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Knee strength symmetry at 4 months is associated with criteria and rates of return to sport after anterior cruciate ligament reconstruction

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Knee strength symmetry at 4 months is associated with criteria and rates of return to sport after anterior cruciate ligament reconstruction

Abstract

Background. Strength limb symmetry index (LSI) is a useful criterion to help in return-to-sport performance (RTP) after anterior cruciate ligament reconstruction (ACLR).
Objectives. We aimed to assess whether knee extensor and flexor LSI values at 4 months after ACLR are associated with those recommended at 8 months after ACLR for RTP (80%, 85% and 90%) and with successful RTP after 2 years.

Methods. This was prospective cohort study of 113 participants who underwent primary ACLR. Personal factors such as demographic and sport information, injury and surgery characteristics were collected at 6 weeks after surgery. Isokinetic strength LSI (60°/s) was calculated at 4 months (LSI[4m]) and 8 months (LSI[8m]) for knee extensors (Q-LSI) and flexors (H-LSI). Participants were followed at 2 years after ACLR to determine their selfreported RTP. Multiple linear regression analysis was used to determine associations between personal factors and LSI at 4 and 8 months. Associations between passing the optimal cut-off thresholds and RTP were tested with chi-square tests and odds ratios (ORs) with effect sizes (ES).

Results. Among the 113 participants (mean age 25.2 [SD 9.7] years; 42% females), extended tourniquet time and lower level of pre-injury sport were associated with lower Q-LSI[4m] and H-LSI[4m]. Bone-patellar tendon-bone graft was associated with lower Q-LSI[4m] and Q-LSI[8m], and older age was associated with lower Q-LSI[4m]. For knee extensors, Q-LSI[4m] >59% was associated with Q-LSI[8m] >80% (OR= 31.50, p <0.001, large ES) and

increased odds of successful RTP (60% vs 31%, OR= 3.45, p= 0.003, medium ES). For knee flexors, H-LSI[4m] >72% was associated with H-LSI[8m] >90% (OR= 6.03, p <0.001, large ES) and increased odds of successful RTP (53% vs 23%, OR= 3.76, p= 0.013, small-to-medium ES).

Conclusions. After primary ACLR, 4-month post-operative strength symmetry was negatively associated with age, pre-injury sport and tourniquet time and bone-patellar tendon-bone graft. Four-month post-operative LSI was associated with 8-month post-operative LSI, and Q-LSI[4m] >59% or H-LSI[4m] >72% was associated with increased RTP rates after 2 years.

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Key words: ACL reconstruction; isokinetic testing; strength; limb symmetry index

Introduction

Anterior cruciate ligament (ACL) injuries are frequent and devasting among athletes [1]. ACL reconstruction (ACLR) is strongly suggested for ACL-deficient athletes who want to return to sport (RTS) participation, especially in pivoting sports requiring satisfactory knee stability [2]. Thus, the patient RTS status is a measure of successful outcome and is associated with patient satisfaction after ACLR [3,4]. This process of the RTS is viewed as a continuum from return to participation, RTS, and return to performance (RTP; performing at or above the preinjury level) [5]. However, the proportion of athletes successfully returning to their preinjury sport is relatively low, especially for amateur athletes (from 30% to 64% at 1 year after surgery)[6]. A systematic review with an average follow-up of 40 months after ACLR

showed that two thirds of individuals returned to unrestricted participation in their sport (RTS), and just 55% practiced at the same level (RTP)[7].

To improve the RTS rate and manage the steps of sport participation after ACLR, various criteria have been described and validated to assess the ability to participate in sport activities [8,9]. RTS decisions are mostly based on time since surgery; however, more individualized criteria are used, including subjective parameters such as patient-reported outcomes or injury-psychological readiness (e.g., the ACL-Return to Sport after Injury scale) [10] but also objective measures of symmetry between the injured and uninjured legs [11]. According to Brugi et al., strength symmetry was the second most frequently used criterion to manage the RTS decision after time since surgery and the most-used individualized criterion for managing the RTS after ACLR [11].

Isokinetic testing is the gold standard for measuring knee flexor-extensor strength; thus, it has been validated as a reliable and useful assessment to measure muscular symmetry after ACLR [12]. This evaluation can be assessed on a short timeline after ACLR (4 months) to optimize the return to running and sport-specific drills during rehabilitation [13–15]. For optimizing RTS decisions, this evaluation is mostly used between 6 and 8 months after surgery [12]. As for functional testing, the isokinetic-strength limb symmetry index (LSI) is an objective index calculated by using isokinetic strength parameters for the injured limb divided by those for the uninjured limb and mostly using peak torques for either knee extensors or flexors [12]. After ACLR, high LSI values at the time of the RTS were found associated with increased functional performance [16,17]; better outcomes at 2 years, including increased patient-acceptable symptom state [18]; and decreased risk of reinjury [19] but also reduced markers of knee cartilage degeneration at 5 years after the RTS [20]. Also, current definitions for optimal strength symmetry to enhance a safe RTS are derived from studies among professional athletes [21], and a few prospective studies have tested the impact of strength symmetry on an effective RTS after ACLR in wider populations of recreational and amateur athletes [22–24].

Defining clinically relevant cut-offs for isokinetic-strength LSI associated with successful RTS is still challenging [12]. Although an LSI >90% is targeted for functional and instrumental tests [25], isokinetic muscle-strength LSI >90% is rarely achieved, especially for knee extensors [26]. According to Burgi et al., who reviewed studies using isokinetic strength tests as RTS criteria after ACLR, the values of LSI >80%, >85% or >90% were equally used as acceptable cut-offs [11]. Specific cut-offs for isokinetic-strength LSI at 4 months have been studied to help in decision-making regarding the return to running [13,14], but little is known about the association of those cut-offs with achieving RTS criteria at 8 months post-operatively and a successful RTS, for all types of sport including pivoting and contact sports. However, an early identification of individuals at risk of not meeting the recommended criteria for strength symmetry at the RTS could provide useful information for physicians and physical therapists, help them to adapt post-ACLR rehabilitation and motivate individuals.

The main objective of this study was to test whether isokinetic-strength LSI values at 4 months after ACLR was associated with the LSI thresholds recommended at 8 months (80%, 85% and 90% for knee extensors, 90% for knee flexors) for successful RTP. Secondary objectives were to identify the individual pre-operative, intra-operative, and post-operative factors affecting the LSI at both 4 and 8 months and test the impact of achieving the cut-offs for LSI at 4 months (LSI[4m]) on the effective RTS. The hypotheses were that the isokinetic evaluation assessed at 4 months is valid and useful for identifying individuals at risk of not achieving the theoretical cut-offs for RTS of muscle symmetry at 8 months and that some individuals (young age, high pre-injury sport participation) and/or surgical factors (hamstring tendon autograft, isolated ACLR, short duration of tourniquet) were associated with a better

LSI. Also, we hypothesised that achieving LSI[4m] would be associated with increased rates of successful RTP.

Materials and Methods

This was a prospective cohort study conducted in the sport medicine department of a university hospital centre between January 2017 and February 2020, with secondary analysis of data.

Regulatory aspects

The protocol was conducted according to the Declaration of Helsinki, the local ethics committee granted approval (Biomedical and Public Health Research Committee, Centre Hospitalier Universitaire Caen Normandie; ID: CLERS-862), and informed consent was obtained from each participant. The study was registered at ClinicalTrials.gov (NCT04071912).

Participants

The study population was all individuals who underwent primary ACLR and were included in the RTS follow-up in the sport medicine department of a university hospital centre. We included individuals with primary ACLR, who were considered amateur and/or recreational athletes (individuals participating in sporting activities) and followed in the sport medicine department. The exclusion criteria were history of ipsilateral or contralateral severe knee injury (ligament or meniscus tear) or surgery, current or recent knee pain with an inability to perform the isokinetic test, unable to read the information form or ask questions, and not participating in the 3 visits. All participants had a patellar tendon autograft or a hamstring autograft, and all surgeons performed both techniques. The graft choice depended on the surgeon's habits, except for 2 specific indications: if a concomitant medial ligament injury had healed, a patellar ligament was indicated. For individuals with a specific profession or religion requiring kneeling, a hamstrings graft was preferred. The addition of a lateral extra-articular tenodesis was performed in case of a grade 3 pivot shift when performed under general anesthesia. The selection of the graft type was not influenced by the present research.

Rehabilitation after ACLR

After surgery, all participants were prescribed physical therapy sessions according to the evidence-based principles of postoperative ACL rehabilitation [27] with the overall physical therapy goals as follows: acute management immediately after surgery and for 3 weeks, focused on reducing swelling, minimizing pain, range of motion exercises, muscle activation, core body training and controlled walking pattern; from 3 weeks, additional strength exercises included progressive submaximal closed kinetic-chain exercises for knee flexors and extensors; at 5 weeks, strengthening exercises with increased loads were prescribed with progressive aerobic conditioning using stationary bikes, and neuromuscular or proprioception exercises were encouraged; open-chain knee extension strengthening was introduced at week 6.

At the 6-week visit (described below), participants were supposed to have no or limited effusion and pain, knee range of motion of at least 0° extension, and 120° to 130° flexion with good extensor control and stability with active resisted knee extension. After 6 weeks, dynamic agility drills and functional strengthening balance and coordination were incorporated. Running and progressive athletic performance-enhancement training techniques with plyometric exercises usually began 12 to 16 weeks after surgery. After 16 weeks, participants were supposed to have specific retraining in agility, plyometrics, functional movements and strengthening exercises according to their needs to return to their

preinjury/desired sport(s). The duration of rehabilitation or number of sessions was not standardized and depended on the individual's progress.

Study procedure

At 6 weeks after the surgery, participants had a first follow-up visit, when personal information, injury information and surgery information were recorded, and participants underwent a clinical examination. Personal information included sex, age, previous sport participation and level of participation. The pre-injury level of sport participation was structured according to the Compass profile [28] (type of participation and frequency of training) and defined as intensive/competitor practice (profiles 1-2, \geq 120 days per year or competitor), regular practice (profiles 3-4, 60-120 days per year) and irregular practice (profiles 5-6, 12-60 days and 1-12 days per year, respectively). Injury information data included the type of injury (isolated ACL, meniscus injury) and delay before surgery. Surgery information collected from the operative reports included the type of surgery (bone-patellar tendon-bone [BPTB] or hamstring tendon autograft, meniscus repair, or lateral extra-articular tenodesis) and duration of the tourniquet.

At 4 months, participants had a second follow-up visit with clinical examination and a muscle strength test on an isokinetic dynamometer according to the protocol described below. This timeframe corresponds to the theoretical stage for a return-to-running decision and optimization of rehabilitation program with return to basic sporting activities. At 8 months after the surgery, participants had a third follow-up visit with clinical examination and a muscle strength test on an isokinetic dynamometer. This timeframe was defined for the RTS decision, that is, the month before the recommended delay for a safe RTS [19,29], and was used in previous studies [15,30]. Furthermore, the national health system supports and covers

the medical evaluations with isokinetic assessment for ACLR follow-up at both times [31]. At each visit, participants were asked about their current physical therapy sessions.

During the standard follow-up after ACLR in the sport medicine department, participants were contacted at 1 and 2 years after the surgery and asked to complete a questionnaire about the RTS and/or RTP, any new injury and psychological readiness to return to sport. In the present study, we collected data on the RTP and considered a successful RTP as a return to performance at the preinjury level of sport after 2 years.

Isokinetic evaluation

The knee isokinetic strength profile was assessed by using a Con-Trex isokinetic dynamometer (Con-Trex MJ; Dübendorf, Switzerland). The testing apparatus was set up as described in the manufacturer's owner manual, and participants were positioned in the seated position for knee flexion/extension testing. All participants had a familiarization set of submaximal repetitions for all conditions. Data were collected from a first set of 4 maximal repetitions at 60°/s in the concentric mode and then a second set of 4 maximal repetitions at 240°/s in the concentric mode and then a second set of 4 maximal repetitions at 240°/s in the concentric mode with constant verbal stimulation [32]. At the 8-month visit, participants performed a similar isokinetic evaluation with an additional set of 3 submaximal then 3 maximal repetitions at 30°/s in the eccentric mode for the knee flexors only for calculating the "mixed" functional eccentric-to-concentric ratio, but this was not investigated in the context of the present study [32]. At all assessments, the participant's legs were passively weighted to provide gravity compensation data, and corrections were incorporated. The studied variables were the maximal peak torque (in Newton.meter [Nm]) and peak torque normalized to body weight (Nm/kg) assessed with a mechanical flat scale (Seca 750, Hamburg, Germany).

The LSI was calculated from the data at 60°/s in the concentric mode by dividing the peak torque on the injured leg by the peak torque on the other leg x 100% [33]. The optimal LSI at 8 months (LSI[8m]) for the hamstring was considered H-LSI[8m] >90%, and for the quadriceps, the optimal LSIs (RTS) for Q-LSI[8m] >80%, >85% or >90% were determined according to the literature [11,34]. LSI[4m] values associated with the optimal theoretical LSI[8m] for a safe RTS were analysed for H-LSI[8m] >90%, Q-LSI[8m] >80%, Q-LSI[8m] >80%, Q-LSI[8m] >85% or Q-LSI[8m] >90%.

RTS and RTP

Participants were followed up at a minimum of 2 years after surgery. They were asked to self-rate their RTS status by a response of yes or no to the following question: Did you return to your preinjury sport activity since the surgery? If so, they were asked to self-rate their RTP status by a response to the following question: Do you feel as though you can play or perform at your preinjury sports activity level?, with the answer being "below", "same level", and "higher". If they did not have an RTS or if the answer was "below", it was considered an unsuccessful RTP, and if the answer was "same level" or "higher", it was

Statistical analyses

Means (SD) or medians (interquartile range [IQR]) were calculated for all variables. The normality of the distribution of the data was checked by the Kolmogorov-Smirnov test. Paired Student *t* test was used to assess the difference in strength between the ACLR and the uninjured leg.

The association between the LSI[4m] and achievement of the optimal theoretical LSI[8m] among Q-LSI >80%, >85% and >90% and H-LSI>90% was assessed by univariate

receiver operating characteristic (ROC) curve analysis, and the area under the ROC curve was tested from the null hypothesis value 0.5 (meaning no discriminating power) with p-values. For each criterion (LSI), the participants were considered "responders" when they achieved the theoretical LSI[8m] for RTS. Optimal cut-off thresholds were determined by using the greater Youden index (J= sensitivity + specificity - 1) with a minimum sensitivity threshold assumed to be 0.8, and chi-square test was used to determine the odds ratios (ORs) of an impaired LSI[8m] at the final evaluation, with 95% confidence intervals (CIs) estimated.

A multivariate exploratory data analysis was used to identify factors associated with LSI. The bivariable selection involved using ANOVA (with F test) and Pearson correlations (r values) to determine the association between the studied covariates or cofactors and the LSI[4M] and LSI[8m]. Then, variables with P < 0.2 on bivariable analysis were included in the multiple linear regression analysis with the Wald test to assess independent factors or variables significantly associated with LSI values after ACLR. To determine the magnitude of the associations between variables and the LSI[4M] and LSI[8m], measures of the effect size using the Cohen's *w* for independence tests were considered to be small if *w*= 0.10, medium if *w*= 0.30, and large if *w*= 0.50 [37].

Associations between achieving the 4-month optimal cut-off corresponding to Q-LSI >80%, >85% and >90% and H-LSI>90% and RTP were tested by chi-square test to determine the ORs of a successful RTP. Effect sizes were calculated with the Phi (Φ) coefficient of association and were interpreted as small if $\Phi = 0.10$, medium if $\Phi = 0.30$, and large if $\Phi = 0.50$ [37].

For an estimated area under the ROC curve of 0.70 considering at least a 5:1 ratio of responders to non-responders (passing LSI criteria) [26], a minimum sample size of 106 was needed (α = 5%, β = 20%). Statistical analyses were performed with IBM SPSS Statistics 25.0 (IBM Corp., Armonk, NY) for Windows and Analyse-it (Analyse-it Software, Ltd., Leeds,

UK) for Excel. P<0.05 was considered statistically significant for all statistical analyses and Bonferroni correction was used to adjust for multiple comparison tests.

Results

Characteristics of participants

We included 113 participants (mean age 25.2 [SD 9.7] years; 42% females) who underwent primary ACLR and participated in both 4-month and 8-month isokinetic tests. The recruitment flowchart is presented in Figure 1 and characteristics of the participants are in Table 1. No professional athletes were included in the study.

Of the 113 included participants, 73 (65%) had a BPTB graft, and 40 (35%) had a hamstring tendon graft. The mean tourniquet time (n=110, 3 missing data) was 56.7 (SD 22.4) min, with a significantly higher duration for ACLRs associated with meniscus repairs and/or lateral extra-articular tenodesis than ACLR alone (mean 62.9 [26.1] vs. 49.8 [18.4], P= 0.003). At the 6-week visit, all participants had physical therapy for a mean of 4 (IQR 3–5) sessions per week, whereas 103 (91%) had physical therapy at 4 months for a mean of 3 (2–3) sessions per week; finally, 55 (49%) participants participated in a mean of 2 (2–2) sessions of physical therapy at 8 months.

Association between LSI[4m] and LSI[8m]

The isokinetic strength peak torques and ratios at the 4-month and 8-month evaluations are in Table 2. At 4 months, the mean Q-LSI[4m] was 60% (SD 18), and the mean H-LSI[4m] was 85% (17). At 8 months, the mean Q-LSI[8m] was 76% (15), and the mean H-LSI[8m] was 96% (17). In total, 50 participants (44%) had a Q-LSI[8m] >80%, 32 (28%) a Q-LSI[8m] >85%, and 19 (17%) a Q-LSI[8m] >90%, whereas 73 (65%) had an H-

LSI[8m] >90% at the same time. The ROC curve analysis with decision thresholds is in Table 3.

The ROC curve graphical representations and distribution of participants according to LSI are in Additional material 1. For knee extensors, on univariate ROC curve analysis of the Q-LSI, the initial Q-LSI[4m] >59% had the best ability to predict a Q-LSI[8m] >80% (J= 0.71, OR 31.50 [95% CI 10.67 ; 92.19], p< 0.001, Φ = 0.674), whereas an initial Q-LSI[4m] >67% had the best ability to predict a Q-LSI[8m] >85% (J= 0.56, OR 14.51 [5.39 ; 38.92], p< 0.001, Φ = 0.547), and a Q-LSI[4m] >71% had the best ability to predict a Q-LSI[8m] >90% (J= 0.51, OR 8.55 [3.12 ; 25.72], p< 0.001, Φ = 0.400) (Table 3). For knee flexors, an initial H-LSI[4m] >72% had the best ability to predict an H-LSI[8m] >90% (J= 0.28, OR 6.03 [2.13 ; 16.89], p< 0.001, Φ = 0.336).

Factors associated with LSI

After including all covariables or cofactors among individual, injury and surgery parameters associated with P< 0.2 on bivariate analysis (Additional material 2), we used multiple linear regression analysis to find independent factors or variables that significantly predicted strength symmetry at 4 and 8 months after ACLR (Table 4).

For extensor muscles, at 4 months, lower Q-LSI[4m] was associated with longer duration of tourniquet during the surgery (p= 0.012, w= 0.219), older age (p= 0.019, w= 0.240), lower level of pre-injury sport participation (p= 0.049, w= 0.193) and the use of a BPTB autograft (p< 0.001, w= 0.619). At 8 months, lower Q-LSI[8m] was associated only with the cofactor use of a BPTB autograft (p< 0.001, w= 0.433) and longer duration of tourniquet was associated but not significantly (p= 0.055, w= 0.183).

For flexor muscles, at 4 months, lower H-LSI[4m] was associated with longer duration of tourniquet (p=0.025, w=0.267) and lower level of pre-injury sport participation (p=0.029,

w= 0.193). At 8 months, the overall model was not significant and no variable/factor was significantly associated with lower H-LSI[8m].

Association between LSI[4m] and RTP

Of the 113 participants, 102 (90%) answered the follow-up questionnaire at a median of 2.4 years (IQR 2.1-2.8) after the surgery; 73 (72%) had returned to the preinjury sport and 47 (46%) had a successful RTP within the first 2 years after the surgery. The RTP rates comparing participants achieving or not achieving the LSI[4m] cut-offs are in Figure 2. Successful RTP rates were significantly higher for participants who had achieved Q-LSI[4m] >59% (OR 3.45 [95% CI 1.52 ; 7.84], χ = 9.08, p= 0.003, Φ = 0.300) or H-LSI[4m] >72% (OR 3.76 [1.26 ; 11.2], χ = 6.16, p= 0.013, Φ = 0.246). We found no significant association for Q-LSI[4m] >67% (OR 1.97 [0.87 ; 4.46], χ = 2.62, p= 0.103) or Q-LSI[4m] >71% (OR 2.27 [0.93 ; 5.52], χ = 3.33, p= 0.068). Passing both Q-LSI[4m] >59% and H-LSI[4m] >72% was associated with increased rate of successful RTP (OR 3.31 [1.47 ; 7.48], χ = 8.56, p= 0.003, Φ = 0.290).

Discussion

The main result of our study is that 4-month post-operative isokinetic assessment could help identify thresholds associated with the 8-month LSI recommended for a successful and safe RTS. Thus, for knee extensors, Q-LSI[4m] >59% should be achieved at 4 months if Q-LSI[8m] >80% is chosen as an RTS criterion at 8 months, Q-LSI[4m] >67% for Q-LSI[8m] >85% or Q-LSI[4m] >71% for Q-LSI[8m] >90%. For flexors, H-LSI[4m] >72% should be targeted at 4 months for an optimal H-LSI[8m] >90% at-8 months. Furthermore, achieving Q-LSI[4m] >59% or H-LSI[4m] >72% was associated with increased rates of successful RTP within the 2 years after the surgery.

Using 4-month isokinetic evaluations with validated cut-offs for LSI could help physicians and physical therapists identify individuals at early risk of low strength recovery and not meeting the criteria of strength for RTS [19,21]. Several previous studies have used a similar approach in attempting to validate clinical cut-offs as useful predictors of a successful RTS [38,39], but this is the first study to assess 4-month post-operative cut-offs associated with muscle asymmetry at 8 months, when an RTS is often considered. Recently, Beischer et al. [40] demonstrated that better strength symmetry at 4 months after ACLR was associated with increased odds of achieving symmetrical muscle function 1 year after ACLR. However, the authors assessed strength measurement using isometric or isokinetic tests, and LSIs were considered comparable and were analysed together, without specific cut-offs at 4 months. Additionally, in a recent paper, Dauty et al. used a similar approach with ROC analysis to test the Q-LSI associated with a return to running after ACLR. The authors found that a Q-LSI of 60% at 4 months after ACLR had good sensitivity and specificity in the decision to allow a return to running [14]. This cut-off is very close to the Q-LSI[4m] > 59% proposed in the present study for a similar timeframe and corresponding to an expected Q-LSI[8m]. Also, in a recent scoping review, Rambaud et al. reported the criteria for decision-making regarding the return to running after ACLR at a median of 12 postoperative weeks [13]. Among the studies using strength evaluation as a criterion, the most common value for isokinetic was LSI >70% (Q-LSI and H-LSI), within a slightly shorter timeframe than the early follow-up of the present study.

The proportion of participants who achieved the Q-LSI[8m] criteria was 44%, 28% and 17% for a Q-LSI[8m] >80%, >85% and >90%, respectively. This finding is consistent with the literature showing that quadriceps muscle symmetry is the least frequently met criterion after ACL surgery, with varying data according to the delay from surgery or the protocol used for the strength assessment [26,41] and greater achievement of symmetrical

knee extension after hamstring tendon autografts (over BPTB) [26]. Because the cut-off criteria for RTS are still debated and biomechanical studies of the impact of LSI on knee kinematics are conflicting [16,17], no consensus is clearly defined and further studies are needed to compare the outcomes when considering different values [19]. However, 65% of participants achieved the criteria for an H-LSI[8m] >90%, which is consistent with the literature finding that hamstring muscle symmetry is more quickly and more often obtained than is quadriceps muscle symmetry [42,43] and may result in an increased H:Q ratio, especially when using BPTB autografts [44].

The follow-up evaluation at 2 years after ACLR among 90% of the included participants showed a 72% rate of successful RTS and 46% rate of successful RTP, which is lower than the usual rates in athletes overall and slightly lower than non-elite athletes, corresponding to our population [2,7]. However, in the present study, competitive athletes were considered to have a successful RTP if returning to competitive sport at the same level (or higher) of participation and training. Ardern et al. [7] showed a mean of 42% of non-elite athletes returning to competitive levels after ACLR. The present study showed 3.5-fold significantly increased odds of successful RTP for participants passing the criteria of Q-LSI[4m] >59% and 3.8-fold significantly increased odds of successful RTP within the first 2 years for those passing the criteria of H-LSI[4m] >72%. These results corroborate findings suggesting that strength symmetry is associated with increased RTP, especially when using the criteria corresponding to an expected LSI >80% for knee extensors and LSI >90% for flexors. Indeed, similar rates of RTP were found with Q-LSI[4m] >59% and Q-LSI[4m] >71%, corresponding to Q-LSI[8m] >80% and >90%, respectively. These results indicate that the optimal threshold for a safe RTS still needs to be discussed because a targeted LSI of >80% is conservative and seemed to be associated with similar RTP rates in the present study of mostly non-elite athletes. However, further studies are needed to confirm these results and

test the impact of the cut-offs on long-term sport practice and reinjury rates. To our knowledge, this is the first study to assess the impact of the 4-month knee strength symmetry on the effective RTP and providing clinically relevant cut-offs associated with increased RTP.

Use of BPTB autografts were associated in lower Q-LSI[4m] and Q-LSI[8m], which is consistent with previous data [15,26,45], and we found no significant asymmetry in hamstring strength after hamstring tendon autografts. The superiority of BPTB over hamstring tendon autografts is still debated, and hamstring tendon grafts could favour an early return to sport participation [7], whereas BPTB grafts could allow participants to return to higher levels of activity and have demonstrated a slightly lower graft failure rate [7,46]. Also, other reconstruction techniques should be discussed (allografts, anterolateral-ligament reconstruction, increased rates of lateral extra-articular tenodesis, etc.), and further studies are needed to compare the strength asymmetry in various reconstruction techniques.

Tourniquet duration was an independent factor associated with reduced early LSIs for both hamstrings and quadriceps, regardless of the surgery. However, it was not associated with muscle asymmetry at the time of RTS, with only a tendency toward a statistically significant association with Q-LSI[8m], which is consistent with previous findings [47,48]. Nicholas et al. compared ACLR individuals with and without tourniquet use during surgery and found tourniquet use associated with decreased thigh girth at 3 weeks but with no effect on strength of knee extensors at 6 months [48]. This finding could be due to immediate and transient postoperative detrimental changes in muscle cell and fiber composition and negative electromyography changes after tourniquet use [49].

Our results suggest that level of pre-injury sport participation was associated with knee strength symmetry after ACLR because individuals with a high level of participation (Compass 1-2) had better H-LSI[4m] and Q-LSI[4m]. The better LSI at a 4-month delay for individuals with a preinjury high-level practice could be explained by the high motivation and

better athletic preparation favouring a return to the pre-injury sport level [7]. Also, older individuals had lower Q-LSI[4m], which confirms previous findings [26]. However, both age and level of pre-injury sport participation were not associated with muscle asymmetry at the time for RTS in our study. These findings should help motivate individuals and intensify strength training, especially for individuals at risk of strength asymmetry at this timeframe.

These results have several potential applications to be used in used in routine clinical practice and research. In a wide population of athletes (mostly nonelite), the isokinetic strength LSI at 4 months, with applicable cut-offs, is a valid method to identify individuals at risk for 1) not achieving the theoretical LSI for a safe RTS at 8 months and 2) not returning to the preinjury level of sport (RTP) after 2 years. For example, for individuals for whom an LSI >80% is expected for a safe RTS, those not achieving Q-LSI[4m] >59% are more likely to fail to meet RTS criteria and RTP after 2 years and may benefit from specific rehabilitation techniques in the later phase of rehabilitation [50]. Also, individual factors such as older age or lower level of practice in the preinjury sport as well as surgical factors such as longer use of a tourniquet and use of a BPTP graft were associated with poorer strength symmetry at 4 months. Thus, identifying individual factors at risk for not achieving acceptable strength symmetry at 4 months could help optimize preoperative and early rehabilitation after ACLR.

These results are presented with caution because of several limitations. First, this was a monocentric study in that we included participants from a single university medical center who underwent surgery by 4 main surgeons but using both hamstring tendon and BPTB grafts each and similar surgical techniques. Also, our participants had a predominance of patellar tendon autografts (65% vs 35% hamstring autografts), whereas the literature seems to show a slight superiority of hamstring autograft use in primary ACLR [51]. Additionally, although physical therapy was uniformly prescribed and session frequency data were collected, the type of exercise and rehabilitation techniques could have varied among participants. Moreover, we

calculated the LSI and ratio by using the peak torque values, as is common in the literature. However, a recent study described an angle-specific approach that could reveal strength deficits and asymmetries better than conventional parameters [52]. Finally, in this study, we focused on strength parameters, and functional testing should also be considered in the RTS decision-making process after ACLR [21]. However, despite good reliability and sensitivity to change, functional testing could still be improved, and data on its impact on RTS lacks consistency [53]. Also, RTS test batteries have been suggested to better incorporate multiple domains of risk factors among strength tests, functional tests and knee-related outcomes and/or psychological readiness for a safe RTS [27,54], but they exhibit low rates of meeting thresholds and limited evidence for validation and predictive value [54].

Conclusions

After ACLR, the use of isokinetic measurements of the strength LSI for both knee flexors and extensors at 4 months after the surgery is strongly associated with symmetrical muscle strength at 8 months, which is a common criterion for determining a safe RTS, with relevant cut-offs for clinical use and research settings. Achieving a Q-LSI[4m] >59% and/or H-LSI[4m] >72% was associated with 3-fold increased odds of successful RTP after 2 years. Early LSI was negatively affected by tourniquet duration, which was reversible over time, and use of a BPTB graft was associated with low Q-LSI persisting over time.

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Conflict of interest. None declared.

Figure legends

Figure 1. Flow of recruitment of study participants (n=113). ACL, anterior cruciate ligament; ACLR, anterior cruciate ligament reconstruction. The 58 individuals who were excluded because they participated only in the 4-month test (mean age 26.9 [SD 8.1] years; 33% females) did not significantly differ from included individuals in terms of age (t = -1.215, p= 0.226), sex ($\chi^2 = 1.26$, p = 0.261), type of autograft ($\chi^2 = 0.11$, p= 0.744), meniscus repair rates ($\chi^2 = 0.02$, p= 0.898) but also the LSI at the 4-month test (Q-LSI: t = 1.49, p = 0.137; H-LSI: t = 0.103, p = 0.918).

Figure 2. Graphical representation and comparison of return-to-performance (RTP) rates within the first 2 years after ACLR for participants achieving or not the 4-month strength LSI cut-offs (n=102). LSI, limb symmetry index; H, hamstrings; Q, quadriceps

Additional material

Additional material 1. Receiver operating characteristic (ROC) curves and distribution of participants meeting the criteria for strength limb symmetry index (LSI) at the time of the return to sport according to the early LSI with decision thresholds for predicting Q-LSI >80%, >85%, >90% and H-LSI >90% (n=113). Q-LSI, knee extensor limb symmetry index; H-LSI, knee flexor limb symmetry index; AUC, area under the ROC curve; TPF, true-positive fraction; FPF, false-positive fraction

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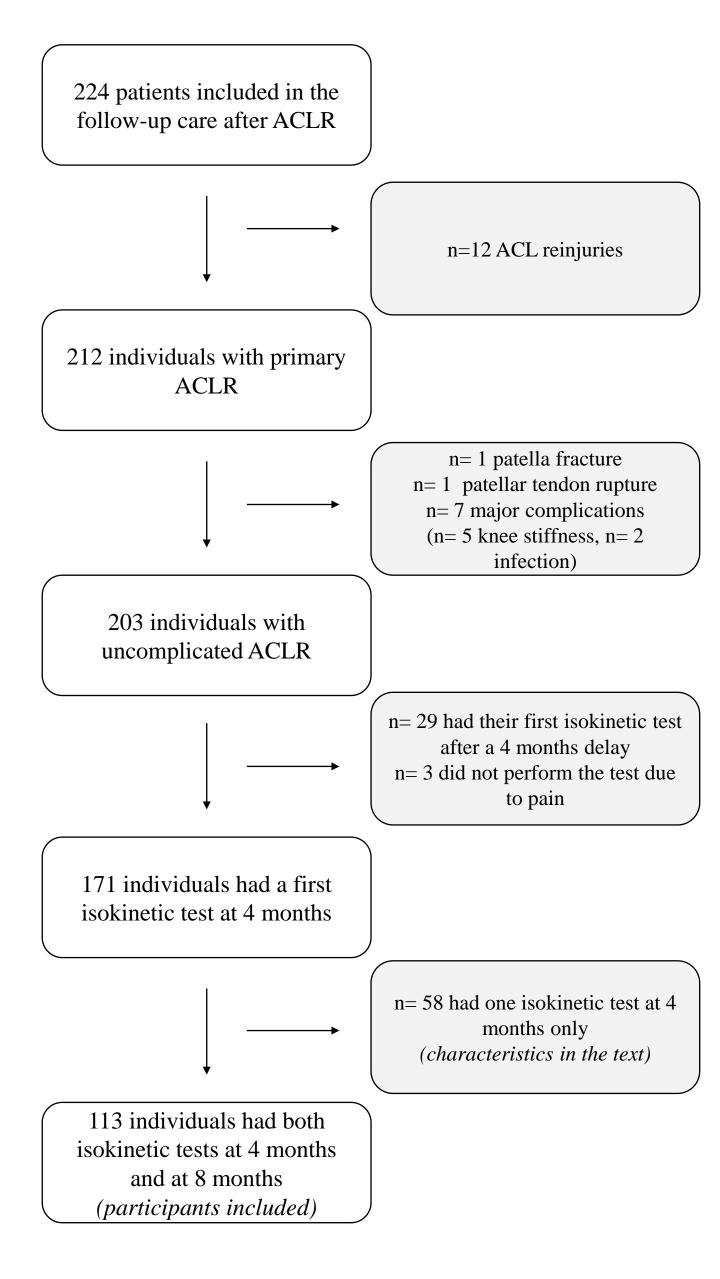
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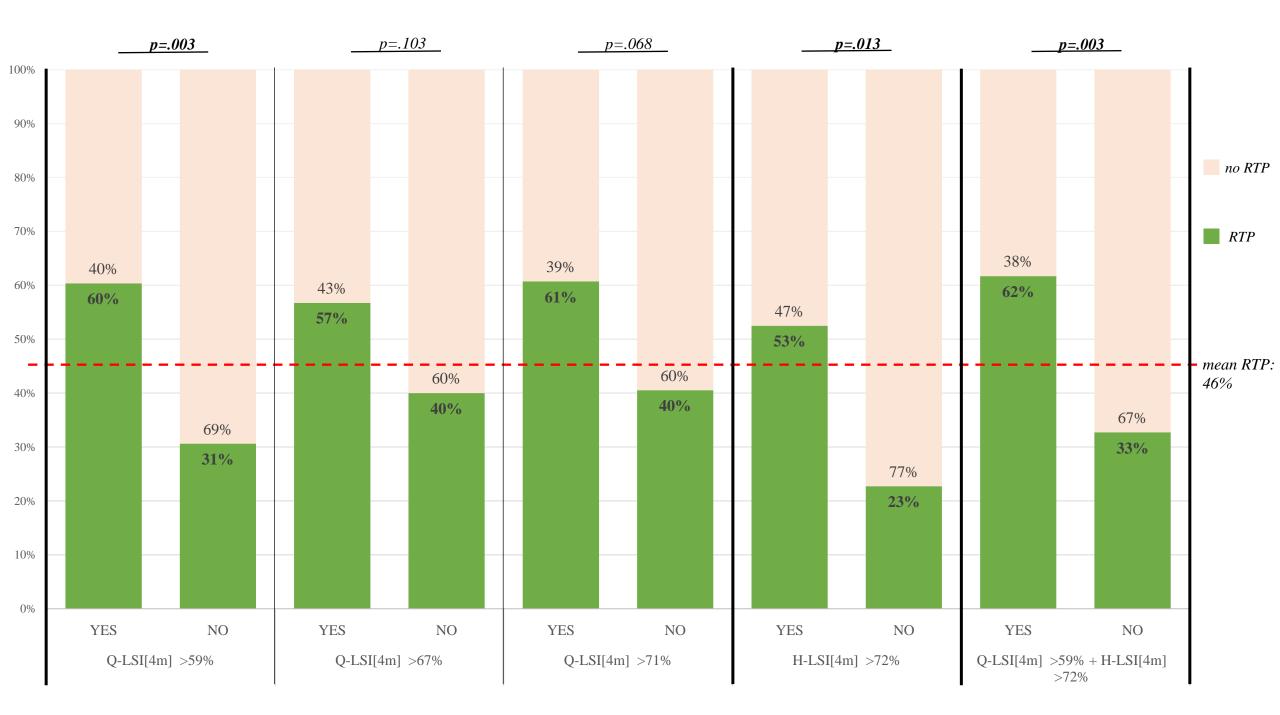


Table 1. Characteristics of participants with anterior cruciate ligament reconstruction (ACLR)
(n=113)

Sex 47 (42%) Male 66 (58%) Age (years) 56 (50%) >20 45 (40%) 20-40 56 (50%) ≥40 12 (11%) Type of pre-injury sport Non-pivoting Non-contact pivoting 28 (25%) Contact pivoting 70 (62%) Sport profile Compass 1-2 Compass 1-2 68 (60%) Compass 3-6 45 (40%) Injury Type Isolated 67 (59%) Combined 46 (41%) Time between injury and ACLR (months) <3 43 (38%) 3-6 37 (33%) >6 33 (29%) Surgery 41 (36%) ACLR + meniscus 41 (36%) ACLR + LEAT 4 (4%) Graft Patellar tendon 73 (65%) Hamstring 40 (35%) Tourniquet duration (min) ≤40 35 (31%) 41-60 46 (41%)	Individual	
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Non-pivoting 15 (13%) Non-contact pivoting 28 (25%) Contact pivoting 70 (62%) Sport profile 70 (62%) Compass 1-2 68 (60%) Compass 3-6 45 (40%) <i>Injury</i> 70 Type 1solated Isolated 67 (59%) Combined 46 (41%) Time between injury and ACLR (months) 43 (38%) 3-6 37 (33%) >6 33 (29%) Surgery 7 Type 44 (4%) ACLR + meniscus 41 (36%) ACLR + tLEAT 4 (4%) Graft 73 (65%) Patellar tendon 73 (65%) Hamstring 40 (35%) Tourniquet duration (min) ≤ 40 ≤ 40 35 (31%) $41-60$ 46 (41%)	Type of pre-injury sport	
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Contact pivoting 70 (62%) Sport profile 68 (60%) Compass 1-2 68 (60%) Compass 3-6 45 (40%) Injury Type Isolated 67 (59%) Combined 46 (41%) Time between injury and ACLR (months) <3 <3 43 (38%) $3-6$ 37 (33%) >6 33 (29%) Surgery Type ACLR 64 (57%) ACLR + meniscus 41 (36%) ACLR + LEAT 4 (4%) Graft Taillar tendon Patellar tendon 73 (65%) Hamstring 40 (35%) Tourniquet duration (min) ≤ 40 ≤ 40 35 (31%) $41-60$ 46 (41%)	Non-contact pivoting	28 (25%)
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Injury Type Isolated $67 (59\%)$ Combined $46 (41\%)$ Time between injury and ACLR (months) <3 $43 (38\%)$ $3-6$ $37 (33\%)$ >6 $33 (29\%)$ Surgery Y Type ACLR ACLR + meniscus $41 (36\%)$ ACLR + LEAT $4 (4\%)$ ACLR + meniscus + LEAT $4 (4\%)$ Graft $73 (65\%)$ Hamstring $40 (35\%)$ Tourniquet duration (min) ≤ 40 ≤ 40 $35 (31\%)$ $41-60$ $46 (41\%)$	Compass 3-6	
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Combined $46 (41\%)$ Time between injury and ACLR (months) 36 3.6 $37 (33\%)$ >6 $37 (33\%)$ >6 $33 (29\%)$ Surgery $33 (29\%)$ Surgery $41 (36\%)$ ACLR + meniscus $41 (36\%)$ ACLR + LEAT $4 (4\%)$ ACLR + meniscus + LEAT $4 (4\%)$ Graft $73 (65\%)$ Hamstring $40 (35\%)$ Tourniquet duration (min) $55 (31\%)$ 41.60 $46 (41\%)$	Туре	
Time between injury and ACLR (months) <3 $43 (38\%)$ $3-6$ $37 (33\%)$ >6 $33 (29\%)$ Surgery $33 (29\%)$ Surgery $41 (36\%)$ ACLR + meniscus $41 (36\%)$ ACLR + LEAT $4 (4\%)$ ACLR + meniscus + LEAT $4 (4\%)$ Graft $73 (65\%)$ Hamstring $40 (35\%)$ Tourniquet duration (min) $46 (41\%)$	Isolated	67 (59%)
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Combined	46 (41%)
$3-6$ $37 (33\%)$ >6 $33 (29\%)$ Surgery Type ACLR $64 (57\%)$ ACLR + meniscus $41 (36\%)$ ACLR + LEAT $4 (4\%)$ ACLR + meniscus + LEAT $4 (4\%)$ Graft 73 (65\%) Hamstring $40 (35\%)$ Tourniquet duration (min) ≤ 40 ≤ 40 $35 (31\%)$ $41-60$ $46 (41\%)$	Time between injury and ACLR (months)	
>6 $33 (29\%)$ Surgery Type ACLR $64 (57\%)$ ACLR + meniscus $41 (36\%)$ ACLR + LEAT $4 (4\%)$ ACLR + meniscus + LEAT $4 (4\%)$ Graft 73 (65\%) Hamstring $40 (35\%)$ Tourniquet duration (min) ≤ 40 ≤ 40 $35 (31\%)$ $41-60$ $46 (41\%)$	<3	43 (38%)
SurgeryTypeACLR $64 (57\%)$ ACLR + meniscus $41 (36\%)$ ACLR + LEAT $4 (4\%)$ ACLR + meniscus + LEAT $4 (4\%)$ Graft $73 (65\%)$ Patellar tendon $73 (65\%)$ Hamstring $40 (35\%)$ Tourniquet duration (min) 540 ≤ 40 $35 (31\%)$ $41-60$ $46 (41\%)$	3-6	37 (33%)
Type 64 (57%) ACLR 64 (57%) ACLR + meniscus 41 (36%) ACLR + LEAT 4 (4%) ACLR + meniscus + LEAT 4 (4%) Graft 73 (65%) Hamstring 40 (35%) Tourniquet duration (min) \leq 40 \leq 40 35 (31%) 41-60 46 (41%)	>6	33 (29%)
ACLR $64 (57\%)$ ACLR + meniscus $41 (36\%)$ ACLR + LEAT $4 (4\%)$ ACLR + meniscus + LEAT $4 (4\%)$ Graft 73 (65%) Hamstring $40 (35\%)$ Tourniquet duration (min) 540 ≤ 40 $35 (31\%)$ $41-60$ $46 (41\%)$	Surgery	
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ACLR + LEAT $4 (4\%)$ ACLR + meniscus + LEAT $4 (4\%)$ Graft $4 (4\%)$ Patellar tendon $73 (65\%)$ Hamstring $40 (35\%)$ Tourniquet duration (min) 540 ≤ 40 $35 (31\%)$ $41-60$ $46 (41\%)$	ACLR	64 (57%)
ACLR + meniscus + LEAT $4 (4\%)$ Graft73 (65\%)Patellar tendon73 (65\%)Hamstring40 (35\%)Tourniquet duration (min) 540 ≤ 40 35 (31\%) $41-60$ 46 (41\%)	ACLR +meniscus	41 (36%)
Graft73 (65%)Patellar tendon73 (65%)Hamstring40 (35%)Tourniquet duration (min) \leq 40 \leq 4035 (31%)41-6046 (41%)	ACLR + LEAT	4 (4%)
Patellar tendon $73 (65\%)$ Hamstring $40 (35\%)$ Tourniquet duration (min) $53 (31\%)$ $41-60$ $46 (41\%)$	ACLR + meniscus + LEAT	4 (4%)
Hamstring $40(35\%)$ Tourniquet duration (min) $35(31\%)$ $41-60$ $46(41\%)$	Graft	
Tourniquet duration (min) ≤ 40 35 (31%) $41-60$ 46 (41%)	Patellar tendon	73 (65%)
	Hamstring	40 (35%)
41-60 46 (41%)	Tourniquet duration (min)	
	≤ 40	35 (31%)
N60 20 (000/.)	41-60	46 (41%)
200 32 (28%)	>60	32 (28%)

LEAT, lateral extra-articular tenodesis

Table 2. Isokinetic knee flexor/extensor peak torques at 60°/s for ACLR and uninjured legs with between-leg differences (a) and limb symmetry index (LSI) ratios (b) at early and return to sport (RTS) stages (n=113)

		Early stage				RTS stage				
		Uninjured leg	ACLR leg	t	P-value	Uninjured leg	ACLR leg	t	P-value	
Peak torque										
	Extensors									
	Nm	170.8 (47.9)	102.4 (39.7)	-19.73	< 0.001	170.6 (49.0)	128.3 (40.4)	-15.30	< 0.001	
	Nm/kg	2.4 (0.5)	1.5 (0.5)	-19.73	< 0.001	2.4 (0.6)	1.8 (0.5)	-15.30	< 0.001	
	Flexors									
	Nm	93.5 (28.9)	79.0 (29.6)	-9.08	< 0.001	96.3 (30.4)	91.6 (29.9)	-3.41	< 0.001	
	Nm/kg	1.3 (0.3)	1.1 (0.4)	-9.08	< 0.001	1.4 (0.4)	1.3 (0.4)	-3.41	< 0.001	
Ratio										
	Unilateral									
	H:Q (%)	55 (9)	82 (26)	-11.01	< 0.001	57 (10)	74 (20)	-9.69	< 0.001	
Data are mear						•				

Data are mean (SD).

ACLR, anterior cruciate ligament reconstruction; H, hamstrings; Q, quadriceps

b)

		Early stage	RTS stage
Ratio			
LSI			
Q-LS	SI (%)	60 (18)	76 (15)
H-LS	SI (%)	85 (17)	96 (17)

Data are mean (SD).

ACLR, anterior cruciate ligament reconstruction; H, hamstrings; Q, quadriceps

a)

		ROC analysis		Decision thresholds				
Criterion to predict	Discriminative	95% CI	<i>p</i> -value	Cut-off	OR	95% CI	<i>p</i> -value	
	power							
Classifier	(AUC-ROC)							
Q-LSI[8m] >80%								
Q-LSI[4m]	0.904	0.85;0.96	< 0.001	Q-LSI[4m] >59%	31.50	10.67 ; 92.19	< 0.001	
Q-LSI[8m] >85%								
Q-LSI[4m]	0.870	0.81;0.94	< 0.001	Q-LSI[4m] >67%	14.51	5.39; 38.92	< 0.001	
Q-LSI[8m] >90%								
Q-LSI[4m]	0.816	0.73; 0.91	< 0.001	Q-LSI[4m] >71%	8.55	3.12;25.72	< 0.001	
H-LSI[8m] >90%								
H-LSI[4m]	0.690	0.59; 0.79	< 0.001	H-LSI[4m] >72%	6.03	2.13;16.89	< 0.001	

Table 3. Receiver operating characteristic (ROC) curve analysis of early limb symmetry index (LSI) with decision thresholds for predicting Q-LSI[8m] >80%, >85%, >90% and H-LSI[8m] >90% (n=113).

AUC, area under the ROC curve; OR, odds ratio; 95% CI, 95% confidence interval; H, hamstrings; Q, quadriceps; 8m, 8 months; 4m,

4 months

Table 4. Multivariate linear regression analysis of covariates and cofactors associated with the knee extensor limb symmetry index (Q-LSI) and knee flexor limb symmetry index (H-LSI) after ACLR (n=113).

		F	β	t	<i>p</i> -value	
Q-LSI[4m]	Overall model	10.44	•		< 0.001	
	Covariates/cofactors					
	Tourniquet duration (min)		-0.21	-2.54	0.012	
	Age (years)		-0.21	-2.39	0.019	
	Sport profile (0=Compass 1-2, 1= Compass 3-6)		-0.18	-1.99	0.049	
	Type of injury (0=isolated, 1= combined)		-0.10	-0.57	0.571	
	Type of surgery ($0 = ACLR$, $l = ACLR + meniscus/LEAT$)		-0.16	-0.95	0.346	
	Type of graft (0=hamstring, 1= patellar tendon)		-0.51	-6.12	< 0.001	
Q-LSI[8m]	Overall model	6.56			< 0.001	
	Covariates/cofactors					
	Tourniquet duration (min)		-0.18	-1.94	0.055	
	Age (years)		-0.12	-1.24	0.218	
	Sport profile (0=Compass 1-2, 1= Compass 3-6)		-0.17	-1.72	0.089	
	Type of injury (0=isolated, 1= combined)		0.04	0.48	0.634	
	Type of graft (0=hamstring, 1= patellar tendon)		-0.41	-4.46	< 0.001	
H-LSI[4m]	Overall model	4.70			0.002	
	Covariates/cofactors					
	Tourniquet duration (min)		-0.23	-2.28	0.025	
	Age (years)		-0.09	-0.84	0.403	
	Sport profile (0=Compass 1-2, 1= Compass 3-6)		-0.24	-2.22	0.029	
	Type of sport (0=non-pivoting, 1=pivoting, 2=pivoting- contact)		0.07	0.66	0.508	
H-LSI[8m]	Overall model	1.81			0.151	
	Covariates/cofactors					
	Tourniquet duration (min)		-0.13	-1.34	0.184	
	Uninjured leg strength (Nm/kg)		-0.11	-1.06	0.293	
	Time to surgery (months)		0.11	1.16	0.251	

H, hamstrings; Q, quadriceps; 4m, 4 months; 8m, 8 months