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Article

Pre- and Post-Operative Limb Symmetry Indexes and Estimated Preinjury Capacity Index of Muscle Strength as Predictive Factors for the Risk of ACL Reinjury: A Retrospective Cohort Study of Athletes after ACLR

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Featured Application: This study provides evidence about the superiority of preoperative knee extension LSI and EPIC index over the generally used postoperative LSI of muscle strength in estimating the risk of secondary injury after ACLR. While the optimal contents of an RTS test battery is still being searched for, this study indicates a potential importance of preoperative knee extension LSI and EPIC to differentiate between low-risk and high-risk patients for secondary ACL injury who need an adjusted rehabilitation plan depending on the degree of limb asymmetry.

Abstract: Long-term muscle weakness may increase the risk of knee reinjury after anterior cruciate ligament reconstruction (ACLR) and of osteoarthritis. The incidence of secondary injuries after ACLR and the predictive value of preoperative and postoperative limb symmetry index (LSI) and estimated preinjury capacity (EPIC) index were studied for predicting the risk of reinjury in a retrospective study. Sixty-three recreational and professional athletes after ACLR with hamstring autograft were followed for secondary injury in the period from 2012 to 2014, 5 years after ACLR. Peak torque values of knee extensor and flexor muscle strength of the involved and uninvolved limb were measured with an isokinetic dynamometer at 60 degrees per second before ACLR and 6 months after ACLR and were used to calculate LSI and EPIC index. The results suggest that the preoperative LSI and EPIC indexes predict a secondary ACL injury better than the postoperative LSI for extensor muscles which is often used as a criterion to determine the time for returning to normal sports activities. Individuals with secondary ACL injuries suffer greater loss of knee extensor muscle strength of the uninvolved limb between preoperative and postoperative ACLR testing compared to the individuals without secondary injury.

Keywords: anterior cruciate ligament; rehabilitation; return to sport; symmetry; strength testing; RTS criteria

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1. Introduction

Anterior cruciate ligament (ACL) knee injuries are common with an estimated incidence of approximately 81 ACL ruptures per 100,000 inhabitants aged 10–64 years [1]. Following ACL reconstruction (ACLR) many short-term and long-term problems may affect the health of the knee. Despite advances in ACLR, a high risk of secondary ACL injury is imminent. Return to sport (RTS) after primary ACL is associated with a 15- to 25-fold higher chance of a secondary ACL injury, as high as 22% for the involved knee and 24% for the contralateral knee five years after ACLR [2–6].

The risk of a secondary injury is a multifactorial phenomenon, the prediction of which should involve a broader approach to understand the complex relationships between risk factors and the occurrence of injuries better [7]. The individual's risk is influenced by different physical, psychological, and other factors. Main physical factors are based on impairments found in patients after ACLR. They include poor neuromuscular control and poor biomechanics known to contribute to secondary ACL injuries, such as greater knee abduction moment, smaller knee flexion angle during landing with compensatory hip flexion, patterns of favoring the uninjured contralateral limb, decreased quadriceps limb symmetry index (LSI) below 90%, decreased rate of force development and hop test LSI below 90% [8–12]. All these variables are influenced by other factors such as sex, age, previous injury, the amount of time elapsed since ACLR, and increased exposure to sports precipitation, unanticipated environmental events, and higher training load [7,8]. There is still a lack of adoption of the simplest RTS tests in clinical practice. The time from ACLR to RTS has been the most frequently reported criterion in the literature [13]. However, the recent consensus statement is that purely time-based RTS decision-making should be abandoned in clinical practice, and it must include objective physical examination data (e.g., clinical tests and measurements) [14]. A general recommendation for unrestricted RTS used to be 6 months, but recent evidence indicates that RTS should be delayed for at least 9 months; some authors even suggest that it should be delayed up to 2 years after ACLR [15,16]. There are many suggested prevention strategies with limited plausibility and dubious efficiency [17]. Currently, the best prevention programs include the restoration of all the reported neuromuscular impairments after primary ACLR; use of objective RTS assessment; and use of a prevention exercise program that includes plyometric, strength, and proprioception training [18,19]. Return to sport assessments are administered following ACLR with the goal of evaluating modifiable risk factors associated with secondary injury, such as physical and mental readiness to safely return to unrestricted activity [20]. Physical readiness is assessed with the goal of capturing the overall impact of knee injury on knee function. Knee function can be assessed with different instruments, such as patient reported outcome measures, performance-based outcome measures, and clinical outcome measures. An important part of RTS assessments is the use of different performance-based outcome measures and screening tools that measure unique constructs. Most of them use LSI for bilateral limb comparison or additional comparison to normative data of healthy controls. Some of the most common assessments are muscle strength measurements, hop tests, agility tests, Y-balance test, tuck jump assessments, or landing error scoring systems [21]. High incidence of secondary ACL injuries has been the matter of debate in the literature regarding the appropriate use of postoperative LSI in currently recommended RTS muscle strength testing criteria [22,23]. Several studies have shown that athletes passing the objective RTS muscle strength assessment are at a lower risk of any knee injury, contralateral ACL injury, and/or ACL graft reinjury [15,23,24].

Persistent knee extension (quadriceps) muscle weakness is the most commonly reported impairment 6 months after ACLR; longitudinal studies have shown, however, that they can persist up to 3 years and longer [9,25–27]. Grindem et al. [15] have shown that the degree of muscle strength deficit in knee extensor is more significant than hop testing in preventing a secondary ACL injury. Being unable to produce sufficient knee extensor force is also associated with changed knee biomechanics during hopping and subjective hop testing assessment is not sufficiently specific to pick up the deficits [27–29]. Isokinetic dynamometry represents the gold standard in the evaluation of muscle strength and is the most commonly used tool in the studies evaluating the strength deficits in RTS following ACLR [15,25]. Muscular weakness may be defined as LSI—the difference between peak torque of the ACLR limb and the uninvolved limb. The commonly used criterion of 90% symmetry between the limbs has been proposed as the minimum standard for the involved limb before the patient returns to unrestricted sports after the injury [15,24,30]. But the use of 90% LSI has been under scrutiny due to the reports of concurrent loss of knee extensor muscle strength of the uninvolved limb after ACLR, which can overestimate muscle strength recovery of the ACLR knee [31,32]. This raises concern of using the LSI to confirm symmetrical muscle function, which could be based on bilateral weakness and could lead to subsequent premature RTS decision. Therefore, the question is whether the comparison of the involved to the uninvolved side (LSI) after ACLR is a good enough measure to evaluate the adequate postoperative rehabilitation status for safe unrestricted RTS [33].

To date, several studies have investigated an interrelationship of isokinetic strength performance before and 6 months after ACLR [28,34,35]. Riesterer et al. [34] have found that preoperative knee extension and flexion strength are moderately correlated to postoperative strength performance after ACLR, but with high intraindividual variability. A preliminary study of Wellsandt et al. [36] has demonstrated a potential benefit of using the estimated preinjury capacity (EPIC) index instead of postoperative LSI. EPIC compares the knee extension strength of the ACLR operated limb with the strength of the uninvolved limb prior to ACLR to determine the readiness for RTS. The same study suggests that inability to restore the knee function exhibited before ACLR (EPIC) may increase the risk of secondary ACL injuries and is a better predictor of secondary injury than postoperative LSI. However, the authors have not reported preoperative LSI. Thus, the objective of our study was to investigate the predictive value of preoperative and postoperative LSI and EPIC index for secondary ACL injury. To our knowledge, there have not been studies investigating these three parameters as predictive factors for secondary ACL injury.

The aims of this study were therefore to assess: (1) if EPIC levels will show greater between-limb differences than preoperative or postoperative LSI, (2) if EPIC levels could predict secondary ACL injuries better than the preoperative or postoperative LSI, and (3) if patients with secondary ACL injuries will suffer greater loss of quadriceps muscle strength of the uninvolved limb in the time interval between preoperative and post ACLR testing, which we called the estimated preinjury capacity index of the healthy limb (EPIC-H).

2. Materials and Methods

We performed a retrospective cohort study of patients following an ACL injury and ACLR performed in the same institution between 2012 and 2014. Patient records were checked for the occurrence of secondary injuries up to 5 years after ACLR. A follow-up of 5 years was chosen to look for a short-term (first 9 months) and medium-term (up to 5 years) incidence of secondary ACL injuries. The incidence reported in the literature appears to be highest in the first 9 months after ACLR and still elevated up to 5 years after the ACLR compared to healthy control subjects [2–6]. All secondary injuries were confirmed by a licensed orthopedic surgeon and MRI. This study was approved by institutional review board (R-42020); all patients provided a voluntary informed consent.

2.1. Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (1) complete ACL rupture in active patients (professional or recreational athletes), (2) peak torque measurements for the strength of the knee extensor and knee flexion muscles of the involved and uninvolved limb prior to ACLR and at 6 months after surgery, (3) follow-up records of a maximum 5-years after ACLR. The exclusion criteria were (1) multiligamentous injuries, (2) severe arthritic changes of the knee evaluated as grade III-IV Kellgren–Lawrence (KL) or grade III-IV ICRS cartilage injury (International Cartilage Regeneration and Joint Society), (3) total or subtotal meniscectomy prior to ACLR on either side, (4) contralateral ACL deficient knee, and (5) contralateral partial ACL tear.

2.2. Patients and Treatment Procedures

In the observation period, 94 patients underwent ACLR using semitendinosus and gracilis tendon autografts. Preoperative patients' evaluations included demographic and anthropometric data (age, gander, height, weight, BMI and preoperative Tegner activity score). Nineteen patients completed only the first, preoperative testing and did not return for the second testing after ACLR; 5 patients did not complete preoperative testing; 5 patients had other symptoms, related to the knee ACL; 2 patients had hamstring autografts taken from the uninvolved leg and were excluded from the study. Thus, 63 patients aged from 14 to 63 years (mean age ± SD: 34.7 ± 12.3 years); 26 (41.3%) women and 37 (58.7%) men were included in further analysis. All patients were treated by the same surgeon (i.e., corresponding author). They all had anatomic single-bundle ACLR. In all patients, a hamstring tendon autograft was used with suspensory fixation on the femoral side and bioabsorbable interference screw fixation on the tibial side.

Patients were instructed to perform rehabilitation program at home while waiting for ACLR to resolve any possible impairments (effusion, range of motion, pain, gait impairments, muscle strength). All patients followed the same rehabilitation protocol with 3 physiotherapy sessions/week in the first 6 weeks after ACLR, and after week 7 post ACLR, 2 weeks of intensive post-operative rehabilitation in a rehabilitation center according to the standard rehabilitation protocol. After that, they received written instructions for late-stage home rehab program that they had to perform in the gym until the second testing; compliance to the rehab program was not measured.

2.3. Outcome Measures

Time intervals between the initial injury, preoperative testing, surgery, postoperative testing, and second injury were well documented and calculated. Isokinetic, concentric knee extension, and flexion strength (peak torque) were measured bilaterally between 0° and 90° using a Humac Norm isokinetic dynamometer (Humac Norm Testing & Rehabilitation System; CSM Inc., Stoughton, MA, USA) at speed of 60°/s, as used in other similar published studies [15,25,37]. Knee extension and flexion strength testing using the Humac Norm dynamometer is reliable when measuring the isokinetic muscle strength (Intraclass Correlation Coefficient = 0.89) [38]. All strength assessments were performed identically before and after ACLR. The second testing was performed six months after ACLR; this being the usual time to begin light non-contact sport activities, it seemed appropriate for evaluating the rehabilitation progress [20].

LSIs were calculated for the muscle strength of knee extension and flexion before and after ACLR using the Equation (1) [36]:

$$\text{LSI} = ((\text{Involved limb})/(\text{Uninvolved limb})) \times 100. \quad (1)$$

In addition to computing LSIs after ACLR, EPIC indexes were calculated for the muscle strength of knee extension and flexion using the Equation (2) [36]:

$$\text{EPIC} = ((\text{Involved Limb (after ACLR)})/(\text{Uninvolved Limb (initial evaluation)})) \times 100 \quad (2)$$

To determine limb-to-limb differences of the uninvolved knee extension and flexion between the initial testing before ACLR and the second one after ACLR, we calculated the EPIC indexes for the uninvolved, healthy limb (EPIC-H) using the Equation (3) [37]:

$$\text{EPIC-H} = ((\text{Uninvolved Limb (after ACLR)})/(\text{Uninvolved Limb (initial evaluation)})) \times 100. \quad (3)$$

A cut-off of 90% was operationally defined as achieving symmetry for all indexes, which is a generally accepted RTS criterion that allows returning to sport activities [15,23,31].

2.4. Statistical Analysis

All results were checked for normality and subsequently reported as mean and standard deviation (SD). Statistical analysis was performed using SPSS (version 25, IBM Corporation Armonk, New York, NY, USA). Chi-square test and independent samples *t*-test following the Levene's test for equality of variances were used to determine the difference between the groups with secondary ACL injury and without secondary injury. The Shapiro–Wilks test for normality was used to verify the adherence to normality assumptions. Statistical significance was set at $p < 0.05$.

The adequacy of sample size was verified by power and sample size calculator using power analysis considering descriptive data of postoperative LSI, EPIC and EPIC-H for knee extension muscle strength (with an alpha of 0.05 and for a power of 0.8) [39].

To assess the predictive value of 90% cut-off criterion of LSI and EPIC levels for the secondary injury risk, sensitivity, specificity, and positive and negative likelihood ratios (LRs) as described by Herbert [40] as well as the positive predictive value (PPV) and negative predictive value (NPV) as suggested by Trevethan [41] were calculated. For calculation of sensitivity, specificity, and positive and negative likelihood ratios (LRs) with 95% confidence intervals (CIs), the web-published tool was used [40].

3. Results

3.1. Baseline Patient Characteristics

Demographic characteristics as well as physical and activity measurements taken on preoperative patient evaluation are presented in Table 1.

Table 1. Patient demographic data and preoperative measurements.

Factor	All (n = 63)	No secondary Injury (n = 51)	Secondary Injury (n = 12)	Difference between Groups
	Mean (SD)	Mean (SD)	Mean (SD)	*p* Value
Age (yrs)	34.7 (12.3)	36.2 (12.1)	28.3 (11.7)	0.045*
Body Mass (kg)	76.7 (17.3)	76.1 (18.8)	79.0 (10.0)	0.611
Body Height (cm)	174.9 (0.1)	174.0 (8.7)	178.6 (9.6)	0.112
Body mass index (kg/m^2)	24.9 (4.4)	24.9 (4.8)	24.7 (1.9)	0.888
Tegner Activity score	6.7 (1.5)	6.5 (1.4)	7.2 (1.6)	0.064
Gender, male/female, n	37/26	29/22	8/4	0.535
Time from injury to surgery (months)	8.5 (9.03)	11 (10.01)	3.4 (2.3)	0.001 *

* indicates significant difference ($p \leq 0.05$) of mean values between secondary injury and no secondary injury groups (independent sample *t*-test). For gender differences between groups, chi-square test was used.

A secondary ACL injury appeared in 12 patients. Patients who sustained a secondary ACL injury were younger than those who did not. There were no gender differences between the groups. In our cohort, 41% of patients (n = 26) were females and 59% were males (n = 37), which is similar to the published data on patients with ACL injuries in the USA (59.5% males, 40.5% females) [42]. Moreover, other demographic and descriptive data did not significantly differ between the groups. Patients with a secondary injury had significantly shorter time form injury to ACLR compared to the no secondary injury group.

3.2. Muscle Strength Testing Results

Patients completed the initial knee extension and flexion strength testing of the involved and uninvolved limb just before ACLR. ACLR was performed at a mean ± SD of 8.5 ± 9.03 months after injury. The second testing was performed at approximately 6 months after ACLR (mean ± SD 5.7 ± 1.0 months).

Thirteen (20.6%) patients achieved over 90% postoperative LSI for knee extension strength, 35 (55.6%) patients achieved over 90% postoperative LSI for knee flexion strength. Twenty-one patients (33%) achieved over 90% preoperative LSI for knee extension strength, 41 (65%) patients achieved over 90% preoperative LSI for knee flexion strength. Only 8 (12.7%) patients met over 90% EPIC knee extension strength levels (comparing the involved limb at approximately 6 months after ACLR to the uninvolved limb before ACLR) and none of them suffered a secondary ACL injury. Forty-one (65.1%) patients met over 90% EPIC knee flexion strength levels. Eight of the 13 patients who achieved postoperative 90% LSI for knee extension did not achieve 90% EPIC levels for knee extension strength 6 months after ACLR.

Fifteen of the 21 patients who achieved preoperative 90% LSI for knee extension did not achieve 90% EPIC levels for knee extension strength 6 months after ACLR. In these patients, the mean knee extension strength deficit ranged from 89.9% to 37.1% (Table 2), and the mean knee flexion strength deficit ranged from 89.8% to 52.6% (Table 3).

Table 2. Mean peak torque (Nm) values for knee extension, LSI, and comparison between groups with secondary ACL injury and without secondary injury.

Extension										
			Preoperative			Postoperative				
Group	**n**		**Peak Torque—ACL Injury**	**Peak Torque—Uninvolved**	**LSI**	**Peak Torque—ACLR**	**Peak Torque—Uninvolved**	**LSI**	**EPIC**	**EPIC-H**
All	63	Mean (SD)	161,8 (58.2)	200.3 (63.9)	82.4 (19.3)	149.2 (52.9)	198.8 (57.5)	78.7 (14.3)	75.5 (16.8)	96.1 (13.6)
No secondary injury	51	Mean (SD)	159.9 (59.0)	186.3 (55.1)	87.1 (17.7)	144.04 (53.1)	183.9 (56.6)	78.3 (15.0)	77.7 (17.4)	99.34 (12.9)
Secondary injury	12	Mean (SD)	170.0 (56.1)	259.9 (66.6)	65.8 (15.2)	170.9 (47.9)	214.6 (56.6)	80.3 (11.3)	66.0 (9.1)	82.5 (5.9)
Sig. (*p* value)			0.593	<0.001 *	0.001 *	0.114	0.096	0.663	0.028 *	<0.001 *

* indicates significant difference ($p \leq 0.05$) of mean values between groups with secondary injury and without secondary injury (*t*-test). ACL injury—limb after anterior cruciate injury; ACLR—limb after anterior cruciate ligament reconstruction; LSI—limb symmetry index; EPIC—estimated preinjury capacity; EPIC-H—EPIC of uninvolved limb.

Table 3. Mean peak torque (Nm) values for knee flexion, LSI, and comparison between groups with secondary ACL injury and without secondary injury.

Flexion										
			Preoperative			Postoperative				
Group	**n**		**Peak Torque—ACL Injury**	**Peak Torque—Uninvolved**	**LSI**	**Peak Torque—ACLR**	**Peak Torque—Uninvolved**	**LSI**	**EPIC**	**EPIC-H**
All	63	Mean (SD)	120.1 (36.3)	126.8 (42.0)	96.9 (19.2)	116.1 (34.9)	123.0 (38.2)	93.0 (14.0)	94.4 (18.6)	102.0 (13.9)
No secondary injury	51	Mean (SD)	116.4 (34.5)	121.0 (37.9)	98.4 (18.8)	113.6 (35.7)	123.7 (37.1)	92.6 (12.6)	96.1 (19.0)	104.0 (16.2)
Secondary injury	12	Mean (SD)	135.8 (41.3)	151.5 (50.6)	91.6 (13.9)	126.4 (30.7)	137.8 (42.4)	94.6 (19.4)	87.0 (15.6)	93.6 (16.8)
Sig. (*p* value)			0.097	0.022 *	0.222	0.258	0.251	0.664	0.127	0.052

* indicates significant difference ($p \leq 0.05$) of mean values between groups with secondary injury and without secondary injury (*t*-test). ACL injury—limb after anterior cruciate injury; ACLR—limb after anterior cruciate ligament reconstruction; LSI limb symmetry index; EPIC—estimated preinjury capacity; EPIC-H—EPIC of uninvolved limb.

In the group of patients with secondary injury, three (2 ipsilateral ACL reinjuries, 1 contralateral ACL injury) of the 12 patients passed 90% of the preoperative LSI return-to-sport criteria in knee extension strength test 6 months after the initial ACLR, but none of these 3 achieved 90% EPIC levels (Table 4). In 10 of the 12 patients with a secondary ACL injury a significant knee extension muscle weakness of the uninvolved limb (EPIC-H) of a mean 17.5% ± 5.9 ($p = 0.001$) between testing before and after ACLR occurred (Table 2).

Twelve patients sustained a secondary ACL injury (median time from ACLR to secondary injury was 96 weeks; range 38–246 weeks) (Table 4).

The group with a secondary ACL injury had a statistically significantly higher preoperative extensor ($p = 0.001$) and flexor ($p = 0.022$) muscle strength of the uninvolved knee. Higher peak torque values of flexor and extensor muscles of the involved limb were observed in a group of patients with a secondary injury compared to the patents with no secondary injury (although this difference was not statistically significant in all variables) at preoperative and postoperative testing was observed (Tables 2 and 3). This might be associated with shorter time from injury to ACLR in patients with a secondary injury.

Table 4. Patients with secondary ACL injuries and LSIs and EPIC levels of knee extension strength.

Patient	Time from ACLR to Secondary ACL Injury, wk	LSIe Preoperative	LSIe Postoperative	EPICe	Side of Injury
1	220	60	64	56	ipsilateral
2	215	80	95	74	ipsilateral
3	58	62	84	72	ipsilateral
4	101	90	100	82	ipsilateral
5	39	43	75	64	ipsilateral
6	146	46	80	64	ipsilateral
7	92	51	72	65	ipsilateral
8	38	78	80	64	ipsilateral
9	42	56	78	58	contralateral
10	50	72	62	58	ipsilateral
11	246	80	90	81	contralateral
12	193	77	82	63	ipsilateral

LSIe—limb symmetry index for extensor muscles; EPICe—estimated preinjury capacity for extensor muscles.

In the secondary injury group, we observed a significantly lower preoperative LSI, but higher (though not significantly) postoperative LSI, significantly higher EPIC and EPIC-H levels for extension compared to the no secondary injury group. Indexes for flexion did not differ significantly between the groups.

3.3. Sensitivity and Specificity of Muscle Strength Indexes

Indexes for extensor muscle strength had superior sensitivity to indexes of flexion muscle strength but very low specificity (Table 5). The use of 90% EPIC extension levels or 90% preoperative LSIe as a cut-off diagnostic criterion was superior to 90% postoperative LSIe in predicting secondary ACL injuries.

Table 5. Sensitivity and specificity of muscle strength indexes as tests for prediction of second ACL injury.

	LSIe Preop	LSIf Preop	LSIe Postop	LSIf Postop	EPICe	EPICf
Sensitivity	**0.92**	**0.5**	**0.75**	**0.5**	**1**	**0.5**
95% CI	0.65–0.99	0.25–0.75	0.47–0.91	0.43–0.69	0.76–1	0.25–0.75
Specificity	**0.41**	**0.68**	**0.21**	**0.57**	**0.15**	**0.68**
95% CI	0.29–0.55	0.55–0.80	0.12–0.35	0.61–2.22	0.08–0.28	0.55–0.80
Positive LR	**1.55**	**1.95**	**0.956**	**1.15**	**1.18**	**1.59**
95% CI	1.17–2.07	0.79–3.20	0.67–1.37	0.48 -1.63	1.05–1.34	0.79–3.20
Negative LR	**0.20**	**0.72**	**0.159**	**0.87**	**0**	**0.72**
95% CI	0.03–1.36	0.40–1.32	0.38–3.52	0.37–4.65	-	0.40–1.32
PPV	**0.26**	**0.27**	**0.18**	**0.21**	**0.23**	**0.27**
NPV	**0.95**	**0.85**	**0.87**	**0.82**	**1**	**0.85**

LSIe—limb symmetry index for extensor muscles; EPICe—estimated preinjury capacity for extensor muscles; LSIf—limb symmetry index for flexor muscles; EPICf—estimated preinjury capacity for flexor muscles; LR—likelihood ratio; PPV—positive predictive value; NPV—negative predictive value.

4. Discussion

The current study shows that knee extension strength EPIC levels and preoperative LSI for extension are more sensitive in predicting a secondary ACL injury compared to the postoperative LSI, which is commonly used for determining the time for RTS. All patients who suffered a secondary injury had statistically greater knee extensor muscle strength loss of the uninvolved limb compared to uninjured patients. This demonstrates that knee extension strength at 6 months after the initial ACLR does not guarantee that pre-injury strength levels of the uninvolved limb have been met and can inflate the LSI post-operatively. Thus 3 of the 12 secondary injuries might have been prevented if the RTS decision had been based on EPIC levels. This study supports evidence from previous observations by Wellsandt et al. [36] who found that 6 of the 8 patients who sustained a secondary ACL injury after ACLR achieved postoperative LSI of 90% but did not achieve

90% EPIC levels. Additionally, in patients who sustained secondary ACL injury after ACLR, greater differences in LSI of preoperative knee extension strength and EPIC levels were found. Piussi et al. 2020 [35], however, found no difference in the proportion of patients who recovered their postoperative knee extension and flexion absolute muscle strength compared to the patients who recovered their postoperative LSI at 8- and 12-months post ACLR. It should be stressed that the authors did not study the incidence of secondary ACL injuries.

In our study, only 1 of the 5 patients achieved criterion of 90% LSI, and only 1 of the 8 patients achieved 90% of EPIC levels at 6 months after ACLR. This finding is consistent with other studies reporting that 6 months after ACLR, most patients have not yet recovered their knee extension muscle strength deficits [15,24]. Furthermore, the patients with postoperative LSI lower than 80% have been reported to exhibit deficits even two years after ACLR [43,44]. Similarly, others have found that more symmetrical preoperative limb-to-limb knee extensor muscle strength above 80% has a positive influence on ACLR outcomes even two years after ACLR [37,38]. Low rates of patients passing this criterion raise concerns regarding the adequacy of the rehabilitation protocols used. On the other hand, it has been proven that patients undergoing supervised rehabilitation/physiotherapy with routine measurements of knee strength at different time points during rehabilitation can restore (LSI $\geq$ 90%) knee extension and flexion muscle strength 6 months after ACLR [45,46].

The decreased knee extension muscle strength of the uninvolved limb (EPIC-H) observed in this study likely indicates that a subgroup of patients exists in whom reduced physical activity may result in larger compensatory adaptations. The mean preoperative knee extension muscle strength of the uninvolved limb was statistically higher ($p = 0.001$) in the group of patients with a secondary ACL injury compared to patients without secondary injury. This might explain why stronger individuals suffer a greater strength decrease of the uninvolved knee extensor muscle and have larger between-limb asymmetry and are therefore at a higher risk of a secondary injury. Persistent asymmetrical knee extension strength is associated with asymmetrical knee biomechanics and plays an important role in the incidence of any knee injury, contralateral and ipsilateral ACL graft reinjury [11,23,27,28], which might be a case in our cohort study.

In our study, LSI of preoperative knee extension and EPIC for extensor muscles had higher sensitivity compared to other tested indexes and could be considered as more reliable predictive factors for second injury compared to other investigated indexes. Although both preoperative knee extension LSI and EPIC have high sensitivity for predicting second ACL injury, they have low specificity, which means that the percentage of correctly identified cases that will not suffer second injury is very low due to a low proportion of patients that reach the cut-off 90% preoperative LSI and EPIC. Consequently, there is a high proportion of false positive results of these tests. However, it has to be noted that in screening predictive values are more relevant than sensitivity and specificity [41]. In all indexes, we have observed relatively low positive predictive values and high negative predictive values; in this view, the indexes are better predictors for no reinjury.

This indicates the necessity for the surgeon to apply these indexes before primary ACLR to identify the patients at a higher risk for secondary injury. The risk of secondary injury, resulting from preoperative limb asymmetry, could be minimized by using an extended preoperative rehabilitation protocol. During waiting for the ACLR patients should be empowered to pursue a more intensive preoperative rehabilitation protocol and should undergo a follow up testing. Moreover, by adopting a preseason testing strategy in the population at a higher risk for ACL, injury could be a good criterion to provide patient-specific rehabilitation milestones after ACLR. Thus, the use of reference matched age, sex and sport specific values could also present a good strategy to patient-specific preinjury data, but literature is still sparse and evolving [21,47].

While in our cohort significant differences in time form injury to surgery were detected between tested groups, we did not find a significant association between the time from the

ACL injury to the initial uninvolved limb testing (before ACLR) and EPIC levels, which is in line with the results of Wellsandt et al. [31] who found that the time form ACL injury to the initial involved-to-uninvolved limb testing did not impact muscle strength and EPIC levels.

This study provides evidence for the superiority of preoperative LSI and EPIC over generally used postoperative LSI in estimating the risk of a secondary ACL injury. We have observed that the preoperative muscle strength of the uninvolved limb (EPIC-H) is not restored sufficiently after ACLR in patients with a secondary injury. The study indicates a potential importance of preoperative knee extension LSI and EPIC to differentiate between low-risk and high-risk patients for a secondary ACL injury who need a better rehabilitation plan depending on degree of limb asymmetry. Our study provides additional data to support the existing body of literature, which emphasizes the importance of preoperative rehabilitation to achieve a better preoperative LSI before ACLR. Rehabilitation after ACLR should focus more on the uninvolved limb so that the involved limb would have to reach even a higher criterion to achieve 90% EPIC levels for RTS and possibly decrease the number of secondary knee injuries, which is of uttermost importance. While we still do not know the optimal contents of an RTS test battery, our study highlights that rigorous knee strength testing of both limbs should be included as an objective RTS criterion to evaluate the patients after ACLR for a safe clearance to RTS.

The limitations of our study include its retrospective nature and lack of more detailed data on patients' preinjury activities, type of exercises, and rehabilitation program between the initial ACL injury and preoperative ACLR testing and other factors associated with reinjury. The study population consist of both recreational and some professional athletes participating in pivoting sports, but only basic data on the type and intensity of physical activity (Tegner activity score) were collected. On the other hand, an important strength of the study is that all patients were operated by the same surgeon with the same technique and underwent the same rehabilitation protocol, thus minimizing the variability of treatment.

A prospective study design in further research could allow a better assessment of different factors affecting the occurrence of secondary injuries, especially different activity measures, and verification of preoperative rehabilitation protocols, to achieve mor symmetrical preoperative LSI to increase the efficiency of postoperative rehabilitation and minimize the risk of reinjury. A multicentric research would provide verification and generalization of these findings.

5. Conclusions

The results of this study suggest that EPIC as well as preoperative LSI of knee extensors predict secondary ACL injuries better than postoperative LSI. While the postoperative LSI did not differ significantly different between the groups, the preoperative LSI revealed a larger limb asymmetry in patients who sustained a secondary ACL injury. Patients with secondary ACL injuries suffer greater muscle loss of knee extensor muscle strength of the injured as well as of the uninvolved limb between preoperative and post ACLR testing (presented as EPIC levels), compared to the patients without secondary injuries no-reinjury group.

The findings of the study highlight the importance of muscle strength testing and muscle strengthening in the rehabilitation programs for preventing of secondary injuries and maintenance of long-term effects of ACLR.

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Abbreviations

ACL	Anterior Cruciate Ligament
ACLR	Anterior Cruciate Ligament Reconstruction
EPIC	Estimated preinjury capacity
EPIC-H	Estimated preinjury capacity of the healthy leg
LSI	Limb symmetry index
RTS	Return to sport

References

1. Frobell, R.B.; Lohmander, L.S.; Roos, H.P. Acute Rotational Trauma to the Knee: Poor Agreement between Clinical Assessment and Magnetic Resonance Imaging Findings. *Scand. J. Med. Sci. Sports* **2007**, *17*, 109–114. [CrossRef]
2. Wright, R.W.; Dunn, W.R.; Amendola, A.; Andrish, J.T.; Bergfeld, J.; Kaeding, C.C.; Marx, R.G.; McCarty, E.C.; Parker, R.D.; Wolcott, M.; et al. Risk of Tearing the Intact Anterior Cruciate Ligament in the Contralateral Knee and Rupturing the Anterior Cruciate Ligament Graft during the First 2 Years after Anterior Cruciate Ligament Reconstruction: A Prospective MOON Cohort Study. *Am. J. Sports Med.* **2007**, *35*, 1131–1134. [CrossRef]
3. Barber-Westin, S.D.; Noyes, F.R. Objective Criteria for Return to Athletics after Anterior Cruciate Ligament Reconstruction and Subsequent Reinjury Rates: A Systematic Review. *Physician Sportsmed.* **2011**, *39*, 100–110. [CrossRef]
4. Ahldén, M.; Samuelsson, K.; Sernert, N.; Forssblad, M.; Karlsson, J.; Kartus, J. The Swedish National Anterior Cruciate Ligament Register: A Report on Baseline Variables and Outcomes of Surgery for Almost 18,000 Patients. *Am. J. Sports Med.* **2012**, *40*, 2230–2235. [CrossRef] [PubMed]
5. Paterno, M.V.; Rauh, M.J.; Schmitt, L.C.; Ford, K.R.; Hewett, T.E. Incidence of Contralateral and Ipsilateral Anterior Cruciate Ligament (ACL) Injury After Primary ACL Reconstruction and Return to Sport. *Clin. J. Sport Med.* **2012**, *22*, 116–121. [CrossRef]
6. Brophy, R.H.; Schmitz, L.; Wright, R.W.; Dunn, W.R.; Parker, R.D.; Andrish, J.T.; McCarty, E.C.; Spindler, K.P. Return to Play and Future ACL Injury Risk After ACL Reconstruction in Soccer Athletes from the Multicenter Orthopaedic Outcomes Network (MOON) Group. *Am. J. Sports Med.* **2012**, *40*, 2517–2522. [CrossRef] [PubMed]
7. Bittencourt, N.F.N.; Meeuwisse, W.H.; Mendonça, L.D.; Nettel-Aguirre, A.; Ocarino, J.M.; Fonseca, S.T. Complex Systems Approach for Sports Injuries: Moving from Risk Factor Identification to Injury Pattern Recognition—Narrative Review and New Concept. *Br. J. Sports Med.* **2016**, *50*, 1309–1314. [CrossRef]
8. Hewett, T.E.; Myer, G.D.; Ford, K.R.; Paterno, M.V.; Quatman, C.E. Mechanisms, Prediction, and Prevention of ACL Injuries: Cut Risk with Three Sharpened and Validated Tools: ACL INJURY PREVENTION. *J. Orthop. Res.* **2016**, *34*, 1843–1855. [CrossRef] [PubMed]
9. Welling, W.; Benjaminse, A.; Seil, R.; Lemmink, K.; Zaffagnini, S.; Gokeler, A. Low Rates of Patients Meeting Return to Sport Criteria 9 Months after Anterior Cruciate Ligament Reconstruction: A Prospective Longitudinal Study. *Knee Surg. Sports Traumatol. Arthrosc.* **2018**, *26*, 3636–3644. [CrossRef] [PubMed]
10. Dingenen, B.; Gokeler, A. Optimization of the Return-to-Sport Paradigm After Anterior Cruciate Ligament Reconstruction: A Critical Step Back to Move Forward. *Sports Med.* **2017**, *47*, 1487–1500. [CrossRef]
11. Bell, D.R.; Trigsted, S.M.; Post, E.G.; Walden, C.E. Hip Strength in Patients with Quadriceps Strength Deficits after ACL Reconstruction. *Med. Sci. Sports Exerc.* **2016**, *48*, 1886–1892. [CrossRef]
12. Šarabon, N.; Kozinc, Z.; Bishop, C.; Maffiuletti, N.A. Factors Influencing Bilateral Deficit and Inter-Limb Asymmetry of Maximal and Explosive Strength: Motor Task, Outcome Measure and Muscle Group. *Eur. J. Appl. Physiol.* **2020**, *120*, 1681–1688. [CrossRef]
13. Barber-Westin, S.D.; Noyes, F.R. Factors Used to Determine Return to Unrestricted Sports Activities after Anterior Cruciate Ligament Reconstruction. *Arthrosc. J. Arthrosc. Relat. Surg.* **2011**, *27*, 1697–1705. [CrossRef]
14. The Panther Symposium ACL Injury Return to Sport Consensus Group; Meredith, S.J.; Rauer, T.; Chmielewski, T.L.; Fink, C.; Diermeier, T.; Rothrauff, B.B.; Svantesson, E.; Senorski, E.H.; Hewett, T.E.; et al. Return to Sport after Anterior Cruciate Ligament Injury: Panther Symposium ACL Injury Return to Sport Consensus Group. *Knee Surg. Sports Traumatol. Arthrosc.* **2020**, *28*, 2403–2414. [CrossRef] [PubMed]

15. Grindem, H.; Snyder-Mackler, L.; Moksnes, H.; Engebretsen, L.; Risberg, M.A. Simple Decision Rules Can Reduce Reinjury Risk by 84% after ACL Reconstruction: The Delaware-Oslo ACL Cohort Study. *Br. J. Sports Med.* **2016**, *50*, 804–808. [CrossRef] [PubMed]
16. Nagelli, C.V.; Hewett, T.E. Should Return to Sport Be Delayed Until 2 Years After Anterior Cruciate Ligament Reconstruction? Biological and Functional Considerations. *Sports Med.* **2017**, *47*, 221–232. [CrossRef] [PubMed]
17. Moran, R.W.; Schneiders, A.G.; Mason, J.; Sullivan, S.J. Do Functional Movement Screen (FMS) Composite Scores Predict Subsequent Injury? A Systematic Review with Meta-Analysis. *Br. J. Sports Med.* **2017**, *51*, 1661–1669. [CrossRef]
18. Hewett, T.E.; Ford, K.R.; Myer, G.D. Anterior Cruciate Ligament Injuries in Female Athletes: Part 2, a Meta-Analysis of Neuromuscular Interventions Aimed at Injury Prevention. *Am. J. Sports Med.* **2006**, *34*, 490–498. [CrossRef]
19. Webster, K.E.; Hewett, T.E. Meta-Analysis of Meta-Analyses of Anterior Cruciate Ligament Injury Reduction Training Programs: Effectiveness of ACL Injury Reduction Training Programs. *J. Orthop. Res.* **2018**, *36*, 2696–2708. [CrossRef]
20. van Melick, N.; van Cingel, R.E.H.; Brooijmans, F.; Neeter, C.; van Tienen, T.; Hullegie, W.; Nijhuis-van der Sanden, M.W.G. Evidence-Based Clinical Practice Update: Practice Guidelines for Anterior Cruciate Ligament Rehabilitation Based on a Systematic Review and Multidisciplinary Consensus. *Br. J. Sports Med.* **2016**, *50*, 1506–1515. [CrossRef] [PubMed]
21. Davies, G.J.; McCarty, E.; Provencher, M.; Manske, R.C. ACL Return to Sport Guidelines and Criteria. *Curr. Rev. Musculoskelet. Med.* **2017**, *10*, 307–314. [CrossRef]
22. Webster, K.E.; Hewett, T.E. What Is the Evidence for and Validity of Return-to-Sport Testing after Anterior Cruciate Ligament Reconstruction Surgery? A Systematic Review and Meta-Analysis. *Sports Med.* **2019**, *49*, 917–929. [CrossRef] [PubMed]
23. Capin, J.J.; Snyder-Mackler, L.; Risberg, M.A.; Grindem, H. Keep Calm and Carry on Testing: A Substantive Reanalysis and Critique of 'What Is the Evidence for and Validity of Return-to-Sport Testing after Anterior Cruciate Ligament Reconstruction Surgery? A Systematic Review and Meta-Analysis'. *Br. J. Sports Med.* **2019**, *53*, 1444–1446. [CrossRef] [PubMed]
24. Kyritsis, P.; Bahr, R.; Landreau, P.; Miladi, R.; Witvrouw, E. Likelihood of ACL Graft Rupture: Not Meeting Six Clinical Discharge Criteria before Return to Sport Is Associated with a Four Times Greater Risk of Rupture. *Br. J. Sports Med.* **2016**, *50*, 946–951. [CrossRef]
25. Petersen, W.; Taheri, P.; Forkel, P.; Zantop, T. Return to Play Following ACL Reconstruction: A Systematic Review about Strength Deficits. *Arch. Orthop. Trauma Surg.* **2014**, *134*, 1417–1428. [CrossRef] [PubMed]
26. Abourezk, M.N.; Ithurburn, M.P.; McNally, M.P.; Thoma, L.M.; Briggs, M.S.; Hewett, T.E.; Spindler, K.P.; Kaeding, C.C.; Schmitt, L.C. Hamstring Strength Asymmetry at 3 Years After Anterior Cruciate Ligament Reconstruction Alters Knee Mechanics During Gait and Jogging. *Am. J. Sports Med.* **2017**, *45*, 97–105. [CrossRef] [PubMed]
27. Ithurburn, M.P.; Altenburger, A.R.; Thomas, S.; Hewett, T.E.; Paterno, M.V.; Schmitt, L.C. Young Athletes after ACL Reconstruction with Quadriceps Strength Asymmetry at the Time of Return-to-Sport Demonstrate Decreased Knee Function 1 Year Later. *Knee Surg. Sports Traumatol. Arthrosc.* **2018**, *26*, 426–433. [CrossRef] [PubMed]
28. Schmitt, L.C.; Paterno, M.V.; Ford, K.R.; Myer, G.D.; Hewett, T.E. Strength Asymmetry and Landing Mechanics at Return to Sport after Anterior Cruciate Ligament Reconstruction. *Med. Sci. Sports Exerc.* **2015**, *47*, 1426–1434. [CrossRef]
29. Kotsifaki, A.; Korakakis, V.; Graham-Smith, P.; Sideris, V.; Whiteley, R. Vertical and Horizontal Hop Performance: Contributions of the Hip, Knee, and Ankle. *Sports Health* **2021**, *13*, 128–135. [CrossRef]
30. Sapega, A.A. Muscle Performance Evaluation in Orthopaedic Practice. *J. Bone Jt. Surg.* **1990**, *72*, 1562–1574. [CrossRef]
31. Chmielewski, T.L.; Stackhouse, S.; Axe, M.J.; Snyder-Mackler, L. A Prospective Analysis of Incidence and Severity of Quadriceps Inhibition in a Consecutive Sample of 100 Patients with Complete Acute Anterior Cruciate Ligament Rupture. *J. Orthop. Res.* **2004**, *22*, 925–930. [CrossRef]
32. Hart, J.M.; Pietrosimone, B.; Hertel, J.; Ingersoll, C.D. Quadriceps Activation Following Knee Injuries: A Systematic Review. *J. Athl. Train.* **2010**, *45*, 87–97. [CrossRef]
33. Wilk, K.E. We Can Do Better. *J. Orthop. Sports Phys. Ther.* **2014**, *44*, 634–635. [CrossRef]
34. Riesterer, J.; Mauch, M.; Paul, J.; Gehring, D.; Ritzmann, R.; Wenning, M. Relationship between Pre- and Post-Operative Isokinetic Strength after ACL Reconstruction Using Hamstring Autograft. *BMC Sports Sci. Med. Rehabil.* **2020**, *12*, 1–10. [CrossRef]
35. Piussi, R.; Broman, D.; Musslinder, E.; Beischer, S.; Thomeé, R.; Senorski, E.H. Recovery of Preoperative Absolute Knee Extension and Flexion Strength after ACL Reconstruction. *BMC Sports Sci. Med. Rehabil.* **2020**, *12*, 1–7. [CrossRef]
36. Wellsandt, E.; Failla, M.J.; Snyder-Mackler, L. Limb Symmetry Indexes Can Overestimate Knee Function after Anterior Cruciate Ligament Injury. *J. Orthop. Sports Phys. Ther.* **2017**, *47*, 334–338. [CrossRef]
37. Czaplicki, A.; Jarocka, M.; Walawski, J. Isokinetic Identification of Knee Joint Torques before and after Anterior Cruciate Ligament Reconstruction. *PLoS ONE* **2015**, *10*, e0144283. [CrossRef]
38. de Araujo Ribeiro Alvares, J.B.; Rodrigues, R.; de Azevedo Franke, R.; da Silva, B.G.C.; Pinto, R.S.; Vaz, M.A.; Baroni, B.M. Inter-Machine Reliability of the Biodex and Cybex Isokinetic Dynamometers for Knee Flexor/Extensor Isometric, Concentric and Eccentric Tests. *Phys. Ther. Sport* **2015**, *16*, 59–65. [CrossRef] [PubMed]
39. Georgiev, G.Z. Sample Size Calculator. Available online: https://www.gigacalculator.com/calculators/power-sample-size-calculator.php (accessed on 15 February 2021).
40. Herbert, R. Confidence Interval Calculator. 2013. Available online: https://pedro.org.au/english/resources/confidence-interval-calculator/ (accessed on 15 February 2021).

41. Trevethan, R. Sensitivity, Specificity, and Predictive Values: Foundations, Pliabilities, and Pitfalls in Research and Practice. *Front. Public Health* **2017**, *5*, 307. [CrossRef]
42. Sanders, T.L.; Kremers, H.M.; Bryan, A.J.; Larson, D.R.; Dahm, D.L.; Levy, B.A.; Stuart, M.J.; Krych, A.J. Incidence of Anterior Cruciate Ligament Tears and Reconstruction: A 21-Year Population-Based Study. *Am. J. Sports Med.* **2016**, *44*, 1502–1507. [CrossRef] [PubMed]
43. De Jong, S.N.; van Caspel, D.R.; van Haeff, M.J.; Saris, D.B.F. Functional Assessment and Muscle Strength Before and After Reconstruction of Chronic Anterior Cruciate Ligament Lesions. *Arthrosc. J. Arthrosc. Relat. Surg.* **2007**, *23*, 21.e1–21.e11. [CrossRef] [PubMed]
44. Shaarani, S.R.; O'Hare, C.; Quinn, A.; Moyna, N.; Moran, R.; O'Byrne, J.M. Effect of Prehabilitation on the Outcome of Anterior Cruciate Ligament Reconstruction. *Am. J. Sports Med.* **2013**, *41*, 2117–2127. [CrossRef]
45. Ebert, J.R.; Edwards, P.; Yi, L.; Joss, B.; Ackland, T.; Carey-Smith, R.; Buelow, J.-U.; Hewitt, B. Strength and Functional Symmetry Is Associated with Post-Operative Rehabilitation in Patients Following Anterior Cruciate Ligament Reconstruction. *Knee Surg. Sports Traumatol. Arthrosc.* **2018**, *26*, 2353–2361. [CrossRef] [PubMed]
46. Welling, W.; Benjaminse, A.; Lemmink, K.; Dingenen, B.; Gokeler, A. Progressive Strength Training Restores Quadriceps and Hamstring Muscle Strength within 7 Months after ACL Reconstruction in Amateur Male Soccer Players. *Phys. Ther. Sport* **2019**, *40*, 10–18. [CrossRef] [PubMed]
47. Hadžić, V.; Erulj, F.; Brai, M.; Dervi, E. Bilateral Concentric and Eccentric Isokinetic Strength Evaluation of Quadriceps and Hamstrings in Basketball Players. *Coll. Antropol.* **2013**, *37*, 859–865.