the ACLR limb, contributed more to medial and lateral redirection respectively. Based on the findings of this study, alterations in lower limb muscle contributions to sidestep cutting could persist in ACLR individuals despite rehabilitation and clearance to RTS.

6 LOWER PATELLOFEMORAL JOINT CONTACT FORCE DURING SIDE-STEP CUTTING FOLLOWING RETURN TO SPORT CLEARANCE AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

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6.1 LINKING PARAGRAPH

Chapter 5 investigated how the different muscles of the lower limbs contribute to the execution of a sidestep cut, with the quadriceps in ACLR limbs showing significant deficits in modulating forces during sidestep cutting compared to healthy limbs. This was despite restoration of isokinetic quadriceps strength above the common clinical cutoff (limb symmetry index, LSI $\geq$ 90). Beyond the ability to execute dynamic tasks, the restoration of normal patellofemoral joint (PFJ) loading (contact forces) has been shown to be important for the long-term outcomes of an ACLR individual. Reduction in PFJ contact forces has been associated with the onset of knee osteoarthritis with 1-5 years following anterior cruciate ligament reconstruction (ACLR). A major factor associated with the reduction in PFJ contact forces after ACLR is quadriceps weakness. However, no study has explored PFJ contact forces after restoration of quadriceps strength asymmetry after ACLR. Therefore, the main aim of this study is to compare PFJ contact forces during sidestep cutting between the ACLR and healthy limbs after restoration of quadriceps strength asymmetry at the time of RTS.

6.2 ABSTRACT

Low patellofemoral joint (PFJ) contact force has been associated with PFJ osteoarthritis. Quadriceps force and knee flexion angles, which are typically altered after an ACLR, primarily influence PFJ contact forces. It is still inconclusive whether differences in PFJ contact forces are present during high knee flexion tasks like sidestep cutting after clearance to return to sport (RTS) following ACLR. This case-control study aims to explore PFJ contact forces in the ACLR limb and compare it with the contralateral and control limbs during sidestep cutting tasks following clearance to RTS. A total of 26 ACLR male athletes who were previously cleared to RTS were matched with 23 healthy control males. Three-dimensional motion capture and force plate data were collected while both groups performed anticipated sidestep cutting tasks. Joint kinematics, kinetics, muscle forces, and PFJ contact forces were calculated using musculoskeletal modeling. Results show peak PFJ force was lower in the ACLR limbs compared to the contralateral limbs (mean difference = 5.89 BW, 95%CI = 4.7 to 7.1, $p < 0.001$) and the control limbs (mean difference = 4.44 BW, SE = 2.1 to 6.8, p = < 0.001). During peak PFJ force, knee flexion angle was lower in ACLR limbs compared to the contralateral (mean difference = 4.88°, 95%CI = 3.0 to 6.7, $p < 0.001$) and control limbs (mean difference = 6.01°, 95%CI = 2.0 to 10.0, $p < 0.002$). Lower quadriceps force compared to the contralateral (mean difference = 4.14 BW, 95%CI = 3.4 to 4.9, $p < 0.001$) and control limbs (mean difference = 2.83 BW, 95%CI = 1.4 to 4.3, $p < 0.001$) were also found at this time. In conclusion, lower PFJ contact forces and a combination of quadriceps force deficits and smaller knee flexion angle were found in the ACLR compared to the contralateral and control limbs even after clearance to RTS.

6.3 INTRODUCTION

Rupture of the anterior cruciate ligament (ACL) is one of the most common injuries in the knee [3]. Typical management of an ACL rupture usually includes ACL reconstruction (ACLR) [208] followed by ~6-12 months of rehabilitation to restore knee joint stability [13]. Despite this, poor patient reported outcomes related to knee function [233], high reinjury risk [9], and accelerated onset of knee osteoarthritis [20] are common after ACLR. The development of knee osteoarthritis has been reported as early as three years following ACLR [208]. Given the high rates of ACLR in young athletes (<25 years) [4], early knee joint degeneration can lead to a significant number of young individuals with impaired function and reduced quality of life due to knee osteoarthritis [21, 234].

Alterations in lower limb biomechanics are common following ACLR [77]. Smaller knee flexion angle, reduced knee flexion excursion as well as lower knee extension moments are commonly reported in the ACLR leg compared to the contralateral leg and healthy controls during tasks like gait and running [77, 79]. Furthermore, lower knee joint contact forces are common after ACLR [75, 83, 90] with lower knee joint contact force during walking associated with the development of knee osteoarthritis five years after ACLR [75]. Most of the studies on knee joint contact force and osteoarthritis risk after ACLR has focused on the tibiofemoral joint (TFJ) [47, 75, 88, 90, 216, 235]. However, patellofemoral joint (PFJ) osteoarthritis is reported to be as high as 80% following ACLR [72] and is associated with greater disabilities compared to osteoarthritis in other knee compartments [22]. Therefore, identifying possible mechanisms related to the increased risk in PFJ osteoarthritis may be important in order to improve patient outcomes following ACLR.

Throughout ACLR rehabilitation, individuals progress from normal gait tasks to more dynamic movements like running, jumping and sidestep cutting [209]. Of these tasks, the sidestep cut is one of most physically demanding and commonly performed task in team sports and is a common mechanism of ACL injury [212, 213]. During sidestep cutting, large loads in the PFJ can occur due to the high knee flexion angles and quadriceps force commonly seen during the execution of the task [231]. The interaction between knee flexion angle and quadriceps force determines the total compressive forces at the PFJ [236]. Given that quadriceps weakness[44] and reduced knee flexion angle during tasks (e.g., sidestep cutting)[88] are common in ACLR individuals, these could potentially lead to alterations in PFJ contact forces. Previous studies have investigated PFJ contact forces following ACLR during walking, running, and single leg forward hopping [80, 85, 92, 237, 238]. Results from these studies suggest reductions in PFJ contact forces could be secondary to the presence or combination of reduced quadriceps strength and lower peak knee flexion angles, as well as psychological factors related to fear of reinjury and/or instability and compensatory strategies to underload the ACLR limb. However, no study has yet to investigate PFJ contact force in ACLR individuals who have successfully passed RTS criteria (e.g., quadriceps strength symmetry >90%). Furthermore, PFJ contact forces during a high-demand task like side-step cutting has yet to be examined.

Therefore, the aim of this study was to investigate PFJ contact forces during the performance of sidestep cutting task in ACLR individuals at the time of return to sport (RTS) clearance and compare this to the contralateral limb and a healthy control group. Our hypothesis was that there will be lower PFJ contact forces in the ACLR limb compared to the contralateral and healthy control limbs. Additionally, differences in knee joint angle and quadriceps muscle forces between the ACLR, contralateral, and healthy control limbs were also explored.

6.4 METHODS

6.4.1 Participants

Forty-nine participants agreed to take part in this study (Figure 6.1). Twenty-six males who had been cleared for RTS following ACLR and 23 healthy males who served as the control group. Participants in the ACLR group were athletes (pre-injury Tegner score ≥ 7) between 18 and 35 years who had a unilateral ACLR either by a hamstring tendon - semitendinosus + gracilis (n=10) or a bone-patellar tendon-bone (n=16) autograft.

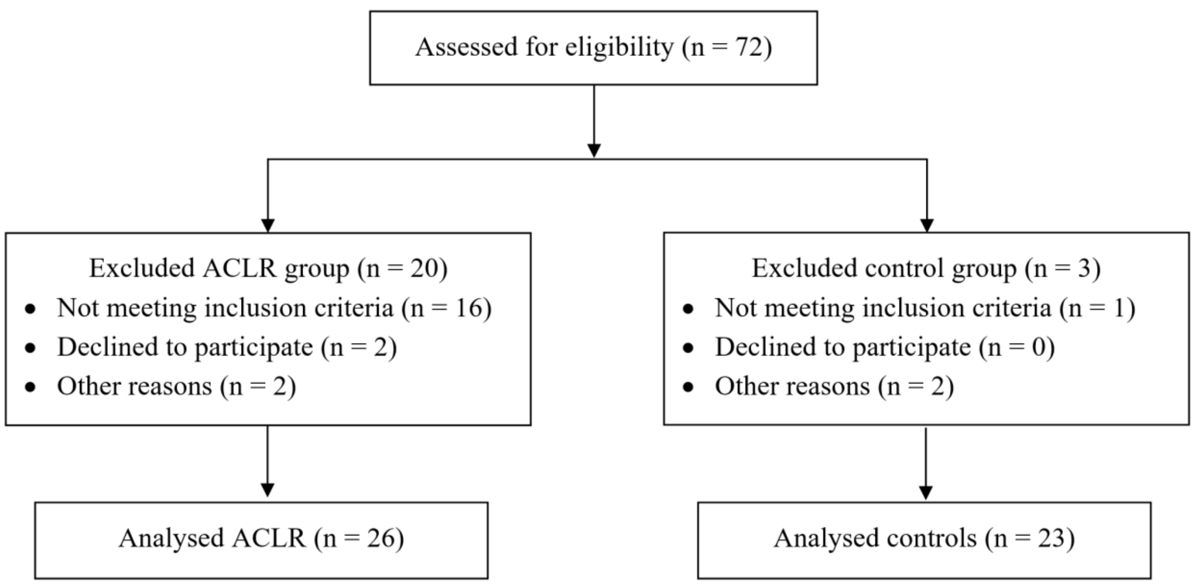

Figure 6.1. Study flow diagram. ACLR, anterior cruciate ligament reconstruction

The ACLR group were recruited for the study after completing supervised rehabilitation at Aspetar Orthopaedic and Sports Medicine hospital and were subsequently enrolled one week after receiving RTS clearance. Clearance to RTS was conducted using a shared decision-making strategy[239] which included consideration of the following: (1) clearance from both their surgeon and physiotherapist, (2) completion of a sports-specific, on-field rehabilitation program, (3) quadriceps strength (LSI ≥ 90%), and (4) hop test performance (LSI ≥ 90%), per previous literature [34]. Participants with concomitant meniscal injury that did not significantly interfere with their rehabilitation were included in the study. Exclusion criteria from the study included full thickness articular cartilage lesion and any other major lower extremity injury in both legs (e.g., concomitant grade III knee ligament injury other than ACL). Activity level for the ACLR (prior to ACL injury) and control groups were assessed using Tegner Actvity Level scale [164]. Patient reported outcomes related to pain, function, and psychological readiness was collected using the International Knee Documentation Committee (IKDC) [158] and Anterior Cruciate Ligament-Return to Sport after Injury (ACL-RSI) [165] questionnaires.

Recruitment for the control group was performed using a convenience sampling from a pool of professional and high-level recreational athletes. Inclusion criteria were age between 18-35 years, Tegner score of ≥ 7, participation in level I or II sports (≥ 3 times/week), no previous lower limb surgery, and no lower limb injury in the three months prior to testing.

6.4.2 Study design

Data collection for this case-control comparative study was performed at the biomechanics laboratory of the Aspetar Orthopaedic and Sports Medicine Hospital. Participants were recruited between November 2018 and October 2019. Informed consent was obtained from all participants prior to participating in the study. This study is part of a larger study investigating RTS criteria following ACLR rehabilitation [84].

Ethics approval for this study was granted (IRB F2017000227). The transfer and use of previously collected and non-identifiable data was approved by the Australian Catholic University Human Research Ethics Committee (Registration number: 2021-29N).

6.4.3 Data collection and instrumentation

Forty-three reflective markers were placed according to a full-body Plug-in Gait marker set which included additional anatomical markers on the sacrum, medial knee, and medial ankle [166].Three marker clusters were also placed laterally on the thigh and shank of both legs [167]. Three-dimensional marker trajectories were collected using a 14-camera motion capture system (250 Hz, Vicon, Oxford, UK) along with ground reaction forces (GRF) using five ground-embedded force plates (1000 Hz, Kistler, Switzerland).

All participants wore shorts and shoes for data collection. Participants were familiarised to all procedures and tasks prior to data collection. Prior to biomechanical testing, participants performed a 7-minute warm up session composed of running, side running, deep squats, and double leg jumps.

For the sidestep cut task, participants started in a standing position six metres away from the force plates. They were then instructed to accelerate towards the force plates, performing three trials of an anticipated 45-degree sidestep cut to the left and to the right. The order of testing for each limb was randomized using a coin toss. For all tests, a clear foot contact of the plant foot (sidestep cutting) on the force plate was needed for a trial to be considered successful.

6.4.4 Musculoskeletal modelling

Data analysis was performed using previous methods as described by Maniar et al. [47, 67, 216] which includes semi-automated analysis via a custom R code (R core team, 2020) interface with OpenSim v4.2 [168]. A generic musculoskeletal model was scaled to each individual's anthropometry based on a static trial [170]. An inverse kinematics algorithm was used to calculate joint angles during the sidestep cut by means of a weighted least-squares optimisation that minimises the difference between model and experimental marker positions during the static and dynamic trials [172]. Inverse dynamics was used to obtain the generalised forces and moments that are responsible for these movements. Static optimisation was used to decompose joint moments into individual lower-limb muscle forces by minimising a cost function (sum of muscle activations squared). To calculate PFJ contact force, we used a separate empirically based model as described previously [188].

$$F_{PFJ} = \sqrt{F_Q^2 + F_P^2 + 2F_Q F_P \cos\beta}$$

Where FPFJ is the PFJ contact force, F_Q is the quadriceps force, F_P is the patella tendon force, and β is the patellar mechanism angle. Note F_P and β were calculated as a function of the knee flexion angle and quadriceps force (calculated from the model), based on data from an in-vitro study [189].

6.4.5 Data analysis

Peak PFJ contact force was extracted during the stance phase (defined as the raw ground reaction force exceeding 20N). Since the primary determinants of the PFJ force is the knee flexion angle and quadriceps force,[188] we also calculated the knee flexion angle and quadriceps force at the time of peak PFJ contact force.

6.4.6 Validation and verification

Qualitative verification of the temporal-varying characteristics of experimental joint angles (Supplementary figure 1) and moments (Supplementary figure 2) were comparable to previous work on sidestep cutting in healthy individuals.[47] Temporal characteristics of predicted muscle forces with that of EMG data from previous work were performed[190] throughout the stance phase of the sidestep cut (Supplementary figure 3) also showed general agreement between model-based predictions and EMG data for most muscles, once accounting for EMG-to-force physiological delays (~100ms) as per recommendations.[180]

6.4.7 Statistical analysis

Descriptive statistics was used to summarise participant characteristics. Shapiro-Wilk test was used to check for normality of distribution of data [191]. An independent sample t-test was used ($p < 0.05$) to determine between group comparisons in participant demographics. A linear mixed effects model [192] approach was used to determine if differences exist between the ACLR leg and the contralateral leg as well as the healthy control legs for each of the previously described outcome variables. For each linear model, leg (ACLR, contralateral, healthy control) was modelled as a fixed effect and participant ID as a random effect, whilst adjusting for approach velocity (i.e., average centre-of-mass forward velocity in the 50ms prior to foot contact). Approach velocity was adjusted for as any variation between groups or trials (e.g., participants may run slower when cutting on their ACLR leg compared to healthy-leg cuts) could confound analysis if unaccounted for. Where significant effects were found for limb, we conducted post-hoc pairwise comparisons using Tukey's method [193]. Data assumptions (e.g., distributions) were verified via the visual inspection of qqplots and residual plots. For all analysis, statistical significance was set at $p < 0.05$.

6.5 RESULTS

Patient demographic and RTS testing results can be found in Table 6.1. Mean approach velocity for the sidestep tasks were 3.7 ± 0.6 m/s for the ACLR leg, 3.9 ± 0.5 m/s for the contralateral leg, and 4.4 ± 0.6 m/s for the healthy control leg. Peak PFJ force was significantly less in the ACLR limbs compared to the contralateral limbs (mean difference = 5.89 BW, 95%CI = 4.7 to 7.1, p < 0.001, Figure 6.2, Table 6.2) and the control limbs (mean difference = 4.44 BW, 95%CI = 2.1 to 6.8, p = < 0.001, Figure 6.2, Table 6.2). At the time of peak PFJ force, ACLR limbs had more extended knee joint angles compared to the contralateral (mean difference = 4.88°, 95%CI = 3.0 to 6.7, p < 0.001, Figure 6.2, Table 6.2) and control limbs (mean difference = 6.01°, 95%CI = 2.0 to 10.0, p < 0.002, Figure 6.2, Table 6.2), as well as lower quadriceps force compared to the contralateral (mean difference = 4.14 BW, 95%CI = 3.4 to 4.9, p < 0.001, Figure 6.2, Table 6.2) and control limbs (mean difference = 2.83 BW, 95%CI = 1.4 to 4.3, p < 0.001, Figure 6.2, Table 6.2). No significant differences between contralateral and control limbs were observed for peak PFJ force (mean difference = 1.45 BW, 95%CI = -0.8 to 3.7, p = 0.281, Figure 6.2, Table 6.2), knee flexion angle (mean difference = 1.12°, 95%CI = -2.8 to 5.0, p = 0.768, Figure 6.2, Table 6.2) or quadriceps force (mean difference = 1.31 BW, 95%CI = -0.1 to 2.7, p = 0.080, Figure 6.2, Table 6.2) at the time of peak PFJ force. The relationship between knee flexion angle and quadriceps force at the time of peak PFJ contact force qualitatively shows that ACLR limbs tend to have a combination of smaller knee flexion angle and lower quadriceps force at peak PFJ contact force compared to healthy limbs (Figure 6.3).

Table 6.1. Participant demographics, patient reported outcome measures, quadriceps strength, and single leg hop for distance performance used as criteria for clearance to RTS

	ACLR group	Control group	P value
Age (years)	23.2±3.4	28.3±4.4	<0.001
Body mass (kg)	71.4±12.1	76.1±7.4	0.10
Height (cm)	173 (166 to 182)	178.2±6.9	0.18
Body mass index ($kg.m^{-2}$)	23.3±2.3	23.9±1.6	0.24
Tegner score pre-injury	9 (9 to 9)	7 (7 to 9)	<0.001
IKDC	94.9±7.0	100	0.002
ACL-RSI	92.0±10.6	NA	NA
Quadriceps strength LSI %	94±6	NA	NA
SLHD LSI %	97±4	100±5	0.011
TRHD LSI %	97±5	100 (98 to 102)	0.07
Return to sport (months)	9.5±2.7	NA	NA
ACL hamstrings autograft, n (%)	10 (38)	NA	NA
Isolated ACL injury, n (%)	15 (58)	NA	NA
Meniscal injury, n (%)	11 (42)	NA	NA
Cartilage lesion, n (%)	2 (8)	NA	NA

Values are presented as mean ± standard deviation for normally distributed data and median (interquartile range) for not normally distributed data, unless otherwise stated. ACLR, anterior cruciate ligament reconstruction; ACL-RSI, Anterior Cruciate Ligament-Return to Sport; IKDC, International Knee Documentation Subjective Knee questionnaire; LSI, Limb Symmetry Index; NA, not available; RTS, return to sports; SLHD, single leg hop for distance; TRHD, triple hop for distance

Table 6.2. Peak PFJ contact force, knee flexion angle at peak PFJ contact force, and quadriceps force at peak PFJ contact force

	Peak PFJ contact force, BW (95% CI)	Knee flexion angle, Deg (95% CI)	Quadriceps force, BW (95% CI)
ACLR	12.6 (11.3 to 14.0)*	51 (49 to 54)*	10.8 (10.0 to 11.7)*
Contralateral	18.5 (17.3 to 19.8)	56 (54 to 58)	15.0 (14.1 to 15.8)
Control	17.1 (15.7 to 18.4)	57 (55 to 60)	13.7 (12.8 to 14.5)

Data are marginal means (95% CI) accounting for approach velocity during the sidestep cut. ACLR, anterior cruciate ligament reconstruction; BW, body weight; Deg, degrees; PFJ, patellofemoral joint. * Significant difference compared to contralateral and control limbs ($p < 0.05$)

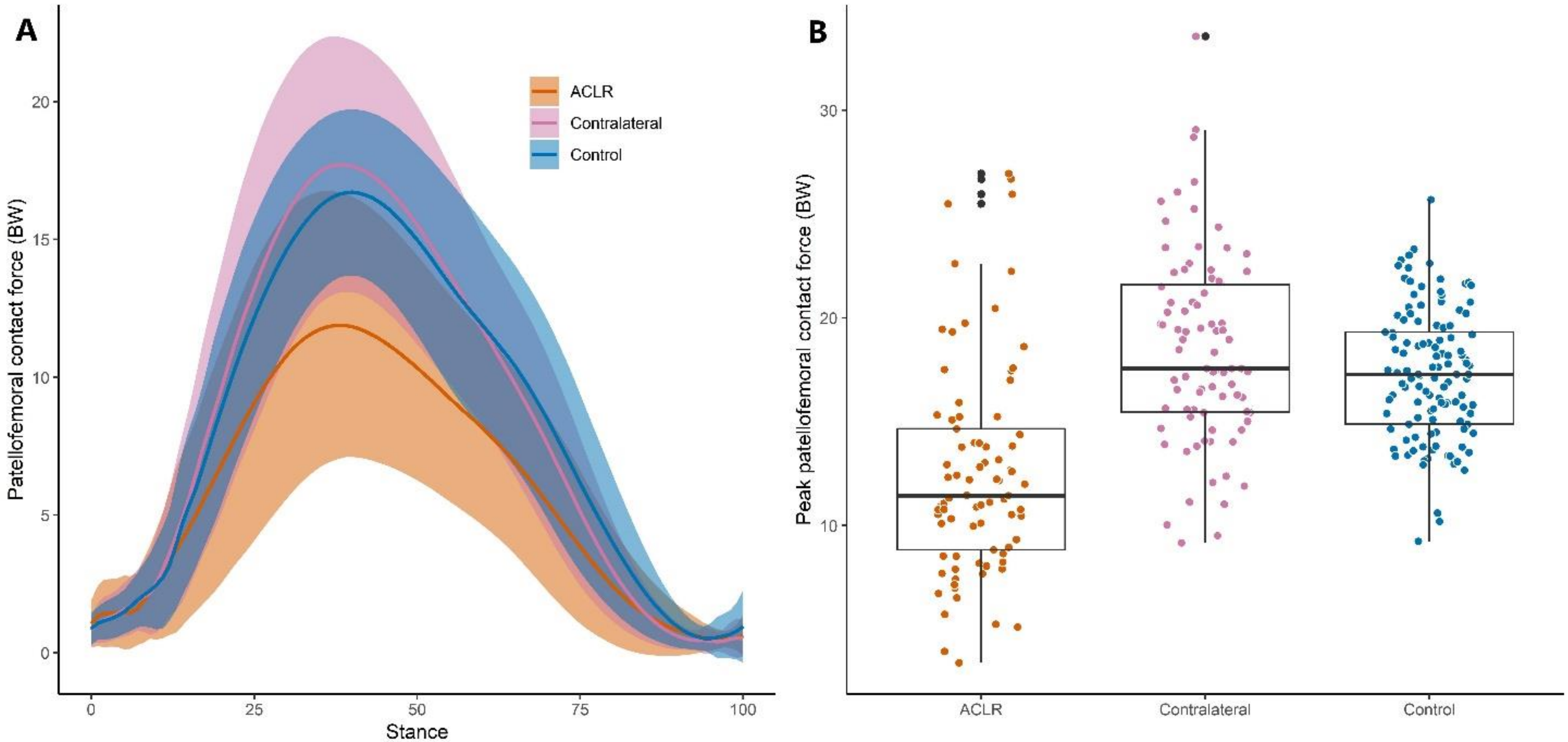

Figure 6.2. A, Patellofemoral contact force during the stance phase of a sidestep cut (solid line and shaded area represent the mean and standard deviation of the patellofemoral contact force across stance phase respectively); and B, Peak patellofemoral contact force between the ACLR, contralateral, and control limb during the stance phase of a sidestep cut (Dots represent all trials, horizontal line inside the box represent the median, edge of the boxes are the 1st and 3rd quartiles, while vertical line represent the range of the peak patellofemoral contact force among the three groups). BW, bodyweight; ACLR, anterior cruciate ligament reconstruction

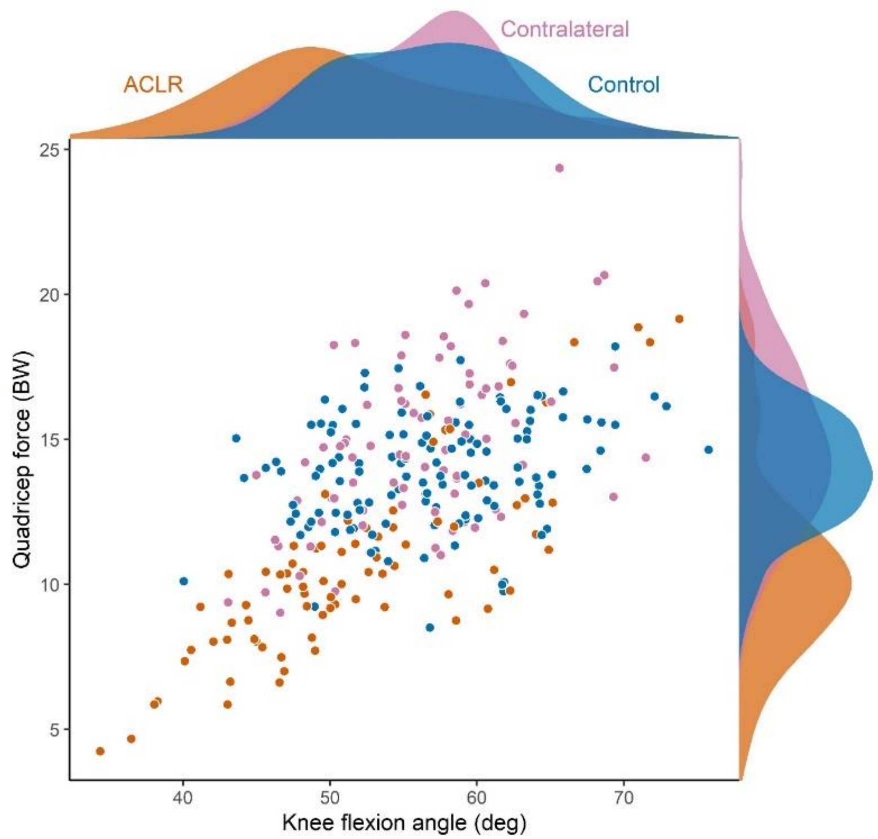

Figure 6.3. Knee flexion angle and quadriceps force at peak patellofemoral contact force for the ACLR, contralateral, and control group legs. Note: The shaded region outside the box represents the probability density of the knee flexion angle (top) and quadriceps force (right) across the three groups. BW, bodyweight; ACLR, anterior cruciate ligament reconstruction

6.6 DISCUSSION

The most important finding of the study is that there werelower PFJ contact forces in the ACLR leg during the stance phase of a sidestep cut when compared to the contralateral and healthy control limb. Additionally, smaller knee flexion angle and lower quadriceps force were also found at the time of peak PFJ contact force in the ACLR leg compared to the contralateral and healthy control limb.

The PFJ contact forces found in this study (12-17 BW, Table 6.2) were larger than the previous studies on walking (1.1-1.6 BW) [238], running (3.4-6.7 BW) [80, 92, 237], and single leg forward hopping (8.6-10.8 BW) [85] following ACLR. As this was the first study to investigate PFJ contact forces during a sidestep cut, a comparative data set on the magnitude of our PFJ contact forces is currently not available. However, the magnitude of forces found in this study was not surprising given the larger knee flexion and knee extension moment required to perform a sidestep cut compared to the abovementioned tasks [240]. Studies on other activities that requires larger knee flexion angles like a squat showed PFJ contact forces can go up to 18 BW [236].

Previous studies have investigated PFJ contact forces during walking, forward hopping and running in ACLR populations compared to non-ACLR limbs [80, 85, 92, 237, 238]. Similar to our results, lower PFJ contact forces in the ACLR limb were found during the stance phase of walking (3-6 months post ACLR) [238] and running (1-2 years after ACLR) [80, 237] as well as the landing phase of a single-leg forward hop (1-2 years after ACLR) [85] compared to the contralateral [80, 85, 92, 237, 238] and healthy control group [85, 92]. In contrast, Herrington et al [92] found larger PFJ contact forces during the stance phase of running (~7 months post ACLR) while Williams et al [238] found no differences between limbs during walking at 2 years. The differences of our results from these two studies could be attributed to the different tasks and time post ACLR. Herrington et al [92] performed their assessments much earlier in the post-ACLR phase than our study during running tasks while Williams et al [238] were from a less demanding task (walking) at 2 years after ACLR.

Low knee flexion angle and extension moment during different tasks is common after ACLR [77, 85, 241]. One of the proposed explanations for this is the presence of quadriceps weakness [91]. The presence of low quadriceps strength could logically explain a subsequent reduction in the ability to produce a knee extension moment. As such, biomechanical compensations such as a smaller knee flexion angle, as seen in the current study, or a relative increase in the joint moments produced at the trunk, hip, and ankle can arise from a reduced knee extension moment.[80, 84]. Another explanation to the "underloading" of the knee joint in this study could be from psychological factors like pain, fear of reinjury, or psychological readiness. Previous studies have shown associations with low psychological readiness or fear of reinjury with aberrant lower limb biomechanics in ACLR individuals.[242, 243] The combination of deficits in these physical and psychological capacities could potentially explain the smaller knee flexion angle, knee extension moment, and quadriceps force that resulted in the low PFJ contact forces in the ACLR limb compared to the healthy limbs in this study. However, the ACLR participants in this study had a relatively symmetrical isokinetic quadriceps strength LSI (Table 6.1), as well as satisfactory subjective perception of knee function and readiness (Table 1). Previous studies have proposed that compensatory strategies can develop during the earlier phases of rehabilitation to achieve task completion despite the presence of deficits in physical and/or psychological capacity.[225] It could be that despite restoration of strength and return of confidence and comfort in the knee, these strategies are still persistent at time of RTS.

Lower PFJ contact force in the ACLR limb during a sidestep cut compared to the contralateral and healthy limb, despite RTS clearance, may have implications for the development of knee osteoarthritis. Lower contact forces in the TFJ during walking, six months following ACLR, has been associated with radiographic signs of TFJ osteoarthritis in the ACLR leg [75]. Similarly, lower PFJ contact forces during forward hop tasks was related to radiographic signs of PFJ osteoarthritis as early as one year after ACLR [76]. The reduction in PFJ contact force may have consequences for the articular cartilage. The cyclic application and removal of joint contact force is necessary for cartilage health [244]. As such, a reduction in PFJ contact force may alter the normal load cycling of the cartilage and trigger a series of mechanical and metabolic changes that eventually leads to cartilage deterioration and onset of osteoarthritis [245, 246]. However, the association between lower PFJ contact forces and the development of PFJ osteoarthritis is still inconclusive and needs further investigations.

In addition to the lower peak PFJ forces, the influence of knee flexion angle on PFJ load location should be considered, given the observed differences in knee flexion during cutting tasks. While not a focus of the current research, understanding the interaction between the location and magnitude of loading in the PFJ during cutting movements may shed light on the development of PFJ osteoarthritis after ACLR. To date, prospective studies investigating the effect of lower PFJ contact forces on the development of PFJ osteoarthritis are lacking. Future prospective studies are needed to better understand cartilage response to PFJ loading and the onset of osteoarthritis after ACLR.

We acknowledge that there were limitations to the current study. First, our PFJ contact force model only considered the sagittal plane biomechanics of the patella. While frontal and transverse plane loading could potentially influence PFJ contact forces, PFJ loading is largely sagittal plane-dominant and the results of our study were relatively comparable to available data [85, 236]. Regardless, future studies could increase complexity of the model to account for other planes. Second, our study is cross-sectional in nature, and we were not able to determine the biomechanical changes following ACLR and rehabilitation. The lower PFJ contact forces, smaller knee flexion angles, and lower quadriceps forces found in this study may have been present prior to ACL injury. Lastly, the participants in this study had either hamstring tendon or patellar tendon graft. While graft-type morbidity is commonly reported in muscle strength [40], previous studies on the effect of graft type on quadriceps muscle morphology [206] or knee osteoarthritis outcomes (radiographic changes, pain, function, symptoms) have been mixed [93, 247]. Given this, future work which compares PFJ contact forces following different ACLR graft types may be warranted. Lastly, this study included a male-only population from a single site which limits the generalisability of our results to females. Future work in the female population is still needed given the previously reported differences in lower limb strength and biomechanics between sex.[248, 249]

6.7 CONCLUSION

In conclusion, this study found that PFJ contact forces during a sidestep cut were lower in the ACLR limb when compared to contralateral and control limbs, despite clearance to RTS. A combination of reduction in quadriceps force and smaller knee flexion angle was found in the ACLR limb compared to the contralateral and healthy control limbs. Current RTS criteria does not appear effective enough to restore biomechanical alterations in the lower limbs that may predispose ACLR individuals to lower PFJ contact forces.

7 DISCUSSION AND CONCLUSIONS

Rehabilitation and subsequent return to sport (RTS) following anterior cruciate ligament reconstruction (ACLR) is typically guided by subjective and objective outcomes related to pain, and restoration of knee joint range of motion (ROM), strength and function (e.g., walking, running, jumping, change of direction) [23-25, 33, 34]. Of the objective measures, hamstrings and quadriceps strength following ACLR have received much attention clinically and in the literature [44, 134, 152, 250]. These muscles are important in providing stability to the knee during dynamic tasks [45-48, 67, 89] hamstrings and/or quadriceps weakness in ACLR individuals being associated with elevated risk of ACL reinjury [33, 34] and the early onset of knee osteoarthritis [35, 71]. Consequently, rehabilitation programs and criteria for RTS has focused heavily restoring the strength of these muscle groups [23, 38, 63, 98, 147].

Conventional assessment of lower limb strength after ACLR has is typically performed on maximal hamstrings and quadriceps strength [33, 50, 123]. Subsequently, restoration of maximal strength has been foci of rehabilitation. However, there is evidence that strength deficits following ACLR extends beyond maximal strength [54]. For example, explosive strength (i.e., rate of force/torque development, RFD or RTD) has been shown to also be affected by ACLR [51]. Given the importance of training specificity in addressing such deficits [50], it is important to better understand the extent of restoration of both maximal and explosive strength following ACLR.

Another important aspect of rehabilitation following ACLR is to restore movement quality and mechanics during activities of daily living as well as during physical activity or sports participation [23, 65]. However, kinematic and kinetic alterations during tasks like gait [77, 78, 251], running [78, 79, 241], jumping/landing [55, 81, 82], and sidestep cutting [86, 87, 214, 252] are common after ACLR. While these impairments in lower limb biomechanics have been associated with hamstrings [197] and quadriceps strength asymmetries [30, 82, 149] and functional alterations [35, 253], impairment of other muscles of the lower limbs could also be important. However, there is limited evidence on lower limb muscle function (e.g., muscle contributions to task and knee joint loading) during the performance of a sidestep cut following ACLR. Given sidestep cutting is common in sports and is a common mechanism of ACL injury [212, 214], a better understanding of lower limb muscle function during this task is needed in order to help improve outcomes after ACLR.

Females have been shown to have worse patient reported outcomes on knee pain and function [254], sports participation/activity [7, 99, 255], and risk of re-injury [9, 10, 14, 16]. It is still unknown whether differences in strength recovery and /or lower limb biomechanics between males and females contribute to this discrepancy in outcomes. However, before associations among strength and/or lower limb biomechanics, and outcomes can be made, it is important to understand whether there are sex differences in hamstrings and quadriceps strength as well as lower limb biomechanics after ACLR in the first place. To date, there are few studies directly exploring potential differences in these variables between males and females.

7.1 SUMMARY OF KEY FINDINGS

In Chapter 2, a systematic review and meta-analysis was conducted to synthesise the evidence on hamstrings and quadriceps strength following ACLR. Firstly, we found that strength deficits are commonly reported using a measure of between limb strength symmetry, often referred to as limb symmetry index (LSI) and that maximal hamstrings and quadriceps strength (e.g., peak torque from an isokinetic dynamometer) are commonly used after ACLR. Maximal hamstrings and quadriceps strength symmetry showed a pattern of improvement (i.e. there was a decrease in the magnitude of asymmetry) from preoperative to 12 months post ACLR regardless of graft type. However, quadriceps strength asymmetries, (using the clinical convention of a LSI $\geq$ 90 [31]) are still present at six (mean LSI = 73, 95%CI = 67 to 79, i^2 = 96%) and 12 (mean LSI = 82, 95%CI = 78 to 86, i^2 = 88%) months following ACLR. These are important timelines as the majority of ACLR individuals are cleared to RTS between these timepoints [13, 25, 209] and the presence of quadriceps strength asymmetry has been associated with a high risk of knee reinjuries [33]. The secondary aim of the systematic review was to conduct a meta-analysis on the influence of sex on strength symmetry following ACLR. However, we were not able to perform this as the majority of the studies did not stratify data between males and females. However, a meta-regression analysis using hamstrings and quadriceps strength LSI as a function of sex distribution of the participants did not show any sex differences in the hamstrings across all timepoints. There were no sex differences in quadriceps strength LSI during the preoperative period and at six months, however, males were found to have greater asymmetries compared to females at 12 months. A caveat for these results, however, is that the majority of included studies had male-dominated populations, with only one study included in this analysis consisting of mostly female participants. Chapter 2 also revealed that rate of force/torque development asymmetries is also affected following ACLR. Explosive strength could be an important variable to assess and target during rehabilitation given its potential transfer to dynamic tasks like running, landing from a jump, and sidestep cutting [53, 256]. Given this, exploring the restoration of explosive strength could provide a better understanding of how lower limb strength recovers during rehabilitation after ACLR.

Unfortunately, we were not able to synthesise the time-course of explosive strength asymmetry as it was not commonly assessed following ACLR.

To address the gaps identified in Chapter 2, in Chapter 4 we employed an observational cohort study to explore both maximal and explosive hamstrings and quadriceps strength in males and females following ACLR [248]. We found significant improvement from early to late ACLR rehabilitation in LSI for both hamstrings (Early: 86 ± 14; Late 92 ± 13; $p = 0.005$) and quadriceps (Early, 73 ± 15; Late 91 ± 12; $p < 0.001$) maximal strength. Limb symmetry index for explosive quadriceps strength (Early: 82 ± 30; Late: 92 ± 25; $p = 0.03$) also improved from early to late rehabilitation, however, there was no significant improvement in explosive hamstrings strength LSI (Early: 86 ± 46; Late: 83 ± 22; $p = 0.746$). Analysis of strength differences between males and females showed that females tend to have greater quadriceps asymmetries compared to males throughout the first year after ACLR [248]. These findings were somewhat unexpected given that participants in Chapter 4 had hamstring tendon (HT) autografts. Graft-related strength asymmetries are common after ACLR [40, 41] but our data indicates that in females, quadriceps strength is more affected by the injury and subsequent surgery compared to males. More work is needed in this area to verify, and potentially extend upon, this finding.

The strength asymmetries described in Chapters 2 and 4 have been associated with impairments in movement mechanics after ACLR [30, 55, 82, 149, 197]. These asymmetries (strength and/or biomechanics) have been proposed to contribute to the risk of reinjury [33, 257-259] and early onset of knee osteoarthritis [71, 74, 260] among ACLR individuals. As such, understanding the interaction between lower limb strength and biomechanics after ACLR has received increasing attention [30, 55, 82, 197, 223, 261]. Initially, the program of research intended to explore the implications of hamstrings and quadriceps strength asymmetry in lower limb biomechanics between males and females. However, as discussed in Chapter 1, the COVID-19 pandemic impacted on the planned trajectory of Chapter 5 and 6. Due to the public health restrictions in place in Victoria, Australia, participant recruitment and data collection was significantly hindered, and we were not able to conduct the intended studies. Fortunately, we were able to access previously collected data of lower limb biomechanics in ACLR individuals who were just cleared to RTS, which had direct relevance to this program of research. The data we were able to access was only collected in male participants and while matched data in females would have been desirable, this is a limitation of the thesis we had to accept based on the impacts of COVID-19.

One of the aims of restoring hamstrings and quadriceps strength during rehabilitation is to ensure the ACLR individual has the physical capacity to progress from normal gait to more demanding tasks such as sidestep cutting [23, 65]. The hamstrings and quadriceps are important modulators of ground reaction forces (GRFs) during the execution of different tasks such as walking [68, 262, 263], running [66, 183], hopping,/jumping/landing [46, 69, 184], and sidestep cutting [47, 67, 89, 216]. Musculoskeletal modelling studies in healthy individuals have also shown the importance of other lower limb muscles in sidestep cutting performance [67]. Prior to this thesis it was still unknown how ACLR might alter the contributions of individual lower limb muscles to the forces acting on the body during a sidestep cut. Chapter 5 investigated the differences in lower limb muscle contributions to vertical support, braking/propulsion, and redirection ground reaction forces (GRF) during sidestep cutting tasks between the ACLR limb and that of the contralateral and control limbs. The findings from Chapter 5 show that there were significant impairments in the lower limb muscle contributions in the ACLR limb during the stance phase of a sidestep cutting task. Compared to the contralateral and/or control limbs, the quadriceps of the ACLR limb made lesser contributions to vertical support (contralateral mean difference = -0.040 BW.s, 95%CI = -

0.049 to -0.031, $p < 0.001$; control mean difference = -0.042 BW.s, 95%CI = -0.061 to -0.022, $p < 0.001$), braking (contralateral mean difference = 0.020 BW.s, 95%CI = 0.014 to 0.027, $p < 0.001$; control mean difference = 0.029 BW.s, 95%CI = 0.017 to 0.041), and medial redirection (contralateral mean difference = -0.006 BW.s, 95%CI = -0.01 to -0.001, $p = 0.011$) GRFs. Differences in muscle contributions to support (gluteus maximus), braking/propulsion (dorsi-flexors/plantar flexors), and medio-lateral redirection (dorsi-flexors, gluteus maximus, hamstrings, plantar flexors) forces were also found between the ACLR and healthy limbs. Based on these findings, asymmetries in quadriceps muscle contributions to GRFs during sidestep cutting are present in the ACLR limb even with "sufficient" quadriceps strength symmetry. Additionally, given the asymmetries in muscle contributions to GRFs from other lower limb muscles (e.g., gastrocnemius, soleus, gluteus maximus), current RTS criteria on strength and functional (e.g., hop tests) symmetry may not be enough to identify biomechanical impairments during tasks like sidestep cutting.

Given the impaired quadriceps function in modulating forces during a sidestep cut, it appears that restoration of isokinetic quadriceps strength does not translate directly to its "normal" contributions to GRFs during a task like sidestep cutting. This may have implications on knee joint stability and loading given the role of the quadriceps [48]. Reductions in knee joint contact forces due to impairments in quadriceps strength have been proposed to influence knee joint degeneration that eventually leads to knee osteoarthritis [150]. Previous studies have reported lower knee joint contact forces, particularly in the patellofemoral joint (PFJ), during tasks like walking [238], running [80, 92, 237], and single leg landing [85] after ACLR. However, no study has investigated PFJ loading in ACLR individuals who have restored quadriceps strength symmetry (i.e., LSI ≥ 90%). Chapter 6 explored PFJ contact forces in the ACLR limb during an anticipated sidestep cut and compare it with the contralateral and control limbs following clearance to RTS (which included quadriceps strength LSI ≥90% as a criteria). The ACLR limb had lower peak PFJ contact forces compared to the contralateral (mean difference = 5.89 BW, 95%CI = 4.7 to 7.1, $p < 0.001$) and control limbs (mean difference = 4.44 BW, SE = 2.1 to 6.8, p = < 0.001) during the stance phase of a sidestep cut. Additionally, the ACLR limb had lower quadriceps force (contralateral mean difference = 4.14 BW, 95%CI = 3.4 to 4.9, $p < 0.001$; control mean difference = 2.83 BW, 95%CI = 1.4 to 4.3, $p < 0.001$) and less knee flexion angle (contralateral mean difference = 4.88°, 95%CI = 3.0 to 6.7, $p < 0.001$; control mean difference = 6.01°, 95%CI = 2.0 to 10.0, $p < 0.002$) at time of peak PFJ force compared to the contralateral and control limbs. These results show that despite restoration of quadriceps strength asymmetry, lower PFJ contact forces can still be present in the ACLR limb compared to the contralateral and control limbs.

7.2 QUADRICEPS STRENGTH AND BIOMECHANICS FOLLOWING ACLR

The quadriceps is an ACL antagonist given the muscle forces it produces can induce anterior tibial translation [264], anterior shear force [265], and ACL loading [48]. However, the production of a knee extension moment (highly dependent on the quadriceps) is critical in attenuating ground reaction forces [236, 240] during tasks such as running, hopping, landing, and sidestep cutting. Broadly, the quadriceps are also critical in modulating the body's centre of mass by producing vertical support and braking forces during tasks like. walking [68, 262, 263], running [66, 183], single leg landing [46, 69], and sidestep cutting [47, 67, 89, 216]. Given the importance of the quadriceps following ACLR, there is a plethora of studies investigating the quadriceps muscle and its role in ACL injury [33, 34], prevention [45], and rehabilitation [23, 38, 65, 266].

Despite the focus on quadriceps function following ACLR, quadriceps muscle inhibition [253], atrophy [206], and explosive and maximal strength deficits (e.g., limb asymmetries) [44, 51] are still common following ACLR. These impairments following ACLR, specifically in maximal quadriceps strength, are associated with poor patient-reported outcomes related to pain and function [26, 196, 267], high risk of reinjury [33], and early onset of knee osteoarthritis [35, 71]. One of the main findings of this program of research suggest that quadriceps strength asymmetries can improve within the first year following ACLR (Chapter 4) [248]. We found that both explosive and maximal quadriceps strength improved within 12 months of ACLR. In contrast with our findings, there is some evidence that explosive quadriceps strength asymmetry can persist even after maximal strength symmetry has been achieved [52, 56]. Other studies have also shown explosive quadriceps strength deficits at different timepoints following ACLR [27, 51, 52, 55-58]. A possible explanation for the difference in our results with that of previous work was that we performed our assessments throughout the early phase- and late phase-rehabilitation [248] whereas previous studies have collected their data either only once [27, 55, 57, 58] or within the early phase-rehabilitation (preoperative to six months) [56]. To the best of our knowledge, only Angelozzi et al [52] have explored explosive quadriceps strength during the early phase- and late phase-rehabilitation. Contrary to our findings, they also found differences in rate of recovery between explosive and maximal strength [52]. However, strength data collection in their study was performed using an instrumented leg press machine which limits the comparison of their data to the present study. Additionally, they found that participants who had included ballistic exercises at six months, showed improvements in explosive strength asymmetry at 12 months compared to those who did not [52]. Taken together, concurrent assessment of both explosive and maximal quadriceps strength should be performed following ACLR. This is important to inform rehabilitation given the potential effectiveness of targeted explosive exercises to the resolution of explosive quadriceps strength asymmetries.

In addition to lower limb strength recovery, the restoration of lower limb biomechanics during daily tasks such as walking to more dynamic tasks like running, jumping/landing, and sidestep cutting is equally important following ACLR [23, 62-64]. The alterations in lower limb biomechanics following ACLR has been proposed to be influenced by the presence of quadriceps strength asymmetries [30, 55, 82, 149, 261]. The quadriceps are the main muscles responsible for producing internal knee extension moment [46] which is necessary to decelerate the knee and ameliorate forces from the external flexion moments and GRFs [46] commonly produced during the stance phase of walking, running, and sidestep cutting or the landing phase of a jump. Therefore, the presence of quadriceps strength deficits could potentially explain the kinematic (e.g. small knee flexion angle) and kinetic (e.g., limb unloading) impairments in the ACLR limbs compared to healthy limbs during the execution of the abovementioned tasks.

Given these associations, quadriceps strength recovery (i.e., LSI ≥90%) following ACLR would hypothetically restore lower limb kinematics and kinetics. However, based on the findings of this program of research (Chapters 5 and 6), it appears that isokinetic quadriceps strength symmetry does not translate to symmetry in lower limb kinematics (e.g., knee flexion angle and knee extension moment) as well as quadriceps force necessary to contribute to GRFs and load the PFJ during a sidestep cut. The persistence of these asymmetries (smaller knee flexion angles, low knee extension moments, reduced muscle forces, contributions) could have implications for return to previous level of sports participation [32, 194] but to the risk of knee reinjury [33]. Furthermore, the kinematic, kinetic, and lower PFJ contact forces found in Chapter 6 have been proposed to initiate morphological changes in the articular cartilage of the knee which could trigger the onset of knee osteoarthritis [75, 76, 268].

While restoration of quadriceps strength is important following ACLR, the ability to translate this strength through movement mechanics could be equally important. However, based on the findings of strength recovery from Chapter 4 [248] and the biomechanical asymmetries in Chapters 5 and 6), it appears that lower limb muscle strength and biomechanics recovery may have different timeframes [224, 225]. Asymmetries in strength earlier in rehabilitation could effected muscle coordination [224, 225, 266] that may lead to compensations in motor task strategies as observed in the differences between the ACLR limb kinematics and kinetics with that of the contralateral and control limbs [225]. These strategies (e.g., quadriceps avoidance) could have persisted even after restoration of muscle strength symmetry which could explain why differences in knee flexion angle, knee extension moment, muscle contributions, and PFJ contact forces were still present at RTS. Given the potential differences in timeframe of recovery between strength and movement mechanics, rehabilitation programs should include motor control interventions as early as possible during rehabilitation [65, 269-271]. Motor control interventions such as feedback [272, 273] (e.g., verbal or visual, internal or external) has shown to be improve limb loading symmetry when performing tasks (i.e., walking, running, jumping) during rehabilitation following ACLR [274-276]. Given this, graded motor control drills from early (e.g., during gait tasks) to late (e.g., running, jumping/landing, sidestep cutting) rehabilitation could be incorporated alongside the current interventions for muscle strength after ACLR.

7.3 HAMSTRINGS STRENGTH AND BIOMECHANICS FOLLOWING ACLR

Hamstrings strength deficits have been a proposed risk factor for lower limb injuries in healthy individuals [277-279]. The hamstrings provide stability in the knee by resisting anterior tibial translation, therefore, reducing the loads on the ACL during dynamic tasks [46]. Reduced hamstring to quadriceps strength ratio have been found to increase the risk of second ACL injuries [34] and individuals who had ACLR have been shown to have deficits in hamstring strength and morphology years after surgery [203, 204, 206]. These deficits in hamstring strength may have implications for lower limb biomechanics with hamstring strength asymmetries associated with changes in gait and jogging mechanics [197] as well as an increase in ACL loading during sidestep cutting [279].

One of the more pertinent findings of this program of research, specific to the hamstrings, is the persistence of explosive hamstrings strength asymmetries (Early: 86 ± 46; Late: 83 ± 22; $p = 0.746$) despite improvement in maximal hamstrings strength found in Chapter 4 [248]. While there has been a plethora of studies that have explored explosive quadriceps strength [29, 35, 44, 103, 134, 253, 267] following ACLR, evidence on explosive hamstrings strength is lacking. To date, there are two studies that have investigated explosive hamstring strength during the early phase of rehabilitation (LSI = 68-89%) [56, 280], one study during late rehabilitation (LSI = 87%) [58], and one study between 3-9 months following ACLR (LSI = 70%) [198]. As, such Chapter 4 was the first study [248] to investigate the time-course of explosive hamstring strength asymmetry following ACLR and compare this concurrently with that of maximal strength. Conventional strength assessment of the hamstrings has focused on maximal strength [198]. Compared to the quadriceps, asymmetries in maximal hamstrings strength are not as common. However, studies that have investigated other qualities of the hamstring such as maximal eccentric strength, and musculotendinous stiffness, albeit in a limited number of papers [152, 202, 203], suggest that the deficits in the hamstrings following ACLR might not lie in maximal strength alone.

A potential explanation for this finding could be related to the alterations in the hamstrings' musculotendinous unit after graft harvest [201]. The compliance and stiffness of aponeurosis and tendon have been associated with late-onset explosive strength [281]. Hence, alterations in the compliance and stiffness of the hamstring musculotendinous junction [282, 283] could explain the persistence of explosive hamstring strength deficits following ACLR. Changes in muscle morphology and tendon quality at the graft site has been previously reported following ACLR [119, 152, 201-204, 206]. While we did not assess these qualities with our participants, there is evidence that tendons do not fully regenerate and muscle volume is reduced in the hamstrings of ACLR individuals [202, 203, 206].

Aside from its role in resisting anterior tibial translation and reducing ACL loading during dynamic tasks, the hamstrings are also important in modulating ground reaction forces during gait [68, 263], running [66], and single-leg landings [46]. The hamstrings are major contributors to propulsion and lateral redirection forces during tasks in healthy individuals and it was unknown how these contributions were affected after ACLR. Findings from Chapter 6 show that there was an increase in muscle contribution to medial redirection forces from the hamstrings of the ACLR limb compared to the contralateral limb during a sidestep cut. This was in contrast to previous work where they reported the hamstrings to be a modulator in lateral-directed forces [68, 284]. Taken together with the reduction in quadriceps contribution to medial redirection, greater hamstring contribution to medial redirection forces during a sidestep cut may be a compensatory mechanism following ALCR to, as best as possible, maintain task performance.

The persistence of explosive hamstrings strength asymmetry despite restoration of maximal strength symmetry during the first year following ACLR (Chapter 4) [248] could have implications in the development of a rehabilitation program. Conventional resistance training programs do not put an emphasis on ballistic exercises. The addition of exercises specifically aimed at improving explosive strength has been shown to improve explosive quadriceps strength deficits [52], however, whether this is true with the hamstrings is still unknown. We could not speculate whether the reductions in hamstring muscle contributions to medial redirection GRFs was influenced by hamstrings strength asymmetries as we did not measure hamstring strength in the current thesis (Chapter 5). We also do not know the implications of these reductions in muscle contributions to patient outcomes yet and future studies should be conducted to better understand this.

7.4 SEX DIFFERENCES

Females have been reported to have poorer outcomes compared to males following ACLR. Previous findings have shown poorer scores in self-reported pain [254], sports participation/activity [7, 99, 255], quality of life [254] and a higher risk of reinjury [9, 10, 14, 16] in females compared to males following ACLR. While multifactorial, differences in strength recovery as well as biomechanics may have an influence on the outcomes between sex. Part of the initial aims of this program of research was to explore the influence of sex on strength recovery and biomechanics following ACLR. While we were able to address some elements of this question in Chapters 2 & 4, we were not able to follow up with subsequent studies due to the aforementioned restrictions due to the COVID-19 pandemic.

Chapter 2 showed that much of the literature looking at the restoration of hamstrings and quadriceps strength following ACLR have not stratified for sex. Given the importance of strength recovery after ACLR on successful outcomes when returning to sport, understanding how males and females respond following ACLR may have implications for the rehabilitation that is prescribed. This gap in the literature is partially addressed in Chapter 4 of this thesis. A significant finding from Chapter 4 is that despite the improvement of both explosive and maximal quadriceps strength asymmetry over time during the rehabilitation period, females tend to have larger quadriceps strength asymmetries than males following ACLR. The reason for the differences in quadriceps strength asymmetries between males and females in Chapter 4 is still not completely understood. A potential explanation for this could be related to the inherent sex differences in muscle morphology between males and females [205, 285]. Healthy females have been reported to have less type II muscle fibers [205], smaller muscle volume and CSA [285] in the quadriceps and hamstrings compared to males. Following ACLR, these cellular and morphological characteristics are also affected [286] and there is a known association between muscle strength and its morphology [152, 202]. Given that females already have less fast twitch muscles as well as smaller muscle volume and CSA [205, 285], these inherent differences between sexes could be magnified following ACLR manifesting in females having larger strength asymmetries than males. This is speculative, however, and presents an area for future work.

While there were greater asymmetries in quadriceps strength in females compared to males, we did not find any influence of sex on the rate of strength recovery during rehabilitation in Chapter 4 [248]. This suggests that the rate of strength recovery in males and females following ACLR is expected to be similar. However, serial assessment and interventions that focus on quadriceps strength recovery should be a major consideration in females given the greater asymmetries found in in this group compared to males following ACLR [248]. Additionally, while participants in Chapter 4 received a similar structure in terms of rehabilitation, the volume, intensity, and overall periodisation of their programs were not controlled [248]. Differences in outcomes following supervised and unsupervised rehabilitation have been previously reported [287]. Together with the evidence that female athletes may have unequal exposure and poorer access to resistance training compared to males [288, 289], this may have confounded the differences in quadriceps strength asymmetry found between sexes.

7.5 PRACTICAL IMPLICATIONS

This program of research has resulted in findings with strong implications for practitioners working with individuals who have undergone an ACLR. The findings of this program of research shines the light on strength and biomechanical variables that may have implications for patient outcomes. Furthermore, the current findings should also be cause for guiding future research efforts in ACLR populations.

The results of Chapter 4 strengthen the evidence on the importance of both maximal and explosive strength assessment following ACLR [248]. Given the persistence of explosive hamstrings strength asymmetries despite resolution of maximal strength, routine testing of both strength variables should be considered. However, one of the limitations for objectively measuring strength in the clinical setting is the high cost and technical requirements of isokinetic dynamometers. The use of externally fixed dynamometers with the ability to measure force over time could provide affordable alternatives [290, 291]. Another option would be the use of improvised sling systems instrumented with in-series load cells, which allows for collection of more comprehensive data while being cost-effective and easy to set up [292].

Based on the results of Chapters 5 and 6, it appears that lower limb biomechanics can still be significantly impaired despite isokinetic strength recovery. Given the implications of these biomechanical deficits to knee degeneration [75, 76, 268] and knee re-injury [257-259], inclusion of lower limb biomechanics assessment should be considered as part of RTS criteria. Furthermore, the asymmetries in kinematics and kinetics found in this program of research (and across ACL research) [76, 77, 79, 81, 82, 86], could also be more feasibly measured clinically using inertial measurement units and portable force plates. Given that the most significant alteration in lower limb kinematics is in the sagittal plane [77, 257], the use of a uniaxial rather than a tri-axial force plate might be more cost-effective while still providing a picture of the ACLR individual's capacity. A battery of strength testing from externally fixed dynamometers or load cells, together with kinematics and kinetics data from the abovementioned alternatives, could provide a clearer picture of the current capacity of the ACLR individual and with advances in more affordable and clinically-friendly technology more comprehensive assessments should increasingly become best practice.

7.6 LIMITATIONS AND FUTURE DIRECTIONS

There were some overarching limitations in this program of research. First, we were not able to follow up on whether the explosive strength asymmetries found in Chapter 4 had implications on lower limb biomechanics. We found reductions in the muscle contributions of the hamstrings in producing medial redirection GRFs in Chapter 5, however, we only collected quadriceps strength from this population. There is some evidence that hamstring strength asymmetry is associated with kinematic alterations during running [197]. However, there is scarcity of studies looking at hamstrings strength and its implications on lower limb biomechanics. Given the explosive strength deficits we found in Chapter 4 [248] and the biomechanical compensations reported in Chapter 5, future studies should consider exploring potential associations.

Secondly, graft type has been shown to influence outcomes after ACLR [40, 41, 130]. Previous work has shown explosive quadriceps strength asymmetry persists in ACLR individuals who had PT autografts [51]. The results of Chapter 4 also show the persistence of explosive strength asymmetries, but in the hamstrings, when using HT autografts [248]. Together, these findings suggest that graft type could influence explosive strength recovery. To date, no study has yet to investigate the effect of graft type on concurrent maximal and explosive strength recovery during rehabilitation after ACLR. These could also potentially influence lower limb biomechanics; however, we were not able to stratify the results of Chapters 5 and 6 based on graft type. Exploration of these variables is warranted to develop rehabilitation programs tailored to specific graft types.

Thirdly, there is evidence that exercise selection can address explosive strength deficits in the quadriceps following ACLR [52]. Whether this is true for explosive hamstrings strength deficits is still unknown as we did not conduct an intervention to address this. Studies exploring explosive hamstrings and quadriceps strength and investigating the effect of different exercise interventions on these strength deficits should be a focus of future work. Additionally, given the sex differences found in quadriceps strength in Chapter 4 [248], exploring sex differences in response to explosive exercise intervention is warranted.

Finally, data collected in Chapters 5 and 6 were from male participants only. Previous studies on PFJ contact forces following ACLR has been on a mixture of males and female participants [80, 85, 92, 237, 238] while muscle contributions studies have been previously conducted on healthy participants without any stratification for sex [66-69, 89, 262, 284]. Additionally, deficits in quadriceps muscle force, PFJ contact force and quadriceps muscle contributions during sidestep cutting tasks were still present despite the recovery of quadriceps strength symmetry during rehabilitation and subsequent clearance to RTS in male athletes (Chapters 5 and 6). Given the larger asymmetries in quadriceps strength in females found in Chapter 4, the implications of these strength deficits with that of the abovementioned biomechanical variables is still unknown and should be explored in future work.

7.7 CONCLUSIONS

Overall, this program of research contributes to the body of knowledge on how explosive and maximal hamstring and quadriceps strength recovers following ACLR. Additionally, the findings of this thesis also show that even with recovery of maximal quadriceps strength symmetry, this does not translate to restoration of the ability of the quadriceps to produce forces needed for the execution of a sidestep cut or maintain normal PFJ contact forces. These findings should provide clinicians and researchers alike with meaningful information to better develop targeted interventions and assessment of recovery following ACLR.

8 REFERENCES

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APPENDICES

The following section contains appendices for the supplementary materials, declaration of contribution by authors, and ethics approval forms related to each study.

Appendix A. Table 2.1. Modified quality assessment tool derived from Downs and Black.

Category	**Item**	**Question**	Score
Reporting			
Yes = 1 **No = 0**	1	**Is the hypothesis/aim/objective of the study clearly described?**	
	2	**Are the main outcomes to be measured clearly described in the Introduction or Methods section?** *If the main outcomes are first mentioned in the Results section, the question should be answered no.*	
	3	**Are the characteristics of the patients included in the study clearly described?** *In cohort studies and trials, inclusion and/or exclusion criteria should be given. In case-control studies, a case-definition and the source for controls should be given.*	
Yes = 2 **Partially = 1** **No = 0**	5	**Are the distributions of principal confounders in each group of subjects to be compared clearly described?** *A list of principal confounders is provided.*	
Yes = 1 **No = 0**	6	**Are the main findings of the study clearly described?** *Simple outcome data (including denominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions. (This question does not cover statistical tests which are considered below).*	

	7	**Does the study provide estimates of the random variability in the data for the main outcomes?** *In non-normally distributed data the inter-quartile range of results should be reported. In normally distributed data the standard error, standard deviation or confidence intervals should be reported. If the distribution of the data is not described, it must be assumed that the estimates used were appropriate and the question should be answered yes.*	
	9	**Have the characteristics of patients lost to follow-up been described?** *This should be answered yes where there were no losses to follow-up or where losses to follow-up were so small that findings would be unaffected by their inclusion. This should be answered no, where a study does not report the number of patients lost to follow-up.*	
	10	**Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?**	
External validity			
Yes = 1 **No = 0** **Unable to determine = 0**	11	**Were the subjects asked to participate in the study representative of the entire population from which they were recruited?** *The study must identify the source population for patients and describe how the patients were selected. Patients would be representative if they comprised the entire source population, an unselected sample of consecutive patients, or a random sample. Random sampling is only feasible where a list of all members of the relevant population exists. Where a study does not report the*	

		proportion of the source population from which the patients are derived, the question should be answered as unable to determine.	
	12	**Were those subjects who were prepared to participate representative of the entire population from which they were recruited?** *The proportion of those asked who agreed should be stated. Validation that the sample was representative would include demonstrating that the distribution of the main confounding factors was the same in the study sample and the source population.*	
Internal validity - bias			
Yes = 1 **No = 0** **Unable to determine = 0**	16	**If any of the results of the study were based on "data dredging", was this made clear?** *Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.*	

	17	**In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?** *Where follow-up was the same for all study patients the answer should yes. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where differences in follow-up are ignored should be answered no.*	
	18	**Were the statistical tests used to assess the main outcomes appropriate?** *The statistical techniques used must be appropriate to the data. For example, nonparametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias, the question should be answered yes. If the distribution of the data (normal or not) is not described, it must be assumed that the estimates used were appropriate and the question should be answered yes.*	
	21	**Were the patients in the different intervention groups (trials and cohorts studies) or cases and controls (case control studies) recruited from the same population?** *For example, patients for all comparison groups should be selected from the same hospital. The question should be answered unable to determine for cohort and case control studies where there is no information concerning the source of patients included in the study.*	

Yes = 2 **Partially = 1** **No = 0**	25	**Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?** *This question should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat; the distribution of known confounders in the different treatment groups was not described; or the distribution of known confounders differed between the treatment groups but was not taken into account in the analyses. In nonrandomised studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as no.*	
(Yes=1/No=0/ **Unable to determine=0)**	26	**Were losses of patients to follow-up taken into account?** *If the numbers of patients lost to follow-up are not reported, the question should be answered as unable to determine. If the proportion lost to follow-up was too small to affect the main findings, the question should be answered yes.*	
Power	27	**Did the study have a calculation of power and was this met?**	
(Yes=1/No=0)	29	**Was the rehabilitation of participants controlled and/or reported?**	
		Total	/21

Appendix A. Table 2.2. Summary data of included studies

Author	Participants	Graft type	Mean age (range)	Concomitant injury	Rehabilitation	Study design	Aim of the study
Anderson et al., 2002	Male (n=18); Female (n=4) Male (n=15); Female (n=8)	BPTB (n=22) 4-strand HT (n=23)	30.5 Y (20-42) 34 (20-53)	Not reported	Standardised; 4-6 months	Prospective (observational)	Concentric and eccentric knee extensor and flexor strength recovery over a one-year period after ACLR using either HT or BPTB graft.
Beard et al., 2001	Sex not reported (n=45)	4-strand HT	Not reported	Exclusion criteria for participant recruitment	Standardised; 4-6 months	Randomised controlled trial	Effect of graft type on patient outcomes in patients undergoing ACLR
de Jong et al., 2007	Male (n=162); Females (n=29)	BPTB (n=167); Quadruple-bundle HT (n=24)	29 ± 7 Y (18-50)	Meniscus treatment (n=37); Chondral treatment (n=4)	Standardised; Prehabilitation 6-9 months	Prospective	Evaluate strength and functional capacity before and after ACLR.
Domingues et al., 2018	Males (n=24)	HT (N=24)	27.5 ± 6.2 Y (20-40)	Not reported	Not controlled; 6 months	Prospective (longitudinal)	Evaluate the dynamic balance of the injured and uninjured limb before and after ACLR
Fu et al., 2013	Male (n=32); Female (n=16) Male (n=18); Female (n=6)	Single-bundle HT (n=39)	25.2 ± 7.3 Y 23.3 ± 5.2 Y	Meniscal repair (n=11) Meniscal repair (n=7)	Standardised (randomised to 1 of 2 rehabilitation programs)	Randomised controlled trial	Investigate the effect of early WBVT on neuromuscular control after ACLR.
Hsiao et al., 2014	Male (n=9); Female (n=3)	BPTB (n=12)	25.7 ± 9.3 Y	Exclusion criteria	Not controlled	Prospective (observational)	Assess length and velocity changes of the knee muscle force before and after ACLR.
Hsu et al., 2018	Males (n=20); Females (n=8)	HT (n=28)	(18-60) Y	Meniscal injury (n=18)	Standardised; Home-based; 4-6 months	Prospective	Compare outcomes after ACLR in patients with different BMIs.

Appendix A. Table 2.2. continued

Author	Participants	Graft type	Mean age (range)	Concomitant injury	Rehabilitation	Study design	Aim of the study
Janssen et al., 2013	Male (n=17); Female (n=5)	4-strand HT + gracilis (n=22)	28.4 ± 5 Y	Exclusion criteria for participant recruitment	Standardised	Prospective (double-blind)	Analysis of knee flexion and extension strength between patients with and without HT regeneration.
Jansson et al., 2003	Sex not reported (n=99)	BPTB (n=51); Double-bundle HT + gracilis (n=48)	Not reported	MCL tear (n=9); Meniscal repair (n=12); Meniscectomy (n=16); Chondral (n=8)	Standardised; 6-12 months	Prospective	Assess outcomes after ACLR using either a BPTB autograft or a HT autograft.
Keays et al., 2000	Male (n=22); Female (n=9)	BPTB (n=31)	27 Y (19-38)	Meniscectomy (n=23)	Standardised; Prehabilitation	Prospective (longitudinal)	Assess knee extensor and flexor strength and functional performance before and six months after ACLR
Keays et al., 2001	Male (n=22); Female (n=9)	4-strand HT (n=31)	27 Y (19-38)	Meniscectomy (n=20)	Standardised; Prehabilitation; Home-based+ physiotherapy visits	Prospective (longitudinal)	Assess the nature of the strength deficits in the quadriceps and hamstring muscles before and after ACLR and its relation to functional performance.
Keays et al., 2003	Male (n=22); Female (n=9)	4-strand HT + gracilis (n=31)	27 ± 6 Y	Partial meniscectomy (n=17)	Standardised PrehabilitationHome-based+ physiotherapy visits	Prospective (longitudinal)	Assess the relationship of knee extensor and flexor strength with functional stability tests score
Knezevic et al., 2014[a]	Male (n=23)	BPTB (n=23)	24.2 ± 5.1 Y	Not reported	Standardised	Experimental (longitudinal)	Explore validity of the IKT, IMT, and ACMC when used to monitor the muscle function recovery after ACLR.

Appendix A. Table 2.2. continued

Author	Participants	Graft type	Mean age (range)	Concomitant injury	Rehabilitation	Study design	Aim of the study
Knezevic et al., 2014[b]	Male (n=23)	BPTB (n=23)	22 ± 0.9 Y	Not reported	Standardised	Prospective observational	Evaluate the changes in explosive strength of the knee extensors and flexors after ACLR.
Lee et al., 2015	Males (n=15); Females (n=5)	4-strand HT + gracilis (n=23)	30.5 Y (17-51)	Exclusion criteria for participant recruitment	Not reported	Prospective longitudinal trial	Evaluate serial changes in knee extensor and flexor strength after ACLR with autologous HT graft.
Melikoglu et al., 2008	Males (n=85); Females (n=13)	BPTB; Quadriceps tendon; Achilles tendon allograft	33 ± 6.8 Y (20-49)	Not reported	Standardised	Cross-sectional	Evaluate effect of time from injury to surgery on knee extensor and flexor strength in patients with ACLD.
Mittlmeier et al., 1999	Males (n=6); Females (n=4)	BPTB (n=10)	28.4 (22-38)	Not reported	Standardised for all participants; At least 3 months	Prospective	Use of gait analysis as a refined quantitative measure into functional restoration after ACLR as a function of time.
Ogrodzka-Ciechanowicz et al., 2018	Males (n=34)	HT (n=31)	28.4 ± 9.5 Y (20-57)	Exclusion criteria for participant recruitment	Standardised; 6 months	Randomised controlled trial	Assess stabilometric measures in patients before and after ACLR.
Radziunas et al., 2012	Males (n=26); Females (n=4)	HT + gracilis (n=30)	25.6 ± 7.5 27.4 ± 7.1 Y	Exclusion criteria for participant recruitment	Standardised; Prehabilitation (assigned to 1 of 2 rehabilitation programs)	Experimental, Intervention	Assess the effectiveness of ACLR rehabilitation on knee extensor and flexor strength.
Risberg et al., 2009	Males (n=47); Females (n=27)	BPTB (n=74)	28.4 Y (16.7-40.3)	Meniscectomy (n=34); Cartilage injury (n=29); Combined (n=19)	Standardised (randomised to 1 of 2 rehabilation programs)	Randomised controlled trial	Examine the long-term outcome of a six-month rehabilitation program after ACLR.

Appendix A. Table 2.2. continued

Author	Participants	Graft type	Mean age (range)	Concomitant injury	Rehabilitation	Study design	Aim of the study
Seo et al., 2017	Males (n=89)	BPTB (n=37); HT (n=34); Allograft (n=2)	30.67 ± 9.81 Y (18-50)	Meniscal injury (n=44); Medial meniscus (n=21); Lateral meniscus (n=10); Both (n=13)	Standardised; 3-5 months	Retrospective, cohort observational	Assess knee extensor and flexor strength as well as the distance jumped in the one-legged hop test in patients after ACLR.
Setuain et al., 2017	Males (n=30); Females (n=10)	Double-bundle HT (n=40)	24 ± 6.9 Y	Meniscal injury (n=20); Meniscal repair (n=8); Meniscectomy (n=12)	Standardised for all participants (randomised to 1 of 2 rehabilation programs)	Randomised controlled trial (Double-blind, Longitudinal)	Analyze knee extensor and flexor CSA and force after ACL rehabilitation, before and one year after ACLR.
Soon et al., 2004	Males (n=66); Females (n=10)	4-strand HT + gracilis	25.2 Y (16-45)	Meniscal injury (n=39); Menisectomy (n=37)	Standardised	Prospective	Document the outcomes associated with ACLR using HT autografts.
Tanaka et al., 2010	Females (n=64)	HT (n=64)	16.2 Y (12-29)	Not reported	Standardised; At least 6 months	Case series	Examine the incidence of ACL retears in female basketball players.
Tashiro et al., 2003	Males (n=51); Females (n=39)	HT + gracilis (n=38); HT (n=52)	24.6 Y (14-49)	Not reported	Standardised; 8 months	Prospective (randomized)	Evaluate the influence of HT harvest on knee flexion strength in patients after ACLR.
Teitsma et al., 2014	Males (n=222); Females (n=153)	BPTB (n=16); HT (n=352); Other (n=7)	28 ± 10 Y; 28 ± 11 Y	Not reported	Not reported	Cohort (Retrospective case series)	Explore the data with regard to the clinical outcomes between sexes after ACLR in a Dutch population.
Thomas et al., 2013	Males (n=8); Females (n=7)	BPTB (n=15)	20.3 ± 5.3 Y; 24.7 ± 3.3 Y	Not reported	Standardised; 3-4 months	Case-control study	Determine hip, knee, and ankle muscle strength after ACL injury and ACLR.

Appendix A. Table 2.2. continued

Author	Participants	Graft type	Mean age (range)	Concomitant injury	Rehabilitation	Study design	Aim of the study
Tyler et al., 2004	Males (n=33); Females (n=27)	BPTB (n=15)	30.4 ± 1.0 Y	Not reported	Standardised; 6 months	Randomized clinical trial (Double-blind, prospective)	Examine the effect of creatine supplementation on recovery of muscle strength after ACLR.
Ueda et al., 2017	Males (n=106); Females (n=87)	Single-bundle HT (n=61); Double-bundle HT (n=132)	21 ± 6.8 Y	Not reported	Standardised; 6 months	Prospective	Identify the factors that affect knee extensor strength recovery after ACLR with a HT autograft
Witvrouw et al., 2001	Males (n=27); Females (n=22)	BPTB (n=17); Double-bundle HT + gracilis (n=32)	24.4 Y (18-63); 24.6 Y (17-34)	Exclusion criteria for participant recruitment	Standardised; 9 months	Prospective	Evaluate the clinical outcomes after ACLR between BPTB and HT graft
Yasuda et al., 1995	Males (n=18) Females (n=13)	HT + gracilis (n=35)	24 ± 7.4	Meniscal injury (n=9) Menisectomy (n=4) Chondral (n=13)	Standardised for all participants; 9-12 months	Prospective (randomized)	Distinguish between morbidity caused by harvesting semitendinosus and gracilis tendons and morbidity associated with ACLR.

Bone-patellar-tendon-bone (*BPTB*); Hamstring tendon (*HT*); Years (*Y*); Anterior cruciate ligament reconstruction (*ACLR*); Whole body vibration training (*WBVT*); Knee Injury and Osteoarthritis Outcome Score (*KOOS*); Body mass index (*BMI*); Isokinetic test (*IKT*); Isometric test (*IMT*); Alternating consecutive maximal contractions (*ACMC*); Anterior cruciate ligament deficiency (*ACLD*); Objective Criteria-Based Rehabilitation (*OCBR*); usual care rehabilitation (*UCR*)

Appendix A. Table 2.3. Strength testing protocol of the included studies

Author	Isokinetic dynamometer	Timeline (months)	Muscle action	Isokinetic dynamometer setting	Strength measure
Anderson et al., 2002	Kincom 125	Preoperative, 6, and 12	Concentric Eccentric	60°/sec	Mean torque
Beard et al., 2001	Kincom 125	Preoperative, 6, and 12	Concentric	60°/sec	Mean torque
de Jong et al., 2007	Cybex II	Preoperative, 6, 9, and 12	Concentric	60°/sec and 180°/sec	Peak torque reported as LSD
Domingues et al., 2018	Biodex	Preoperative and 12	Concentric	60°/sec	Peak torque
Fu et al., 2013	Biodex	Preoperative, 1, 3, and 6	Concentric	60°/sec, 180°/sec, and 300°/sec	Peak torque and LSI
Hsiao et al., 2014	KIN-COM	Preoperative, 3, and 6	Isometric Concentric	10°, 30°, 50°, 70°, and 90° knee flexion 50°/sec, 100°/sec, 150°/sec, 200°/sec, and 250°/sec	Peak force reported as percentage of strength per kilogram of body weight (%BW) and LSI
Hsu et al., 2018	Humac	Preoperative, 3, and 6	Concentric	60°/sec	Peak torque normalised to participant body mass (Nm/Kg), modulus knee muscle strength and LSI
Janssen et al., 2013	Biodex	Preoperative, 6, and 12	Concentric	60°/sec, 180°/sec, and 300°/sec	Peak torque and total work
Jansson et al., 2003	Lido Multijoint II	Preoperative, 12, and 24	Concentric	60°/sec	Peak torque reported as LSI
Keays et al., 2000	Cybex	Preoperative and 6	Concentric	60°/sec and 120°/sec	Peak torque and LSD
Keays et al., 2001	Cybex	Preoperative and 6	Concentric	60°/sec and 120°/sec	Peak torque and LSD
Keays et al., 2003	Cybex	Preoperative and 6	Concentric	60°/sec and 120°/sec	Peak torque, LSI, and LSD
Knezevic et al., 2014a	Kin-Com AP125	Preoperative, 4, and 6	Isometric Concentric	45° knee flexion 60°/sec and 180°/sec	Peak torque, LSI, and H:Q ratio

Appendix A. Table 2.3. continued

Author	Isokinetic dynamometer	Timeline (months)	Muscle action	Isokinetic dynamometer setting	Strength measure
Knezevic et al., 2014b	Kin-Com AP125	Preoperative, 4, and 6	Isometric	45° knee flexion	Peak force, RFD, and LSI
Lee et al., 2015	Biodex	Preoperative, 6, and 12	Concentric	60°/sec and 180°/sec	Peak torque, total work, LSI, and H:Q ratio
Melikoglu et al., 2008	Cybex	Preoperative, 2, 4, 6, and 12	Concentric	60°/sec and 240°/sec	Peak torque reported as MD
			Concentric	240°/sec	Total work and endurance ratio reported as MD
Mittlmeier et al., 1999	Biodex	Preoperative, 3, and 6	Concentric	60°/sec and 180°/sec	Peak torque reported as LSD
Ogrodzka-Ciechanowicz et al., 2018	Not reported	Preoperative and 6	Isometric	90° knee flexion	Peak torque and Peak torque normalised to participant body mass (Nm/Kg)
Radziunas et al., 2012	Biodex	Preoperative and 6	Concentric	30°/sec, 180°/sec, and 300°/sec	Peak torque
Risberg et al., 2009	Cybex	Preoperative, 6, 12, and 24	Concentric	60°/sec and 240°/sec	Total work reported as LSI
Seo et al., 2017	Biodex	Preoperative, 3, 6, and 12	Concentric	60°/sec	Peak torque reported as LSI
Setuain et al., 2017	Humac	Preoperative and 12	Concentric	180°/sec	Peak torque and total work
Soon et al., 2004	Cybex	Preoperative, 3, and 6	Concentric	60°/sec and 240°/sec	Peak torque reported as LSI
Tanaka et al., 2010	Cybex	Preoperative and 6	Concentric	60°/sec	Peak torque, LSI, BWR%, and H:Q ratio

Appendix A. Supplementary table 2.3. continued

Author	Isokinetic dynamometer	Timeline (months)	Muscle action	Isokinetic dynamometer setting	Strength measure
Tashiro et al., 2003	Cybex	Preoperative, 6, 12, and 18	Concentric (KE)	60°/sec and 180°/sec	Peak torque reported as LSI
		Preoperative, 6, 12, and 18	Concentric (KF)	60°/sec @ 70°, 90°, and 110° knee flexion	
		Preoperative, 6, 12, and 18	Isometric (KF)	70° and 90° knee flexion (sitting position)	
		Preoperative and 18	Isometric (KF)	70° and 90° knee flexion (prone position)	
Teitsma et al., 2014	Biodex	Preoperative, 3, 6, 9, and 12	Concentric	60°/sec and 180°/sec	Peak torque reported as LSD
Thomas et al., 2013	Biodex	Preoperative and 6	Concentric	60°/sec	Peak torque normalised to participant body mass (Nm/Kg)
Tyler et al., 2004	Biodex	Preoperative, 1.5, 3, and 6 months	Concentric	60°/sec and 180°/sec	Peak torque and power reported as LSD
Ueda et al., 2017	MYORET RZ-450	Preoperative, 6, and 12 months	Concentric	60°/sec	Peak torque and LSI
Witvrouw et al., 2001	Cybex 350	Preoperative, 6, and 12 months	Concentric	60°/sec and 240°/sec	Peak torque reported as LSI
Yasuda et al., 1995	Cybex	Preoperative and 6 months	Concentric	60°/sec	Peak torque reported as LSI
		Preoperative, 1, 3, 6, 9, and 12 months	Isometric	60° and 90° knee flexion	

Limb stength deficit (*LSD*); Limb symmetry index (*LSI*); Percentage body weigth (*%BW*); Newton meter per kilogram (*Nm/Kg*); Hamstring:Quadriceps (*H:*Q); Rate of force development (*RFD*); Mean difference (*MD*); Body weight ratio % (*BWR%*); Knee extensors (*KE*); Knee flexors (*KF*); Not reported (*NR*)

Appendix A. Supplementary Table 4.1. Descriptive statistics for quadriceps and hamstring strength data for males and females across early and late rehabilitation after anterior cruciate ligament reconstruction.

Strength measure	LSI (%)			
	Early rehabilitation		Late rehabilitation	
	Females (n=38)	Males (n=51)	Female (n=23)	Males (n=19)
Concentric hamstring MVC (60°/sec)	85 ± 12	86 ± 15	94 ± 11	90 ± 15
Concentric hamstring MVC (180°/sec)	88 ± 10	88 ± 14	93 ± 10	90 ± 16
Isometric hamstring MVC	74 ± 18	76 ± 16	85 ± 13	82 ± 15
Isometric hamstring RTD	84 ± 22	87 ± 58	86 ± 26	80 ± 16
Concentric quadriceps MVC (60°/sec)	67 ± 15	77 ± 14	89 ± 10	93 ± 14
Concentric quadriceps MVC (180°/sec)	70 ± 13	81 ± 13	86 ± 10	88 ± 13
Isometric quadriceps MVC	83 ± 18	91 ± 21	92 ± 23	95 ± 16
Isometric quadriceps RTD	73 ± 31	88 ± 27	92 ± 29	92 ± 21

Data presented as mean ± standard deviation; *LSI* limb symmetry index, *MVC* maximum voluntary contractions, *RTD* rate of torque development.

Appendix A. Supplementary Table 4.2. Post-hoc sensitivity analysis of quadriceps and hamstring strength data in early and late-stage rehabilitation after anterior cruciate ligament reconstruction collapsed across males and females who had data at both the early and late rehabilitation time points.

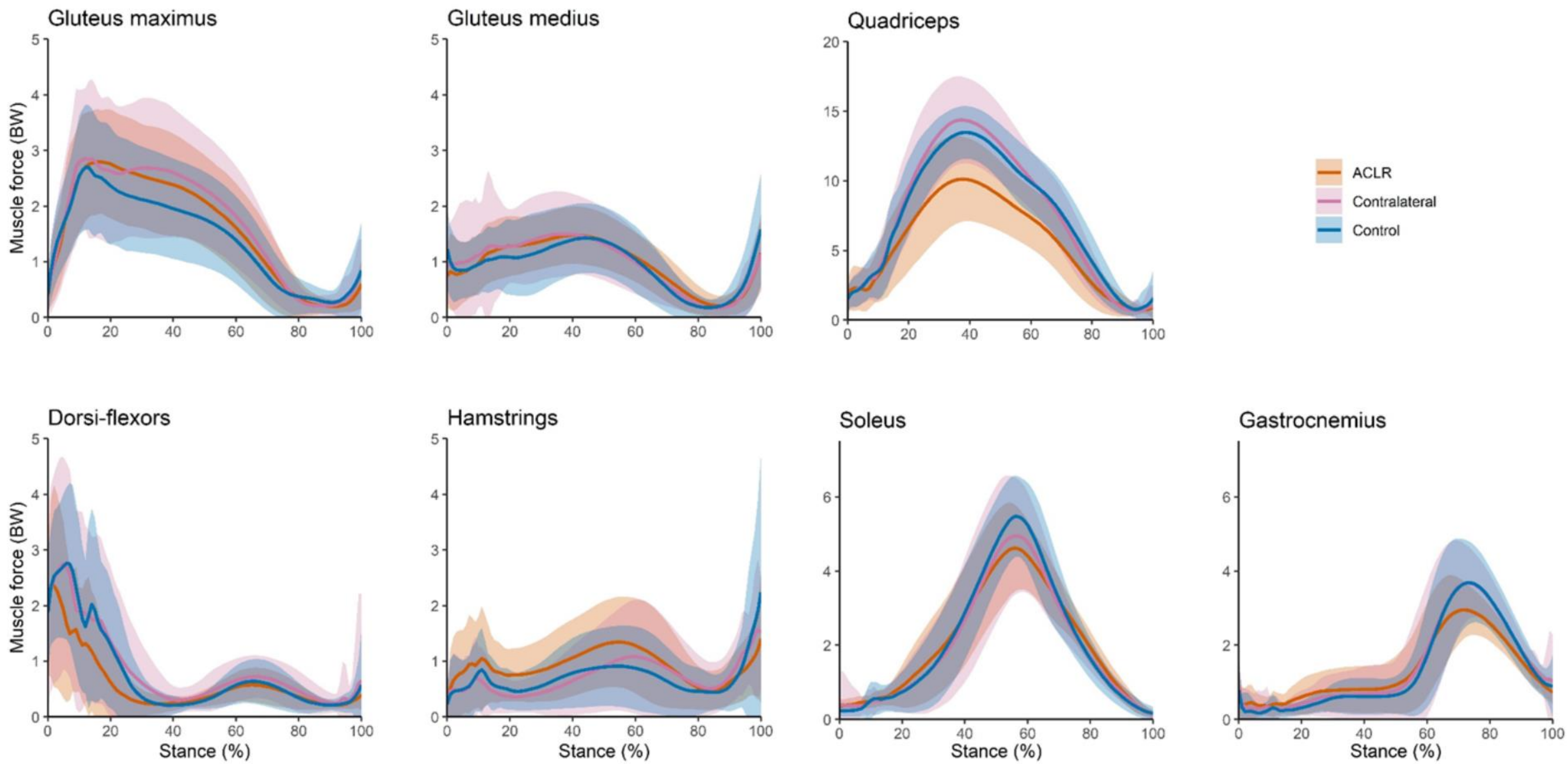
Strength measure	LSI (%)		Main effect
	Early rehabilitation	Late rehabilitation	Time
Concentric hamstring MVC (60°/sec)	85 ± 16	94 ± 12	0.003*
Concentric hamstring MVC (180°/sec)	88 ± 13	93 ± 13	0.010*
Isometric hamstring MVC	78 ± 20	85 ± 13	0.018*
Isometric hamstring RTD	90 ± 66	84 ± 22	n.s.
Concentric quadriceps MVC (60°/sec)	71 ± 15	92 ± 12	<0.001*
Concentric quadriceps MVC (180°/sec)	76 ± 14	87 ± 11	0.001*
Isometric quadriceps MVC	91 ± 22	95 ± 20	n.s.
Isometric quadriceps RTD	82 ± 35	91 ± 24	n.s.

Data presented as mean ± standard deviation; *LSI* limb symmetry index, *MVC* maximum voluntary contractions, *RTD* rate of torque development. *$p \leq 0.05$

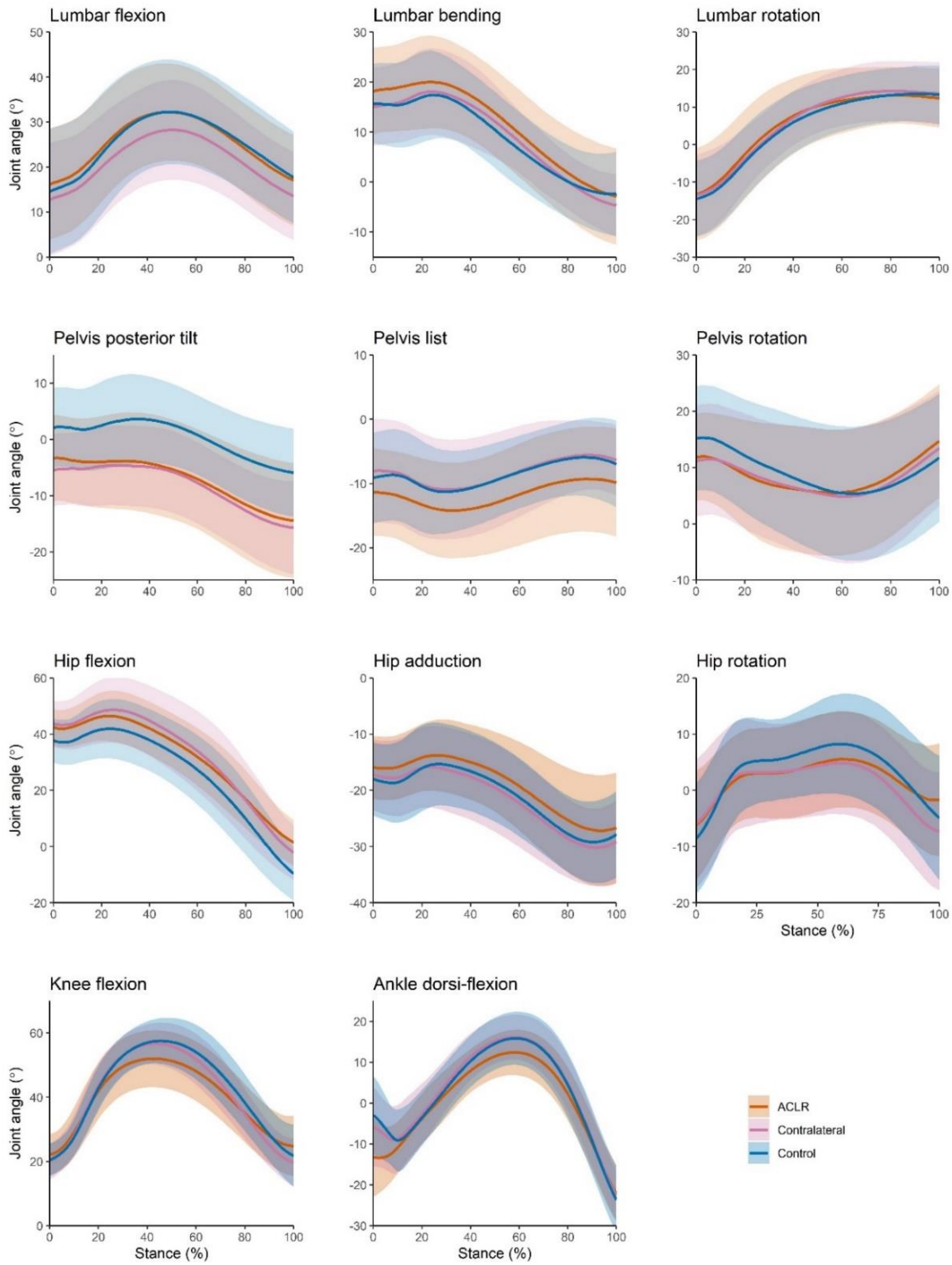
Appendix A. Supplementary Table 4.3. Post-hoc sensitivity analysis of quadriceps and hamstring strength data for males and females collapsed across early and late rehabilitation after anterior cruciate ligament reconstruction collapsed across time for participants who had data at both the early and late rehabilitation time points.

Strength measure	LSI (%)		Main effect
	Females	Males	Sex
Concentric hamstring MVC (60°/sec)	90 ± 13	89 ± 16	n.s.
Concentric hamstring MVC (180°/sec)	91 ± 10	90 ± 16	n.s.
Isometric hamstring MVC	83 ± 18	81 ± 15	n.s.
Isometric hamstring RTD	85 ± 24	89 ± 64	n.s.
Concentric quadriceps MVC (60°/sec)	78 ± 17	84 ± 17	n.s.
Concentric quadriceps MVC (180°/sec)	79 ± 13	84 ± 14	0.045*
Isometric quadriceps MVC	91 ± 21	96 ± 21	n.s.
Isometric quadriceps RTD	84 ± 33	90 ± 25	n.s.

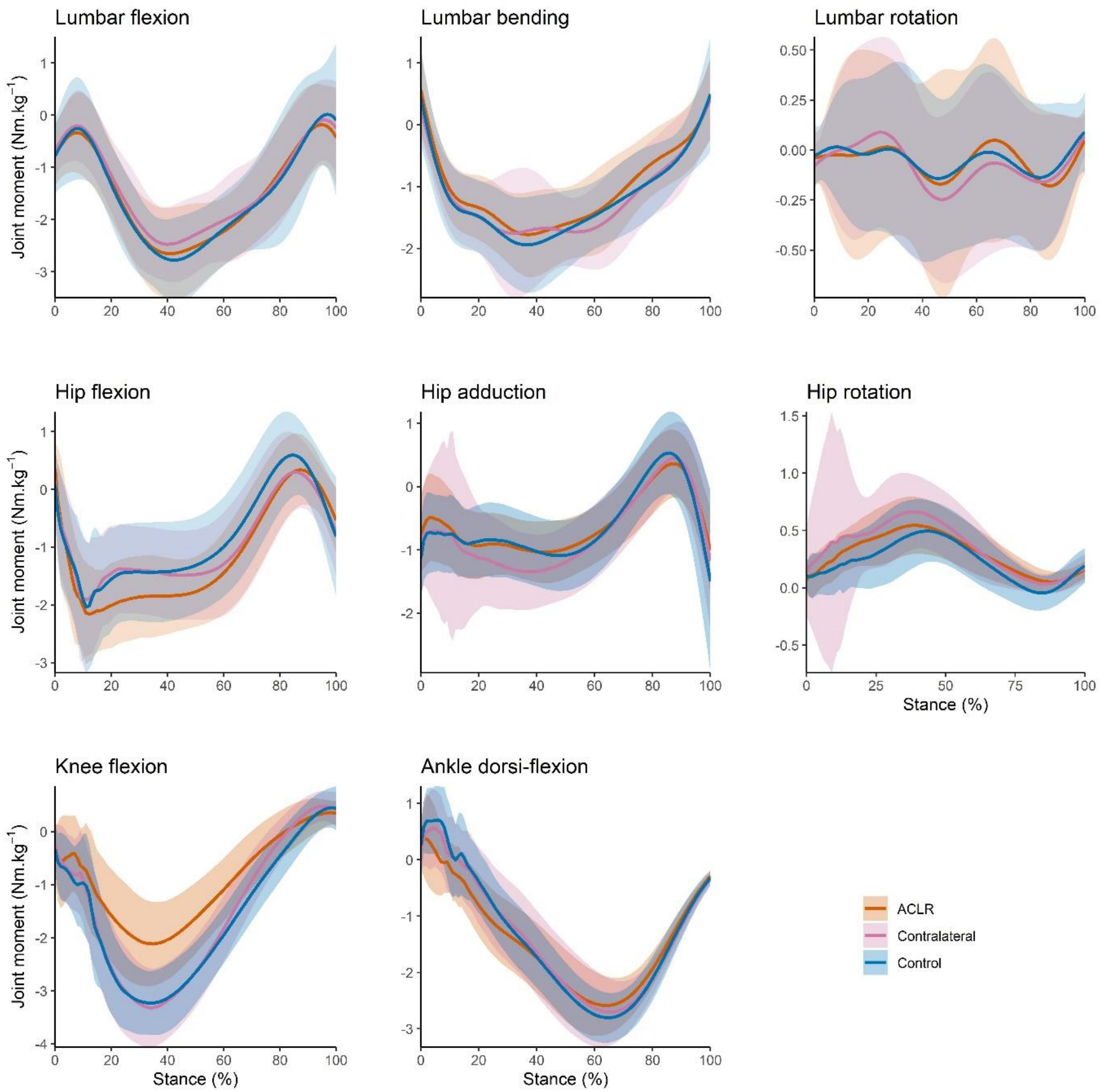
Data presented as mean ± standard deviation; *LSI* limb symmetry index, *MVC* maximum voluntary contractions, *RTD* rate of torque development. *$p \leq 0.05$



Appendix A. Figure 5.1. Lower limb muscle forces during the stance phase of the anticipated sidestep cut between the ACLR (orange line), Contralateral (pink line), and Control (blue line) limbs. Values are averaged across all participants and reported as body weight. *ACLR*, anterior cruciate ligament reconstruction; *BW*, body weight



Appendix A. Figure 6.1. Joint angles during the stance phase of the anticipated sidestep cut between the ACLR (orange line), Contralateral (pink line), and Control (blue line) limbs. Values are averaged across all participants and reported in degrees. *ACLR*,anterior cruciate ligament reconstruction.



Appendix A. Figure 6.1. Lower limb joint moments during the stance phase of the anticipated sidestep cut between the ACLR (orange line), Contralateral (pink line), and Control (blue line) limbs. Values are averaged across all participants and reported as Newton metres of torque normalised to body mass. *ACLR*,anterior cruciate ligament reconstruction; *Nm.kg*, Newton metres of torque normalised to body mass.

Appendix B. Research portfolio

Publications

1. San Jose AJ, Maniar N, Timmins RG, Beerworth K, Hampel C, Tyson N, Williams MD, Opar DA. Explosive hamstrings strength asymmetry persists despite maximal hamstring strength recovery following anterior cruciate ligament reconstruction using hamstring tendon autografts. Knee Surg Sports Traumatol Arthrosc. 2022 Aug 23. doi: 10.1007/s00167-022-07096-y. Epub ahead of print. PMID: 35999280.

Contribution statement:

ASJ participated in study design, data processing, data analysis, statistical analysis, manuscript preparation, and manuscript editing, DO participated in study conception, study design, statistical analysis, manuscript preparation and manuscript editing; NM participated in data processing, data analysis, statistical analysis, and manuscript editing; RT participated in manuscript preparation, and manuscript editing, KB participated in study conception, study design, participant recruitment, and data collection, and manuscript editing; CH participated in data collection, participant recruitment, and manuscript editing; NT participated in data collection, participant recruitment, and manuscript editing; MW participated in data analysis, statistical analysis, and manuscript editing. All authors have read and approved the final version of the manuscript and agree with the order of presentation of the authors.

Approximate percentage contributions – San Jose AJ 70%, Maniar N 10%, Timmins RG 2%, Beerworth K 2%, Hampel C 2%, Tyson N 2%, Williams MD 2%, Opar DA 10%.

I acknowledge that my contribution to the above publication is 70%:

[redacted]

Argell J San Jose

As principal supervisor, I certify that the above contributions are true and correct:

[redacted]

David A Opar

Co-author signatures:

[redacted]

Nirav Maniar

[redacted]

Ryan G Timmins

[redacted]

Kate Beerworth

[redacted]

Chris Hampel

[redacted]

Natalie Tyson

[redacted]

Morgan D Williams

Under review

1. **San Jose AJ,** Maniar N, Whiteley R, Opar DA, Timmins, RG, Kotsifaki A. Lower patellofemoral joint contact force during side-step cutting following return to sport clearance after anterior cruciate ligament reconstruction. American Journal of Sports Medicine. Under review.

Contribution statement:

ASJ participated in study design, data processing, data analysis, statistical analysis, manuscript preparation, and manuscript editing, NM participated in data processing, data analysis, statistical analysis, and manuscript editing; RW participated in study conception, study design, participant recruitment, and data collection, and manuscript editing; DO participated in study conception, study design, manuscript preparation and manuscript editing; RT participated in manuscript preparation, and manuscript editing, AK study conception, study design, participant recruitment, and data collection, and manuscript editing. All authors have read and approved the final version of the manuscript and agree with the order of presentation of the authors.

Approximate percentage contributions – San Jose AJ 70%, Maniar N 10%, Whiteley R 5%, Opar DA 2.5%, Timmins RG 2.5%, Kotsifaki A 10% .

I acknowledge that my contribution to the above publication is 70%:

[redacted]

Argell J San Jose

As principal supervisor, I certify that the above contributions are true and correct:

[redacted]

David A Opar

Co-author signatures:

[redacted]

Nirav Maniar

[redacted]

Rod Whiteley

[redacted]

Ryan G Timmins

[redacted]

Argyro Kotsifaki

Under preparation

1. **San Jose AJ,** Kotsifaki A, Whiteley R, Opar DA, Timmins, RG, Maniar N. Lower limb muscle contributions to sidestep cutting tasks at return to sport after anterior cruciate ligament reconstruction. British Journal of Sports Medicine. Under preparation.

Contribution statement:

ASJ participated in study design, data processing, data analysis, statistical analysis, manuscript preparation, and manuscript editing, AK study conception, study design, participant recruitment, and data collection, and manuscript editing, statistical analysis, and manuscript editing; RW participated in study conception, study design, participant recruitment, and data collection, and manuscript editing; DO participated in study conception, study design, manuscript preparation and manuscript editing; RT participated in manuscript preparation, and manuscript editing, NM participated in data processing, data analysis. All authors have read and approved the final version of the manuscript and agree with the order of presentation of the authors.

Approximate percentage contributions – San Jose AJ 70%, Kotsifaki A 10%, Whiteley R 5%, Opar DA 2.5%, Timmins RG 2.5%, Maniar N 10%.

I acknowledge that my contribution to the above publication is 70%:

[redacted]

Argell J San Jose

As principal supervisor, I certify that the above contributions are true and correct:

[redacted]

David A Opar

Co-author signatures:

[redacted]

Nirav Maniar

[redacted]

Rod Whiteley

[redacted]

Ryan G Timmins

[redacted]

Argyro Kotsifaki

Conference presentation

1. **San Jose AJ,** Maniar N, Timmins RG, Beerworth K, Hampel C, Tyson N, Williams MD, Opar DA. Explosive hamstrings strength asymmetry persists despite maximal. hamstring strength recovery following anterior cruciate ligament reconstruction using hamstring tendon autografts. Sports Medicine Australia – Gold Coast, Australia. November 2022.

Contribution statement: This presentation is based on the work from Chapter 4 (see above for author contributions). The presentation will be designed and delivered by ASJ. RT, NM, and DO will review the presentation and provide feedback.

Appendix C. Ethics approval information

The following section contains materials related to ethics approval on the studies conducted in Chapters 4, 5, and 6.

Appendix C. Study 2 Ethics approval letter

2017-17H Ethics application approved!

Pratigya Pozniak <Pratigya.Pozniak@acu.edu.au>
on behalf of
Res Ethics <Res.Ethics@acu.edu.au>
Fri 2/06/2017 11:36 AM
To: David Opar <David.Opar@acu.edu.au>;Argell San Jose <Argell.SanJose@acu.edu.au>
Cc: Res Ethics <Res.Ethics@acu.edu.au>

Dear Applicant,

Principal Investigator: Dr David Opar
Co-Investigator: Kate Beerworth
Research Assistant: Argell San Jose
Ethics Register Number: 2017-17H
Project Title: Assessing hamstring function throughout rehabilitation from anterior cruciate ligament reconstructive surgery: association with age and gender.
Date Approved: 02/06/2017
Ethics Clearance End Date: 31/12/2021

This is to certify that the above application has been reviewed by the Australian Catholic University Human Research Ethics Committee (ACU HREC). The application has been approved for the period given above.

Researchers are responsible for ensuring that all conditions of approval are adhered to, that they seek prior approval for any modifications and that they notify the HREC of any incidents or unexpected issues impacting on participants that arise in the course of their research. Researchers are also responsible for ensuring that they adhere to the requirements of the National Statement on Ethical Conduct in Human Research, the Australian Code for the Responsible Conduct of Research and the University¿s Code of Conduct.

Any queries relating to this application should be directed to the Ethics Secretariat (res.ethics@acu.edu.au). It is helpful if quote your ethics approval number in all communications with us.

If you require a formal approval certificate in addition to this email, please respond via reply email and one will be issued.

We wish you every success with your research.

Kind regards,

Kylie Pashley
on behalf of ACU HREC Chair, Dr Nadia Crittenden

Senior Research Ethics Officer | Research Services Office of the Deputy Vice Chancellor (Research)
Australian Catholic University

Appendix C. Study 2 Research flyer

ACU exercise science	PARTICIPATE IN RESEARCH Information for Prospective Participants

The following research activity has been reviewed via ACU arrangements for the conduct of research involving human participation.

If you choose to participate, you will be provided with more detailed participant information, including who you can contact if you have any concerns.

Assessing hamstring function throughout rehabilitation from anterior cruciate ligament reconstructive surgery: association with age and gender

Research Team Contacts

Kate Beerworth

Phone: 0402 421 084

Email: katebeerworth@hotmail.com

David Opar (Lecturer)

Phone: 03 9953 3742

Email: david.opar@acu.edu.au

Please contact the researcher team members to have any questions answered or if you require further information about the project.

What is the purpose of the research?

To investigate the association between age and gender on the recovery of hamstring strength throughout rehabilitation from ACL reconstructive surgery and to determine if poor recovery of hamstring strength at the conclusion of ACL reconstruction rehabilitation is a risk factor for recurrent ACL injury, regardless of age and gender.

Are you looking for people like me?

The research team is looking for male and female (aged 15-40) who have had an ACL reconstruction, via hamstring graft technique, within the previous 4 months.

What will you ask me to do?

Participation will be involve three (3) visits each lasting up to 60 minutes. These visits will be approximately 4 and 8 months into rehabilitation as well as at the conclusion of rehabilitation and will coincide with the participant's rehabilitation program with Wakefield Sports Clinic, Adelaide.

Participants will be asked to answer subjective questionnaires on physical activity levels, knee function and symptoms, and pain-related fear of movement. Furthermore, clinical and functional assessment of knee joint range of motion (ROM), knee joint laxity, single leg squat and one leg rise test, hop tests, and hamstrings and quadriceps strength will be performed.

Are there any risks for me in taking part?

The research team does not anticipate any major risks.

Are there any benefits for me in taking part?

It is not expected that this project will benefit you in the short term. In the long term, information gathered from this study could provide significant information for the development of better rehabilitation programs for ACL reconstruction.

I am interested – what should I do next?

If you would like to participate in this study, please contact the research team (contact details are given above) for details of the next step. You will be provided with further information to ensure that your decision and consent to participate is fully informed.

Thank You!	ACU Approval Number:	*2017-17H*

Appendix C. Study 2 Participant information letter

PARTICIPANT INFORMATION LETTER

PROJECT TITLE: Assessing hamstring function throughout rehabilitation from anterior cruciate ligament reconstructive surgery: association with age and gender.

PRINCIPAL INVESTIGATOR: Dr David Opar
CO-INVESTIGATOR: Ms Kate Beerworth
RESEARCH ASSISTANT: Mr Argell San Jose

Dear Participant,

You are invited to participate in the research project described below.

What is the project about?

Individuals with a history of anterior cruciate ligament (ACL) rupture and reconstructive surgery are 9-11 times more likely to sustain another ACL injury in the same leg, compared to individuals without a history of injury. The most common surgical technique used in Australia to reconstruct the ACL is to take part of the tendon of semitendinosus, one of the hamstring muscles on the back of the thigh, to use as a graft for the ruptured ACL.

Using the semitendinosus tendon to reconstruct the ACL can have an impact on the function and structure of the hamstring muscles, particularly the strength of the hamstrings. Regaining function in the hamstrings is a focus of a well-rounded rehabilitation program following ACL reconstructive surgery because the hamstrings are one of the primary muscles used to protect the ACL from injury during change of direction and landing. We still require a better understanding of how the hamstrings recover throughout ACL rehabilitation and whether age or gender influences the rate of recovery.

The project aims to assess hamstring function throughout rehabilitation from ACL reconstructive surgery and to investigate the association between age and gender on the recovery of hamstring strength. We would also like to determine if poor recovery of hamstring strength at the conclusion of ACL reconstruction rehabilitation, regardless of age or gender, is a risk factor for recurrent ACL injury.

The research team requests your assistance because you are a male or female aged between 15-40, who has had an ACL reconstruction, via a hamstring graft technique, at least 4 months ago.

Who is undertaking the project?
This project will be conducted by Dr David Opar (Bachelor of Applied Science – Human Movement, PhD) and Mr Argell San Jose (Bachelor of Exercise and Sports Science) from the School of Exercise Science at Australian Catholic University and Ms Kate Beerworth (Bachelor of Applied Science - Physiotherapy, Graduate Certificate – Sports Physiotherapy) Physiotherapist and Partner from the Wakefield Sports Clinic, Adelaide.
What is the experience of the research team?
Dr. Opar has been a lecturer and researcher for 6 years, with expertise in sports injury prevention and rehabilitation. He has published over 30 papers in scientific journals.

Mr. San Jose has completed a Bachelor of Exercise and Sports Science and has experience working as a strength and conditioning coach for the last two years.

Ms Beerworth is an APA Sports Physiotherapist with over 20 years clinical experience, including 10 years as the Head Physiotherapist for the Australian Women's Soccer team.

Potential conflicts of interests
Dr David Opar is the co-inventor of one of the devices which you will use as part of the study to assess your hamstring strength. This device is known commercially as the "NordBord" and is manufactured and distributed by Vald Performance Pty Ltd. Dr Opar maintains approximately a 5% share in the intellectual property of the "NordBord".

Are there any risks associated with participating in this project?
As with any injury, there is risk of re-injury during ACL rehabilitation. It should be noted that this research is not introducing anything beyond what is considered best-practice rehabilitation. The risk of re-injury will be minimised because your assessment will be overseen by experienced physiotherapists, who will employ best-practice, evidence based strategies to guide rehabilitation. The methods to assess your hamstring strength have been used extensively and are best practice following ACL reconstruction. Similarly, testing your hopping ability is best practice. Should either yourself or your physiotherapist decide that you are not ready to complete any of the testing procedures outlined these assessments will be omitted.

In the event that you sustain an ACL re-injury during an assessment at Wakefield Sports Clinic you may be required to undergo a second ACL reconstruction. It should be noted that Wakefield Sports Clinic has not had a patient suffer an ACL re-injury during such an assessment over the last 10 years. Should you sustain a re-injury as part of your assessment you will be provided information and guidance by your treating practitioner as to the best course of action for you.

Unless it can be proven that your treating practitioner or Wakefield Sports Clinic acted in a negligent manner that ultimately resulted in your ACL re-injury, the cost incurred and any subsequent consequences as a result of an ACL re-injury will be borne by the participant.

If you do not feel uncomfortable at any stage during your participation in this research project, you are free to withdraw from the study at any time without reason or further explanation.

What will I be asked to do?

Involvement in this project will require you to do nothing more than what you would normally do as part of your typical program of rehabilitation and follow up assessments with your physiotherapist, which normally occur four (4) and eight (8) months into your rehabilitation and once you are cleared to return to sport (approximately 12 month). We just request that we are able to record some of the data collected during these assessments. In addition, we would like to contact you once a year for five years to see if you have remained injury free.

The elements of the follow up assessments that we would like to collect data for are:

1) Questionnaires on your physical activity levels, knee function and symptoms, and pain-related fear of movement.
2) The amount of range of motion you have in your knee joint, specifically how far you can extend and flex your knee (both legs assessed).
3) How much laxity is in your knee (how "loose" is your knee) when pulled forward (both legs assessed).
4) The furthest distance you can hop with one single hop (both legs assessed).
5) The furthest distance you can hop with three consecutive hops (both legs assessed).
6) Maximal hamstring strength during an isometric contraction (both legs assessed).
7) Maximal hamstring strength during the Nordic hamstring exercise (both legs assessed).
   -

If you do not feel comfortable or confident in doing any of the aforementioned assessments, or your physiotherapist does not feel as though you are capable of performing these assessments, you can choose not to complete any of these assessments.

After your final assessment, we ask that we can maintain record of your contact details for the next five years. We will contact you once a year to check to see if you have remained injury free.

How much time will the project take?
Participation will coincide with your follow up assessments with your physiotherapist approximately on the fourth and eight month of your rehabilitation as well as at the conclusion of your rehabilitation program. These assessments are estimated to be no longer than 60 minutes each. The follow up contact to check on your injury status should be no more than a 5 minute phone call, once a year for five years.

Will participation in the project cost me anything financially?
There is no additional cost to you should you choose to participate in this project. You should note, however, that you are still required to pay Wakefield Sports Clinic for your assessment time, however the cost of this assessment would be the same regardless of whether your chose to participate in this project or not.

What are the benefits of the research project?

You will be given instant feedback on the results of your tests which will help your treating practitioner to further plan your rehabilitation and will help to frame discussion in regards to the return to sport decision making process. In the long term, information gathered from this study could provide significant information for the development of better rehabilitation programs for ACL reconstruction.

Can I withdraw from the study?

Participation in this study is completely voluntary. You are not under any obligation to participate. If you agree to participate, you can withdraw from the study at any time without adverse consequences. Your decision to participate will in no way impact upon your current or future relationship with Australian Catholic University, Wakefield Sports Clinic or with any of the investigators. If you do choose to withdraw from participation, the data collected up until that point may still be used by the investigators for the research purposes stated, unless otherwise requested by you. Should you choose to request that your data not be used, you will face no adverse consequences.

Will anyone else know the results of the project?

If you agree to participate in this project, the data will be provided to the research team in a de-identified format. No information will be provided to the research team that will enable your identity to be determined. It is intended that the results of this research will be submitted for publication within scholarly journals. All test results, comments and responses are anonymous and will be treated confidentially.

All data obtained:

- Will be stored for at least 5 years by the research team after your participation in the research project is complete.
- Will not be used for any other purpose (e.g. as an instructional aide).
- Can be accessed only by the research team.

As is standard clinical practice, the results of your testing will be shared with your attending orthopaedic surgeon and/or other allied health professionals who are assisting with your rehabilitation. This data will be provided to your surgeon and other allied health professionals whether you choose to participate in this research project or not. Should you not wish to have your data shared with these individuals please inform your treating practitioner at Wakefield Sports Clinic at the time of your consultation.

Will I be able to find out the results of the project?

All results will be available to be communicated to the participants upon their request for the data once their involvement within the project is complete. Participants are encouraged to contact the research team once this occurs. No distribution of data to the participants will occur without this prior request. Upon the request for the data, the participants will be given an individualised letter, outlining the specific information obtained. Participants will also be informed of any publication from the study (pending its acceptance).

Who do I contact if I have questions about the project?

Dr David Opar

Phone: 61 3 9953 3742
Email: david.opar@acu.edu.au

What if I have a complaint or any concerns?
This research has been reviewed by the Human Research Ethics Committee at Australian Catholic University (review number XXXX). If you have any complaints or concerns about the conduct of the project, you may write to the Chair of the Human Research Ethics Committee care of the Office of the Deputy Vice Chancellor (Research).

Manager, Ethics
c/o Office of the Deputy Vice Chancellor (Research)
Australian Catholic University
North Sydney Campus
PO Box 968
North Sydney, NSW, 2059
Ph: 02 9739 2519
Fax: 02 9739 2870
Email: res.ethics@acu.edu.au

Any complaint or concern will be treated in confidence and fully investigated. You will be informed of the outcome.

I want to participate! How do I sign up?

Please contact Ms Kate Beerworth or Dr David Opar to have any questions answered or if you require further information about the project.

If you would like to participate we would like to ask you to sign a written consent form (enclosed) to confirm your agreement to participate.

Yours sincerely,

Dr David Opar
Ms Kate Beerworth
Mr Argell San Jose

Appendix C. Study 2 Participant consent forms

PARTICIPANT CONSENT FORM

Copy for Researcher / Copy for Participant to Keep

TITLE OF PROJECT: Assessing hamstring function throughout rehabilitation from anterior cruciate ligament reconstructive surgery: association with age and gender.

PRINCIPAL INVESTIGATOR: Dr David Opar
CO-INVESTIGATOR: Ms Kate Beerworth
RESEARCH ASSISTANT: Mr Argell San Jose

I *.. (the participant)* have read (*or, where appropriate, have had read to me)* and understood the information provided in the Letter to Participants. Any questions I have asked have been answered to my satisfaction.

I agree to participate in the elements of this study which I have ticked below:

- ☐ I agree to participate in three 60-minute visits with my physiotherapist (which coincide with my scheduled follow-up consultations), following ACL reconstructive surgery at approximately:
  - ☐ 4 months post-surgery,
  - ☐ 8 months post-surgery
  - ☐ clearance for return to sport/conclusion of rehabilitation
- ☐ I understand that these visits will involve the answering of subjective questionnaires on physical activity levels, knee function and symptoms, and pain-related fear of movement as well as clinical and functional assessment of knee joint range of motion (ROM), knee joint laxity, single leg squat, one leg rise, hop tests, and hamstrings and quadriceps strength tests.
- ☐ I agree to allow the research team to contact me once a year for five years after the completion of my rehabilitation to check whether I have sustained a subsequent knee injury or not.
- ☐ I understand that I can withdraw my consent at any time for any reason (without adverse consequences)
- ☐ I agree that research data collected for the study may be published or may be provided to the research team or to other researchers in a form that does not identify me in any way.

Note that if you are under the age of 18, you and your parent/guardian are also required to read and sign a guardian consent form.

Please sign over the page

NAME OF PARTICIPANT: ....

SIGNATURE .... DATE

....

SIGNATURE OF INVESTIGATOR: ....

DATE:………………………..

Appendix C. Study 2 Participant consent forms (Guardian for minors)

GUARDIAN CONSENT FORM

Copy for Researcher / Copy for Parent/Guardian to Keep

TITLE OF PROJECT: Assessing hamstring function throughout rehabilitation from anterior cruciate ligament reconstructive surgery: association with age and gender.

PRINCIPAL INVESTIGATOR: Dr David Opar
CO-INVESTIGATOR: Ms Kate Beerworth
RESEARCH ASSISTANT: Mr Argell San Jose

I *.. (the parent or guardian)* have read (*or, where appropriate, have had read to me)* and understood the information provided in the Letter to Participants. Any questions I have asked have been answered to my satisfaction.

I agree to provide consent for the minor under my care to participate in the elements of this study which I have ticked below:

- ☐ I agree for the minor under my care to participate in three 60-minute visits with their physiotherapist (which coincide with their scheduled follow-up consultations), following ACL reconstructive surgery at approximately:
    - ☐ 4 months post-surgery,
    - ☐ 8 months post-surgery
    - ☐ clearance for return to sport/conclusion of rehabilitation
- ☐ I understand that these visits will involve the minor under my care answering subjective questionnaires on physical activity levels, knee function and symptoms, and pain-related fear of movement as well as clinical and functional assessment of knee joint range of motion (ROM), knee joint laxity, single leg squat test, one leg rise test, hop tests, and hamstrings and quadriceps strength tests.
- ☐ I agree to allow the research team to contact me and then subsequently the minor under my care once a year for five years after the completion of my rehabilitation to check whether the minor under my care has sustained a subsequent knee injury or not.
- ☐ I understand that I can withdraw my consent for the minor under my care at any time for any reason (without adverse consequences)
- ☐ I agree that research data collected for the study may be published or may be provided to the research team or to other researchers in a form that does not identify the minor under my care in any way.

Note that this form is required to be completed as you are the parent or guardian of a minor under the age of 18, who has been identified as eligible to participate in this study.

Please sign over the page

NAME OF MINOR: ....
(Note that the minor is required to sign a separate assent form which is provided to the minor by the research team)

NAME OF GUARDIAN: ....

SIGNATURE .... DATE

....

SIGNATURE OF INVESTIGATOR: ....

DATE:………………………..

Appendix C. Study 2 Participant consent forms (For minors)

MINOR ASSENT FORM
Copy for Researcher / Copy for Minor to Keep

TITLE OF PROJECT: Assessing hamstring function throughout rehabilitation from anterior cruciate ligament reconstructive surgery: association with age and gender.

PRINCIPAL INVESTIGATOR: Dr David Opar
CO-INVESTIGATOR: Ms Kate Beerworth
RESEARCH ASSISTANT: Mr Argell San Jose

I *.. (the participant)* have read (*or, where appropriate, have had read to me)* and understood the information provided in the Letter to Participants. Any questions I have asked have been answered to my satisfaction.

I agree to provide assent to participate in the elements of this study which I have ticked below:

- ☐ I agree to participate in three 60-minute visits with my physiotherapist (which coincide with my scheduled follow-up consultations), following ACL reconstructive surgery at approximately:
    - ☐ 4 months post-surgery,
    - ☐ 8 months post-surgery
    - ☐ clearance for return to sport/conclusion of rehabilitation

- ☐ I understand that these visits will involve the answering of subjective questionnaires on physical activity levels, knee function and symptoms, and pain-related fear of movement as well as clinical and functional assessment of knee joint range of motion (ROM), knee joint laxity, single leg squat test, one leg rise test, hop tests, and hamstrings and quadriceps strength test.

- ☐ I agree to allow the research team to contact me once a year for five years after the completion of my rehabilitation to check whether I have sustained a subsequent knee injury or not.

- ☐ understand that I can withdraw my assent at any time for any reason (without adverse consequences)

- ☐ I agree that research data collected for the study may be published or may be provided to the research team or to other researchers in a form that does not identify me in any way.

Please sign over the page

NAME OF PARTICIPANT: ....

SIGNATURE .... DATE

....

SIGNATURE OF INVESTIGATOR: ....

DATE:………………………..

Appendix C. Studies 3-4 Ethics approval letter

[2021-134H] - Ethics application approved!

Kylie Pashley <Kylie.Pashley@acu.edu.au>
on behalf of
Res Ethics <Res.Ethics@acu.edu.au>
Wed 7/28/2021 11:38 AM

To: David Opar <David.Opar@acu.edu.au>;Argell Joseph San Jose <argelljoseph.sanjose@myacu.edu.au>
Cc: Frances Taylor <Frances.Taylor@acu.edu.au>;Res Ethics <Res.Ethics@acu.edu.au>

Dear Applicant,

Chief Investigator: Dr David Opar
Co-Investigators: Dr Ryan Timmins, Nirav Maniar. (Admin Contact - Frances Taylor)
Student Researcher: Argell Joseph San Jose (Doctoral student)
Ethics Register Number: 2021-134H
Project Title: Lower limb muscle and joint forces during bilateral and unilateral exercises in healthy and anterior cruciate ligament reconstructed (ACLR) individuals
Date Approved: 28/07/2021
End Date: 31/08/2022

This is to certify that the above human ethics application has been reviewed by the Australian Catholic University Human Research Ethics Committee (ACU HREC). The application has been approved for the period given above.

Continued approval of this research project is contingent upon the submission of an annual progress report which is due on/before each anniversary of the project approval. A final report is due upon completion of the project. A report proforma can be downloaded from the ACU Research Ethics website.

Researchers are responsible for ensuring that all conditions of approval are adhered to and that any modifications to the protocol, including changes to personnel, are approved prior to implementation. In addition, the ACU HREC must be notified of any reportable matters including, but not limited to, incidents, complaints and unexpected issues.

Researchers are also responsible for ensuring that they adhere to the requirements of the National Statement on Ethical Conduct in Human Research, the Australian Code for the Responsible Conduct of Research and the University's Research Code of Conduct.

Any queries relating to this application should be directed to the Ethics Secretariat (res.ethics@acu.edu.au). Please quote your ethics approval number in all communications with us.

We wish you every success with your research.

Kind regards,

Kylie Pashley
on behalf of ACU HREC Chair, Assoc Prof. Michael Baker

Senior Research Ethics Officer | Research Services | Office of the Deputy Vice-Chancellor (Research)
Australian Catholic University
T: +61 2 9739 2646 E: res.ethics@acu.edu.au

Appendix C. Studies 3-4 Data sharing agreement letter

inspired by aspire®

ASPETAR سبيتار

TO:	Mr. Mohammed k. Al Suwaidi, DG
From:	Buthaina Mahmoud, Senior Specialist - Risk Management
DATE:	Tuesday, March 2, 2021
REF:	02 03 2021 1
SUBJECT:	Risk Assessment: Data Transfer and Use Agreement - ACU - IRB F2017000227

Dear Mr. Mohammed,

The above referenced Agreement is between Aspetar and the Australian Catholic University (ACU) for a term of three (3) years from the date of last signature.

This agreement is at no cost. Aspetar will be sharing de-identified data with ACU electronically. The data will be used for research purposes, specifically for a project titled: "*Risk factors associated with ACL injury and correlates of recovery following ACL reconstruction in athletic populations*".

The agreement template has been previously reviewed and approved by AZF Legal and Risk. The Research Department has another ongoing agreement with ACU; no issues or concerns were reported. Signing this agreement will be reasonable and demonstrates low risk to Aspetar.

Thank you for your consideration of this request. I am available to discuss at your convenience.

Sincerely,

[redacted]

Buthaina Mahmoud

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أحد أعضاء A member of
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