The Prognosis and Predictors of Sports Function and Activity at Minimum 6 Years After Anterior Cruciate Ligament Reconstruction

A Population Cohort Study

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Background: The predictors of anterior cruciate ligament reconstruction (ACLR) outcome at 6 years as measured by validated patient-based outcome instruments are unknown.

Hypothesis: Certain variables evaluated at the time of ACLR will predict return to sports function (as measured by the International Knee Documentation Committee [IKDC] questionnaire and the Knee injury and Osteoarthritis Outcome Score [KOOS] Sports and Recreation subscale), knee-related quality of life (KOOS Knee Related Quality of Life subscale), and activity level (Marx Activity Scale). Potential predictor variables include demographic factors, surgical technique and graft choice for ACLR, and intra-articular injuries and treatment.

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

Methods: All patients with unilateral ACLRs from 2002 currently enrolled in the MOON (Multicenter Orthopaedic Outcomes Network) cohort were evaluated. Patients completed the validated outcome instruments preoperatively. Physicians documented intra-articular pathologic abnormalities, treatment, and surgical techniques used at the time of surgery. At 2 and 6 years postoperatively, patients completed the same validated outcome instruments.

Results: Follow-up was obtained at 2 years (88%) and at 6 years (84%). The cohort was 57% male with a median age of 23 years at enrollment. The ability to perform sports function was maintained at 6 years, but the Marx activity level continued to decline from baseline. Revision ACLR and use of allograft predicted worse outcomes on the IKDC and both KOOS subscales. Lateral meniscus treatment, smoking status, and body mass index at baseline were each predictors on 2 of 3 scales. The predictors of lower activity level were revision ACLR and female sex.

Conclusion: Six years after ACLR, patients could perform sports-related functions and maintain a high knee-related quality of life similar to their 2-year level, although their physical activity level (Marx) dropped over time. Choosing autograft rather than allograft, not smoking, and having normal body mass index are advised to improve long-term outcomes.

Keywords: anterior cruciate ligament reconstruction; sports function; activity; Knee injury and Osteoarthritis Outcome Score; International Knee Documentation Committee; Marx Activity Scale; 6-year follow-up

The prognosis and predictors of anterior cruciate ligament reconstruction (ACLR) outcome at 6 years as measured by modern validated patient-based outcome instruments and assessed by multivariable analysis are unknown. Knowing prognostic information would be valuable in physicians' counseling of patients regarding likely results of ACLR. Identification of modifiable predictors (ie, risk factors) would provide future interventions to improve ACLR in those projected to have worse outcomes. The development of validated patient-reported outcome instruments for an athletically active population established methods of measuring and quantifying patient activity, symptoms, function, and quality of life. This MOON (Multicenter Orthopaedic Outcomes Network) study is based on a consortium network that was established to follow a population cohort of sufficient size to perform multivariable analysis for identifying prognosis and modifiable predictors for both short-term and long-term outcomes after an ACLR.

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Other groups and studies have looked at outcomes in ACLR patients at a minimum of 5 years after surgery. Eighteen Level 1 or 2 studies provided the highest evidence for prognosis and predictors at greater than 5 years after ACLR.[||||] However, no previous study contained all of the following: (1) preoperative and postoperative administration of outcome instruments, (2) modern validated sports-related instruments, (3) greater than 80% follow-up, and (4) multivariable analysis. Multivariable analysis is necessary to see how factors affect outcome and how important each is, in context together. In cohort studies, where variables cannot be randomly and equally distributed, this is the only way to account for uneven distributions of factors and potential confounders.[18] Risk factors that are likely to be relevant to outcomes of ACLR include age, sex, mechanism of injury, body mass index (BMI), concomitant medial and lateral meniscal tears and treatment, articular cartilage injuries and treatment, ACLR technique, and graft choice. Large sample sizes with excellent follow-up are necessary for this type of analysis. The largest sample size of a previously reported randomized controlled trial had an enrollment of 225,[35] which limits risk factor analysis. A previous cohort study using multivariable analysis had 69% follow-up, and results were weakened by lack of preoperative validated outcomes measures for each patient.[52]

Outcomes evaluation after ACLR can be broadly divided into 2 categories. Traditionally, measurements that are performed on-site in a limited number of patients (usually around 100) are used to differentiate results among treatments based on physical examination, instrumented knee laxity, and imaging (primarily standard radiographs). Recently, partly as a result of an increasing focus on evidence-based medicine, patient-reported outcome questionnaires have been psychometrically designed and clinically validated. Several research studies have compared the validity of patient-reported outcome measures with clinician-based measures (ie, clinical assessment), such as range of motion, knee laxity, and physical examination.[5,10,40,50] These tools were designed to capture the effect of a knee injury and treatment on patients' activities and sports function. Included in our study are the International Knee Documentation Committee (IKDC) questionnaire,[14] the Knee injury and Osteoarthritis Outcome Score (KOOS),[45] and the Marx Activity Scale,[28] which are designed for self-administration of an athletically active population. Their validity,[31] reliability,[30] responsiveness to clinical change,[45] and minimal clinically meaningful differences have been documented (IKDC[13-15,46]; KOOS[26,37,42-45]; Marx[7,28,32]). The IKDC is designed as a tool to evaluate knee injuries.[14] The KOOS includes 5 subscales; of particular interest are the Sports and Recreation subscale ($\text{KOOS}_{\text{sports/rec}}$) and the Knee Related Quality of Life subscale ($\text{KOOS}_{\text{krqol}}$) because these are aimed at evaluating the relevance of functional disability of the knee in a younger (not elderly) population and are reported to change the most after surgery.[45] The Marx Activity Scale is useful for differentiating those with high demands on their knees, usually due to participation in sports activities, from those who are more sedentary and thus have less demand on their knees.[28]

Our multicenter group was initiated in 2002 to prospectively enroll a sample size with sufficient generalizability that encompassed a timeliness of ACLR treatments to identify prognosis and modifiable predictors of validated outcomes through multivariable analysis. The purpose of this prospective longitudinal cohort study was to investigate patient-reported outcomes and predictors for sports function, knee related quality of life, and physical activity level at an intermediate term (6 years after ACLR).

We address 3 questions in the current study: (1) What are the predictors of sports function and activity as measured by the IKDC and $\text{KOOS}_{\text{sports/rec}}$? (2) What are the predictors of knee-related quality of life as measured by the $\text{KOOS}_{\text{krqol}}$? (3) What are the predictors of return to physical activity level as measured by the Marx Activity Scale? These results will aid physician counseling regarding an individual patient's prognosis after ACLR, provide highest level of evidence for physician decision making, and identify future modifiable risk factors to improve ACLR outcomes.

MATERIALS AND METHODS

Study Design and Setting

This MOON group began on January 1, 2002, as a consortium of 6 sites with 8 physicians to conduct a multicenter

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||||References 2, 3, 8, 9, 12, 19, 24, 25, 29, 35, 36, 41, 47, 48, 51, 52, 55, 56.

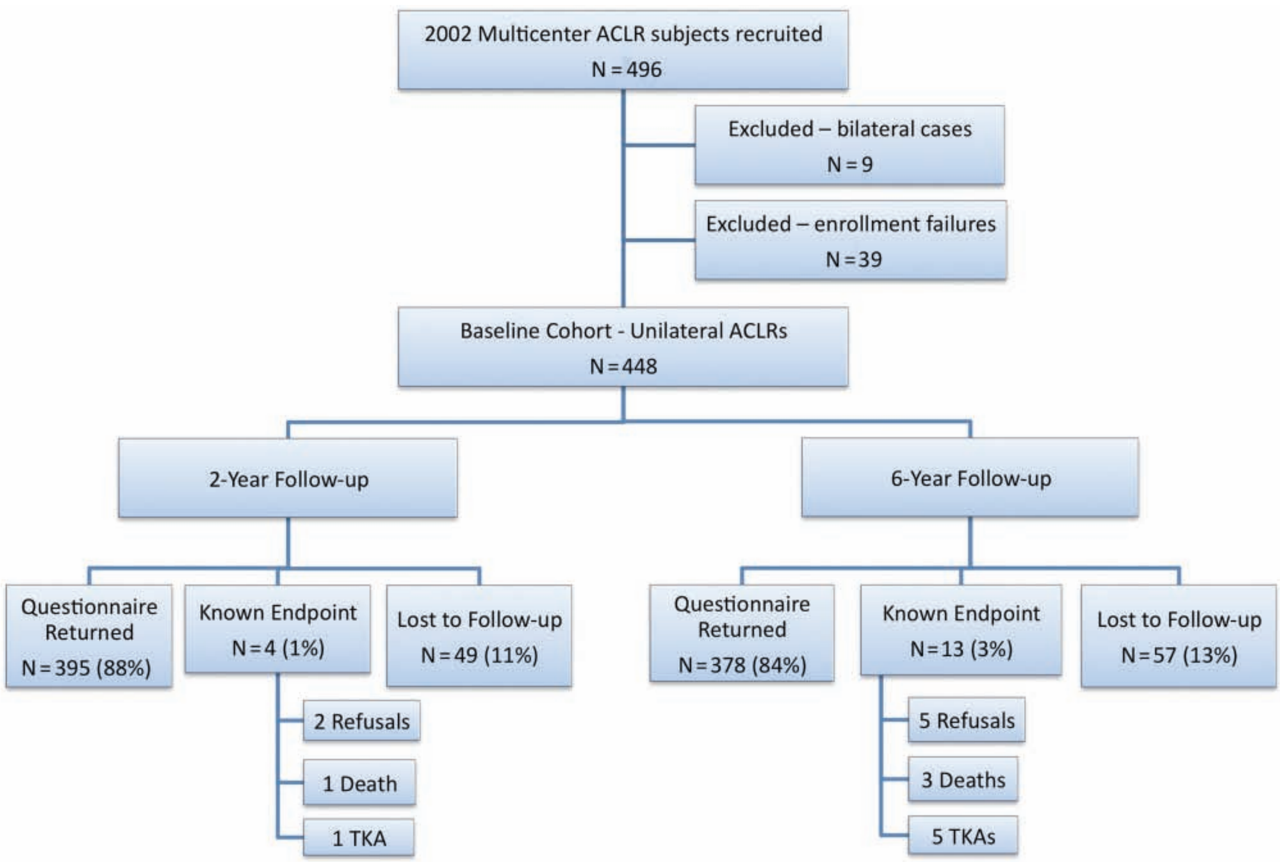

Figure 1. Flow diagram of study cohort. All anterior cruciate ligament reconstruction (ACLR) patients were enrolled during calendar year 2002. The follow-up for each interval, a minimum of 2 or 6 years, for the validated patient-reported outcome questionnaires is indicated as *returned*. In addition, the lost-to-follow-up patients with known results (ie, endpoints) are shown, including death, subsequent total knee arthroplasty (TKA), and refusals.

population-based cohort study following patients after ACLR. One university serves as the data-coordinating center for the study and is responsible for entering baseline data and collecting follow-up data. Institutional review board approval was obtained from all participating centers.

Participants

All participants having ACLR at participating sites in 2002 (from January 1, 2002, to December 31, 2002) were invited to enroll in the study (see Figure 1). There were 8% enrollment failures (39 of 496) and 9 simultaneous bilateral cases excluded, leaving a final baseline cohort of 448 unilateral ACLRs.

Data Sources and Measurement

After documentation of informed consent, participants completed a 13-page questionnaire examining self-reported demographics, injury characteristics, sports participation history, and health status. Regarding the last item, the following validated instruments were included: the KOOS (which includes the Western Ontario and McMaster Universities Arthritis Index), the IKDC, and the Marx Activity Scale. This questionnaire was typically completed the day of surgery; otherwise, it was completed within 2 weeks of the surgery date.

Surgeons completed a 49-page questionnaire that included sections on history of knee injury and/or surgery on both knees, the results of the general knee examination done under anesthesia, the grade of all intra-articular injuries and treatments to the meniscus and articular cartilage, and the surgical technique used for the ACLR. Classification of the general knee examination findings follows the recommendations of the updated 1999 IKDC guidelines.[14,16] Surgeon documentation of articular cartilage injury is recorded on the modified Outerbridge classification.[1,27] Meniscal injuries are classified by size, location, and partial versus complete tears, and treatment is recorded as *not treated*, *repair*, or by extent of resection.[4] Patients were given a standardized evidence-based rehabilitation protocol for ACLR rehabilitation.

Completed data forms were mailed from the participating sites to the data-coordinating center. Data from the patient and surgeon questionnaires were scanned with

Teleform software (Version 9.0; Cardiff Software, Inc, Vista, California) using optical character recognition to avoid manual data entry; the scanned data were then verified and exported to a database. A series of logical error checks was subsequently performed before data analysis.

Follow-Up

Six-year patient follow-up was obtained by mail using the same outcome questionnaire completed at baseline. The questionnaire documented any additional surgeries subsequent to the index ACLR performed in 2002. Patient follow-up was initiated on January 1, 2008, and completed on October 1, 2009.

Quantitative Variables and Statistical Methods

Patient-reported outcomes treated as continuous dependent variables were (1) $KOOS_{krqol}$, (2) $KOOS_{sports/rec}$, (3) IKDC, and (4) Marx Activity Scale. The IKDC and the KOOS subscales were transformed to a score of 0 to 100, where 100 constituted the best score and 0 the worst score. The Marx activity level was scored on a scale from 0 to 16, where 16 constituted the highest activity level and 0 the lowest.

Several categorical variables were reduced because of low-prevalence categories. Articular cartilage variables were grouped by compartment (medial, lateral, anterior), and severity of chondromalacia was dichotomized into positive or negative, with grade II chondromalacia or higher (ie, worse) being positive for chondrosis in that compartment. Lateral collateral ligament injury and medial collateral ligament injury were dichotomized from severity of grade into *yes* or *no*.

To evaluate the association of baseline predictors with knee function, multivariable linear multiple regression models were fit using the continuous scores of the KOOS subscales, IKDC score, and the Marx activity level as the dependent variables. The independent variables included in these models were current age; sex; race; baseline marital status; baseline smoking status; baseline BMI from self-reported height and weight; whether or not a "pop" was heard at the time of injury; medial and lateral meniscus status and treatment; collateral ligament injury; chondrosis in the medial, lateral, and anterior compartments; graft type; and type of reconstruction. Therefore, in our multivariable analysis, each independent variable studied (see Table 1) was controlled to identify variables that significantly determined the patient-reported outcome scale (KOOS, IKDC, Marx). Over time, as patients age, other measured exposures may change as well, such as smoking status and BMI. To that end, all regression models were fit using baseline and current smoking and BMI. The former approach is to determine if a baseline exposure predicts an outcome regardless of whether a patient's exposure status has changed, whereas the latter approach is a means of adjusting for the current exposure status, which is the way that age was handled in the models. The clinically meaningful effect based on the responsiveness is approximately 11 points for the IKDC and 8 points on the KOOS.[13,42] The clinically meaningful effect of the Marx scale has not been determined, but consensus believes it to be approximately 2 points. A nomogram was constructed to display the relationship of predictor variables and the outcomes. A nomogram can be used to estimate the mean response for individual patients and to show the relationship between the different predictor variables and how this affects the response.

We did not assume linearity of covariate effects, only smoothed relationships using restricted cubic regression splines. Missing values of predictor variables were imputed using multiple imputation, incorporating predictive mean matching and flexible additive imputation models, as implemented in the *aregImpute* function available in the Hmisc package in R (free open-source statistical software; http://www.r-project.org). Data reduction methods used to preserve degrees of freedom in models included pooling of low-prevalence categories, variable grouping, and hierarchical clustering (using squared Spearman rank correlation coefficients as the singularity matrix) to identify colinear variables that could be deleted from the model. Statistical analysis was performed with R.

RESULTS

Participants

From January 1, 2002, to December 31, 2002, 448 patients met the inclusion criteria of having a unilateral ACLR and were included in our final enrollment (Figure 1). Of the initial 448, repeat questionnaires were obtained on 395 (88%) at 2 years (median, 2.08 years; 25th percentile, 2.02 years; 75th percentile, 2.19 years) and on 378 (84%) at 6 years (median, 6.7 years; 25th percentile, 6.6 years; 75th percentile, 6.8 years).

Table 1 provides baseline demographic and clinical characteristics of the cohort that were analyzed at 6 years. The median age of the female cohort at the time of ACLR was 20 years, whereas in the male cohort it was 26 years (Table 1). Seventy-eight percent (290 of 372) reported that they were nonsmokers at the time of their ACLR. The cohort was composed of 92% primary reconstructions and 8% revision candidates. The participating surgeons opted for bone–patellar tendon–bone grafts 43% of the time and hamstring grafts 48% of the time (semitendinosus + gracilis, 32%; semitendinosus only, 16%), using an arthroscopic, 1-incision approach 72% of the time. The surgeons used autografts 84% of the time and allografts 16%. When an allograft was used, it originated from 1 of 4 tissue banks. Just over half the allografts were irradiated with less than 2.5 Mrad. Table 1 summarizes concomitant injuries and treatments. There were no drastic changes in smoking habits or BMI over the 6-year follow-up period. Less than 9% of patients changed smoking status from current to quit/never or vice versa, and the median change in BMI was an increase of only 3%.

TABLE 1
Patient and Surgical Characteristics: Baseline

	n	Female (n, 174)	Male (n, 201)
Age, y	375		
Lower quartile, median, upper quartile		17.0, 20.0, 34.5	19.0, 26.0, 36.0
Mean ± SD		25.4 ± 11.4	28.4 ± 10.9
Body mass index	368		
Lower quartile, median, upper quartile		21.1, 22.8, 26.2	23.6, 25.8, 28.1
Mean ± SD		24.1 ± 4.4	26.1 ± 3.9
		% (n)	% (n)
Smoking status	372		
Never		82 (142)	75 (148)
Quit		10 (17)	14 (28)
Current		9 (15)	11 (22)
Ethnicity	371		
Asian		2 (4)	6 (11)
Black		8 (13)	2 (4)
Hispanic		1 (1)	1 (1)
Other		1 (1)	4 (7)
White		89 (154)	88 (175)
Marital status	374		
Single/other		61 (107)	45 (90)
Married		39 (67)	55 (110)
"Pop" heard at time of injury	358		
No		21 (36)	22 (41)
Yes		79 (133)	78 (148)
Reconstruction type	375		
Primary		95 (165)	89 (179)
Revision		5 (9)	11 (22)
Graft type	375		
Allograft		13 (23)	18 (37)
Autograft		87 (151)	82 (164)
Graft source	374		
Achilles tendon		1 (2)	<1 (1)
Bone–patellar tendon–bone		40 (69)	45 (90)
Hamstring (semitendinosis)		14 (25)	18 (35)
Hamstring (semitendinosis + gracilis)		39 (67)	26 (53)
Other		6 (11)	10 (21)
Surgical exposure	375		
Arthroscopic, 1 incision		74 (129)	70 (140)
Arthroscopic, 2 incisions		26 (45)	30 (61)
Medial collateral ligament injury	375		
No		91 (159)	86 (173)
Yes (grades 1, 2 only)		9 (15)	14 (28)
Lateral collateral ligament injury	375		
No		98 (170)	95 (190)
Yes (grades 1, 2 only)		2 (4)	5 (11)
Medial compartment chondrosis	375		
No		81 (141)	80 (160)
Yes (grades II, III, or IV)		19 (33)	20 (41)
Lateral compartment chondrosis	375		
No		85 (148)	80 (161)
Yes (grades II, III, or IV)		15 (26)	20 (40)
Anterior compartment chondrosis	375		
No		84 (147)	81 (163)
Yes (grades II, III, or IV)		16 (27)	19 (38)
Medial meniscus status	375		
Normal		67 (116)	57 (114)
No treatment		5 (9)	7 (15)
Repair		11 (19)	13 (26)
Excision		17 (30)	23 (46)
Lateral meniscus status	375		
Normal		40 (69)	40 (80)
No treatment		32 (55)	23 (46)
Repair		7 (12)	5 (11)
Excision		22 (38)	32 (64)

TABLE 2
Outcome Scores Over Time: Median (25%, 75% Quartile)

Outcome Measure	Scale	Baseline	2 Years	6 Years
IKDC[a]	0-100	45 (34, 56)	75 (66, 83)	77 (66, 84)
KOOS[b]	0-100	50 (25, 75)	85 (70, 95)	90 (70, 100)
Sports/recreation				
Knee-related	0-100	38 (19, 50)	75 (63, 88)	81 (63, 94)
Marx Activity Scale	0-16	12 (8, 16)	9 (4, 13)	7 (3, 11)

[a]International Knee Documentation Committee questionnaire.
[b]Knee injury and Osteoarthritis Outcome Score: Sports and Recreation subscale and Knee Related Quality of Life subscale.

Changes in IKDC, KOOS, and Marx Over Time

The data were found to be nonnormally distributed; hence, medians and interquartile ranges are presented. Table 2 shows the median with 25% and 75% quartiles for each outcome measure at baseline, 2 years, and 6 years. The IKDC and KOOS at 2 years demonstrate a large improvement, which was maintained at the 6-year follow-up. In contrast, the Marx activity level continued to decline over time.

Predictors of Outcome

Multivariable analysis was used to determine which baseline factors are significant predictors of patient-reported outcome 6 years after ACLR. Additionally, this analysis was used to establish a patient-specific predictive model of the IKDC, KOOS, and Marx scores. The candidate predictor variables, time of measurement, and levels of significance are listed in Table 3, and the significant predictors are summarized in the online appendix (Table A-1, available in the online version of this article at http://ajs.sagepub.com/supplemental/). For every model, the baseline score was a significant predictor of the current score. Revision ACLR was a significant predictor of poorer outcomes on all metrics (ie, lower IKDC and KOOS subscale scores and lower activity level). The use of an allograft was found to be a significant predictor of poorer IKDC and KOOS ($KOOS_{sports/rec}$, $KOOS_{krqol}$) outcomes. Baseline BMI was a significant predictor of the IKDC and $KOOS_{sports/rec}$ at 6 years, whereas baseline smoking status was a predictor of the IKDC at 6 years. When the IKDC and $KOOS_{sports/rec}$ models were repeated using current BMI and smoking status, the results were similar; that is, current BMI and smoking status were associated with the outcome having significant *P* values similar to those listed in Table 3 for baseline BMI and smoking status. There were only 2 slight differences in the results of the models when current BMI and smoking status were used instead of the baseline variable, and these are noted in Table 3. For example, for the $KOOS_{krqol}$ model, baseline smoking status was not a significant predictor (P = .102) of outcome; however, there was a significant association between current smoking status and $KOOS_{krqol}$ score (P = .034). Lateral meniscus status was significant on the 2 KOOS subscales ($KOOS_{sports/rec}$, $KOOS_{krqol}$). The Marx activity scores were lower for patients who were female and had undergone revision ACLR. We evaluated whether these significant differences were clinically meaningful; thus, the 95% confidence intervals for each value for each outcome measure are displayed in Figure 2 (and in Figures A-1, A-2, and A-3, in the online appendix). These figures display the comparison as negative (delineating a worse outcome score) or positive (better outcome score) with the mean (± 95% confidence interval) for IKDC, 2 KOOS subscales, and activity level. The clinically meaningful difference is represented by a green line for better outcomes and a red line for worse outcomes on each graph.

For the IKDC, only revision ACLR reached a clinically meaningful difference (Figure A-1). For the $KOOS_{sports/rec}$, revision ACLR, use of allograft, and lateral meniscus status were both statistically significant and clinically relevant differences. For the $KOOS_{krqol}$, revision ACLR, use of allograft, lateral meniscus status, and smoking status were all individually meaningful (Figure 2). With 2 points as an estimate of clinically relevant change in activity level, being female and undergoing revision ACLR may portend a clinically meaningful decline in activity level.

The final models are presented as nomograms; as such, IKDC (Figure A-4), KOOS (Figure 3 and Figure A-5), and Marx (Figure A-6) can be used to predict outcomes on future patients. To determine a specific patient outcome at 6 years, identify that patient's status for each predictor listed on the left-hand column, use the top line to get the corresponding points for each predictor, and sum them. Then, this total score for all the risk factor variables is transferred to the total points axis, and the patient's predicted outcome can be estimated by the direct vertical correspondence from total points axis to the bottom line on the nomogram. The number of points assigned for an individual predictor is proportional to the strength of the association with the outcome. For example, a patient undergoing primary ACLR (~ 98 points) with an autograft (~ 55 points) who has never smoked (~ 52 points) and has a BMI of 15 (~ 100 points)—while letting the other predictors default to categories contributing 0 points—would have 305 total points, corresponding to a predicted $KOOS_{krqol}$ of 65. This is in contrast to a patient undergoing revision ACLR (0 points) with allograft (0 points) who has never smoked (~ 52 points) and has a BMI of 15 (~ 100 points). This patient would have 152 total points, corresponding to a predicted $KOOS_{krqol}$ of 40. This represents a clinically relevant difference of 25 points.

TABLE 3
Predictor Variables and Results

Variable	Timepoint[a]	Comparison	Significance at T_6 (P) IKDC	$KOOS_{sports/rec}$	$KOOS_{krqol}$	Marx
Patient-reported outcomes[b]	T_0		< .001	< .001	.011	< .001
Age, y	T_6	42:24	.031 (.096)[c]	.558	.616	.070
Body mass index	T_0	28:23	.022	.0497	.130	.421
Sex	T_0	Female:male	.587	.983	.694	<.001
Smoking status[d]	T_0	Never:quit:current	.021	.448	.102 (.034)[c]	.899
Ethnicity	T_6	Other:white	.451	.599	.476	.294
Marital status	T_6	Married:other	.872	.293	.865	.245
Reconstruction type	T_0	Revision:primary	<.001	.008	<.001	.038
Anterior cruciate ligament graft type	T_0	Allograft:autograft	.008	.021	.014	.405
"Pop" heard at time of injury	T_0	No:yes	.729	.745	.503	.866
Medial collateral ligament injury[e]	T_0	Yes:no	.668	.136	.962	.899
Lateral collateral ligament injury[e]	T_0	Yes:no	.818	.723	.993	.454
Medial compartment chondrosis[f]	T_0	Yes:no	.399	.550	.938	.226
Anterior compartment chondrosis[f]	T_0	Yes:no	.858	.334	.911	.548
Lateral compartment chondrosis[f]	T_0	Yes:no	.718	.678	.395	.710
Medial meniscus status	T_0	Normal to no treatment of tear, repair, and excision	.742	.713	.714	.145
Lateral meniscus status	T_0	Normal to no treatment of tear, repair, and excision	.127	.017	.027	.144

[a]T_0, baseline; T_6, 6-year follow-up.
[b]For IKDC, $KOOS_{sports/rec}$, $KOOS_{krqol}$, and Marx outcome instruments. IKDC, International Knee Documentation Committee questionnaire; $KOOS_{sports/rec}$ and $KOOS_{krqol}$, Knee injury and Osteoarthritis Outcome Score, Sports and Recreation subscale and Knee Related Quality of Life subscale; Marx, Marx Activity Scale.
[c]If there were a difference in the P value when the models were repeated using T_6 instead of T_0 body mass index and smoking status, it is denoted in parentheses. Only 2 variables changed from slightly above .05 to slightly below, or vice versa.
[d]Comparison of never smoked, quit smoking, currently smokes.
[e]*Yes* is defined as grade I or II only.
[f]*Yes* is any chondromalacia of grades II, III, or IV.

DISCUSSION

This is the most comprehensive multivariable analysis of a prospective multicenter cohort of sufficient size and rate of follow-up to demonstrate that variables measured at the time of ACLR (revision ACLR, allograft, lateral meniscus status, BMI, smoking status) are predictors of 6-year sports activity and function as measured by the IKDC, KOOS, and Marx outcome instruments. Each predictor (variable) is modifiable except for revision ACLR. Thus, avoiding allograft as a graft choice, leaving "stable" partial and complete lateral meniscal tears alone, not smoking, and maintaining a relatively lower BMI could improve ACLR outcomes. In contrast to the modifiable predictors for IKDC and KOOS, the predictors of declining Marx activity (revision ACLR and female sex) are not modifiable. However, despite the decline in activity level, the population medians of the cohort remain at the same 2-year levels of the IKDC and KOOS subscales.

The maintenance of IKDC and KOOS outcomes at 6 years was an unexpected result. We anticipated a decline from the 2-year outcomes in all 3 scales, which were clearly not observed. These results indicate that our present technique of ACLR is durable at the 6-year mark. The potential role of declining Marx activity level to reducing knee-related stress and therefore preserving joint health, as would be measured in the future by IKDC and KOOS, is unknown. Although it may take more time before decline of knee function is observed in this cohort, the similar group score at 2 and 6 years for the validated, patient-reported outcomes provides a good prognosis to be conveyed to our patients preoperatively.

A comprehensive systematic review by Oiestad et al[34] evaluated knee osteoarthritis (OA) after ACLR and found that concomitant meniscal tears were associated with radiographic OA using univariate analysis. Unfortunately, the authors were unable to perform a meta-analysis because of the heterogeneous classification systems defining OA, the lack of interrater agreement, and the lack of multivariable analysis.[34] They concluded that future studies that define the prognosis and predictors of OA after ACLR should be prospective with clearly defined aims and endpoints, include clear inclusion and exclusion criteria, and use a common radiographic classification system with reliability data and independent blinded examiners; furthermore, the rehabilitation protocol should be reported, and regression analysis should be used to evaluate risk factors.[34] We believe that the majority of these points characterize the current cohort. The strengths of this study include the application of a multicenter

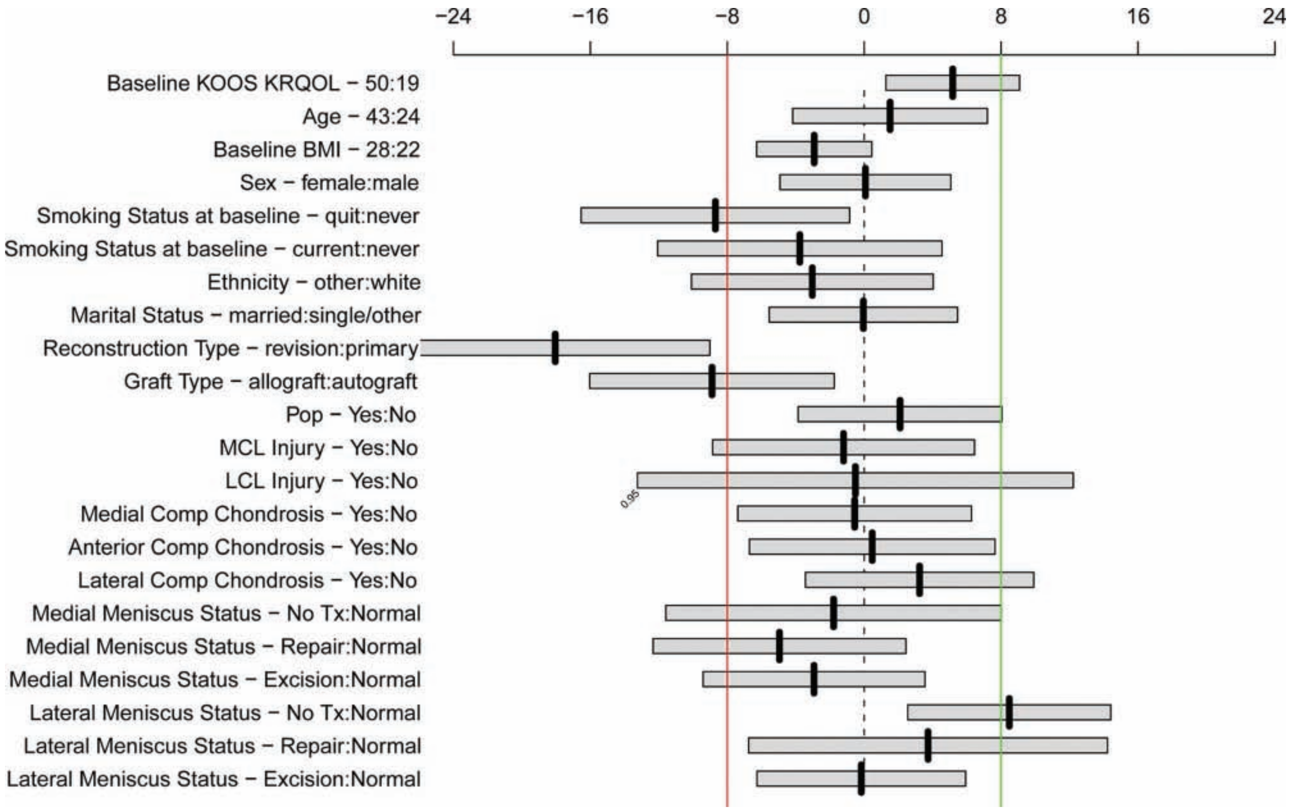

Figure 2. Knee injury and Osteoarthritis Outcome Score: Knee Related Quality of Life ($KOOS_{krqol}$)—results of potential predictor variables (mean ± 95% confidence interval). For each potential predictor variable listed and the comparison, the change is shown, either positive (better outcome) or negative (worse outcome). A result is statistically significant if the 95% confidence interval does not cross the zero line. A result is thought to be clinically meaningful if the mean is outside the red and green lines. These lines represent the positive (green) and negative (red) clinically meaningful differences based on development of outcome instruments. BMI, body mass index; MCL, medial collateral ligament; LCL, lateral collateral ligament; Comp, compartment; Tx, treatment.

prospective longitudinal assessment using the same validated outcome measures over time and accruing greater than 85% follow-up, which is the preferred research design (level 1) to evaluate prognosis and modifiable predictors through multivariable analysis.[34] In clinical practice, patients have many combinations of potential predictors that can be independently scaled and then summed to yield a patient-specific result. This result can be obtained through use of an equation where individual values are entered or through the use of a nomogram. Patients present with an almost-infinite combination of these variables, and an individual's specific outcome can now be estimated. Alternatively, a surgeon can avoid allograft ACLR, counsel patients on smoking cessation and maintaining healthy weight, and leave stable lateral meniscal tears alone in an effort to improve the outcomes of his or her patients. The multicenter nature of this consortium lends the results to be generalizable to patients treated by fellowship-trained sports medicine physicians.

There are several weaknesses in this analysis. Despite being the largest prospective cohort using multivariable analysis for ACLR outcomes, our sample size is still too small to provide a more detailed analysis of the injuries involving the articular cartilage and meniscus. Because of the relatively low frequency of chondromalacia grades II, III, and IV, these are grouped in the current analysis. Ideally, as additional patients are prospectively enrolled and evaluated at 6 years, our modeling can be divided into more clinically applicable chondromalacia grades (II vs III vs IV). Previous interrater agreement[27] has shown our ability to divide by individual grade. Likewise, all meniscus excisions are currently grouped instead of stratified by one-third, two-thirds, or whole, which would have greater clinical meaning. Another weakness is the lack of important complementary information gathered by clinician observation and testing of knee joint laxity, physical characteristics, and radiologic images of the ACLR knee. The logistic and financial requirements of on-site follow-up impede performing sufficiently powered multivariable analysis on equally important patient-reported outcomes (eg, sports function, knee quality of life, and activity level) specifically designed to follow much larger cohorts. However, information regarding the principal outcomes that influence a surgeon's and a patient's decision

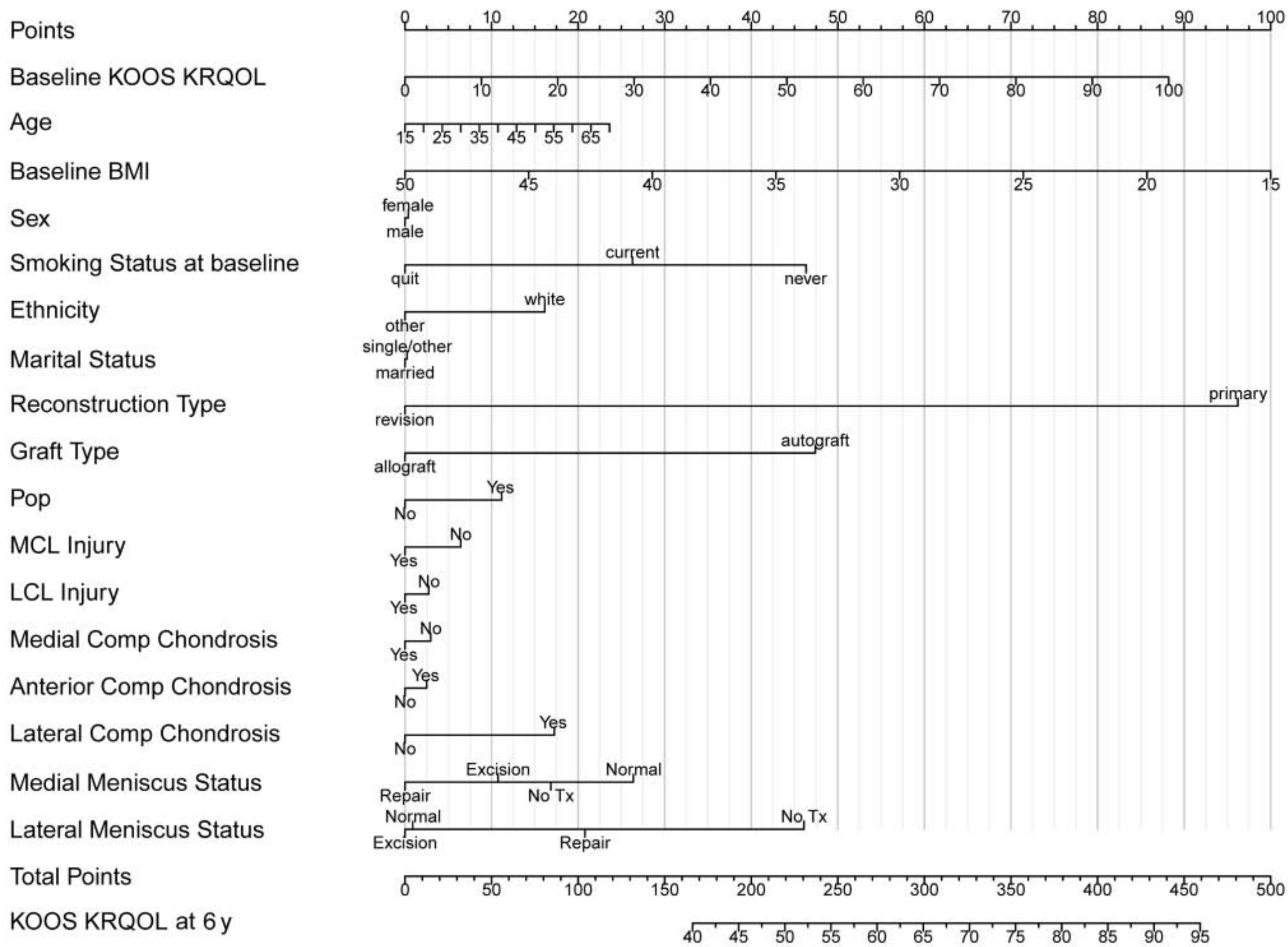

Figure 3. Knee injury and Osteoarthritis Outcome Score: Knee Related Quality of Life ($KOOS_{krqol}$)—patient-specific results at 6 years. The nomogram is used to predict a patient-specific outcome score at 6 years based on summing the individual point total for each variable on the left. For each variable, the patient's result is indicated, and the points based on the top scale are recorded. Then, the sum of the points is placed on the total points line on the bottom. After the total points are marked, the predicted outcome score at 6 years is read below. BMI, body mass index; MCL, medial collateral ligament; LCL, lateral collateral ligament; Comp, compartment; Tx, treatment.

making—clinical failure, restoration of functional stability, activity level and sports participation or function, pain, reoperation, and function in activities of daily living—can be gathered through the use of validated questionnaires and patient interview.

Several prospective and retrospective studies have explored predictors or risk factors for ACLR through a variety of statistical methods. Recently, a randomized controlled trial at 10-year follow-up showed no difference between autograft hamstring and patellar tendon in clinical assessment (laxity, hop, isokinetic strength), radiographic OA, or patient-reported outcomes (Cincinnati and Lysholm).[11] Likewise, a randomized controlled trial between neuromuscular versus traditional strength rehabilitation did not demonstrate a difference for Cincinnati or Lysholm at 2 years.[39] Similarly, several studies failed to demonstrate a correlation between clinical assessments and validated patient-reported outcomes (KOOS, SF-36, IKDC).[21,23,33,49] However, 2 studies found that several clinical assessments significantly predicted ACLR outcome.[38,51] Decreased range of motion in knee extension, meniscectomy, presence of articular cartilage damage, and time from injury to surgery all led to significantly worse IKDC outcomes and radiologic OA.[51] However, a 7- to 10-year longitudinal cohort study on both patellar tendon and hamstring tendon ACLR did not find extension range of motion as a risk factor for radiologic OA.[38,41] However, they did observe that patients undergoing a patellar tendon autograft ACLR had more radiologic OA. Like our study, several prior studies have demonstrated that BMI and smoking are risk factors for patient-reported outcomes.[17,22,52] Likewise, age and sex were not risk factors for patient-reported outcomes.[33,41] In our multivariable analysis, education level, prior meniscectomy, and medial meniscus status were not risk factors, as shown by others.[6,22,23,49,52,54] In addition, other factors not explored in our model that have been shown to be risk factors include preoperative quadriceps strength,[6] knee self-efficacy scale,[53] pivot shift,[21] and patient satisfaction.[20] We believe that our study was underpowered to test the effect of meniscal and/or articular injury and treatment with a single year's cohort. When a second year is followed, we expect adequate sample size to evaluate.

The multivariable analysis most similar to ours found a pop at injury (KOOS, IKDC, Lysholm), no change in educational level (KOOS and IKDC), and weight gain greater than 15 pounds (IKDC) to be predictors of its outcomes.[52] Our analysis found high baseline BMI to be predictive of poorer IKDC and $KOOS_{sports/rec}$ scores. However, just as in the prior study, the individual differences in outcome were below a clinically meaningful difference for each measure. We did not find a pop heard at the time of injury to be significant in any outcome. The prior study did not evaluate smoking, allograft, or revisions, and the current study did not evaluate education level. However, both studies found that age and sex were not related to outcomes.

The major role that revision versus primary ACLR has on every outcome measure clearly supports the role of additional research aimed at understanding and improving outcomes after revision ACLR. Thus, the importance of a multicenter study of revision ACLR is once again confirmed. Multivariable analysis of a large group of revision ACLRs will be necessary to determine the predictors in revision surgery for these poor outcomes. Because revision ACLR has such a large negative effect on outcome, even when controlling through multivariable analysis for articular cartilage and meniscus injuries and treatment, every effort should be made for secondary prevention of ACLR graft tear.

In conclusion, our MOON results revealed that choosing an autograft would significantly, and in a clinically meaningful way, improve sports function (IKDC, $KOOS_{sports/rec}$) and knee-related quality of life ($KOOS_{krqol}$), whereas not smoking is associated with better IKDC and $KOOS_{krqol}$ scores, and a lower BMI is predictive of better IKDC and $KOOS_{sports/rec}$ scores. The actual improvement in outcomes can be predicted for each outcome by use of the nomograms. Unfortunately, no modifiable predictors were identified for the declining Marx Activity Scale. Because revision ACLR has the most powerful negative effect on outcome, secondary prevention strategies should be explored and tested.

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