



Acute and subacute anterior cruciate ligament reconstructions are associated with a higher risk of revision and reoperation

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Abstract

Purpose (1) Report concomitant cartilage and meniscal injury at the time of anterior cruciate ligament reconstruction (ACLR), (2) evaluate the risk of aseptic revision ACLR during follow-up, and (3) evaluate the risk of aseptic ipsilateral reoperation during follow-up.

Methods Using a United States integrated healthcare system's ACLR registry, patients who underwent primary isolated ACLR were identified (2010–2018). Multivariable Cox proportional-hazards regression was used to evaluate the risk of aseptic revision, with a secondary outcome evaluating ipsilateral aseptic reoperation. Outcomes were evaluated by time from injury to ACLR: acute (< 3 weeks), subacute (3 weeks–3 months), delayed (3–9 months), and chronic (≥ 9 months).

Results The final sample included 270 acute (< 3 weeks), 5971 subacute (3 weeks–3 months), 5959 delayed (3–9 months), and 3595 chronic (≥ 9 months) ACLR. Medial meniscus [55.4% (1990/3595 chronic) vs 38.9% (105/270 acute)] and chondral injuries [40.0% (1437/3595 chronic) vs 24.8% (67/270 acute)] at the time of ACLR were more common in the chronic versus acute groups. The crude 6-year revision rate was 12.9% for acute ACLR, 7.0% for subacute, 5.1% for delayed, and 4.4% for chronic ACLR; reoperation rates a 6-year follow-up was 15.0% for acute ACLR, 9.6% for subacute, 6.4% for delayed, and 8.1% for chronic ACLR. After adjustment for covariates, acute and subacute ACLR had higher risks for aseptic revision (acute HR 1.70, 95% CI 1.07–2.72, $p=0.026$; subacute HR 1.25, 95% CI 1.01–1.55, $p=0.040$) and aseptic reoperation (acute HR 2.04, 95% CI 1.43–2.91, $p<0.001$; subacute HR 1.31, 95% CI 1.11–1.54, $p=0.002$) when compared to chronic ACLR.

Conclusions In this cohort study, while more meniscal and chondral injuries were reported for ACLR performed ≥ 9 months after the date of injury, a lower risk of revision and reoperation was observed following chronic ACLR relative to patients undergoing surgery in acute or subacute fashions.

Level of evidence

III.

Keywords Anterior cruciate ligament · Reconstruction · Timing · Reoperation · Revision · Acute · Chronic · Registry

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Abbreviations

ACL	Anterior cruciate ligament
ACLR	Anterior cruciate ligament reconstruction
ACLRR	Anterior cruciate ligament reconstruction registry
ASA	American Society of Anesthesiologists
BMI	Body mass index
BPTB	Bone patellar tendon bone
CI	Confidence interval
CIF	Cumulative incidence function
EHR	Electronic health record
HR	Hazard ratio

IQR	Interquartile range
ROM	Range of motion
SD	Standard deviation
US	United States

Introduction

Anterior cruciate ligament (ACL) tears are common injuries in the young, active population, most frequently occurring in patients under the age of 30 [30]. In the United States (US), the incidence of ACL tears in 2016 was estimated to be 68 per 100,000 person-years [36]. ACL reconstruction (ACLR) aims to restore the ligamentous integrity of the joint to reach a pre-injury level of knee function, with well over 200,000 ACLR performed in the US annually [37]. In addition, surgical reconstruction prevents further knee instability and damage to cartilage and other intra-articular structures [40]. ACL tears are generally managed in one of two fashions: (1) immediate ACLR or (2) functional rehabilitation with optional delayed ACLR if instability persists.

The optimal timing of surgical reconstruction is debated. Studies investigating the possible effect of early ACLR on postoperative stiffness and range of motion (ROM) have reported conflicting results and, as such, an optimal time from injury to surgery has yet to be determined [5, 8, 13]. More recently, it is thought that restoring knee ROM preoperatively and reducing overall inflammation in the knee should be achieved prior to surgical reconstruction rather than a relying on a specific time from injury [2, 28]. Delayed ACLR, with or without functional rehabilitation, has also been associated with a higher incidence of meniscal tears, particularly in the medial meniscus, and cartilage wear [10, 25, 27, 31–33, 36, 41].

Several systematic reviews and meta-analyses have failed to demonstrate differences in outcomes following ACLR according to time of the procedure relative to the injury [7, 16, 20]. However, these studies are limited by significant heterogeneity in the definitions of early and delayed surgery. More research is needed to evaluate the impact of timing of ACLR on outcomes, specifically on risks of revision and reoperation where less information on the impact of surgical timing is available [42].

Therefore, in a cohort of ACLR patients, this study aimed to: (1) report concomitant cartilage and meniscal injury at the time of ACLR according to timing of the ACLR procedure, (2) evaluate the risk of aseptic revision ACLR during follow-up, and (3) evaluate the risk of aseptic ipsilateral reoperation during follow-up. Our hypothesis was the risk of aseptic revision and aseptic reoperation would differ depending on timing of when the ACLR was performed, using four mutually exclusive timing groups: acute (< 3 weeks),

subacute (3 weeks–3 months), delayed (3–9 months), and chronic (≥ 9 months). To our knowledge, this is the largest study looking at timing from ACL injury to ACLR in a heterogenous, community-based cohort. This can provide clinicians important information in their discussion with patients when considering timing of the ACLR.

Materials and methods

Ethics statement

This study was approved by Kaiser Permanente's Institutional Review Board (#5691) prior to commencement. No outside funding was obtained.

Study design, setting, and data source

A retrospective cohort study was conducted using data from Kaiser Permanente's ACLR Registry. Kaiser Permanente is an integrated healthcare system which covers over 12 million people throughout 8 geographical regions in the US, including Colorado, Georgia, Hawaii, the Mid-Atlantic, Northern California, the Northwest, Southern California, and Washington. Healthcare plan membership has previously been shown to be demographically representative of the geographical areas in which it covers [17, 19].

A detailed summary of data collection procedures, coverage, and participation rates for the ACLR Registry has been published previously [21, 29]. Briefly, patient, procedure, implant, surgeon, and hospital information for all ACLR procedures performed within our healthcare system is collected into this surveillance tool using electronic intraoperative forms that are completed at the point-of-care by the operating surgeon. Information is then supplemented using data from the electronic health record (EHR), administrative claims data, membership data, and mortality records. Outcomes, such as revisions and reoperations, are prospectively monitored using electronic screening algorithms and validated by trained clinical content experts using the EHR.

Study sample

The study sample included patients who underwent a primary isolated ACLR between January 1, 2010 and December 31, 2018. Patients were excluded if they had a multi-ligament injury ($n = 1494$), underwent double bundle or bilateral procedures ($n = 138$), as well as the Georgia and Washington regions due to incomplete data ($n = 666$). Patients with a missing injury date were excluded as timing of the ACLR could not be determined ($n = 11,063$).

Exposure of interest

The reported time from injury to primary ACLR was the exposure of interest and classified as follows: acute (< 3 weeks of injury), subacute (3 weeks to < 3 months after injury), delayed (3 months to < 9 months after injury), and chronic (≥ 9 months after injury). The final study sample included 270 acute, 5971 subacute, 5959 delayed, and 3595 chronic ACLR.

Outcomes of interest

Outcomes that required a subsequent surgical intervention were evaluated. The primary outcome was first aseptic revision surgery. Aseptic revision was defined as the aseptic failure of the primary ACLR graft where removal and replacement of the original graft was required. The secondary outcome was first ipsilateral aseptic reoperation. Reoperation was defined as any procedure after the index ACLR, not including a revision surgery. Revisions and reoperations were reported by the operating physician on the registry data collection form and validated by trained clinical research associates. Patients are continuously monitored for revisions and reoperations following the index ACLR until either healthcare plan membership termination or death.

Covariates

Covariates included patient age (< 20, 20–29, 30–39, and ≥ 40 years), gender (male vs female), body mass index (BMI, < 22, 22–24.9, 25–29.9, and ≥ 30 kg/m²), race/ethnicity (Asian, Black, Hispanic, Native American/Multi, and White), American Society of Anesthesiologists (ASA) classification (< 3, ≥ 3 , and missing/unknown), activity at the time of injury (motor vehicle accident, sport, work, and other), graft selection (allograft, autograft: BPTB, autograft: hamstring, autograft: quad tendon/other, and hybrid graft), femoral fixation device type (combination, crosspin, interference, and suspensory), tibial fixation device type (combination, crosspin, interference, and suspensory), meniscal tears at index surgery (lateral and medial), and cartilage injuries at index surgery. Hybrid graft was defined as a graft using both hamstring autograft and allograft. Combination fixation was defined as more than one fixation device used on the same side.

Statistical analysis

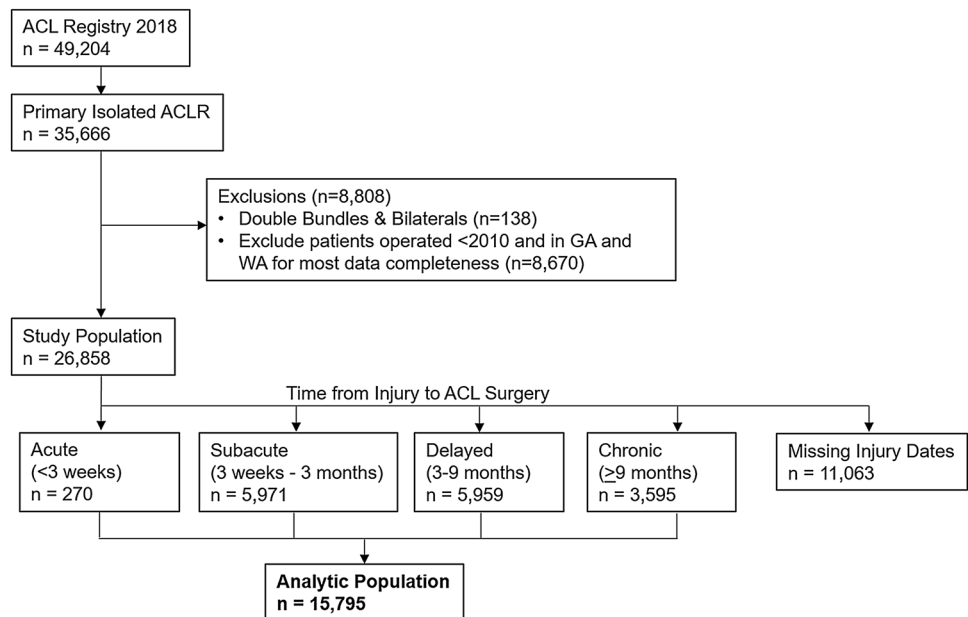
Both revisions and reoperations were modelled as time-to-events with no restrictions on minimum follow-up. Follow-up time for those who experienced one of the outcomes of interest was defined as the difference between the index ACLR date and the date of the outcome. Patients who did

not experience an outcome of interest were censored at the date of last surveillance (date lost to follow-up, death, or study end date [December 31, 2018], whichever came first). For the reoperation outcome, patients who experienced a revision surgery before any reoperation were also censored at the date of revision surgery as any reoperation after would no longer be attributable to the original graft from the index ACLR. Crude cumulative revision and reoperation probabilities were calculated as one minus the Kaplan–Meier estimator and cumulative incidence curves were shown up to the time point at which there were still 50 ACLR at risk in the smallest group to ensure a reliable estimate with sufficient number of patients at risk (6-year follow-up for the entire study cohort, 5-year follow-up for the age-stratified groups).

Multivariable Cox proportional-hazards regression was used to evaluate the risk of aseptic revision and aseptic reoperation by exposure group. All models included the covariates listed above and a surgeon-level cluster-robust variance estimator to account for correlation of ACLR performed by the same operating surgeon. Age-specific models within two age groups, < 22 years and ≥ 22 years, were also presented for the evaluation of revision and reoperation risk as it was observed to be an effect modifier in the association between ACLR timing and risk of revision. Hazard ratios (HR), 95% confidence intervals (CI), and *P* values are presented with chronic ACLR as the reference group. The proportional-hazards assumption for the exposure variable was checked by testing time interaction terms and the assumption was met, implying that the factors investigated have a constant impact on the hazard over time. Uncategorised missing values were not included in the models. Analyses were performed using SAS Enterprise Guide 7.1. *P* < 0.05 was the statistical significance threshold used for this study and all tests were two-sided.

Results

The final study sample included 15,795 ACLR procedures performed by 281 surgeons at 47 healthcare centres (Fig. 1). The median age for the total cohort was 25 years [interquartile range (IQR) = 18–36] and the median BMI was 25.8 kg/m² (IQR = 23.2–29.4). More ACLR patients in the sample were male (60.4%), White (51.8%), with an ASA of 1–2 (77.7%). Most (77.8%) suffered ACL injury from sporting activity. Hamstring autograft was more frequently utilised during the primary procedure (36.2%) and more grafts were fixed with a suspensory device on the femoral side (43.6%) and an interference device on the tibial side (72.3%). Demographics, patient, and surgical characteristics by exposure group are summarised in Table 1.

Fig. 1 Study sample flowchart

Cartilage and meniscal injuries at the time of ACLR

A similar proportion of lateral meniscus tears were reported at the time of acute (42.2%) and chronic (41.3%) ACLR; however, a larger percentage of medial meniscus tears were reported for chronic (55.4%) compared acute ACLR (38.9%). Similarly, cartilage injury was more frequently reported in chronic (40.0%) versus acute ACLR (24.8%).

Timing of ACLR and revision risk

Figure 2 presents cumulative aseptic revision probabilities during follow-up; the crude 6-year revision rate is presented in Table 2. After adjustment for covariates, both acute and subacute ACLR had higher risks for aseptic revision (acute HR 1.70, 95% CI 1.07–2.72, $p=0.026$; subacute HR 1.25, 95% CI 1.01–1.55, $p=0.040$) when compared to chronic ACLR patients.

Pairwise comparisons of the ACLR timing groups for aseptic revision indicated higher risks in both the acute (HR 1.71, 95% CI 1.07–2.73, $p=0.026$) and subacute groups (HR 1.26, 95% CI 1.06–1.48, $p=0.007$) compared with delayed ACLR (Table 3).

Age at index surgery was identified as an effect modifier for aseptic revision; age-stratified 5-year cumulative revision rates are included in Table 4. In the adjusted models, acute surgery had a higher revision risk (HR 2.21, 95% CI 1.21–4.05, $p=0.010$), as did subacute surgery (HR 1.69, 95% CI 1.21–2.36, $p=0.002$) in younger ACLR patients.

Timing of ACLR and reoperation risk

The cumulative aseptic reoperation probability is presented in Fig. 3 and the 6-year cumulative reoperation incidence is presented in Table 2. Similar to aseptic revision, both acute and subacute ACLR had higher risks for aseptic reoperation (acute HR 2.04, 95% CI 1.43–2.91, $p<0.001$; subacute HR 1.31, 95% CI 1.11–1.54, $p=0.002$) when compared to chronic ACLR patients.

Pairwise comparisons for aseptic reoperation identified additional differences between the timing groups including acute and subacute (HR 1.56, 95% CI 1.12–2.19, $p=0.009$), acute and delayed (HR 2.29, 95% CI 1.60–3.27, $p<0.001$), and subacute and delayed (HR 1.46, 95% CI 1.28–1.67, $p<0.001$) (Table 3).

Crude age-stratified aseptic reoperation 5-year incidences are included in Table 4. After adjustment for covariates, younger ACLR patients had a higher reoperation risk in the acute group (HR 1.76, 95% CI 1.06–2.93, $p=0.029$) compared with chronic ACLR (Table 4). Older patients had a higher reoperation risk amongst acute (HR 2.31, 95% CI 1.39–3.85, $p=0.001$) and subacute (HR 1.30, 95% CI 1.06–1.59, $p=0.014$) when compared with chronic ACLR patients.

Discussion

The most important finding of the present study was the lower risk of revision and reoperation following chronically treated ACLR relative to patients undergoing surgery in an acute or subacute fashion. In a large cohort of 15,795

Table 1 Baseline data of included 15,795 primary isolated anterior cruciate ligament reconstruction (ACLR) patients (2010–2018)

Characteristic, n (%) unless specified	Acute (< 3 weeks)	Subacute (3 weeks–3 months)	Delayed (3–9 months)	Chronic (≥ 9 months)
Total N	270	5971	5959	3595
<i>Patient characteristics</i>				
Age, in years, median (IQR)	21 (17–33)	22 (17–33)	25 (18–36)	29 (22–38)
< 20	121 (44.8)	2515 (42.1)	1936 (32.5)	614 (17.1)
20–29	64 (23.7)	1515 (25.4)	1674 (28.1)	1200 (33.4)
30–39	46 (17.0)	1018 (17.1)	1193 (20.0)	984 (27.4)
≥ 40	39 (14.4)	920 (15.4)	1155 (19.4)	796 (22.1)
Female	117 (43.3)	2676 (44.8)	2292 (38.5)	1167 (32.5)
<i>Race/ethnicity</i>				
Asian	34 (12.6)	708 (11.9)	743 (12.5)	516 (14.4)
Black	24 (8.9)	494 (8.3)	453 (7.6)	250 (7.0)
Hispanic	43 (15.9)	1246 (20.9)	1599 (27.0)	1124 (31.4)
Other	6 (2.2)	134 (2.3)	114 (1.9)	67 (1.9)
White	163 (60.4)	3368 (56.6)	3023 (51.0)	1624 (45.4)
<i>ASA classification</i>				
1–2	196 (72.6)	4648 (77.8)	4621 (77.5)	2804 (78.0)
≥ 3	5 (1.9)	61 (1.0)	76 (1.3)	75 (2.1)
Missing	69 (25.6)	1262 (21.1)	1262 (21.2)	716 (19.9)
<i>BMI, in kg/m², median (IQR)</i>				
< 22	66 (24.4)	1095 (18.4)	869 (14.6)	354 (9.9)
22–24.9	85 (31.5)	1823 (30.6)	1511 (25.4)	778 (21.7)
25–29.9	86 (31.9)	2006 (33.7)	2185 (36.8)	1398 (39.0)
≥ 30	33 (12.2)	1028 (17.3)	1379 (23.2)	1059 (29.5)
<i>Activity at injury</i>				
Motor vehicle accident	8 (3.0)	144 (2.5)	182 (3.1)	158 (4.5)
Sports	211 (80.2)	4857 (82.7)	4600 (78.6)	2619 (75.4)
Work-related	3 (1.1)	54 (0.9)	73 (1.2)	43 (1.2)
Other	41 (15.6)	820 (14.0)	995 (17.0)	655 (18.8)
<i>Procedure characteristics</i>				
<i>Graft source</i>				
Allograft	89 (33.0)	1753 (29.4)	2017 (33.8)	1423 (39.6)
Autograft: BPTB	72 (26.7)	1790 (30.0)	1564 (26.2)	811 (22.6)
Autograft: hamstring	104 (38.5)	2227 (37.3)	2153 (36.1)	1237 (34.4)
Autograft: quad tendon/other	1 (0.4)	24 (0.5)	29 (0.5)	13 (0.3)
Hybrid	4 (1.5)	177 (3.0)	196 (3.3)	111 (3.1)
<i>Femoral fixation</i>				
Combination	15 (6.1)	252 (4.4)	287 (5.0)	166 (4.8)
Crosspin	30 (12.1)	601 (10.5)	616 (10.7)	375 (10.8)
Interference	94 (38.1)	2247 (39.2)	2303 (40.1)	1334 (38.3)
Suspensory	108 (43.7)	2635 (45.9)	2539 (44.2)	1610 (46.2)
<i>Tibial fixation</i>				
Combination	35 (14.2)	1149 (20.1)	1313 (22.9)	788 (22.7)
Interference	203 (82.5)	4417 (77.1)	4231 (73.9)	2565 (74.0)
Suspensory	8 (3.3)	161 (2.8)	184 (3.2)	114 (3.3)
<i>Meniscus and cartilage injuries</i>				
Lateral meniscus tear	114 (42.2)	2516 (42.1)	2338 (39.2)	1484 (41.3)
Medial meniscus tear	105 (38.9)	1741 (29.2)	2059 (34.6)	1990 (55.4)
Cartilage injury	67 (24.8)	1379 (23.1)	1699 (28.5)	1437 (40.0)

Missing values: age = 5 (0.0%), gender = 3 (0.0%), race = 62 (0.4%), ASA = 3309 (20.9%), BMI = 40 (0.3%), activity at injury = 332 (2.1%), femoral fixation = 583 (3.7%), tibial fixation = 627 (4.0%)

ASA American Society of Anesthesiologists, BMI body mass index, BPTB bone patellar tendon bone, IQR interquartile range

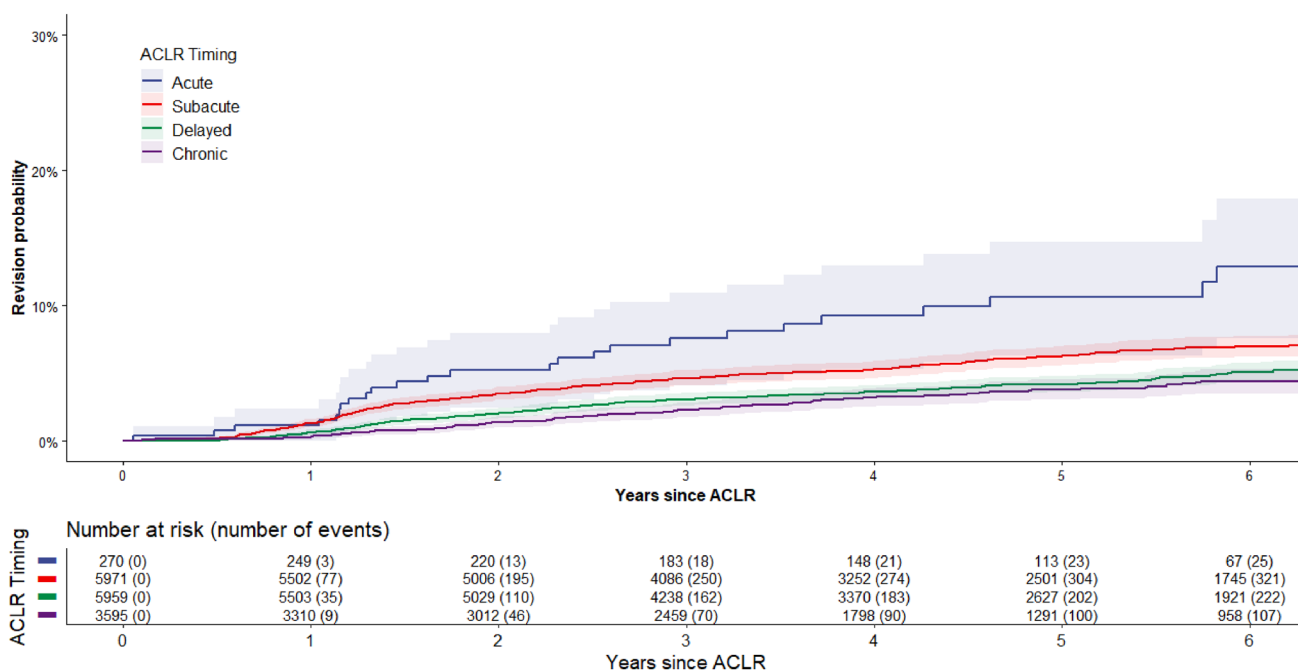


Fig. 2 Cumulative aseptic revision probability (solid line) and 95% confidence limits (shaded area) during follow-up. Number of patients at risk (number of cumulative events) by each year of follow-up

Table 2 Cumulative incidence and adjusted risk of aseptic revision and reoperation by timing of the isolated primary anterior cruciate ligament reconstruction (ACLR)

Outcome	Crude 6-year CIF ^a (95% CI)	Adjusted ^b HR (95% CI)	<i>p</i>
<i>Aseptic revision</i>			
Acute	12.9 (8.3–18.5)	1.70 (1.07–2.72)	0.026
Subacute	7.0 (6.3–7.8)	1.25 (1.01–1.55)	0.040
Delayed	5.1 (4.4–5.8)	1.00 (0.79–1.26)	n.s.
Chronic	4.4 (3.6–5.4)	Reference	
<i>Aseptic reoperation</i>			
Acute	15.0 (9.2–22.1)	2.04 (1.43–2.91)	<0.001
Subacute	9.6 (8.6–10.7)	1.31 (1.11–1.54)	0.002
Delayed	6.4 (5.6–7.3)	0.89 (0.77–1.03)	n.s.
Chronic	8.1 (6.9–9.5)	Reference	

CI confidence interval, CIF cumulative incidence function, HR hazard ratio, n.s. not statistically significant

^aCumulative incidence function calculated as one minus the Kaplan–Meier estimate. Cumulative incidence at 6-year follow-up is reported

^bAdjusted for age, gender, race/ethnicity, American Society of Anesthesiologists classification, body mass index, activity at injury, lateral meniscus tear, medial meniscus tear, cartilage injury, graft type, femoral fixation, tibial fixation, and operating surgeon. Bold indicates statistically significant result (*p* < 0.05)

Table 3 Pairwise comparisons of adjusted risk of aseptic revision and reoperation by timing of the isolated primary anterior cruciate ligament reconstruction (ACLR)

Timing	Aseptic revision		Aseptic reoperation	
	Adjusted ^a HR (95% CI)	<i>p</i>	Adjusted ^a HR (95% CI)	<i>p</i>
Acute vs subacute	1.36 (0.86–2.17)	n.s.	1.56 (1.12–2.19)	0.009
Acute vs delayed	1.71 (1.07–2.73)	0.026	2.29 (1.60–3.27)	<0.001
Acute vs chronic	1.70 (1.07–2.72)	0.026	2.04 (1.43–2.91)	<0.001
Subacute vs delayed	1.26 (1.06–1.48)	0.007	1.46 (1.28–1.67)	<0.001
Subacute vs chronic	1.25 (1.01–1.55)	0.040	1.31 (1.11–1.54)	0.002
Delayed vs chronic	1.00 (0.79–1.26)	n.s.	0.89 (0.77–1.03)	n.s.

CI confidence interval, HR hazard ratio, n.s. not statistically significant

^aAdjusted for age, gender, race/ethnicity, American Society of Anesthesiologists classification, body mass index, activity at injury, lateral meniscus tear, medial meniscus tear, cartilage injury, graft type, femoral fixation, tibial fixation and operating surgeon. Bold indicates statistically significant result (*p* < 0.05)

Table 4 Age-stratified cumulative incidence and adjusted risk of aseptic revision and aseptic reoperation by timing of the isolated primary anterior cruciate ligament reconstruction (ACLR)

Timing	Aseptic revision			Aseptic reoperation		
	Crude 5-year CIF ^a (95% CI)	Adjusted ^b HR (95% CI)	<i>p</i>	Crude 5-year CIF ^a (95% CI)	Adjusted ^b HR (95% CI)	<i>p</i>
<i>< 22 years old</i>						
Acute	16.4 (10.1–24.4)	2.21 (1.21–4.05)	0.010	7.1 (2.7–14.2)	1.76 (1.06–2.93)	0.029
Subacute	9.2 (8.1–10.4)	1.69 (1.21–2.36)	0.002	7.8 (6.7–9.1)	1.27 (0.99–1.62)	n.s.
Delayed	7.1 (6.0–8.3)	1.38 (0.99–1.92)	n.s.	4.7 (3.7–5.9)	0.87 (0.67–1.12)	n.s.
Chronic	6.0 (4.3–8.1)	Reference	–	6.0 (4.2–8.2)	Reference	–
<i>≥ 22 years old</i>						
Acute	3.9 (1.2–8.9)	1.39 (0.61–3.21)	n.s.	8.2 (3.8–14.9)	2.31 (1.39–3.85)	0.001
Subacute	3.4 (2.7–4.2)	0.94 (0.67–1.31)	n.s.	5.5 (4.5–6.6)	1.30 (1.06–1.59)	0.014
Delayed	2.3 (1.7–2.9)	0.74 (0.51–1.07)	n.s.	4.5 (3.7–5.4)	0.90 (0.74–1.09)	n.s.
Chronic	3.1 (2.3–3.9)	Reference	–	5.7 (4.6–7.0)	Reference	–

CI confidence interval, CIF cumulative incidence function, HR hazard ratio, n.s. not statistically significant

^aCumulative incidence function calculated as one minus the Kaplan–Meier estimate. Cumulative incidence at 5-year follow-up is reported

^bAdjusted for age, gender, race/ethnicity, American Society of Anesthesiologists classification, body mass index, activity at injury, lateral meniscus tear, medial meniscus tear, cartilage injury, graft type, femoral fixation, tibial fixation, and operating surgeon. Bold indicates statistically significant result (*p* < 0.05)

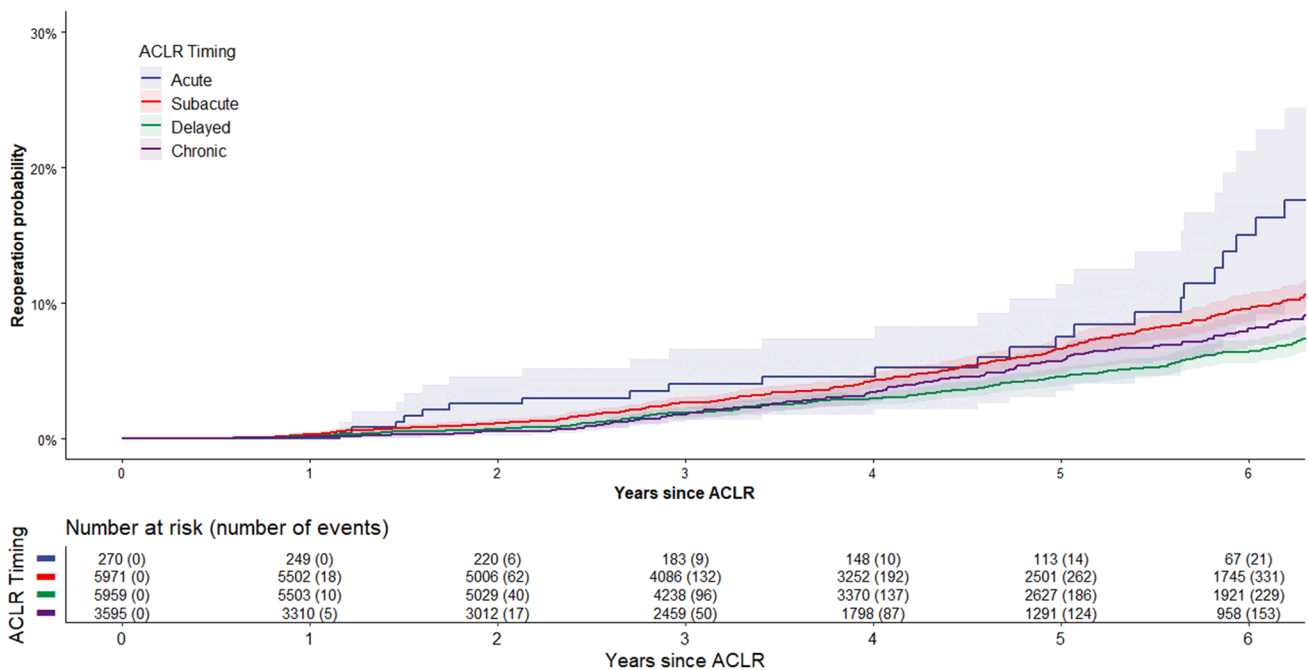


Fig. 3 Cumulative aseptic reoperation probability (solid line) and 95% confidence limits (shaded area) during follow-up. Number of patients at risk (number of cumulative events) by each year of follow-up

patients, more concomitant medial meniscus and cartilage injuries were reported in chronic ACLR patients. However, chronic ACLR was also associated with a lower risk for both aseptic revision and reoperation during follow-up relative to the acute and subacute ACLR. Patients < 22 years of age in

particular had a lower aseptic revision risk during follow-up for ACLR performed ≥ 9 months after injury.

Since the posterior horn of the medial meniscus serves as a secondary stabiliser to anteroposterior translation, when the ACL is torn, the medial meniscus is subject to higher

forces and risk of injury with each instability event [40]. This corresponds to our findings of a higher frequency of medial meniscus injuries for patients with chronic ACLR, but comparable frequencies in lateral meniscus injuries between chronic and acute study groups. The results presented here are similar to those of Chen et al. [4] who reported meniscal injuries to be present in 53.7% of delayed ACLR (defined as ≥ 1 year) and 29.1% of early ACLR (defined as < 1 year) with no observed difference in lateral meniscus tears. Brambilla et al. [3] also found delaying surgery beyond 12 months increased the risk of developing medial meniscus tear but not lateral meniscus tear.

The greater frequency of cartilage lesions at the time of chronic ACLR is consistent with previous studies. Studies have reported a higher likelihood of cartilage injury and high grade cartilage lesions for ACLR performed more than 1 year after injury [18, 25, 26], with similar findings in the paediatric population [1]. The Norwegian National Knee Ligament Register suggested a higher odds of cartilage lesion by close to 1% with each month from the time of injury and close to twice the odds if a meniscal lesion is present [9].

Higher risks of revision following ACLR performed within 3 months of injury were also reported in prior studies from the Norwegian and Swedish registries [39]. Sutherland et al. [42] also found a higher risk for revision in ACLR performed within 1 year from injury. In our investigation separating out acute and subacute groups, we also observed a dose–response relationship as ACLR were performed closer to the time of injury (i.e. HR 1.25 for subacute vs chronic and HR 1.70 for acute vs chronic in overall analysis; HR 1.69 for subacute vs chronic and HR 2.21 for acute vs chronic in < 22 years analysis). Future investigation is needed to evaluate if those undergoing ACLR earlier have higher Marx activity scores which may increase their revision risk [15], particularly in patients < 22 years where the observed association was the strongest.

Reoperations outside of revision may derive from secondary injuries. Evidence generally supports the theory that nonoperative or delayed management of ACL tears increases the risk of secondary meniscal and chondral injury [11, 32, 35, 38], though definitions for early and delayed are varied. Hagmeijer et al. [11] reported lower rates of secondary meniscal tears with ACLR within 6 months (7%) compared to after 6 months (33%) or nonoperative management (19%). Other studies have observed similar findings when using early/delayed cut-points at 6 months [25] and 1 year [35]. In paediatric patients, a meta-analysis pooling results from observational studies indicated a lower risk of medial meniscal injury in those reconstructed early (26%) compared to delayed (47%) [18]. Despite this theoretical higher risk of secondary injuries, we observed a lower risk of aseptic

reoperation for those with a chronic ACLR when compared to acute and subacute ACLR.

Current literature is heterogenous in its definitions of early/acute/subacute and delayed/chronic ACLR. Early reconstruction has been defined as soon as 48 h and as long as up to 2 years after injury [13, 20]. One of the long-standing arguments against performing ACLR early after injury is the risk of arthrofibrosis [2, 34]. However, a recent randomised controlled trial evaluated patients undergoing ACLR within 8 days after injury and found no increase in stiffness relative to those undergoing surgery 6–10 weeks after injury [43]. Similar studies have also reported no difference with respect to surgical timing [6, 12, 43]. Two meta-analyses failed to observe a difference in ROM, graft rupture, or functional outcomes in those undergoing early reconstruction within 3 weeks of injury relative to delayed, defined as either at least 4 weeks or 10 weeks after injury [5, 24]. Many of these studies, however, would have fallen into the early reconstruction categories of the present study [14, 22]. The benefit of incorporating a chronic group with ACLR ≥ 9 months after injury is it allows more than adequate time for patients to resume normal activities of daily living and trial return to sports if desired. Despite the varying definitions of ACLR timing in the literature, there does appear to be a clear delineation between early (days to weeks) versus chronic (≥ 9 months).

Younger age is a known risk factor for revision surgery [21, 23]. While higher revision risks have previously been reported for ACLR performed early and in younger patients, the relationship between both timing of surgery and age is limited. When stratifying by age, the lower revision risk following chronic ACLR relative to acute and subacute ACLR was within patients < 22 years of age specifically; no associations between surgical timing and subsequent aseptic revision were observed in older patients. On the other hand, acute or subacute ACLR had higher risks of surgical reoperations relative chronic ACLR in the older age group. This may be of use to surgeons to discuss with their prospective patients as a counselling to younger patients who are undergoing ACLR. For older patients undergoing ACLR, they should also be counselled that they have a higher risk of subsequent surgeries (outside of revision ACLR).

This study has several strengths. Our ACLR registry captures information on all ACLR performed within the integrated healthcare system and longitudinally monitors healthcare plan members for outcomes. This is of value since the rates of patients undergoing surgery with different surgeons than their primary is not insignificant [42]. The healthcare system includes 8 geographical regions and more than 300 surgeons, so that our findings are likely representative of community-based practices in the US. Furthermore, there is longitudinal follow-up for outcomes, allowing for time-to-event analyses, and manual validation of identified

outcomes. The large cohort size made it possible to account for potential confounders, such as age, gender, BMI, race, ASA classification, activity at injury, meniscus tear, cartilage injury, graft type, and graft fixation, in the regression analysis.

Limitations of the present study align with those of other observational studies in that causation cannot be inferred. While we attempted to account for additional factors in our multivariable analysis, residual influence due to unmeasured covariates is possible. The registry does not capture data on activity level, nor is there information on return to play. While we included activity at the time of injury in our multivariable analysis, patients who choose to undergo surgery earlier may have a higher activity level or returned to play at an earlier timeframe postoperatively, which can also impact the risk of revision. Still, these factors would occur after ACLR exposure and be considered an intermediary step in the causal pathway rather than a confounder. While surgeon volume was also not included as a covariate in the regression analysis, all models accounted for the individual surgeon who performed the index ACLR. Furthermore, no information on arthrofibrosis, patient-reported outcomes, or functional outcomes were collected in the registry and, therefore, could not be evaluated. Only outcomes requiring surgical intervention were examined, which may underestimate the true incidence of ACLR graft failure as patients who experienced clinical failure but chose not to undergo subsequent revision or reoperation were not evaluated. Therefore, inferences regarding the risk of graft re-tear and clinical failure cannot be made. Loss to follow-up was high at 25.8%, and there is potential for selection bias as 20% acute, 25% subacute, 28% delayed, and 27% chronic ACLR patients terminated healthcare membership during follow-up. However, our statistical analysis accounted for this, including follow-up time in the regression models and censoring at the date lost to follow-up. Finally, a large proportion of patients in the registry were excluded due to missing information on the date of injury. However, when these patients were compared to those included in the study sample, demographics and patient and surgical characteristics were similar. Therefore, we do not anticipate there to be selection bias in reporting of injury date. Despite these limitations, the present study contributes to literature on timing of ACLR after injury.

Conclusion

In this cohort study, while more meniscal and chondral injuries were reported for ACLR performed ≥ 9 months after the date of injury, lower risks of revision and reoperation were observed in the chronic group relative to patients undergoing acute or subacute ACLR. The lower revision risk was

observed especially for chronic ACLR performed in patients younger than 22 years old. Clinicians may use this information in their discussion with patients when considering timing of the ACLR. Specifically, while more medial meniscus and cartilage injuries were observed in the patients with a chronic ACLR, these patients had lower aseptic revision and reoperation risks when compared to acute and subacute ACLR. This provides evidence for a patient that delaying surgery to a more convenient time does not increase the risk of revision ACLR.

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Author contributions DYD, SA, MJC, HAP, and GBM contributed to overall conception and design of the study. RNC and HAP took part in data acquisition. RNC completed the statistical analysis. DYD, RNC, SA, and MJC drafted the manuscript. DYD, RNC, SA, MJC, HAP, and GBM reviewed the manuscript, contributed to revisions, gave approval of the final draft, and agree to be accountable for all aspects of the work.

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Declarations

Conflict of interest The authors report no conflicts.

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References

1. Anderson AF, Anderson CN (2015) Correlation of meniscal and articular cartilage injuries in children and adolescents with timing of anterior cruciate ligament reconstruction. *Am J Sports Med* 43:275–281
2. Bierke S, Abdelativ Y, Hees T, Karpinski K, Häner M, Park H et al (2021) Risk of arthrofibrosis in anatomical anterior cruciate ligament reconstruction: the role of timing and meniscus suture. *Arch Orthop Trauma Surg* 141:743–750
3. Brambilla L, Pulici L, Carimati G, Quaglia A, Prospero E, Bait C et al (2015) Prevalence of associated lesions in anterior cruciate ligament reconstruction: correlation with surgical timing and with patient age, sex, and body mass index. *Am J Sports Med* 43:2966–2973
4. Chen KH, Chiang ER, Wang HY, Ma HL (2019) Correlation of meniscal tear with timing of anterior cruciate ligament reconstruction in patients without initially concurrent meniscal tear. *J Knee Surg* 32:1128–1132
5. Deabate L, Previtali D, Grassi A, Filardo G, Candrian C, Delcogliano M (2020) Anterior cruciate ligament reconstruction within 3 weeks does not increase stiffness and complications compared with delayed reconstruction: a meta-analysis of randomized controlled trials. *Am J Sports Med* 48:1263–1272
6. Eriksson K, von Essen C, Jönhagen S, Barenius B (2018) No risk of arthrofibrosis after acute anterior cruciate

- ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 26:2875–2882
7. Ferguson D, Palmer A, Khan S, Oduoza U, Atkinson H (2019) Early or delayed anterior cruciate ligament reconstruction: Is one superior? A systematic review and meta-analysis. *Eur J Orthop Surg Traumatol* 29:1277–1289
 8. Forsythe B, Lu Y, Agarwalla A, Ezuma CO, Patel BH, Nwachukwu BU et al (2021) Delaying ACL reconstruction beyond 6 months from injury impacts likelihood for clinically significant outcome improvement. *Knee* 33:290–297
 9. Granan LP, Bahr R, Lie SA, Engebretsen L (2009) Timing of anterior cruciate ligament reconstructive surgery and risk of cartilage lesions and meniscal tears: a cohort study based on the Norwegian National Knee Ligament Registry. *Am J Sports Med* 37:955–961
 10. Hagino T, Ochiai S, Senga S, Yamashita T, Wako M, Ando T et al (2015) Meniscal tears associated with anterior cruciate ligament injury. *Arch Orthop Trauma Surg* 135:1701–1706
 11. Hagmeijer MH, Hevesi M, Desai VS, Sanders TL, Camp CL, Hewett TE et al (2019) Secondary meniscal tears in patients with anterior cruciate ligament injury: relationship among operative management, osteoarthritis, and arthroplasty at 18-year mean follow-up. *Am J Sports Med* 47:1583–1590
 12. Helito CP, Sobrado MF, Giglio PN, Bonadio MB, Pécora JR, Gobbi RG et al (2021) Surgical timing does not interfere on clinical outcomes in combined reconstruction of the anterior cruciate ligament and anterolateral ligament: a comparative study with minimum 2-year follow-up. *Arthroscopy* 37:1909–1917
 13. Herbst E, Hoser C, Gföller P, Hepperger C, Abermann E, Neumayer K et al (2017) Impact of surgical timing on the outcome of anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 25:569–577
 14. Hu B, Gao F, Li C, Zhang B, An M, Lu M et al (2020) A comparative analysis of the efficacy of anterior cruciate ligament reconstruction with autologous ligament grafting at different time points. *J Clin Lab Anal* 34:e23543
 15. Kaeding CC, Pedroza AD, Reinke EK, Huston LJ, Spindler KP (2015) Risk factors and predictors of subsequent ACL injury in either knee after ACL reconstruction: prospective analysis of 2488 primary ACL reconstructions from the MOON cohort. *Am J Sports Med* 43:1583–1590
 16. Karikis I, Åhlén M, Sernert N, Ejerhed L, Rostgård-Christensen L, Kartus J (2018) The long-term outcome after early and late anterior cruciate ligament reconstruction. *Arthroscopy* 34:1907–1917
 17. Karter AJ, Ferrara A, Liu JY, Moffet HH, Ackerson LM, Selby JV (2002) Ethnic disparities in diabetic complications in an insured population. *JAMA* 287:2519–2527
 18. Kay J, Memon M, Shah A, Yen YM, Samuelsson K, Peterson D et al (2018) Earlier anterior cruciate ligament reconstruction is associated with a decreased risk of medial meniscal and articular cartilage damage in children and adolescents: a systematic review and meta-analysis. *Knee Surg Sports Traumatol Arthrosc* 26:3738–3753
 19. Koebnick C, Langer-Gould AM, Gould MK, Chao CR, Iyer RL, Smith N et al (2012) Sociodemographic characteristics of members of a large, integrated health care system: comparison with US Census Bureau data. *Perm J* 16:37–41
 20. Lee YS, Lee OS, Lee SH, Hui TS (2018) Effect of the timing of anterior cruciate ligament reconstruction on clinical and stability outcomes: a systematic review and meta-analysis. *Arthroscopy* 34:592–602
 21. Maletis GB, Inacio MC, Funahashi TT (2013) Analysis of 16,192 anterior cruciate ligament reconstructions from a community-based registry. *Am J Sports Med* 41:2090–2098
 22. Manandhar RR, Chandrashekar K, Kumaraswamy V, Sahanand S, Rajan D (2018) Functional outcome of an early anterior cruciate ligament reconstruction in comparison to delayed: are we waiting in vain? *J Clin Orthop Trauma* 9:163–166
 23. Matar HE, Platt SR, Bloch BV, James PJ, Cameron HU (2021) A systematic review of randomized controlled trials in anterior cruciate ligament reconstruction: standard techniques are comparable (299 trials with 25,816 patients). *Arthrosc Sports Med Rehabil* 3:e1211–e1226
 24. Matthewson G, Kooner S, Rabbani R, Gottschalk T, Old J, Abou-Setta AM et al (2021) Does a delay in anterior cruciate ligament reconstruction increase the incidence of secondary pathology in the knee? A systematic review and meta-analysis. *Clin J Sport Med* 31:313–320
 25. Mehl J, Otto A, Baldino JB, Achtnich A, Akoto R, Imhoff AB et al (2019) The ACL-deficient knee and the prevalence of meniscus and cartilage lesions: a systematic review and meta-analysis (CRD42017076897). *Arch Orthop Trauma Surg* 139:819–841
 26. Michalitsis S, Vlychou M, Malizos KN, Thriskos P, Hantes ME (2015) Meniscal and articular cartilage lesions in the anterior cruciate ligament-deficient knee: correlation between time from injury and knee scores. *Knee Surg Sports Traumatol Arthrosc* 23:232–239
 27. Mok YR, Wong KL, Panjwani T, Chan CX, Toh SJ, Krishna L (2019) Anterior cruciate ligament reconstruction performed within 12 months of the index injury is associated with a lower rate of medial meniscus tears. *Knee Surg Sports Traumatol Arthrosc* 27:117–123
 28. Monk AP, Davies LJ, Hopewell S, Harris K, Beard DJ, Price AJ (2016) Surgical versus conservative interventions for treating anterior cruciate ligament injuries. *Cochrane Database Syst Rev* 4:Cd011166
 29. Paxton EW, Kiley ML, Love R, Barber TC, Funahashi TT, Inacio MC (2013) Kaiser Permanente implant registries benefit patient safety, quality improvement, cost-effectiveness. *Jt Comm J Qual Patient Saf* 39:246–252
 30. Prentice HA, Lind M, Mouton C, Persson A, Magnusson H, Gabr A et al (2018) Patient demographic and surgical characteristics in anterior cruciate ligament reconstruction: a description of registries from six countries. *Br J Sports Med* 52:716–722
 31. Prodromidis AD, Drosatou C, Mourikis A, Sutton PM, Charalambous CP (2021) Relationship between timing of anterior cruciate ligament reconstruction and chondral injuries: a systematic review and meta-analysis. *Am J Sports Med*. <https://doi.org/10.1177/036354652110361413635465211036141>
 32. Prodromidis AD, Drosatou C, Thivaos GC, Zreik N, Charalambous CP (2021) Timing of anterior cruciate ligament reconstruction and relationship with meniscal tears: a systematic review and meta-analysis. *Am J Sports Med* 49:2551–2562
 33. Ralles S, Agel J, Obermeier M, Tompkins M (2015) Incidence of secondary intra-articular injuries with time to anterior cruciate ligament reconstruction. *Am J Sports Med* 43:1373–1379
 34. Rushdi I, Sharifudin S, Shukur A (2019) Arthrofibrosis following anterior cruciate ligament reconstruction. *Malays Orthop J* 13:34–38
 35. Sanders TL, Kremers HM, Bryan AJ, Fruth KM, Larson DR, Pareek A et al (2016) Is anterior cruciate ligament reconstruction effective in preventing secondary meniscal tears and osteoarthritis? *Am J Sports Med* 44:1699–1707
 36. Sanders TL, Maradit Kremers H, Bryan AJ, Kremers WK, Levy BA, Dahm DL et al (2016) Incidence of and factors associated with the decision to undergo anterior cruciate ligament reconstruction 1 to 10 years after injury. *Am J Sports Med* 44:1558–1564

37. Sanders TL, Maradit Kremers H, Bryan AJ, Larson DR, Dahm DL, Levy BA et al (2016) Incidence of anterior cruciate ligament tears and reconstruction: a 21-year population-based study. *Am J Sports Med* 44:1502–1507
38. Sanders TL, Pareek A, Kremers HM, Bryan AJ, Levy BA, Stuart MJ et al (2017) Long-term follow-up of isolated ACL tears treated without ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 25:493–500
39. Snaebjörnsson T, Hamrin Senorski E, Svantesson E, Westin O, Persson A, Karlsson J et al (2019) Graft fixation and timing of surgery are predictors of early anterior cruciate ligament revision: a cohort study from the Swedish and Norwegian knee ligament registries based on 18,425 patients. *JB JS Open Access* 4:e0037
40. Sommerfeldt M, Raheem A, Whittaker J, Hui C, Otto D (2018) Recurrent instability episodes and meniscal or cartilage damage after anterior cruciate ligament injury: a systematic review. *Orthop J Sports Med* 6:2325967118786507
41. Stone JA, Perrone GS, Nezwik TA, Cui Q, Vlad SC, Richmond JC et al (2019) Delayed ACL reconstruction in patients ≥ 40 years of age is associated with increased risk of medial meniscal injury at 1 year. *Am J Sports Med* 47:584–589
42. Sutherland K, Clatworthy M, Chang K, Rahardja R, Young SW (2019) Risk factors for revision anterior cruciate ligament reconstruction and frequency with which patients change surgeons. *Orthop J Sports Med* 7:2325967119880487
43. von Essen C, Eriksson K, Barenius B (2020) Acute ACL reconstruction shows superior clinical results and can be performed safely without an increased risk of developing arthrofibrosis. *Knee Surg Sports Traumatol Arthrosc* 28:2036–2043

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