Preoperative Risk Factors for Subsequent Ipsilateral ACL Revision Surgery After an ACL Restoration Procedure

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Background: Anterior cruciate ligament (ACL) revision surgery is challenging for both patients and surgeons. Understanding the risk factors for failure after bridge-enhanced ACL restoration (BEAR) may help with patient selection for ACL restoration versus ACL reconstruction.

Purpose: To identify the preoperative risk factors for ACL revision surgery within the first 2 years after BEAR.

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

Methods: Data from the prospective BEAR I, II, and III trials were used to determine the preoperative risk factors for ACL revision surgery. All patients with a complete ACL tear (aged 13-47 years, depending on the trial), who met all other inclusion/exclusion criteria and underwent a primary BEAR procedure within 30 to 50 days from the injury (dependent on the trial), were included. Demographic data (age, sex, body mass index), baseline patient-reported outcomes (International Knee Documentation Committee [IKDC] subjective score, Marx activity score), preoperative imaging results (ACL stump length, notch size, tibial slope), and intraoperative findings (knee hyperextension, meniscal status) were evaluated to determine their contribution to the risk of ipsilateral ACL revision surgery.

Results: A total of 123 patients, with a median age of 17.6 years (interquartile range, 16-23 years), including 67 (54%) female patients, met study criteria. Overall, 18 (15%) patients required ACL revision surgery in the first 2 years after the BEAR procedure. On bivariate analyses, younger age (P = .011), having a contact injury at the time of the initial tear (P = .048), and increased medial tibial slope (MTS; P = .029) were associated with a higher risk of ipsilateral revision surgery. Multivariable logistic regression analyses identified 2 independent predictors of revision: patient age and MTS. The odds of ipsilateral revision surgery were decreased by 32% for each 1-year increase in age (odds ratio, 0.684 [95% CI, 0.517-0.905]; P = .008) and increased by 28% for each 1° increase in MTS (odds ratio, 1.280 [95% CI, 1.024-1.601]; P = .030). Sex, baseline IKDC or Marx score, knee hyperextension, and meniscal status were not significant predictors of revision.

Conclusion: Younger age and higher MTS were predictors of ipsilateral ACL revision surgery after the BEAR procedure. Younger patients with higher tibial slopes should be aware of the increased risk for revision surgery when deciding to undergo ACL restoration.

Keywords: anterior cruciate ligament (ACL); ACL restoration; outcomes; failure; retear; revision surgery

Anterior cruciate ligament (ACL) injuries are common, particularly in the high school athletic population. ACL reconstruction (ACLR) with autografts has become the widely accepted treatment for these patients; however, graft failure rates have been reported to range from about 10% to 25%.[3,4,8,10,33] Repair of the ACL in this population has also been found to have a failure rate as high as 49%.[7] Bridge-enhanced ACL restoration (BEAR) is a procedure in which the environment surrounding the injured ACL is augmented with the placement of an extracellular matrix–based implant at the repair site. The repaired ACL, with the implant saturated with the patient's blood to stimulate healing,[22] has been shown to be restored to its previous cross-sectional area and orientation.[15] In addition, the BEAR procedure does not require graft harvest, thereby avoiding donor-site morbidity, and does not disrupt the native ACL insertion sites. A recent blinded randomized controlled trial has demonstrated similar efficacy of this procedure compared with ACLR with autografts in terms of patient-reported outcomes and instrumented knee laxity out to 2 years and has reported a failure rate of 14% in young patients.[22]

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Multiple risk factors for a retear of a reconstructed ACL have been previously identified, including younger age,[14] higher baseline Marx activity score,[14] preoperative knee hyperextension greater than 5°,[18] and higher posterior tibial slope.[1,28,32] These risk factors have yet to be analyzed in patients undergoing the BEAR procedure.

The primary objective of this study was to identify the preoperative risk factors associated with ACL failure requiring revision surgery within the first 2 years after the BEAR procedure. The identification of risk factors would facilitate data-driven conversations between patients and surgeons when selecting a surgical procedure. We hypothesized that previously identified risk factors for revision surgery after ACLR, such as age, baseline activity level, preoperative knee hyperextension, and posterior tibial slope, would be significant risk factors for a reinjury and revision surgery after BEAR.

METHODS

Patient Population

After institutional review board approval, we reviewed all patients prospectively enrolled in the BEAR I (NCT02292004, IRB-P00012985), BEAR II (NCT02664545, IRB-P00021470), and BEAR III (NCT03348995, IRB-P00026162) trials between February 2015 and January 2019. Previous institutional review board approval was obtained from the relevant institutions (Boston Children's Hospital for all 3 trials and Rhode Island Hospital for the BEAR III trial) before each trial's initiation, and all patients provided written informed consent before data collection. BEAR I was a nonrandomized controlled cohort study with 10 patients in the BEAR arm,[23] BEAR II was a randomized controlled trial with 65 patients in the BEAR arm,[22] and BEAR III was a prospective multicenter cohort study with 49 patients in the BEAR arm. Eligibility criteria were similar between trials; however, the inclusion criteria were expanded from BEAR I to BEAR III (Table 1) to increase generalizability. Patients were excluded if they had a history of ipsilateral knee surgery, previous knee infections, or risk factors that could adversely affect ligament healing (nicotine/tobacco use, corticosteroid use in the past 6 months [BEAR I and II] or 3 months [BEAR III], chemotherapy, diabetes, inflammatory arthritis). For the BEAR I and BEAR III trials, all 59 patients were included. One patient in the BEAR II trial was unable to be contacted and was excluded from the analysis, leaving a total of 123 patients in this study.

The following data were collected preoperatively for all patients: sex, race, age, body mass index (BMI), contact versus noncontact injury, participation in a level I sport, International Knee Documentation Committee (IKDC) subjective score,[12] Marx activity score,[19] time from the injury to surgery, pivot-shift grade on the operative knee, hyperextension of the operative knee, presence of a medial or lateral meniscal tear at surgery, and magnetic resonance imaging (MRI) measurements. Level I sports were those that involved jumping, pivoting, and hard cutting and included football, soccer, basketball, field hockey, rugby, volleyball, lacrosse, and ultimate frisbee. The dichotomous outcome of interest was a reinjury requiring revision surgery before the 2-year follow-up visit.

Preoperative MRI Measurements

Preoperative MRI was used to measure tibial stump length as a percentage of the total ACL length, anterior notch

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TABLE 1
Eligibility Criteria[a]

	BEAR I	BEAR II	BEAR III
Age, y	18-35	13-35	12-80
ACL tear	Complete	Complete	Complete or partial with positive pivot shift
Time from injury to surgery, d	≤35	≤45	≤50
Medial collateral ligament injuries	Grade I or II may be included	Grade I or II may be included	All included
Meniscal injuries	No displaced bucket-handle injuries	No displaced bucket-handle injuries	All included

[a]ACL, anterior cruciate ligament; BEAR, bridge-enhanced ACL restoration.

width, posterior notch width, medial tibial slope (MTS), and lateral tibial slope (LTS) (Appendix Figure A1, available in the online version of this article). Measurements were made based on established techniques,[15,24] by an experienced member of the team (A.M.K.), using a commercially available image viewer (OsiriX Viewer Version 8.5; Pixmeo). Tibial stump length was defined as the linear distance from the center of the ACL tibial insertion to the most superior fibers of the tibial remnant.[15] The stump length was then normalized to the ACL length, measured as the linear distance between the center of the femoral and tibial insertions on the same MRI scan obtained from the ACL-injured knee.[2] ACL and stump lengths were measured on a sagittal slice with complete coverage of the ACL. Anterior notch width was measured parallel to a line along the most inferior aspects of the femoral condyles on an axial slice corresponding to the front of the notch.[15] Posterior notch width was measured parallel to a line along the most inferior aspects of the femoral condyles on a coronal slice corresponding to the back of the notch.[24] For both measurements, notch width was measured at multiple spots from the middle to the bottom of the notch, and the maximum value was used as the notch width.[26] MTS and LTS were measured on a sagittal slice at the center of the medial and lateral plateaus as the angle between a line that joined the peak points on the anterior and posterior rims of the plateau and a line perpendicular to the longitudinal axis of the tibia.[9,11]

Surgical Procedure

A schematic of the BEAR procedure is shown in Figure 1 (arthroscopic views of the procedure are shown in Appendix Figure A2, available online). After the induction of general anesthesia, an examination was performed to verify a positive pivot shift on the injured side and to record the Lachman test, range of motion, and pivot-shift test results of both knees. A tourniquet was then applied to the surgical limb. Knee arthroscopic surgery was performed, and any meniscal injuries were treated if present. A tibial aimer (ACUFEX Director Drill Guide; Smith & Nephew) was used to place a 2.4-mm guide pin through the tibia and the tibial footprint of the ACL. The pin was overdrilled with a 4.5-mm reamer (Endoscopic Drill; Smith & Nephew). Notchplasty was performed using a combination

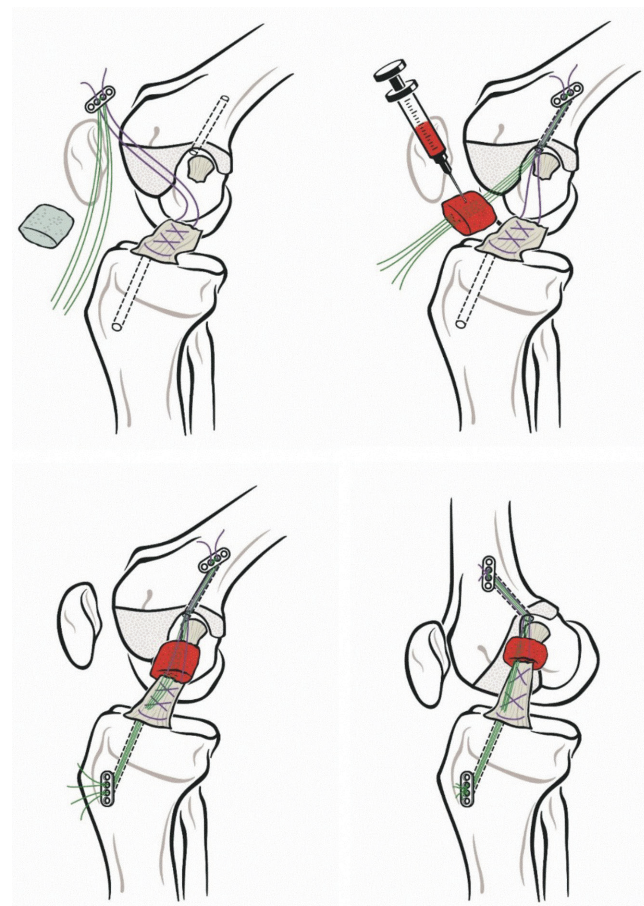

Figure 1. Schematic of the technique used to place the bridge-enhanced ACL restoration (BEAR) implant. Upper left: a suture (purple) is placed through the tibial stump using a whipstitch and secured with 2 free sutures (green) to an extracortical button. Upper right: after a cortical button carrying free sutures (green) is passed up through the femoral tunnel, the BEAR implant is loaded onto the free sutures (green) and soaked with up to 10 mL of autologous blood. Lower left: the free suture ends (green) at the tibial end of the BEAR implant (which was positioned between the 2 ends of the torn ACL) are passed through the tibial tunnel to be tied over a second extracortical button. Lower right: the sutures and extracortical buttons are secured. (From Murray et al.[22])

of a shaver and curette to facilitate visualization of the femoral footprint. A guide pin was then placed in the femoral ACL footprint, drilled through the femur, and then overdrilled with the 4.5-mm reamer. Next, a 4-cm arthrotomy was performed at the medial border of the patellar tendon, and a whipstitch of No. 2 absorbable braided suture (Vicryl; Ethicon) was placed into the tibial stump of the torn ACL. In some cases, these sutures were placed arthroscopically before performing arthrotomy. Once the sutures were placed into the ACL, 2 No. 2 nonabsorbable braided sutures (Ethibond; Ethicon) were looped through the 2 center holes of a cortical button (Endobutton; Smith & Nephew). The free ends of a No. 2 absorbable braided suture from the tibial stump were passed through the cortical button, which was then passed through the femoral tunnel and engaged on the lateral femoral cortex. Both looped No. 2 nonabsorbable braided sutures (4 matched ends) were passed through the BEAR implant (Boston Children's Hospital), which was manufactured from bovine connective tissue as previously described.[22] Then, 10 mL of autologous blood obtained from the antecubital vein was added to the implant. The implant was passed up along the sutures into the femoral notch, and the nonabsorbable braided sutures were passed through the tibial tunnel and tied over a second cortical button on the anterior tibial cortex with the knee in full extension. The remaining pair of suture ends coming through the femur was tied over the femoral cortical button to bring the ACL stump into the implant using an arthroscopic surgeon's knot and knot pusher. The arthrotomy site was closed in layers and the tourniquet deflated. Sterile dressing, followed by a cold therapy unit (Polar Care; Breg) and a locking hinge knee brace (T Scope; Breg), was applied. No surgical drain was used.

Postoperative Rehabilitation and Return to Sport

The physical therapy protocols for the BEAR I and BEAR II trials[22,23] were adapted from the Multicenter Orthopaedic Outcomes Network (MOON) recommendations for ACLR.[35] Changes to the MOON protocol include the use of a locking hinge brace (T Scope), which was set to limit knee flexion from 0° to 50° for 2 weeks and then from 0° to 90° for an additional 4 weeks. Partial weightbearing was permitted within the first 2 weeks and then weightbearing as tolerated with crutches until 4 weeks postoperatively. The use of a functional ACL brace (CTi brace; Ossur) was encouraged from 6 to 12 weeks postoperatively and for 2 years when participating in cutting and pivoting sports. Running was allowed at 3 months, and a graded return-to-sport strategy was initiated at 6 months.

For the BEAR III trial, modifications were made to the rehabilitation protocol. The locking hinge brace limited flexion from 0° to 30° for 2 weeks, from 0° to 60° for 2 to 4 weeks, and from 0° to 90° for 4 to 6 weeks. Partial weightbearing with crutches was permitted for the first 6 weeks and then weightbearing as tolerated after 6 weeks. Running was allowed at 4 months, and a graded return-to-sport strategy was initiated at 8 to 9 months postoperatively.

ACL Failure

Failure was defined as the need for revision surgery. If a patient sustained a reinjury to the knee when he or she returned to sport (with or without clearance), a clinical examination was performed to assess knee stability and ACL integrity (ie, Lachman or pivot shift), and MRI was performed to evaluate ACL failure. Clinical failure on examination was confirmed with an MRI scan read by a pediatric musculoskeletal radiologist (K.E.) with expertise in reading MRI scans after the BEAR procedure. The patient was then scheduled for revision surgery.

Patient Follow-up

Patients returned for a follow-up visit at 2 years after surgery. Patients who were unable to attend the follow-up in person were contacted by a telemedicine chat, telephone call, or email to determine if they had any subsequent knee injury or surgery on either knee after the index BEAR procedure. The study cohort, which was formed from the 3 trials, is summarized in a STROBE diagram in Figure 2.

Statistical Analysis

Logistic regression analyses were used to identify baseline characteristics that were risk factors for patients undergoing ACL revision surgery before their 2-year assessment. First, unadjusted odds ratios were estimated for each baseline variable using univariable logistic regression (ie, 1 predictor at a time). Next, a multivariable logistic regression model was constructed based on a backward elimination process using the criterion of $P < .05$ for inclusion to determine the set of independent predictors of revision and their associated adjusted odds ratios. To limit the number of potential predictors, only variables with $P < .20$ for their bivariate relationship with revision were considered as candidates for the multivariable model. Because listwise deletion of cases has the potential to adversely affect the sample size used for multivariable regression models, multiple imputation was used (n = 5 iterations) to include all cases in these analyses.[34] All analyses were conducted using statistical software (SAS Version 9.4; SAS Institute) with statistical significance based on $P < .05$. With 123 total patients and 18 revision cases, the current study has an estimated power of 82%, using $\alpha = .05$ (two-sided) to detect doubling of the risk of revision (ie, 15% vs 30%) for a 1-SD change from the mean for each risk factor. This corresponds to an odds ratio of 2.43.

RESULTS

Patient Characteristics

A total of 123 patients (54% female) underwent the BEAR procedure and attended the 2-year follow-up visit across the 3 BEAR trials (99% of all enrolled patients) (Table 2).

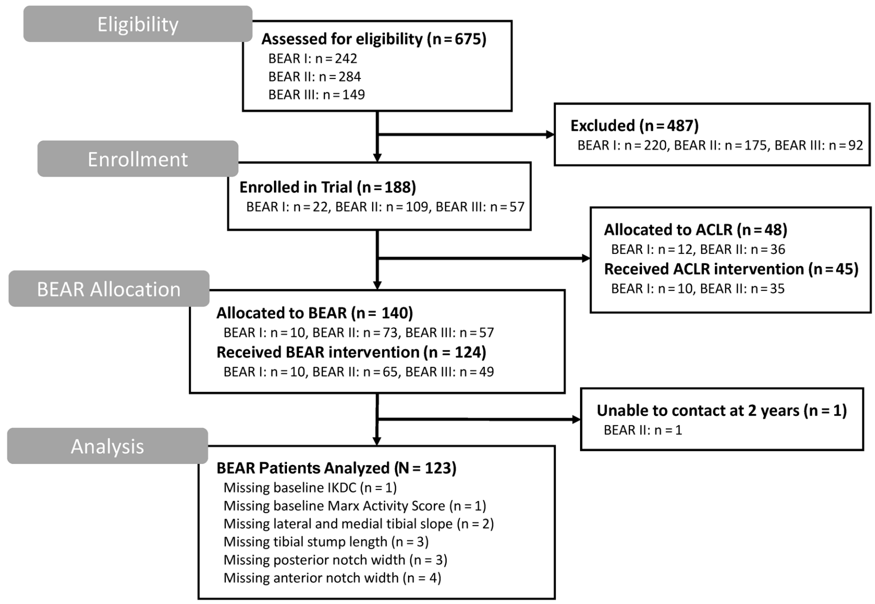

Figure 2. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) diagram detailing the flow of patients through the analysis. ACLR, anterior cruciate ligament reconstruction; BEAR, bridge-enhanced ACL restoration; IKDC, International Knee Documentation Committee.

The breakdown of baseline characteristics for those undergoing and not undergoing ACL revision surgery is provided in Appendix Table A1 (available online).

Unadjusted Odds Ratios for Baseline Variables Predicting Revision

Baseline risk factors that might contribute to ACL revision surgery by 2 years were examined using univariable logistic regression to obtain unadjusted odds ratios (Table 3). Factors associated with an increased risk of ACL revision surgery were younger age (P = .011), contact injury (P = .048), and increased MTS (P = .029). A 1-year increase in age corresponded to a 28% decrease in the odds of ACL revision surgery. Figure 3 displays observed revision surgery rates for different age groups based on approximate quartiles as cut points. It is worth noting that there were no revision surgery cases in patients aged $\geq$20 years. Patients who sustained their initial ACL tear as a contact injury had an almost 3-fold higher risk of undergoing ACL revision surgery. Additionally, each degree increase in MTS was associated with a 25% increase in the odds of revision (95% CI, 1.024-1.536). Lower BMI, decreased tibial stump length, decreased anterior notch width, and increased LTS were marginally associated with increased odds of revision ($P < .10$ for all).

Adjusted Odds Ratios for Baseline Variables Predicting Revision

Multivariable logistic regression identified 2 baseline factors, age and MTS, as predictors of revision surgery after the BEAR procedure (Table 4). The odds of revision by 2 years were decreased by 32% for each 1-year increase in

TABLE 2
Baseline Patient Characteristics[a]

	Value (N = 123)
Female sex	67 (54)
White (non-Hispanic) race	98 (80)
Age, median (IQR), y	17.6 (16-23)
BMI, kg/m^2	23.9 ± 3.4
Weight, kg	70.2 ± 14.3
Contact injury	31 (25)
Level I sport	87 (71)
IKDC subjective score (n = 122)	46.6 ± 14.9
Marx score (n = 122), median (IQR)	16 (13-16)
Time from injury to surgery, d	34.8 ± 9.1
Pivot-shift grade	
0	1 (1)
1	27 (22)
2	82 (67)
3	13 (10)
Hyperextension (≥5°)	31 (25)
Medial meniscal tear	15 (12)
Lateral meniscal tear	40 (33)
Tibial stump length (n = 120), %	54.2 ± 11.3
Anterior notch width (n = 119), mm	18.9 ± 2.3
Posterior notch width (n = 120), mm	18.4 ± 2.3
LTS (n = 121), deg	6.4 ± 2.8
MTS (n = 121), deg	5.3 ± 2.5
Revision by 2 y	18 (15)

[a]Data are shown as mean ± SD or n (%) unless otherwise indicated. BMI, body mass index; IKDC, International Knee Documentation Committee; IQR, interquartile range; LTS, lateral tibial slope; MTS, medial tibial slope.

TABLE 3
Unadjusted Odds Ratios Associated With Revision by 2 Years[a]

	Odds Ratio	95% CI	*P* Value
Female sex	1.375	0.495-3.822	.541
Age	0.717	0.555-0.926	.011
BMI	0.843	0.699-1.018	.075
Contact injury	2.852	1.010-8.056	.048
Level I sport	1.089	0.358-3.316	.881
IKDC subjective score (per 10-unit increase)	0.932	0.665-1.318	.699
Marx score	1.024	0.881-1.190	.759
Time from injury to surgery (per week increase)	0.820	0.562-1.196	.304
Pivot-shift grade			.460
0 or 1[b]	1.000		
2	2.676	0.569-12.590	
3	2.363	0.294-18.970	
Hyperextension (≥5°)	2.148	0.751-6.146	.154
Medial meniscal tear	1.550	0.391-6.147	.533
Lateral meniscal tear	1.825	0.659-5.053	.247
Tibial stump length (per 10% increase)	0.638	0.411-1.000	.051
Anterior notch width	0.805	0.629-1.030	.084
Posterior notch width	0.840	0.674-1.046	.120
LTS	1.177	0.976-1.420	.088
MTS	1.254	1.024-1.536	.029

[a]BMI, body mass index; IKDC, International Knee Documentation Committee; LTS, lateral tibial slope; MTS, medial tibial slope.
[b]One patient had a pivot-shift grade of 0.

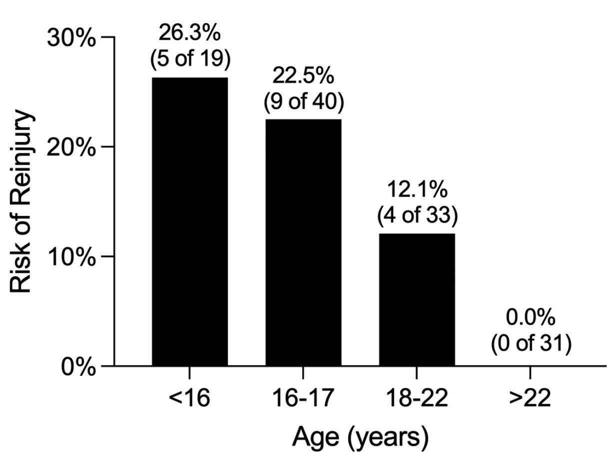

Figure 3. Observed revision surgery rates broken down by age.

TABLE 4
Adjusted Odds Ratios Associated With Revision by 2 Years[a]

	Odds Ratio	95% CI	*P* Value
Age	0.684	0.517-0.905	**.008**
MTS	1.280	1.024-1.601	**.030**

[a]MTS, medial tibial slope. Bolded values represent p<.05.

age and increased by 28% for each 1° increase in MTS. It is worth noting that there were no revision surgery cases in patients aged ≥20 years.

DISCUSSION

Understanding the risk factors for ligament or graft failure after ACL surgery is crucial to support physician-patient discussions about surgical treatment options. In the present study, univariable logistic regression identified 3 factors that were significantly associated with an increased risk for ACL revision surgery after the BEAR procedure: younger age, higher MTS, and contact injury. Lower BMI, decreased tibial stump length, decreased anterior notch width, and increased LTS were marginally associated with increased odds of revision ($P < .10$). Sex, level I sport, Marx activity score, IKDC subjective score, and presence of a meniscal tear were not associated with the risk of a second ipsilateral revision procedure within 2 years of BEAR. Using a multivariable logistic regression model, both age and MTS were significant independent predictors.

The finding that younger age was predictive for ACL revision surgery within 2 years is consistent with findings in the ACLR literature, in which younger age has been found to be predictive of revision ACLR.[13,14] Revision rates in adolescents after ACLR are reported to range from 10% to 25%.[3,4,8,10,33] We found that patients who underwent the BEAR procedure who were younger than 16 years had a revision surgery rate of 27.3% and that those aged between 16 and 17 years had a revision surgery rate of 18.6%. No revision surgery was performed in patients aged ≥20 years. These findings in the younger ACL restoration population are surprising, as animal studies have demonstrated that ACL cells in juvenile and adolescent animals have improved proliferation and migration abilities,[20,21] an increased number of growth factor receptors,[31] increased responsiveness to platelet concentrates,[16] and superior ACL healing compared with adult animals.[25] We believe that age may be a surrogate for activity level and that increased exposure to cutting and pivoting activities for the younger high school athlete may play a role in the increased reinjury rates observed in that age group. Another possibility is that synovial fluid (containing plasmin and plasminogen) may reconstitute faster in younger patients. Even though blood clots are stabilized by the implant, a quicker formation of normal levels of synovial fluid may affect the ability of the implant to protect the clot that has formed at the repair area. Future studies are needed to clarify the role of these factors.

The association of increased MTS with an increased risk of revision surgery is also consistent with that noted in the ACLR literature, in which posterior tibial slope (ie, MTS and LTS) has been reported to be predictive of revision surgery.[27,29,30,32] A recent study has demonstrated that adolescent age combined with a posterior tibial slope of over 12° resulted in a 78% failure rate by 20 years after ACLR.[28] Thus, in the context of our findings, younger patients with higher tibial slopes should be counseled about the increased risk for revision surgery before undergoing ACL restoration or ACLR. The acceptable threshold for the MTS remains to be determined. Nonetheless, surgical techniques that might decrease this risk, such as tibial osteotomy to correct the tibial slope or lateral extra-articular tenodesis (LET), could potentially be successful, although clinical studies are required to demonstrate this.

Recent literature has shown that the addition of LET to ACLR with hamstring tendon autografts decreased the odds of a retear by up to 60%.[6,8] The addition of LET has also been shown to decrease forces on the ACL graft.[5,17] By decreasing forces on the ACL in the postoperative period, this technique may provide protection for younger patients undergoing the BEAR procedure. Future studies could explore combining the BEAR procedure with LET, or other anterolateral procedures, to determine if they would decrease the odds of revision surgery in the younger population or in patients with higher tibial slopes.

This study has several limitations. While the postoperative rehabilitation protocol and return-to-sport criteria were defined for the trials, patient compliance was not documented. Also, the rehabilitation and return-to-sport timelines for the BEAR I and BEAR II trials were different from those of BEAR III. Unfortunately, the sample size was not large enough to compare failure rates between trials; however, they appear to have remained consistent between the BEAR II and BEAR III trials. Furthermore, we did not document daily or weekly activity levels for each patient. Thus, it is possible that the differences in rehabilitation, return to sport, and activity level could have influenced the results. These topics are areas that would benefit from future research. In addition, while the number of patients lost to follow-up was exceedingly low (n = 1), the study only included 123 patients; a relatively small sample size limits statistical power to detect more subtle predictors. Thus, the influence of other variables with smaller effect sizes (eg, knee hyperextension, presence of a meniscal tear, BMI) cannot be ruled out. However, the finding that younger age and MTS were associated with the need for revision surgery is clinically valuable. Another limitation is that multiligamentous injuries were included in the BEAR III trial but not in BEAR I or BEAR II. However, this should not affect the current analysis, as only 3 patients in the BEAR III trial had a concomitant medial collateral ligament injury. None of these concomitant medial collateral ligament injuries required repair or reconstruction at the time of ACL surgery. Obtaining data from a larger cohort may identify more variables that are predictors of risk. Finally, while our results were compared with ACLR outcomes reported in the literature, this study did not include an ACLR control group for direct comparison. Nonetheless, it is important to note that previous studies evaluating ACLR outcomes have shown that age and tibial slope are predictors of revision.[27,29,30,32]

In conclusion, younger age and higher MTS were associated with increased odds of ipsilateral ACL revision surgery after the BEAR procedure. Therefore, younger patients with higher tibial slopes should be advised about the increased risk for revision surgery when choosing a surgical intervention.

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