Predictors of Osteoarthritis Development at a Median 25 Years After Anterior Cruciate Ligament Reconstruction Using a Patellar Tendon Autograft

Line Lindanger,*†‡ MD, Torbjørn Strand,†§ MD, Anders Odd Mølster,‡ MD, PhD, Eirik Solheim,†‡ MD, PhD, Cornelia Fischer-Bredenbeck,‖ MD, PhD, Olga Therese Ousdal,¶ MD, PhD, and Eivind Inderhaug,‡# MD, PhD
Investigation performed at Haraldsplass Deaconess Hospital, Bergen, Norway

Background: Few studies have investigated the outcome ≥20 years after an anterior cruciate ligament reconstruction (ACLR) with a bone–patellar tendon–bone autograft, and there is a wide range in the reported rates of radiographic osteoarthritis (OA).

Purpose: To report on radiographic OA development and to assess risk factors of knee OA at a median 25 years after ACLR with a bone–patellar tendon–bone autograft.

Study Design: Case-control study; Level of evidence, 3.

Methods: Unilateral ACLRs performed at a single center from 1987 to 1994 were included (N = 235). The study population was followed prospectively with clinical testing and questionnaires. Results from the 3-month, 12-month, and median 25-year follow-up are presented. In addition, a radiographic evaluation was performed at the final follow-up. Radiographic OA was defined as Kellgren-Lawrence grade ≥2 or having undergone ipsilateral knee replacement surgery. Possible predictors of OA development included patient age, sex, time from injury to surgery, use of a Kennedy ligament augmentation device, any concomitant meniscal surgery, and return to preinjury sports after surgery.

Results: At long-term follow-up, 60% (141/235) of patients had radiographic OA in the involved knee and 18% (40/227) in the contralateral knee ($P < .001$). Increased age at surgery, male sex, increased time between injury and surgery, a Kennedy ligament augmentation device, and medial and lateral meniscal surgery were significant predictors of OA development in univariate analyses. Return to preinjury level of sports after surgery was associated with less development of OA. In the multivariate model, medial meniscal surgery and lateral meniscal surgery were independently associated with OA development. The adjusted odds ratio was 1.88 (95% CI, 1.03-3.43; $P = .041$) for medial meniscal surgery and 1.96 (95% CI, 1.05-3.67; $P = .035$) for lateral meniscal surgery. Patients who had developed radiographic signs of OA had significantly lower Knee injury and Osteoarthritis Outcome Score and Lysholm scores at long-term follow-up.

Conclusion: At 25 years after ACLR, 60% of patients had developed OA in the involved knee, and these patients reported significantly lower subjective outcomes. Medial meniscal surgery and lateral meniscal surgery were independent predictors of OA development at long-term follow-up.

Keywords: ACL; return to sports; meniscus; osteoarthritis; long-term follow-up

Injury to the anterior cruciate ligament (ACL) leads to an increase in lifetime risk of knee osteoarthritis (OA) in the ipsilateral knee.[1,31,42] As compared with a noninjured population, those with an ACL injury have a 7-fold increased risk of developing OA[41] or undergoing knee replacement surgery.[19] Pathologic knee laxity, with episodes of instability, contributes to further injuries to the cartilage, subchondral bone, and menisci, which can predispose the knee to OA.[9,25] Meniscal injuries—in particular, a medial meniscal tear at the time of ACL rupture or later—has been found to relate to degenerative changes in the knee.[5,31,38,47] Whether a reconstruction of the torn ACL will reduce the incidence of OA is still uncertain,[1,22] and conflicting results have been presented among studies comparing nonoperative treatment with operative treatment.[20,37,46,48]

Other important factors possibly related to OA development are older age at surgery, male sex, early loss of knee extension, and persistent increased knee laxity after the

The American Journal of Sports Medicine
1–10
DOI: 10.1177/03635465221079327

ACL reconstruction (ACLR).[3,7,21,38,47] Continued participation in pivoting sports also comes with a high risk of new ACL injuries to both the ipsilateral and the contralateral knee.[24,49] One could therefore suspect that those going back to pivoting sports are more prone to develop knee OA. However, there is a paucity in the literature supporting or rejecting such a hypothesis.[6]

Across the few studies that have reported on outcomes ≥20 years after an ACLR with a bone–patellar tendon–bone (BPTB) autograft, the OA incidence ranges from 20% to 80%.[5,7,11,32,38,44,48] With a need for more knowledge on the long-term outcome after reconstruction of a torn ACL, the primary aim of this study was to report OA development at 25 years after ACLR with a BPTB autograft. The secondary aim was to evaluate how factors such as addition of a Kennedy ligament augmentation device (LAD), meniscal injuries, loss of knee extension, increased knee laxity, or return to sports would affect the incidence of OA. First, we hypothesized that the prevalence of OA would be higher in the ACL-reconstructed knee as compared with the uninjured knee after 25 years. Second, we hypothesized that increasing time between injury and surgery, any meniscal surgery to the involved knee, or return to preinjury sports would increase the incidence of radiographic OA at long-term follow-up.

METHODS

Patient Population

All ACLRs performed at a single center from 1987 to 1994 using an ipsilateral BPTB autograft qualified for inclusion. Data were extracted from a prospectively held database; only patients with a unilateral ACL injury at the time of index surgery were included. Patients with concomitant injuries to the posterior cruciate ligament or collateral ligaments requiring surgery were excluded. A flowchart of the participants is presented in Figure 1.

The study population was followed prospectively with clinical testing and questionnaires. Results from the 3-month, 12-month, and 25-year follow-up are presented. At the final follow-up, radiographic evaluation was performed in addition to clinical testing and evaluation by patient-reported outcome measures. For analyses regarding OA development, patients who had undergone an ipsilateral knee replacement before the last follow-up were defined as having a Kellgren-Lawrence (K-L) grade ≥2. Furthermore, knee replacement surgery led to exclusion from the clinical and subjective evaluations. Any contralateral ACL injury experienced during the follow-up period did not lead to exclusion from the study, but range of motion and knee laxity results were not analyzed in these patients at the follow-up.

The study was approved by the regional ethical committee (REK 2016-00571). Eligible patients first received a study invitation by post, and nonresponders received a phone call or text message with a reminder after 2 weeks.

Surgical Technique and Postoperative Rehabilitation Protocol

All ACLRs were performed or supervised by the same 2 experienced knee surgeons.

The BPTB autograft was harvested from the central third of the patellar tendon of the ipsilateral knee. Initially, ACL surgery was performed as a mini-open procedure performed "through the defect" created by the patellar tendon harvest, using outside-in drilling of the femoral tunnels. A limited notchplasty was performed.[13] The tibial tunnel was positioned anteriorly and medially, whereas the femoral tunnel was placed in a posterior and superior position relative to the femoral anatomic center.[4] The last 53 reconstructions were performed arthroscopically by drilling the femoral tunnel through the tibial tunnel.[26] The tibial tunnel aimed for a central anteromedial position, and the femoral tunnel ended up in a proximal and posterior position dependent of the tibial tunnel placement. A moderate notchplasty was performed in every case. The graft was tested for isometry throughout the flexion movement and was normally fixed in nearly full extension.

Meniscal surgery, mostly partial resection, was performed arthroscopically assisted. Most ruptures of the medial and lateral meniscus were treated with a partial resection. Bucket-handle injuries and unstable meniscocapsular tears in the vascularized zone were treated with meniscal repair if possible. A severe knee extension deficit at the 3-month follow-up led to a repeat arthroscopic procedure to remove a cyclops lesion and, where needed, perform an extended notchplasty.

A Kennedy LAD was used in 25 cases.[18] The Kennedy LAD was sutured to the graft and fixed with staples to the femoral and tibial condyles through a mini-open procedure. This polypropylene band was intended to take the main load in the early phase before gradually transferring the load over to the autograft and hence facilitating safer and faster healing of the graft.[14,18] The Kennedy LAD

*Address correspondence to Line Lindanger, MD, Department of Orthopedics, Haraldsplass Deaconess Hospital, Ulriksdal 8, 5009, Norway (email: line.lindanger@haraldsplass.no).
†Department of Orthopedics, Haraldsplass Deaconess Hospital, Bergen, Norway.
‡Department of Clinical Science, Faculty of Medicine, University of Bergen, Bergen, Norway.
§Department of Orthopedics, Haukeland University Hospital, The Coastal Hospital at Hagevik, Bergen, Norway.
||Department of Radiology, Haraldsplass Deaconess Hospital, Bergen, Norway.
¶Department of Radiology, Haukeland University Hospital, Bergen, Norway.
#Department of Orthopedics, Haukeland University Hospital, Bergen, Norway.
Submitted June 9, 2021; accepted January 3, 2022.
The authors declared that they have no conflicts of interest in the authorship and publication of this contribution. AOSSM checks author disclosures against the Open Payments Database (OPD). AOSSM has not conducted an independent investigation on the OPD and disclaims any liability or responsibility relating thereto.

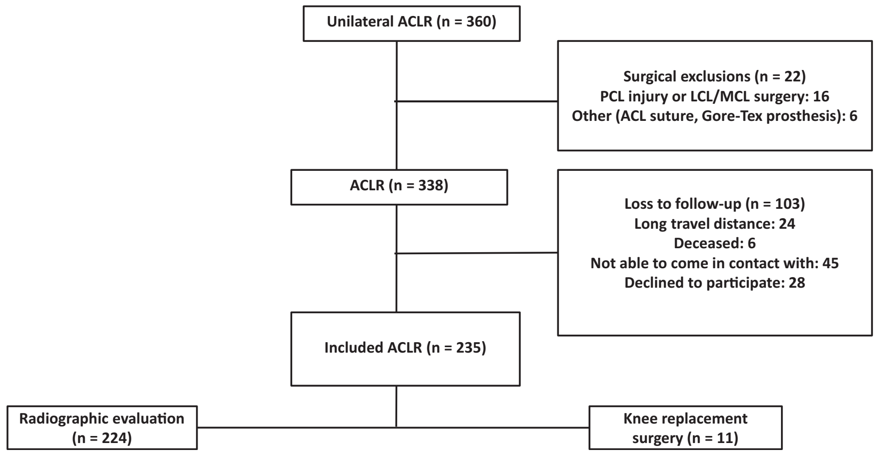

Figure 1. Flowchart of the study participants. ACL, anterior cruciate ligament; ACLR, ACL reconstruction; LCL, lateral collateral ligament; MCL, medial collateral ligament; PCL, posterior cruciate ligament.

was dynamized after 6 months by surgically removing staples from the lateral femoral condyle.

All patients underwent structured rehabilitation guided by physical therapists for 6 months after surgery. The patients underwent a rehabilitation program assisted by an in-house physical therapist when hospitalized and at local institutes after discharge. Between 1987 and 1991, all patients used a DonJoy® orthosis that initially allowed them full range of motion without weightbearing but with restriction on the last 20° of knee extension during weightbearing until postoperative 6 weeks. After 1991, the rehabilitation was based on a protocol by Shelbourne and Nitz[40] with no restriction in range of motion during weightbearing, but patients were recommended partial weightbearing and use of a DonJoy® orthosis for the first 6 weeks.

Radiographic Assessment

A Synaflexer frame (Synarc Inc) was used for standardization of the bilateral weightbearing radiographs. The patients' knees were placed in 45° of flexion in the frame, with a 15° craniocaudal radiographic beam for a posteroanterior view of the tibiofibular joint. A lateral view of both knees in maximum extension was also included. The radiographs were evaluated by 1 experienced musculoskeletal radiologist (C.F-B) at 2 time points with at least a 6-week interval between evaluations. Interrater reliability was established with a second radiologist (O.T.O), who evaluated 30 radiographs (60 knees) blinded from the previous radiographic evaluation.

Radiographs were evaluated according to the K-L classification[17]:

Grade 0: no radiographic features of OA are present
Grade 1: doubtful joint space narrowing (JSN) and possible osteophytic lipping
Grade 2: definite osteophytes and possible JSN
Grade 3: moderate multiple osteophytes, definite JSN, some sclerosis, and possible bony end deformity
Grade 4: large osteophytes, marked JSN, severe sclerosis, and definite bony end deformity

Radiographic OA was defined as K-L grade ≥2.

Clinical Evaluation

At the long-term follow-up evaluation, the patients were examined by an independent experienced knee surgeon. However, in cases where classification was unclear, 2 senior surgeons independently examined patients, and cases were discussed and agreed upon in each case by consensus. Knee extension was recorded as absolute values for each knee, and the side-to-side difference (STS) between knees was graded according to the International Knee Documentation Committee (IKDC) classification system.[16] Normal knee extension should be <3° different from the noninvolved knee.

Evaluation of knee laxity included arthrometer measures (KT-1000; MEDmetric), Lachman test, and pivot-shift evaluation. The maximum manual difference between knees was used for analyses of the arthrometer testing.[8] A side-to-side difference was graded according to the IKDC classification: normal, <3 mm; nearly normal, 3 to 5 mm; abnormal, 6 to 10 mm; severely abnormal, >10 mm.[16] The Lachman test[45] was graded accordingly. Anterolateral rotational instability was assessed by the pivot-shift test,[12,28] graded as 0 (negative), 1+ (glide), 2+ (clunk), or 3+ (gross)[16] or as "guarding" if muscular tension prevented accurate classification. Abnormal residual knee laxity was defined as a KT-1000 side-to-side difference >5 mm, a Lachman test result ≥2+, or pivot-shift test result ≥2+.

Patient-Related Outcome Measures

A return-to-sports questionnaire was used routinely at follow-ups after surgery.[24] Patients were classified into 4 levels of sports participation based on self-reported preinjury and postoperative levels: elite, high competitive, lower competitive, and recreational. Elite level was defined as a professional level of sports or the highest possible national level of sports participation. *Overall successful return to sports* was defined as any sports participation at one of the defined levels for a minimum of 12 months after surgery. *Return to preinjury level* was defined as return to the same level of participation as before injury. Return to pivoting sports included team handball, basketball, and soccer.

Lysholm evaluation and Tegner score before surgery, after 12 months, and after 25 years were acquired.[43] Knee injury and Osteoarthritis Outcome Score (KOOS) was acquired at the median 25-year follow-up. It has been suggested that 8 to 10 points may represent the minimal perceptible clinical improvement of the KOOS.[33]

Statistical Analysis

Data analyses were performed using SPSS Version 25 (IBM Inc). $P < .05$ was considered statistically significant. Descriptive statistics were calculated. Categorical variables were presented as numbers or percentages. Continuous variables were presented as median and range when nonnormally distributed or as mean and standard deviation when normally distributed. The Shapiro-Wilk test was used to test for normality of data.

Comparison between groups (ie, presence or absence of radiographic OA) was made with odds ratio analyses, Mann-Whitney *U* test, or Kruskal-Wallis test as appropriate. Logistic regression analysis was used to assess the relative contribution of selected variables on a dichotomous outcome: presence of radiographic OA (K-L $\geq$2) 25 years after surgery. Multivariate analysis was performed to evaluate which factors were significant for predicting the presence of radiographic OA 25 years after surgery: sex, age at surgery, time between injury and surgery, medial meniscal surgery, lateral meniscal surgery, the use of a Kennedy LAD, or return to preinjury sports.

RESULTS

There were 235 patients available for long-term evaluation at a median 25 years (range, 20-31) after surgery. At follow-up, 20% of the patients had experienced a contralateral ACL injury, and 9% had undergone ACL revision surgery of the ipsilateral knee. The median time between ACL injury and primary reconstruction was 14 months (range, 0-267). Patient characteristics are presented in Table 1.

A Kennedy LAD was used in 11% of cases while the mini-open technique was used in 77%. For the remaining, the procedure was performed arthroscopically assisted. Medial meniscal surgery was performed in 49% (n = 114) of patients before, at the time of, or after the ACLR. The median time between the first medial meniscal surgery and follow-up was 26 years (range, 2-49). Lateral meniscal surgery was performed in 32% (n = 75) of patients. The median time between the first lateral meniscal surgery and follow-up was 26 years (range, 10-33).

TABLE 1
Patient Characteristics (N = 235)[a]

	No. (%)[b]
Age at injury, y	
Median (range)	22 (12-47)
Mean (SD)	22.9 (6.6)
Age at surgery, y	
Median (range)	24 (15-52)
Mean (SD)	25.4 (7.1)
Time, median (range)	
Between injury and surgery, mo	14 (0-267)
Between surgery and follow-up, y	25 (20-31)
Male sex	115 (49)
Tegner score before injury, median [range]	7 [4-10]
Participation in pivoting sports before injury	177 (75)
Team handball	67
Soccer	101
Basketball	9
LAD	25 (11)
ACL reconstruction	
Arthroscopic	53 (23)
Mini-open	182 (77)
During follow-up	
Contralateral ACL injury	48 (20)
ACL revision surgery	20 (9)
Knee replacement surgery	14 (6)
Ipsilateral	11 (5)
Contralateral	3 (1)
K-L radiographic grading at final follow-up	
Involved knee	224 (95)
0	47 (20)
1	47 (20)
2	57 (24)
3	57 (24)
4	16 (7)
Contralateral knee	224 (95)
0	135 (57)
1	52 (22)
2	18 (8)
3	17 (7)
4	2 (1)

[a]ACL, anterior cruciate ligament; K-L, Kellgren-Lawrence; LAD, ligament augmentation device.
[b]Values are presented as No. (%) unless noted otherwise.

TABLE 2
Meniscal Surgery (Partial Resection) From Preoperative Evaluation Until Long-term Follow-up (N = 235)[a]

Meniscal Surgery	No. (%)
Medial	
Before ACLR	49 (21)
At the time of ACLR	38 (16)
Secondary to ACLR	25 (15)
Lateral	
Before ACLR	37 (16)
At the time of ACLR	32 (14)
Secondary to ACLR	11 (5)

[a]ACLR, anterior cruciate ligament reconstruction.

TABLE 3
IKDC Distribution of Knee Extension at 3-Month and Long-term Follow-up[a]

	Normal, <3°	Nearly Normal, 3°-5°	Abnormal, 6°-10°	Severely Abnormal, >10°
Knee extension				
At 3 mo (n = 228)	104 (46)	74 (33)	32 (14)	18 (8)
At long-term follow-up (n = 179)	86 (48)	75 (42)	18 (10)	0 (0)

[a]Values are presented as No. (%). IKDC, International Knee Documentation Committee.

TABLE 4
Knee Ligament Evaluation at 1-Year and Long-time Follow-up[a]

Follow-up	Normal	Nearly Normal	Abnormal	Severely Abnormal
1 y				
KT-1000 STS difference (n = 213)	141 (66)	59 (28)	12 (6)	1 (1)
Lachman test (n = 211)	121 (57)	82 (39)	8 (4)	0 (0)
Pivot-shift test (n = 215)[b]	158 (74)	39 (18)	13 (6)	0 (0)
Long term				
KT-1000 STS difference (n = 171)	84 (49)	67 (39)	20 (12)	0 (0)
Lachman test (n = 179)	87 (49)	72 (40)	20 (11)	0 (0)
Pivot-shift test (n = 176)[c]	87 (49)	51 (29)	28 (16)	1 (1)

[a]Values are presented as No. (%). STS, side-to-side.
[b]Guarding (n = 5).
[c]Guarding (n = 9).

The median time between injury and ACLR was 24 months (range, 0-267) in patients who had undergone medial meniscal surgery, as compared with 5 months (range, 0-148) in patients not in need of medial meniscal surgery during the follow-up period ($P < .001$). There was no difference in median time from injury to ACLR between lateral meniscal surgery and no surgery (median, 11 months [range, 0-267] vs 15 months [range, 0-267]; $P = .49$). An overview of the meniscal surgery is presented in Table 2. At final follow-up, 68% (105/154) of the patients who had undergone surgery to either meniscus had developed OA vs 44% (36/81) who did not undergo meniscal surgery ($P < .001$).

Clinical Evaluation

Knee Extension. The IKDC grading of knee extension is presented in Table 3. Of total patients, 54% had a knee extension deficit at 3-month follow-up and 52% at long-term follow-up. Surgery attributed to an extension deficit was performed in 21 patients (9%) after a median 6 months (range, 1-39) after the ACLR. Extension deficit at the 3-month follow-up did not increase the odds of having an extension deficit at long-term follow-up (odds ratio, 1.04 [95% CI, 0.57-1.90]; $P = .90$). Having an extension deficit at long-term follow-up increased the odds of having OA by 2.22 (95% CI, 1.20-4.41; $P = .010$).

Knee Laxity. The graft laxity evaluation at 1-year and long-term follow-up is presented in Table 4. Fifteen patients (12%) were classified as having abnormal residual knee laxity at the 1-year follow-up, and the odds of having this residual laxity at long-term follow-up was 5.56 (95% CI, 1.82-16.98). However, 75% of those (27/36) with residual knee laxity at final follow-up had a normal knee laxity at the 1-year follow-up ($P = .002$). Having residual knee laxity at long-term follow-up was associated with less development of OA (odds ratio, 0.43 [95% CI, 0.21-0.87]; $P = .019$).

Radiographic Evaluation

The OA evaluation of the involved and contralateral knees is presented in Table 1. Sixty percent (141/235) of patients had OA in the involved knee and 18% (40/227) in the contralateral knee at long-term follow-up ($P < .001$). Patients with a contralateral ACL injury had 3.49 (95% CI, 1.66-7.39) increased odds of developing contralateral OA at long-term follow-up as compared with those with an uninjured contralateral knee ($P = .001$). In patients with an LAD, 76% (n = 19) had developed OA and 8% (n = 2) had undergone knee replacement surgery at follow-up. The intra- and interrater reliability test of the radiographic evaluation using the K-L classification revealed weighted kappas of 0.9 and 0.8, respectively.

Variables Associated With OA at Long-term Follow-up

The univariate and multivariate analyses of factors associated with the development of OA at long-term follow-up are presented in Tables 5 and 6. In the univariate analyses, patients with older age at surgery, increasing time between injury and surgery, medial meniscal surgery, or

TABLE 5
Odds Ratio for Developing Osteoarthritis (K-L ≥2) at the 25-Year Follow-up[a]

Variable	K-L, Median (Range) or No. (%)		Odds Ratio (95% CI)	P Value
	<2 (n = 94)	≥2 (n = 141)		
Age at surgery, y	23 (15-47)	25 (15-52)	1.046 (1.005-1.088)	.023
Sex: male vs female	39/55	76/65	0.606 (0.358-1.027)	.062
Time				
From injury to surgery, mo	11 (0-153)	17 (0-267)	1.010 (1.002-1.018)	.011
From ACLR to long-term follow-up, y	25 (22-32)	26 (19-31)	1.003 (0.993-1.013)	.588
LAD	6 (6)	19 (13)	2.284 (0.876-5.953)	.075
Arthroscopic procedure	25 (27)	28 (20)	0.684 (0.369-1.267)	.229
ACL revision surgery	7 (7)	13 (9)	1.262 (0.484-3.291)	.631
Return to				
Sports	76 (81)	102 (72)	0.619 (0.329-1.166)	.132
Preinjury level	53 (56)	62 (44)	0.607 (0.359-1.027)	.062
Duration of sport participation at preinjury level, y	8 (1-25)	8 (1-25)	0.999 (0.951-1.049)	.967
Meniscal surgery				
Medial	33 (35)	81 (57)	2.495 (1.455-4.279)	.001
Lateral	23 (24)	52 (37)	1.804 (1.008-3.226)	.043
Time from first meniscal surgery to follow-up, mo				
Medial	302 (25-380)	309 (47-590)	1.002 (0.998-1.007)	.281
Lateral	307 (269-393)	307 (119-389)	0.998 (0.985-1.011)	.785
Knee extension deficit at 3-mo follow-up[b]	44 (48)	80 (58)	1.499 (0.879-2.556)	.136
Abnormal residual knee laxity at the 1-y follow-up[c]	9 (11)	11 (9)	0.800 (0.316-2.025)	.640

[a]ACL, anterior cruciate ligament; ACLR, ACL reconstruction; K-L, Kellgren-Lawrence; LAD, ligament augmentation device.
[b]n = 44/91; n = 80/137.
[c]n = 9/83; n = 11/124.

lateral meniscal surgery were more likely to have developed OA at long-term follow-up. A trend was also seen for sex and the use of a Kennedy LAD ($P < .1$). Return to preinjury level of sports after surgery was, however, associated with less development of OA ($P = .062$). In the multivariate analysis, medial and lateral meniscal surgery were independently associated with OA development at long-term follow-up, after adjusting for the aforementioned variables. The adjusted odds ratio was 1.88 (95% CI, 1.03-3.43; $P = .041$) for medial meniscal surgery and 1.96 (95% CI, 1.05-3.67; $P = .035$) for lateral meniscal surgery.

TABLE 6
Multivariate Analysis of Factors Associated With Osteoarthritis (Kellgren-Lawrence ≥2) at 25-Year Follow-up (N = 235)

Variable	Adjusted Odds Ratio (95% CI)	P Value
Age at surgery	1.025 (0.978-1.074)	.304
Sex	0.777 (0.424-1.424)	.414
Time from injury to surgery	1.006 (0.997-1.015)	.206
Ligament augmentation device	1.723 (0.619-4.798)	.298
Return to preinjury level	0.766 (0.430-1.362)	.364
Meniscal surgery		
Medial	1.876 (1.026-3.431)	.041
Lateral	1.960 (1.048-3.669)	.035

Return to Sports

Of total patients, 75% participated in pivoting sports before injury (see Table 1). Of these, 76% returned to their pivoting sports (135/177). Overall 178 patients (76%) returned to any kind of sports, and 115 (49%) returned at their preinjury level. The median postoperative duration of sports participation in those who returned to their preinjury levels was 8 years (range, 1-25). Return to the preinjury level of sports after surgery decreased the odds of developing OA in univariate analyses by 0.607 ($P = .06$) (Table 5).

Subjective Evaluation

Patients presenting with OA had significantly lower KOOS outcomes for all 5 subscales at long-term follow-up ($P <$ .001) as compared with those with no significant OA (K-L <2) (Table 7, Figure 2). In addition, the median Lysholm score was 10 points lower in the group presenting with OA vs the group with no significant OA (K-L <2). The median Lysholm score at preoperative evaluation and after 1-year follow-up was not significantly different between those who developed OA and those who did not (Figure 3).

DISCUSSION

The main finding of the present study, investigating the ACL injury outcome at a median 25 years after ACLR,

TABLE 7
KOOS, Lysholm, and Tegner Scores Among Patients With and Without Radiographic OA (K-L $\geq$2 vs <2) at 25-Year Follow-up[a]

	Score, Median (Range)		
Measure	OA (n = 130)	No OA (n = 91)	*P* Value
KOOS			
Pain	80.5 (13.8-100)	97.2 (47.2-100)	<.001
Symptoms	73.2 (14.2-100)	89.2 (42.8-100)	<.001
Activities of Daily Living	94.1 (25.0-100)	100 (50.0-100)	<.001
Sport/Recreation	60.0 (0-100)	90 (15-100)	<.001
Quality of Life	56.2 (0-100)	81.2 (18.7-100)	<.001
Lysholm	80 (26-100)	90 (52-100)	<.001
Tegner	4 (0-9)	4 (0-7)	.087

[a]K-L, Kellgren-Lawrence; KOOS, Knee injury and Osteoarthritis Outcome Score; OA, osteoarthritis.

was an OA development rate of 60% (K-L $\geq$2) in the involved knee as opposed to just 18% in the contralateral knee (P < .001). Older age at surgery, prolonged time between injury and surgery, male sex, use of Kennedy LAD reinforcement, medial meniscal surgery, or lateral meniscal surgery increased the odds of having developed OA at long-term follow-up. Return to preinjury level of sports after surgery was associated with lower odds of OA development. In the adjusted regression analysis, medial meniscal surgery and lateral meniscal surgery were the only variables independently associated with OA development. Patients who had developed radiographic signs of OA had significantly lower KOOS and Lysholm scores at long-term follow-up.

Just a few studies have evaluated the rate of radiographic OA >20 years after ACLR.** The current study reports results from 235 patients with a median follow-up of 25 years. Although 60% of the current patients had developed signs of OA at follow-up, only 36% (including 11 knees that had undergone arthroplasty) had developed severe OA in the involved knee (K-L grade 3 or 4). Also using the K-L classification of OA (K-L $\geq$2), Risberg et al,[32] Zaffagnini et al,[50] and van Yperen et al[48] reported the following rates of OA development 20 years after ACLR: 42%, 65%, and 80%, respectively. Shelbourne et al[38] evaluated the prevalence in >400 knees at a minimum 20 years after ACLR using a BPTB autograft. In their study, 29% had an IKDC radiographic rating of abnormal or severely abnormal, and 65% had an IKDC rating of less than normal. If we assume that a K-L classification $\geq$2 is similar but not identical to the IKDC classification of less than normal, the rate of long-term development of OA found in our study seems to be in accordance with the study by Shelbourne et al. Costa-Paz et al[5] presented results in 72 knees >20 years after ACLR with a BPTB autograft. In that study, 28% had an IKDC classification of abnormal or severely abnormal, but 85% were rated as less than normal. Curado et al[7] presented results in 182 patients >20 years after ACLR (92.8% BPTB auto-

**References 5, 7, 11, 15, 32, 34, 38, 44, 48.

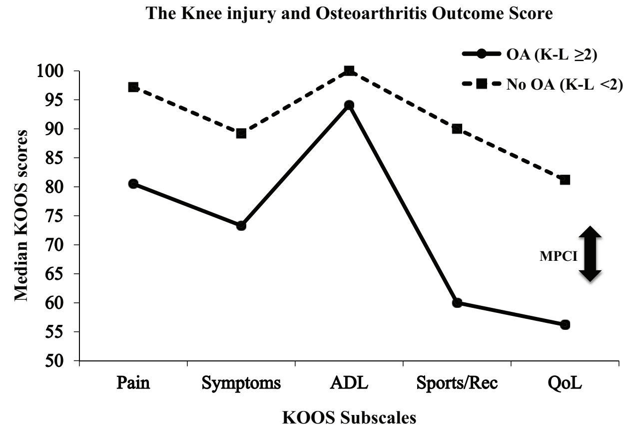

Figure 2. The KOOS at long-term follow-up related to OA. The MPCI of the KOOS represents a difference of 8 to 10 points. ADL, Activities of Daily Living; K-L, Kellgren-Lawrence; KOOS, Knee injury and Osteoarthritis Outcome Score; MPCI, minimal perceptible clinical improvement; OA, osteoarthritis; QoL, Quality of Life.

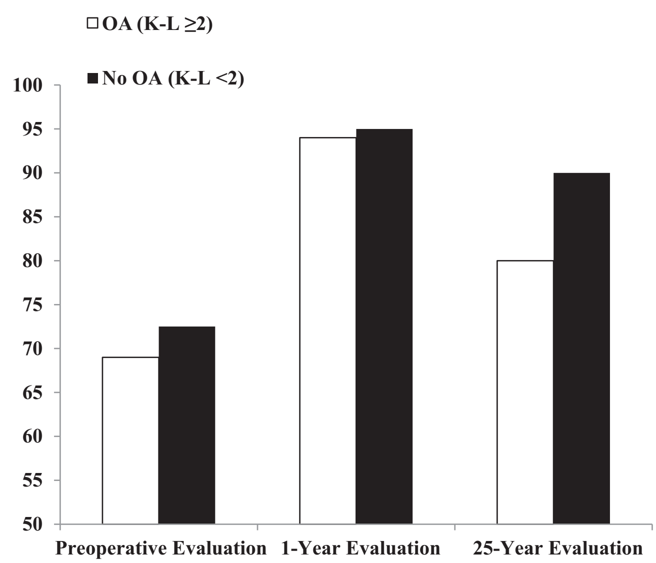

Figure 3. Median Lysholm score at preoperative, 1-year, and 25-year evaluation related to OA. K-L, Kellgren-Lawrence; OA, osteoarthritis.

graft). Twenty-nine percent of patients had developed OA according to the IKDC classification (abnormal or severely abnormal) and 50% had developed signs of OA. These results reflect the variations in reports of long-term development of OA after ACLR and the challenges in comparing results across various studies and different radiological classification systems.[4] Although there is high variability in rates of OA in long-term studies, the conclusion remains the same: the rate of OA development after ACL surgery is higher than the expected prevalence rate of a comparable noninjured knee and often results in “young patients with old knees.”

Several studies have evaluated risk factors for the development of OA after an ACLR. In the present study, increasing age at surgery was associated with increased odds of developing OA in the univariate analyses. This result is in line with comparable studies.[7,38]

Elveos et al[11] evaluated ACLRs using a BPTB autograft with and without the Kennedy LAD after 25 years. No significant difference in outcomes, including the development of OA, was seen between the groups. In the current cohort, a Kennedy LAD was used in 11% of patients. The development of OA was not statistically higher than in patients without this augmentation, but in the univariate analysis, the odds of developing OA after 25 years was 2.28 if the Kennedy LAD was added (P = .075). This trend toward a less favorable result supports the earlier recommendations to avoid the use of reinforcement with synthetic bands.[2,10,27]

The importance of intact menisci to protect against OA development after ACLR has been noted by several authors.[5,15,30,38] Results of the current study are in line with these findings, as the odds of developing OA in the involved knee was 1.9 times as likely in patients with a medial meniscal resection and 2.0 times as likely in patients with a lateral meniscal resection. One could also suspect that the odds of developing OA is related to the time between injury and surgery, as increasing time until surgery places the involved knee at risk of reinjury. However, high-quality evidence supporting this notion is lacking.[14] In the current study, the time between injury and surgery significantly influenced the rate of medial meniscal surgery, and patients developing OA underwent surgery later than those with normal radiographs (17 vs 11 months; P = .011); however, the differences were not significant in the final regression model. The time until surgery was longer in the current study than in our current practice (and others). Furthermore, more effort is now placed on preserving the menisci. Thus, the rate of meniscal resections in the current patient series is probably higher than what will be seen in future long-term studies. This will ideally reduce the long-term prevalence of OA.

A loss of knee extension after ACLR has been shown to affect the development of OA.[35,39] In the current study, a loss of knee extension 3 months after surgery was not unusual, but it did usually resolve with time and was therefore not a significant predictor of OA development. In contrast with our findings, Shelbourne et al[38] noted that if the knee lacked normal extension at discharge, the odds of lacking normal extension at follow-up was 19.7. Furthermore, the early extension deficit increased the odds of OA development. Similar to the current study, their study revealed that lacking normal knee extension at follow-up increased the odds of having developed OA at the same time. However, the loss of knee extension seen at long-term follow-up is probably due to the development of degenerative changes in the knee joint over time and should probably not be considered a risk factor for OA development.

Early residual knee laxity after ACLR is associated with increased risk of revision surgery.[23] However, the presence of abnormal residual knee laxity at 12 months or long-term follow-up did not increase the odds of having developed long-term OA in this study, as supported by Shelbourne et al.[38] On the contrary, in the current study it seems as though residual knee laxity could be considered favorable after 25 years. Because restriction in range of motion is the natural path in the development of OA, it might affect knee laxity, causing the knee to become more stable in anteroposterior translation and in anterolateral rotation movement over time. Furthermore, a knee with a very tight ACLR might be at risk of loss of motion over time and hence develop OA attributed to overconstraint of the knee joint.[36] Thus, when residual knee laxity does not cause bothersome symptoms of instability, it could be considered favorable for knee function at long-term evaluations.

Oiestad et al[29] investigated the association between return to sports and the risk of developing OA 15 years after ACLR. Patients who returned to pivoting sports had lower odds of long-term knee OA and better self-reported activities of daily living as compared with those who did not return to sports. These results are in line with the current study, as we found that the return to preinjury level of sports was associated with less development of OA. Athletes who aim for a return to sports after surgery may be more motivated during the phase of rehabilitation. This could lead to better restoration of knee stability and function after surgery and, by this, further improve the long-term outcome. However, the knee-related causes for not returning to sports after surgery are potential biases to this finding, as patients with concomitant injuries (eg, meniscal or cartilage injuries) are probably less likely to return to sports after surgery and at the same time have an increased risk of OA development. This could partially explain the counterintuitive finding of lower odds of OA in those who returned to their preinjury levels of sports

In the current study, the KOOS at long-term follow-up was significantly lower in patients with radiographic OA (K-L $\geq$ 2) as compared with patients without significant OA. The suggested minimal meaningful clinical difference of 8 to 10 points between groups was reached in all subscales except in activities of daily living. Furthermore, the Lysholm score was 10 points lower in the group classified with radiographic OA. Although a direct association between the subjective scores and the presence of OA on radiographs cannot be established, this finding unsurprisingly shows that patients with radiographic OA development have a less favorable subjective long-term outcome. Other long-term studies have shown that patients had progressively lower subjective scores as the level of OA increased.[5,30,38]

The strength of the current study is the long follow-up period (median, 25 years). Furthermore, to our best knowledge, this is one of the largest prospectively held cohorts after ACLR all performed with a BPTB autograft. However, long-term studies have some inherent limitations. The surgical technique and rehabilitation protocol have evolved over the past 25 years, and the results of the current study may therefore be inferior to results from future long-term studies. Moreover, during the current follow-up, meniscal injuries were mainly treated with a partial resection. Today's shift toward saving the menisci by repair instead of partial resection may improve the rates of OA development in the future. Cartilage damage at the time of ACLR or during the follow-up period might affect the OA development rate. Unfortunately, we were not able to report the cartilage status, as the data were partially missing and of poor quality and no classification system for cartilage status was established at our clinic when the current patient cohort underwent surgery. Finally, data on body mass index were not analyzed.

CONCLUSION

At a median 25 years after ACLR with a BPTB autograft, 60% of patients had developed OA in the involved knee, and 18% had radiographic signs of OA in the contralateral knee. Medial meniscal surgery and lateral meniscal surgery were the only variables independently associated with the development of OA. This finding suggests that as more effort is placed on saving the menisci by repair instead of partial resection, the rates of OA development may improve in the future. Finally, patients who had developed radiographic OA had significantly lower subjective scores at long-term evaluation as compared with patients with normal radiographic evaluation results.

REFERENCES

1. Ajuied A, Wong F, Smith C, et al. Anterior cruciate ligament injury and radiologic progression of knee osteoarthritis. *Am J Sports Med*. 2014;42(9):2242-2252.
2. Asahina S, Yamamoto H, Muneta T, et al. Evaluation of anterior cruciate reconstruction reinforced by the Kennedy ligament augmentation device. *Int Orthop*. 1995;19:229-233. doi:10.1007/BF00185228
3. Cinque ME, Dornan GJ, Chahla J, et al. High rates of osteoarthritis develop after anterior cruciate ligament surgery: an analysis of 4108 patients. *Am J Sports Med*. 2018;46(8):2011-2019.
4. Clancy WG, Nelson DA, Reider B, Narechania RG. Anterior cruciate ligament reconstruction using one-third of the patellar ligament, augmented by extra-articular tendon transfers. *J Bone Joint Surg Am*. 1982;64(3):352-359.
5. Costa-Paz M, Garcia-Mansilla I, Marciano S, et al. Knee-related quality of life, functional results and osteoarthritis at a minimum of 20 years' follow-up after anterior cruciate ligament reconstruction. *Knee*. 2019;26(3):666-672.
6. Culvenor AG, Crossley KM. Accelerated return to sport after anterior cruciate ligament injury: a risk factor for early knee osteoarthritis? *Br J Sports Med*. 2016;50(5):260-261.
7. Curado J, Hulet C, Hardy P, et al. Very long-term osteoarthritis rate after anterior cruciate ligament reconstruction: 182 cases with 22-year follow-up. *Orthop Traumatol Surg Res*. 2020;106(3):459-463.
8. Daniel DM, Stone ML, Sachs R, Malcolm L. Instrumented measurements of anterior knee laxity in patients with acute anterior cruciate ligament disruption. *Am J Sports Med*. 1985;13(6):401-407.
9. Dare D, Rodeo S. Mechanisms of post-traumatic osteoarthritis after ACL injury. *Curr Rheumatol Rep*. 2014;16(10):622-625.
10. Drogset JO, Grøntvedt T. Anterior cruciate ligament reconstruction with and without a ligament augmentation device. *Am J Sports Med*. 2002;30(6):851-856.
11. Elveos MM, Drogset JO, Engebretsen L, et al. Anterior cruciate ligament reconstruction using a bone–patellar tendon–bone graft with and without a ligament augmentation device: a 25-year follow-up of a prospective randomized controlled trial. *Orthop J Sports Med*. 2018;6(11):2325967118808778.
12. Galway HR, MacIntosh DL. Lateral pivot shift: a symptom and sign of anterior cruciate ligament insufficiency. *Clin Orthop Relat Res*. 1980;147:45-50.
13. Gächter A. Reconstruction through a transligamentous approach. In: Jacob RP, Staübli HU, eds. *The Knee and the Cruciate Ligaments*. Springer; 1992:384-385.
14. Grøntvedt T, Engebretsen L, Bredland T. Arthroscopic reconstruction of the anterior cruciate ligament using bone–patellar tendon–bone grafts with and without augmentation. *J Bone Joint Surg Br*. 1996;78(5):817-822.
15. Hagemans FJA, Jonkers FJ, van Dam MJJ, et al. Clinical and radiographic outcomes of anterior cruciate ligament reconstruction with hamstring tendon graft and femoral cortical button fixation at minimum 20-year follow-up. *Am J Sports Med*. 2020;48(12):2962-2969.
16. Hefti F, Müller W, Jakob RP, Staübli HU. Evaluation of knee ligament injuries with the IKDC form. *Arthroscopy*. 1993;1(3-4):226-234.
17. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. *Ann Rheum Dis*. 1957;16(4):494-502.
18. Kennedy JC, Roth JH, Mendenhall HV, Sanford JB. Presidential address: intraarticular replacement in the anterior cruciate ligament-deficient knee. *Am J Sports Med*. 1980;8(1):1-8.
19. Khan T, Alvand A, Prieto-Alhambra D, et al. ACL and meniscal injuries increase the risk of primary total knee replacement for osteoarthritis: a matched case-control study using the Clinical Practice Research Datalink (CPRD). *Br J Sports Med*. 2019;53(15):965-968.
20. Kvist J, Filbay S, Andersson C, et al. Radiographic and symptomatic knee osteoarthritis 32 to 37 years after acute anterior cruciate ligament rupture. *Am J Sports Med*. 2020;48(10):2387-2394.
21. Lebel B, Hulet C, Galaud B, et al. Arthroscopic reconstruction of the anterior cruciate ligament using bone–patellar tendon–bone autograft. *Am J Sports Med*. 2008;36(7):1275-1282.
22. Lien-Iversen T, Morgan DB, Jensen C, et al. Does surgery reduce knee osteoarthritis, meniscal injury and subsequent complications compared with non-surgery after ACL rupture with at least 10 years follow-up? A systematic review and meta-analysis. *Br J Sports Med*. 2020;54(10):592-598.
23. Lindanger L, Strand T, Mølster AO, et al. Effect of early residual laxity after anterior cruciate ligament reconstruction on long-term laxity, graft failure, return to sports, and subjective outcome at 25 years. *Am J Sports Med*. 2021;49(5):1227-1235.
24. Lindanger L, Strand T, Mølster AO, et al. Return to play and long-term participation in pivoting sports after anterior cruciate ligament reconstruction. *Am J Sports Med*. 2019;47(14):3339-3346.
25. Louboutin H, Debarge R, Richou J, et al. Osteoarthritis in patients with anterior cruciate ligament rupture: a review of risk factors. *Knee*. 2009;16(4):239-244.
26. McGuire D, Hendricks SD, Grinstead GL, et al. Use of an endoscopic aimer for femoral tunnel placement in anterior cruciate ligament reconstruction. *Arthroscopy*. 1996;12(1):26-31.
27. Muren O, Dahlstedt L, Dalén N. Reconstruction of acute anterior cruciate ligament injuries: a prospective, randomised study of 40 patients with 7-year follow-up. *Arch Orthop Trauma Surg*. 2003;123(4):144-147.
28. Musahl V, Hoshino Y, Ahldén M, et al. The pivot shift: a global user guide. *Knee Surg Sports Traumatol Arthrosc*. 2012;20(4):724-731.
29. Oiestad BE, Holm I, Risberg MA. Return to pivoting sport after ACL reconstruction: association with osteoarthritis and knee function at the 15-year follow-up. *Br J Sports Med*. 2018;52(18):1199-1204.
30. Pernin J, Verdonk P, Si Selmi TA, et al. Long-term follow-up of 24.5 years after intra-articular anterior cruciate ligament reconstruction with lateral extra-articular augmentation. *Am J Sports Med*. 2010;38(6):1094-1102.
31. Poulsen E, Goncalves GH, Bricca A, et al. Knee osteoarthritis risk is increased 4-6 fold after knee injury—a systematic review and meta-analysis. *Br J Sports Med*. 2019;53(23):1454-1463.
32. Risberg MA, Oiestad BE, Gunderson R, et al. Changes in knee osteoarthritis, symptoms, and function after anterior cruciate ligament reconstruction: a 20-year prospective follow-up study. *Am J Sports Med*. 2016;44(5):1215-1224.

33. Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes*. 2003;1:64
34. Salmon LJ, Heath E, Akrawi H, Roe JP, et al. 20-year outcomes of anterior cruciate ligament reconstruction with hamstring tendon autograft: the catastrophic effect of age and posterior tibial slope. *Am J Sports Med*. 2018;46(3):531-543.
35. Salmon LJ, Russell VJ, Refshauge K, et al. Long-term outcome of endoscopic anterior cruciate ligament reconstruction with patellar tendon autograft. *Am J Sports Med*. 2006;34(5):721-732.
36. Samitier G, Marcano AI, Alentorn-Geli E, et al. Failure of anterior cruciate ligament reconstruction. *Arch Bone Jt Surg*. 2015;3(4):220-240.
37. Sanders TL, Kremers HM, Bryan AJ, et al. Is anterior cruciate ligament reconstruction effective in preventing secondary meniscal tears and osteoarthritis? *Am J Sports Med*. 2016;44(7):1699-1707.
38. Shelbourne D, Benner RW, Gray T. Results of anterior cruciate ligament reconstruction with patellar tendon autografts: objective factors associated with the development of osteoarthritis at 20 to 33 years after surgery. *Am J Sports Med*. 2017;45(12):2730-2738.
39. Shelbourne D, Gray T. Minimum 10-year results after anterior cruciate ligament reconstruction. *Am J Sports Med*. 2009;37(3):471-480.
40. Shelbourne K, Nitz P. Accelerated rehabilitation after anterior cruciate ligament reconstruction. *Am J Sports Med*. 1990;18(3):292-299.
41. Snoeker B, Turkiewicz A, Magnusson K, et al. Risk of knee osteoarthritis after different types of knee injuries in young adults: a population-based cohort study. *Br J Sports Med*. 2020;54(12):725-730.
42. Suter LG, Smith SR, Katz JN, et al. Projecting lifetime risk of symptomatic knee osteoarthritis and total knee replacement in individuals sustaining a complete anterior cruciate ligament tear in early adulthood. *Arthritis Care Res*. 2016;69(2):201-208.
43. Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries. *Clin Orthop Relat Res*. 1985;198:43-49.
44. Thompson S, Salmon L, Waller A, et al. Twenty-year outcomes of a longitudinal prospective evaluation of isolated endoscopic anterior cruciate ligament reconstruction with patellar tendon autografts. *Am J Sports Med*. 2015;43(9):2164-2174.
45. Torg JS, Conrad W, Kalen V. Clinical diagnosis of anterior cruciate ligament instability in the athlete. *Am J Sports Med*. 1976;4(2):84-93.
46. Tsoukas D, Fotopoulos V, Basdekis G, Makridis KG. No difference in osteoarthritis after surgical and non-surgical treatment of ACL-injured knees after 10 years. *Knee Surg Sports Traumatol Arthrosc*. 2016;24(9):2953-2959.
47. van Meer BL, Meuffels DE, van Eijsden WA, et al. Which determinants predict tibiofemoral and patellofemoral osteoarthritis after anterior cruciate ligament injury? A systematic review. *Br J Sports Med*. 2015;49(15):975-983.
48. van Yperen DT, Reijman M, van Es EM, Bierma-Zeinstra SMA, Meuffels DE. Twenty-year follow-up study comparing operative versus nonoperative treatment of anterior cruciate ligament ruptures in high-level athletes. *Am J Sports Med*. 2018;46(5):1129-1136.
49. Wiggins AJ, Grandhi RK, Schneider DK, et al. Risk of secondary injury in younger athletes after anterior cruciate ligament reconstruction. *Am J Sports Med*. 2016;44(7):1861-1876.
50. Zaffagnini S, Marcheggiani Muccioli GM, Grassi A, et al. Over-the-top ACL reconstruction plus extra-articular lateral tenodesis with hamstring tendon grafts: prospective evaluation with 20-year minimum follow-up. *Am J Sports Med*. 2017;45(14):3233-3242.