Prognostic Factors for Patient-Reported Outcomes at 32 to 37 Years After Surgical or Nonsurgical Management of Anterior Cruciate Ligament Injury

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Background: Knowledge to inform the identification of individuals with a poor long-term prognosis after anterior cruciate ligament (ACL) injury is limited. Identifying prognostic factors for long-term outcomes after ACL injury may inform targeted interventions to improve outcomes for those with a poor long-term prognosis.

Purpose: To determine whether ACL treatment (early augmented or nonaugmented ACL repair plus rehabilitation, rehabilitation alone, or rehabilitation plus delayed ACL reconstruction [ACLR]) and 4-year measures (quadriceps and hamstrings strength, single-leg hop, knee laxity, flexion and extension deficit, self-reported knee function, activity level) are prognostic factors for patient-reported outcomes at 32 to 37 years after acute ACL injury.

Study Design: Cohort study; Level of evidence, 2.

Methods: A total of 251 patients aged 15 to 40 years with acute ACL rupture between 1980 and 1985 were allocated to early ACL repair (augmented or nonaugmented) plus rehabilitation or to rehabilitation alone, based on birth year. One hundred ninety of 234 completed 32- to 37-year follow-up questionnaires (response rate, 81%); 18 people were excluded, resulting in 172 patients available for analysis (mean age, 59 ± 6 years; 28% female). Potential prognostic factors assessed 4 years after ACL injury were ACL treatment (early ACL repair, rehabilitation alone, or delayed ACLR), isokinetic quadriceps and hamstrings strength, single-leg hop performance, knee flexion and extension deficit, knee laxity, Tegner activity scale, and Lysholm score. Outcomes included Knee injury and Osteoarthritis Outcome Score (KOOS) subscales and the Anterior Cruciate Ligament Quality of Life (ACL-QOL) measure. Linear regression adjusted for age, sex, baseline meniscal injury, and contralateral ACL injury was used to assess potential prognostic factors for 32- to 37-year outcomes. Multiple imputation accounted for missing data.

Results: A fair/poor Lysholm score (vs excellent/good) at 4 years was a prognostic factor for worse KOOS Pain (adjusted regression coefficient, −12 [95% confidence interval (CI), −19 to −4]), KOOS Symptoms (−15 [95% CI, −23 to −7]), KOOS Sport and Recreation (−19 [95% CI, −31 to −8]), and ACL QOL (−9 [95% CI, −18 to −1]) scores. A 4-year single-leg hop limb symmetry index <90% was a prognostic factor for worse KOOS Pain (adjusted regression coefficient, −9 [95% CI, −17 to −1]) and ACL QOL (−13 [95% CI, −22 to −3]) scores at long-term follow-up. A lower activity level, delayed ACLR, and increased knee laxity were prognostic factors in the crude analysis. Rehabilitation alone versus early repair, quadriceps and hamstring strength, and flexion and extension deficit were not related to 32- to 37-year outcomes.

Conclusion: Reduced self-reported knee function and single-leg hop performance 4 years after ACL injury were prognostic factors for worse 32- to 37-year outcomes. Estimates exceeded clinically important thresholds, highlighting the importance of assessing these constructs when managing individuals with ACL injuries.

Registration: NCT03182647 (ClinicalTrials.gov identifier).

Keywords: nonoperative management; ACL repair; knee injury; patient-reported outcomes; long-term follow-up

The annual incidence of anterior cruciate ligament (ACL) reconstructive surgery is increasing rapidly.[48] This is a great concern considering 1 in 2 individuals will not return to their

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previous level of physical activity after ACL injury,[5] 1 in 3 people will develop painful posttraumatic knee osteoarthritis within 15 years of injury,[30] and a substantial number of individuals will experience reduced quality of life (QOL) because of their knee 5 to 20 years after ACL injury.[13,14] Of further concern is that one-third of young, active individuals experience a second ACL injury after ACL reconstruction (ACLR),[46] and the annual incidence of revision ACL surgery is increasing rapidly.[48] Despite the wealth of literature investigating short- and midterm outcomes of ACL injury, little is known about outcomes beyond 30 years after ACL injury. Investigating outcomes beyond 30 years after ACL injury is important for understanding the long-term burden and consequences of ACL injury.

Importantly, not all individuals will have poor outcomes after ACL injury. A systematic review of prospective studies investigating prognostic factors for poor patient-reported outcomes at a minimum 10 years after ACL injury found that the longest follow-up was 17 years and most studies had high dropout rates.[22] Factors related to worse outcomes within 10 years of ACL injury include reduced preoperative quadriceps strength, range of motion, and activity level; concomitant meniscal or cartilage injury; worse single-leg hop performance; subsequent knee injury; and revision ACL surgery.[15] However, no research to date has investigated prognostic factors for poor outcomes 30 to 40 years after ACL injury. Specifically, it is not clear if impaired measures of knee function assessed within 5 years of injury are prognostic factors for poor outcome 30 to 40 years after injury. Identifying modifiable functional deficits within 5 years of injury that are prognostic factors for poor outcome could inform objectives for rehabilitation strategies aimed at improving long-term prognosis.

The aim of the study was to determine whether ACL treatment (early augmented or nonaugmented ACL repair plus rehabilitation, rehabilitation alone, or rehabilitation plus delayed ACLR) and 4-year measures (quadriceps and hamstrings strength, single-leg hop for distance, knee laxity, flexion and extension deficit, self-reported knee function, activity level) are prognostic factors for knee pain, symptoms, reduced sport and recreational function, and knee-related QOL 32 to 37 years after acute ACL injury.

METHODS

Procedures

This long-term follow-up of a prospective cohort study (NCT03182647) was granted ethical approval from a regional ethics committee. Between November 1980 and December 1985, all patients who presented to the emergency department at University Hospital (Linköping, Sweden) within 14 days of a traumatic knee injury underwent diagnostic arthroscopy under anesthesia. During this time, 251 patients aged 15 to 40 years were diagnosed with acute ACL rupture.

Patients were allocated to early augmented or nonaugmented ACL repair plus rehabilitation or rehabilitation alone based on an even or odd birth year. Patients with an even birth year were allocated to the early ACL repair group, which comprised augmented ACL repair using a 1.5 cm–wide strip of the iliotibial band as described previously (n = 56)[4,29] or nonaugmented ACL repair (n = 19) performed a mean (± standard deviation) of 5 ± 4 days after injury. After surgery, patients wore a nonweightbearing long-leg cast for 6 weeks with the knee in 30° of flexion; after that, they underwent approximately 9 months of physiotherapist-supervised structured rehabilitation.

Patients with an odd birth year were allocated to the rehabilitation-alone group, which comprised structured rehabilitation supervised by a physiotherapist and was typically completed 4 to 6 months after injury. Structured rehabilitation focused on restoration of strength and coordination.[4] Based on birth year, 41 out of 251 patients (16%) were allocated the wrong ACL treatment.

All patients had to regain at least 85% of quadriceps torque (compared with the uninjured side) before receiving clearance to return to sports participation. The guidelines for crossing over to delayed ACLR were disabling instability in addition to an activity level that was unacceptable to the patient, despite adequate rehabilitation.[4] Delayed ACLRs were performed utilizing allograft or autograft (patellar tendon, hamstrings tendon, or iliotibial band graft) techniques. Concomitant meniscal, cartilage, and ligamentous injuries (medial collateral ligament, posterior oblique ligament, and arcuate ligament complex) were diagnosed arthroscopically within 21 days (mean, 5 ± 4 days) of injury. Meniscal injuries were treated using surgical repair or partial meniscectomy or managed nonoperatively (if graded as minor severity) irrespective of ACL treatment.[4] Patients who received meniscal repair without ACL repair wore a nonweightbearing cast for 4 weeks.

Research has been performed on smaller subgroups of this cohort, including a 5-year follow-up of a consecutive sample of 111 patients who were allocated to early ACL repair (augmented or nonaugmented) or rehabilitation-alone between 1980 and 1982 and a 15-year follow-up of 167 patients who were recruited between 1980 and

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Ethical approval for this study was obtained from the Regional Ethical Committee of Linköping (Dnr: 2017/119-31).

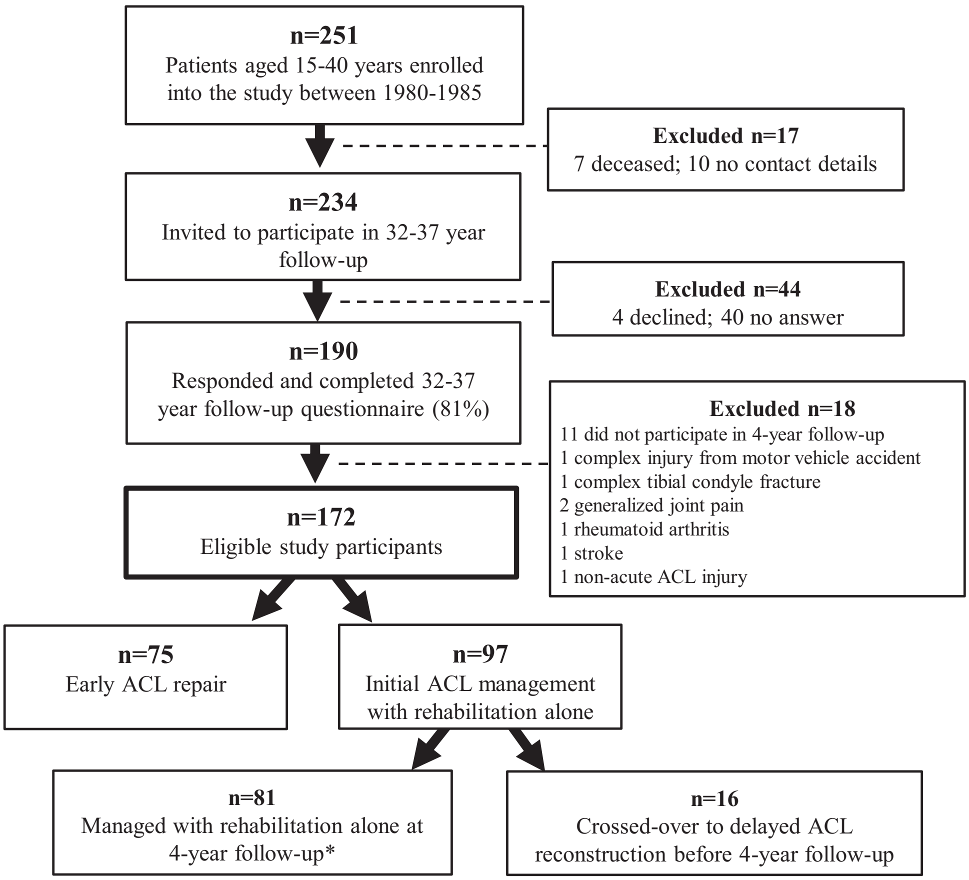


Figure 1. Participant recruitment. *Includes 9 participants who had delayed ACL reconstruction 5 to 21 years after ACL injury. ACL, anterior cruciate ligament.

1983.[4,23] Despite previous studies only using data from patients recruited before 1983, recruitment continued until December 1985. For the 32- to 37-year follow-up, all patients who were recruited into the study between November 1980 and December 1985 were assessed for eligibility.

Neither patients nor the public were directly involved in the design or conduct of this study, and authors were physiotherapists (S.F., J.K.) or orthopedic surgeons (C.A., H.G.) with experience treating individuals with ACL injury.

Follow-Up at 4 Years

All patients who were enrolled into the study between 1980 and 1985 were invited to complete a range of assessments at a mean of 4 ± 1 years (range, 3-6 years) after ACL injury. Assessments included isokinetic quadriceps and hamstrings strength, single-leg hop for distance, knee flexion and extension, arthrometer-assessed anterior-posterior knee laxity, the Tegner Activity Scale, and the Lysholm score to evaluate self-reported knee function.[3]

Follow-Up at 32 to 37 Years

Eligibility criteria for 32- to 37-year follow-up were as follows: aged 15 to 40 years at the time of ACL injury; enrolled in the study with a primary acute ACL injury (diagnosed arthroscopically within 3 weeks of injury); and no disease or trauma (other than those related to the ACL injury) causing limitations in function, joint pain, or cognitive deficits (eg, rheumatoid arthritis, fibromyalgia, stroke, cancer treatment). Of the 251 potentially eligible patients, 234 living patients with contact details were invited to complete a 32- to 37-year follow-up questionnaire, a clinical assessment, and knee radiographs. Study information, an informed consent form, a paper-based questionnaire, and a reply-paid envelope were sent to potentially eligible participants via mail, and up to 3 reminder letters were sent if no response was received. Individuals could consent to complete 1, 2, or all of the components of the 32- to 37-year follow-up. All participants who consented to take part in the long-term follow-up completed the questionnaire. This study used data from individuals who participated in the 4-year follow-up and completed the 32- to 37-year follow-up questionnaire.

Of the 234 people invited for the 32- to 37-year follow-up, 4 declined, and 40 did not respond (response rate, 81%). Seven people were ineligible, and 11 were excluded because of not participating in the 4-year follow-up, leaving data from 172 participants available for analysis (Figure 1).

TABLE 1
Potential Prognostic Factors Included in Regression Models[a]

Variable	Method of Measurement
ACL treatment	Defined as (1) early ACL repair (underwent early augmented or nonaugmented ACL repair at a mean of 5 ± 4 d after injury) plus rehabilitation, (2) rehabilitation alone (allocated rehabilitation alone, did not undergo ACLR at 4-y follow-up), or (3) delayed ACLR (initially allocated to rehabilitation alone but underwent ACLR before 4-y follow-up).
4-y Quadriceps and hamstring strength	Assessed using with a Cybex II Dynamometer (Lumex Inc) isokinetically at an angular velocity of 30 deg/s.[38] The peak torque values were recorded,[38] and an LSI was calculated ([ACL-injured knee/contralateral knee] × 100%) for isokinetic quadriceps and hamstrings strength. This was converted to a binary variable whereby an LSI of ≥90% represented sufficient strength, and an LSI <90% represented insufficient strength. A quadriceps and hamstrings strength LSI ≥90% is commonly used as criteria to determine if patients are ready to return to sports.[40]
4-y Single-leg hop performance	A single-leg hop for distance was performed 3 times with each leg, hopping and landing on the same leg with the hands behind the back.[38] The best distance for the injured and uninjured leg was used to calculate an LSI. A binary variable was created using an LSI cutoff of ≥90%. An LSI ≥90% is recommended as a cutoff point to determine whether an individual is ready to return to sports after ACL injury.[44] The single-leg hop for distance is the most frequently used functional test within the ACL injury literature.[1]
4-y Knee extension and flexion deficit	Assessed for the ACL-injured knee using a handheld goniometer. Maximal passive knee extension was converted to a binary variable, whereby an extension deficit was defined as ≥5° of knee extension deficit. Maximal passive knee flexion was converted to a binary variable: no flexion deficit (≥135° of knee flexion) vs flexion deficit (<135° of knee flexion).
4-y Knee laxity	Anterior-posterior laxity was assessed bilaterally using the Stryker Knee Laxity Tester (Stryker)[43] with the knee at 20° of flexion and anterior- and posterior-directed forces on the proximal tibia of 90 and 180 N applied.[31] Data from the 90-N anterior and posterior translation tests were summed and compared with data from the contralateral knee to calculate an SSD, whereby an SSD near zero is considered normal.[32] We defined increased knee laxity as an SSD ≥3 mm, which is commonly used as a threshold for increased knee laxity.[31]
4-y Activity level	The TAS was intended to provide a standardized method of grading sports and work activities in patients with ACL injury and to complement the Lysholm score since knee functional limitations may be masked by low activity levels.[37] Scores range from 0 (receiving a disability pension because of disability of the knee) to 10 (competing in soccer at a national or elite level). In individuals with knee injury, the TAS has been found to have good test-retest reliability (intraclass correlation coefficient range, 0.82-0.92), an MDC of 1, and an SEM in the range of 0.4-0.6.[8] Scores of 6-10 can only be achieved if the person participates in recreational or competitive sport. Given linearity issues, the TAS was converted to a binary score (0-5 vs 6-10).
4-y Self-reported knee function	Evaluated using the Lysholm score, which assesses 8 items (pain [25 points], instability [25 points], locking [15 points], swelling [10 points], limp [5 points], stair climbing [10 points], squatting [5 points], and need for gait support [5 points]). Scores range from 0 (extreme disability) to 100 (no symptoms or disability). Scores are commonly categorized as *excellent* (95-100), *good* (84-94), *fair* (65-83), and *poor* (≤64).[2,4,8] Owing to linearity issues, scores were converted to a binary variable: *excellent*/*good* vs *fair*/*poor*. The Lysholm score has acceptable test-retest reliability, criterion and construct validity, responsiveness to change, and floor and ceiling effects, for use in individuals with ACL injuries.[7] The Lysholm score has a reported MDC of 8.9-10.1 points and SEM of 3.2-3.6 points.[8]

[a]ACL, anterior cruciate ligament; ACLR, anterior cruciate ligament reconstruction; LSI, limb symmetry index; MDC, minimal detectable change; SEM, standard error of measurement; SSD, side-to-side difference; TAS, Tegner Activity Scale.

Potential Prognostic Factors Included in Regression Models

Potential prognostic factors (Table 1) for inclusion in regression models were selected a priori based on clinical reasoning and a comprehensive review of the literature.

Outcomes at 32 to 37 Years

Knee injury and Osteoarthritis Outcome Score. The Knee injury and Osteoarthritis Outcome Score (KOOS) comprises 5 subscales, scored from 0 (severe impairment) to 100 (no impairment). For the purpose of this study, we used data from the Pain, Symptoms, Sport and Recreational Function (Sport/Rec) and QOL subscales. The KOOS has adequate content validity, internal consistency, test-retest reliability, and construct validity in patients with ACL rupture.[9]

Knee-Related Quality of Life. The ACL QOL is the only ACL-specific knee-related QOL instrument[24] and contains more items of relevance to individuals with ACL injuries than do other commonly used knee measures.[36] The Swedish version of the ACL QOL contains 32 items in 5 domains:

"symptoms and physical complaints"; "work-related concerns"; "recreational activities and sport participation or competition"; "lifestyle"; and "social and emotional."[24] Item scores are summed to calculate the overall ACL QOL score (range, 0-100 [best]). The ACL QOL is valid for use in individuals with ACL injury.[24] A minimal clinically important difference (MCID) for the ACL QOL for use in groups with ACL injuries has been estimated to range from 6.9 to 8.9 points, although further investigations are needed.[21]

Statistical Methods

Linear regression was used to assess potential prognostic factors for 32- to 37-year KOOS Pain, KOOS Symptoms, KOOS Sport/Rec, and ACL QOL scores. Underlying assumptions for linear regression, including linearity between independent and dependent variables, assessment for outliers, multivariate normality, multicollinearity, autocorrelation, and homoscedasticity of residuals, were assessed and met. Nonlinearity of 4-year measures was handled by converting continuous to binary measures using clinically meaningful categories. Crude and adjusted effect estimates are reported in terms of regression coefficients, and 95% confidence intervals (CIs) present the estimated uncertainty. Potential prognostic factors and covariates were identified via clinical reasoning and literature review. Multivariable models were adjusted for age at injury, sex, baseline meniscal injury, and contralateral ACL injury (before 32- to 37-year follow-up).

Missing Data. Incomplete data for potential prognostic factors (quadriceps and hamstring strength, n = 10 missing [6%]; single-leg hop performance, n = 11 missing [6%]; knee extension and flexion deficit, n = 14 missing [8%]; knee laxity, n = 12 missing [7%]; activity level, n = 1 missing [<1%]; self-reported knee function, n = 4 missing [2%]) were assessed for systematic patterns and monotonicity and assumed to be missing at random. Multiple imputation using 40 iterations was performed to account for missing values using the Markov Chain Monte Carlo technique.[34] Consistency between imputation iterations and convergence between complete data and imputed data were assessed by comparing proportions and regression coefficients. There was ≤2% missing data for 32- to 37-year outcomes (KOOS Pain, n = 2 [1%]; KOOS Symptoms, n = 2 [1%]; KOOS Sport/Rec, n = 4 [2%]; ACL QOL, n = 1 [<1%]); therefore, the sample size for each regression model was 170, 170, 168, and 171, respectively.

Sample Size. With 6 independent variables in a multivariable regression model, an anticipated effect size of 0.15, a probability level of .05, and a statistical power level of 0.90, 123 participants were required to achieve a 90% probability of not committing a type II error. To increase the probability of not committing a type II error to 95%, 146 participants were required.

Exploratory Analyses. Exploratory analyses compared outcomes between key subgroups of interest to determine whether specific variables should be accounted for in the multivariable analyses. This included patients who had undergone a knee arthroplasty (n = 10; 6%) compared with those who had not (better outcomes in patients who had a knee arthroplasty may falsely portray a positive outcome). Since people who had knee arthroplasty reported worse scores on all 32- to 37-year outcomes, these individuals remained in the analysis. Outcomes were also compared between patients who had experienced a contralateral ACL injury during the follow-up period (n = 19; 11%) and those who had not. People who had a contralateral ACL injury reported worse (potentially clinically meaningful) 32- to 37-year outcomes. Slubsequently, contralateral ACL injury was included as a potential confounder in the multivariable models. Since 32- to 37-year patient-reported outcomes were similar between patients managed using augmented (n = 56) versus nonaugmented (n = 19) ACL repair and between patients receiving correct (n = 143; 83%) and incorrect (n = 29; 17%) baseline ACL treatment according to birth year (i.e. incorrect treatment = patients with an even birth year underwent rehabilitation alone or patients with an odd birth year underwent early ACL repair), these were not accounted for in the analyses.

The potential for selection bias was assessed by comparing characteristics between the 172 study participants and the 11 individuals who were excluded because of nonparticipation in the 4-year follow-up. The 11 excluded individuals had similar characteristics to those of the eligible study participants, including concomitant injuries, age, sex, preinjury activity level, contralateral injuries, and 32- to 37-year outcomes.

RESULTS

Participant Characteristics

A total of 172 participants completed the long-term follow-up at a mean of 34.2 ± 1.5 years after ACL injury. Of the participants, 28% were women, with a mean age of 59 ± 6 years and a median body mass index of 26.9 (interquartile range, 24.6-28.8) (Table 2). The most common sports played at the time of ACL rupture were football (n = 99; 58%), alpine skiing (n = 19; 11%), and handball (n = 10; 6%). Of the participants, 75 (44%) were allocated to augmented or nonaugmented early ACL repair, 16 (9%) had crossed over to delayed ACLR before 4-year follow-up (none had delayed reconstruction during the 12 months before 4-year follow-up), and 81 (47%) had been managed using rehabilitation alone at the time of 4-year follow-up (of those, 9 had delayed ACLR 5 to 21 years after ACL injury). The characteristics of these groups and 32- to 37-year outcomes are presented in Table 2.

Prognostic Factors for 32- to 37-Year Patient-Reported Outcomes

Fair/poor Lysholm score (compared with excellent/good) at 4-year follow-up was a prognostic factor for worse 32- to 37-year outcomes on all measures in the crude and adjusted analyses: KOOS Pain (adjusted regression coefficient, −11.6; 95% CI, −19.1 to −4.1); KOOS Symptoms (−15.1; 95% CI, −23.3 to −6.9); KOOS Sport/Rec (−19.4; 95% CI, −31.4 to −7.5); and ACL QOL (−9.0; 95% CI, −17.6 to −0.5) (Figures 2 and 3).

TABLE 2
Participant Characteristics (N = 172)[a]

		ACL Treatment Status at 4-y Follow-up		
	All Participants (N = 172)	Early ACL Repair (n = 75)	Rehabilitation Alone (n = 81)	Delayed ACLR (n = 16)
Characteristics				
Female sex	49 (28)	17 (23)	24 (30)	8 (50)
Age at injury, y	24 ± 6	25 ± 6	24 ± 6	21 ± 4
Age at 32- to 37-y follow-up, y	59 ± 6	59 ± 6	58 ± 7	56 ± 4
BMI at 32- to 37-y follow-up	26.9 (24.6-28.8)	27.0 (24.1-29.7)	26.6 (24.6-28.5)	27.0 (24.3-28.7)
Baseline meniscal injury	101 (59)	42 (56)	51 (63)	8 (50)
Baseline meniscal surgery	54 (31)	25 (33)	40 (49)	8 (50)
Preinjury TAS level	8 (7-9)	9 (7-9)	8 (7-9)	7 (7-9)
Contralateral ACL injury	19 (11)	7 (9)	8 (10)	4 (25)
Outcomes at 4 y				
Quadriceps strength <90% LSI	50 (29)	20 (27)	21 (26)	9 (56)
Hamstring strength <90% LSI	28 (16)	10 (13)	15 (19)	3 (19)
Single-leg hop <90% LSI	33 (19)	10 (13)	17 (21)	6 (38)
Knee extension deficit ≥5°	36 (21)	28 (37)	3 (4)	5 (31)
Knee flexion <135°	53 (31)	31 (41)	17 (21)	5 (31)
Knee laxity (>3 mm SSD)	65 (38)	17 (23)	41 (51)	7 (44)
Lower activity level (TAS score 0-5)	64 (37)	21 (28)	32 (39)	11 (69)
Fair/poor Lysholm score (vs excellent/good)	38 (22)	9 (12)	25 (31)	4 (25)
Patient-reported outcomes at 32 to 37 y				
KOOS Pain	83 (64-97)	82 (64-97)	89 (79-97)	69 (54-90)
KOOS Symptoms	75 (54-89)	70 (54-82)	79 (54-89)	64 (38-75)
KOOS Sport/Rec	55 (30-75)	55 (30-83)	60 (28-80)	25 (9-55)
KOOS QOL	56 (38-69)	56 (38-68)	56 (44-69)	44 (36-63)
ACL QOL	71 (51-88)	73 (51-92)	70 (52-87)	46 (36-86)

[a]Data are reported as n (%), mean ± SD, or median [interquartile range]. ACL, anterior cruciate ligament; ACLR, anterior cruciate ligament reconstruction; BMI, body mass index; KOOS, Knee injury and Osteoarthritis Outcome Score; LSI, limb symmetry index; QOL, Quality of Life; Sport/Rec, Sport and Recreation; SSD, side-to-side difference; TAS, Tegner Activity Scale.

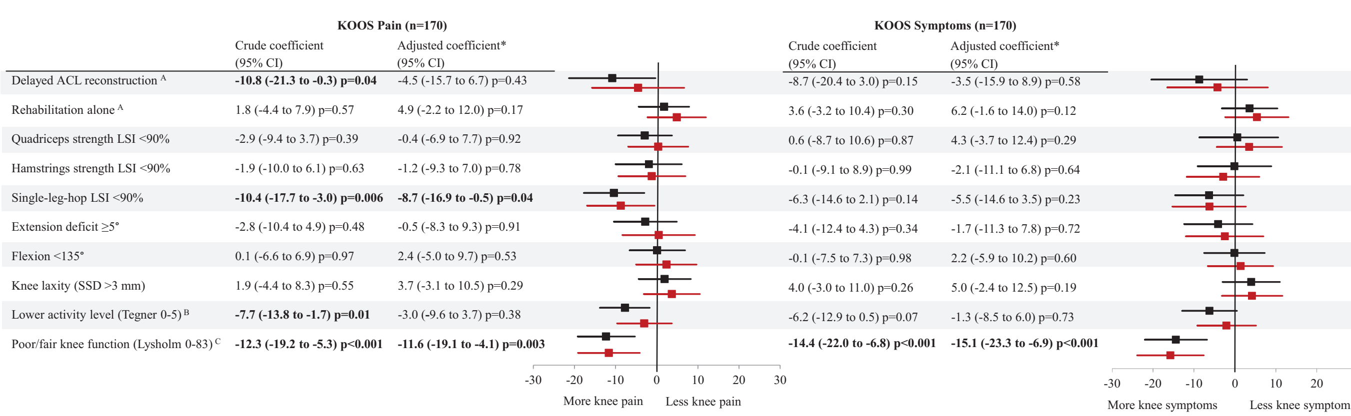
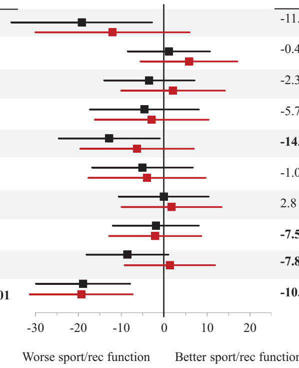


Figure 2. Crude and adjusted linear regression analyses investigating prognostic factors for pain and symptoms 32-37 years after acute ACL injury. Black boxes and error bars represent crude coefficients and 95% CIs, respectively; red boxes and error bars represent adjusted coefficients and 95% CIs, respectively. Bolded text indicates statistical significance. *Adjusted for age, sex, contralateral ACL injury, and baseline meniscal status. Delayed ACL reconstruction received before 4-year follow-up: [A]Reference category = early augmented or nonaugmented ACL repair; [B]Reference category = Tegner Activity Scale score 6-10 (good/excellent); [C]Reference category = Lysholm score good/excellent (84-100). ACL, anterior cruciate ligament; KOOS, Knee injury and Osteoarthritis Outcome Score; LSI, limb symmetry index; SSD, side-to-side difference.

	KOOS Sport Rec (n=168) Crude coefficient (95% CI)	KOOS Sport Rec (n=168) Adjusted coefficient * (95% CI)	ACL QOL (n=171) Crude coefficient (95% CI)	ACL QOL (n=171) Adjusted coefficient * (95% CI)
Delayed ACL reconstruction [A]	**-19.2 (-35.6 to -2.8) p=0.02**	-12.2 (-30.1 to 5.7) p=0.18	-11.0 (-23.1 to 1.1) p=0.07	-2.0 (-14.9 to 11.0) p=0.77
Rehabilitation alone [A]	1.1 (-8.5 to 10.7) p=0.82	5.6 (-5.7 to 16.8) p=0.33	-0.4 (-7.4 to 6.7) p=0.91	4.7 (-3.4 to 12.8) p=0.25
Quadriceps strength LSI <90%	-3.5 (-14.0 to 7.1) p=0.52	1.8 (-10.2 to 13.9) p=0.77	-2.3 (-10.0 to 5.3) p=0.55	2.1 (-6.5 to 10.8) p=0.63
Hamstrings strength LSI <90%	-4.6 (-17.3 to 8.1) p=0.48	-3.1 (-16.3 to 10.1) p=0.65	-5.7 (-15.0 to 3.6) p=0.23	-2.6 (-12.2 to 7.0) p=0.60
Single-leg-hop LSI <90%	**-12.8 (-24.6 to -1.0) p=0.03**	-6.5 (-19.7 to 6.7) p=0.34	**-14.1 (-22.6 to -5.5) p=0.001**	**-12.5 (-22.2 to -2.8) p=0.01**
Extension deficit ≥5°	-5.1 (-16.8 to 6.7) p=0.40	-4.2 (-17.8 to 9.4) p=0.55	-1.0 (-9.7 to 7.8) p=0.83	-1.8 (-11.8 to 8.1) p=0.72
Flexion <135°	-0.1 (-10.6 to 10.4) p=0.99	1.5 (-10.1 to 13.1) p=0.80	2.8 (-5.0 to 10.5) p=0.48	4.0 (-4.4 to 12.4) p=0.35
Knee laxity (SSD >3 mm)	-1.9 (-12.0 to 8.1) p=0.71	-2.3 (-13.0 to 8.4) p=0.68	**-7.5 (-14.7 to -0.3) p=0.04**	-5.9 (-13.7 to 1.9) p=0.14
Lower activity level (Tegner 0-5) [B]	-8.6 (-18.1 to 1.0) p=0.08	-1.1 (-9.4 to 11.6) p=0.84	**-7.8 (-14.7 to -0.9) p=0.03**	-2.5 (-10.0 to 5.1) p=0.52
Poor/fair knee function (Lysholm 0-83) [C]	**-18.9 (-29.9 to -7.9) p<0.001**	**-19.4 (-31.4 to -7.5) p=0.001**	**-10.2 (-18.3 to -2.2) p=0.01**	**-9.0 (-17.6 to -0.5) p=0.04**



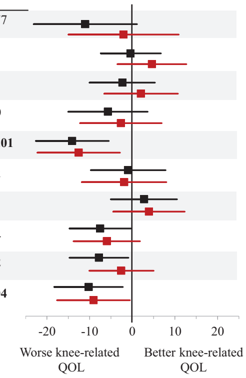


Figure 3. Crude and adjusted linear regression analyses investigating prognostic factors for reduced sport and recreational function and knee-related quality of life 32-37 years after acute ACL injury. Black boxes and error bars represent crude coefficients and 95% CIs, respectively; red boxes and error bars represent adjusted coefficients and 95% CIs, respectively. Bolded text indicates statistical significance. *Adjusted for age, gender, contralateral ACL injury, and baseline meniscal status. Delayed ACL reconstruction received before 4-year follow-up: [A]Reference category = early augmented or nonaugmented ACL repair. [B]Reference category = Tegner Activity Scale score 6-10 (good/excellent). [C]Reference category = Lysholm score good/excellent (84-100). ACL, anterior cruciate ligament; KOOS, Knee injury and Osteoarthritis Outcome Score; LSI, limb symmetry index; QOL, Quality of Life; Sport/Rec, Sport and Recreation; SSD, side-to-side difference.

A worse single-leg hop test was a prognostic factor for worse KOOS Pain and ACL QOL scores in the crude and adjusted analysis and worse KOOS Sport/Rec scores in the crude analysis. After adjusting for potential confounding, a 4-year single-leg hop limb symmetry index (LSI) <90% was associated with a KOOS Pain score that was an estimated −8.7 points (95% CI, −16.9 to −0.5) worse and an ACL QOL score that was −12.5 points (95% CI, −22.2 to −2.8) worse at 32 to 37 years compared with an LSI ≥90% (Figures 2 and 3).

In the crude analysis, a lower activity level at 4 years (ie, not participating in recreational or competitive sports) was associated with worse KOOS Pain (regression coefficient, −7.7; 95% CI, −13.8 to −1.7) and ACL QOL scores (−7.8; 95% CI, −14.7 to −0.9). Increased knee laxity at 4 years was also a prognostic factor for worse ACL QOL scores in the crude analysis (−7.5; 95% CI, −14.7 to −0.3). Delayed ACLR before 4-year follow-up was associated with worse KOOS Pain (−10.8; 95% CI, −21.3 to −0.3) and KOOS Sport/Rec scores (−19.2; 95% CI, −35.6 to −2.8]) compared with early ACL repair; however, this relationship did not remain after adjustment. Quadriceps and hamstrings strength and a knee extension or flexion deficit were not related to 32- to 37-year outcomes (Figures 2 and 3).

DISCUSSION

This study found that reduced self-reported knee function 4 years after acute ACL rupture was a prognostic factor for worse patient-reported outcomes at the 32- to 37-year follow-up. Reduced single-leg hop performance 4 years after ACL injury was a prognostic factor for worse knee pain and knee-related QOL at 32- to 37-year follow-up. Estimates exceeded the MCID for these measures, highlighting the importance of targeting these constructs when managing individuals with ACL injuries.

Patient-Reported Outcomes 32 to 37 Years After ACL Injury

Comparison of patient-reported outcomes from our cohort with those reported in other cohorts suggests that knee problems are just as common 32 to 37 years after ACL injury as they are during the acute injury period and less severe compared to a population with knee osteoarthritis. On average, 32 to 37 years after acute ACL injury, patient-reported knee pain, symptoms, and sport and recreational function scores were better than scores reported by cohorts with knee osteoarthritis of a similar age (exceeded the MCID).[9] This is expected since not all participants in our cohort had knee osteoarthritis at the 32- to 37-year follow-up.[18] Of the 153 who underwent knee radiographs, 62% had radiographic tibiofemoral osteoarthritis, and 35% had patellofemoral osteoarthritis.[18] Surprisingly, KOOS Pain and Symptoms scores were similar to those reported by individuals with an acute ACL injury and similar or worse than KOOS subscale scores reported within the first year after ACLR.[9,19] Additionally, KOOS scores were worse in individuals 5 to 16 years after ACLR[13] and in individuals with ACL-deficient knees 5 to 23 years after ACL injury.[14] Knee-related QOL assessed using the ACL QOL was similar to that of people with knee symptoms and no radiographic osteoarthritis and better than that of people with knee symptoms and radiographic osteoarthritis, 5 to 20 years after ACLR.[11]

Self-Reported Knee Function

The most consistent prognostic factor for worse 32- to 37-year outcomes was reporting a fair or poor Lysholm score 4 years after ACL injury. The constructs assessed in the Lysholm score may be more meaningful to patients than objective measures of knee function, including knee strength and a flexion or extension deficit that were not associated with 32- to 37-year outcomes. Increased knee laxity was only a prognostic factor for worse QOL in the crude analysis and was not related to any outcomes after adjusting for confounding. Measures of knee laxity assessed clinically are poorly correlated with patient-reported knee instability and self-reported function.[15,33,45] Self-reported knee function takes into account an individual's perception of one's knee and can be affected by a range of contextual and psychological factors. Psychological factors including pessimism, reduced self-efficacy, and external locus of control are related to worse self-reported outcomes and dissatisfaction with knee function after ACL injury.[27,28,35,39] Such psychological factors might have contributed to our study finding, whereby self-reported function was a prognostic factor for poor long-term self-reported outcomes but objective measures of function were not. A discord between objective measures of function and self-reported function has also been evidenced in the broader medical literature, in patients receiving intensive care,[6] in patients with hip fracture,[10] and in patients with chronic low back pain.[47] Additionally, self-reported knee function 2 years after ACLR was found to predict symptomatic knee osteoarthritis at 10- to 15-year follow-up; however, functional tests did not predict symptomatic osteoarthritis in this cohort.[30] Thus, self-reported measures of knee function may provide an important means of predicting long-term outcomes after ACL injury.

Single-Leg Hop Performance

We found that reduced single-leg hop performance at 4-year follow-up was a prognostic factor for worse knee pain and knee-related QOL 32 to 37 years after acute ACL injury. The single-leg hop test is commonly used to evaluate whether a patient is ready to return to sports after ACL injury. A better single-leg hop test LSI measured 6 months after ACLR was found to predict return to preinjury level of sports at 1 and 2 years after ACLR.[25] Not returning to preinjury level of sport after ACL injury has been associated with worse QOL outcomes 5 to 20 years after ACL injury.[12] Additionally, individuals with <90% LSI at the time of return to sport are more likely to sustain a new knee injury or rupture their ACL graft.[17,20] Subsequent ACL injury and revision ACL surgery have also been identified as prognostic factors for worse long-term pain and QOL.[15] Notably, previous research has used the single-leg hop test within 12 months of ACL injury to evaluate rehabilitation progress or predict short-term outcomes. Our findings support the use of the single-leg hop test 3 to 6 years after injury as a screening tool for long-term outcomes after ACL injury and suggest that targeting single-leg hop function may be of value when managing individuals with ACL injuries beyond the typical 12-month rehabilitation period.

ACL Injury Management Strategy

Patients in our cohort allocated to early ACL repair received ACL repair with or without augmentation, and although this technique is regaining popularity,[26] this is not common practice or considered the gold standard for ACL surgical management today. Despite the need for further high-quality research, recent systematic reviews suggest ACL repair may be a viable alternative to ACLR, particularly when the tear is located in the proximal portion of the ACL.[26,41,42] Our findings demonstrate that individuals who underwent early ACL repair plus rehabilitation for an acute ACL rupture reported similar patient-reported outcomes to those of individuals who underwent rehabilitation alone at the 32- to 37-year follow-up. However, it is important to note that although only 16% of people managed via rehabilitation alone crossed over to ACL surgery before 4-year follow-up, these individuals reported worse patient-reported outcomes compared with those managed via early ACL repair or rehabilitation alone. This was the first study to investigate prognostic factors for outcomes beyond 30 years of ACL injury, providing important information to inform ACL management strategies.

Strengths and Potential Limitations

The key strengths of this study include the prospective longitudinal study design; the recruitment of consecutive patients with ACL injury over a 5-year period; and the very high response rate (81%), which was higher than expected 32 to 37 years after the baseline assessment. To our knowledge, this is the longest follow-up of acute ACL injury performed to date, which addresses significant knowledge gaps related to long-term outcomes after ACL injury managed using augmented or nonaugmented ACL repair or rehabilitation alone. Notably, our regression models did not account for possible measurement error in the independent variables. Errors in the measurement of these variables could result in inconsistent estimates and attenuation bias. An important consideration is that all patients received a diagnostic arthroscopy and many patients managed via rehabilitation only underwent surgery for concomitant injuries. While this may be advantageous in diagnosing concomitant injuries that can be misdiagnosed clinically, the effect of arthroscopic knee surgery shortly after ACL injury on long-term patient-reported outcomes is unclear.[16] Additionally, immobilization in a long-leg cast for up to 6 weeks after surgery is not recommended as current practice. Although this aligned with best practice in the early 1980s, patients receiving today's best practice recommendations may experience different long-term outcomes from those of patients treated in the 1980s.

CONCLUSION

Worse self-reported knee function 4 years after ACL injury was a prognostic factor for more knee pain and symptoms, worse sport and recreational function, and reduced QOL 32 to 37 years after acute ACL injury managed using augmented or nonaugmented ACL repair or rehabilitation alone. Reduced 4-year single-leg hop performance was a prognostic factor for more knee pain and worse QOL 32 to 37 years after ACL injury.

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