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Effect of Graft Choice on the Outcome of Revision Anterior Cruciate Ligament Reconstruction in the Multicenter ACL Revision Study (MARS) Cohort

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Background: Most surgeons believe that graft choice for anterior cruciate ligament (ACL) reconstruction is an important factor related to outcome; however, graft choice for revision may be limited due to previously used grafts.

Hypotheses: Autograft use would result in increased sports function, increased activity level, and decreased osteoarthritis symptoms (as measured by validated patient-reported outcome instruments). Autograft use would result in decreased graft failure and reoperation rate 2 years after revision ACL reconstruction.

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

Methods: Patients undergoing revision ACL reconstruction were identified and prospectively enrolled by 83 surgeons at 52 sites. Data collected included baseline demographics, surgical technique, pathologic abnormalities, and the results of a series of validated, patient-reported outcome instruments (International Knee Documentation Committee [IKDC], Knee injury and Osteoarthritis Outcome Score [KOOS], Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC], and Marx activity rating score). Patients were followed up at 2 years and asked to complete the identical set of outcome instruments. Incidences of additional surgery and reoperation due to graft failure were also recorded. Multivariate regression models were used to determine the predictors (risk factors) of IKDC, KOOS, WOMAC, Marx scores, graft rerupture, and reoperation rate at 2 years after revision surgery.

Results: A total of 1205 patients (697 [58%] males) were enrolled. The median age was 26 years. In 88% of patients, this was their first revision, and 341 patients (28%) were undergoing revision by the surgeon who had performed the previous reconstruction. The median time since last ACL reconstruction was 3.4 years. Revision using an autograft was performed in 583 patients (48%), allograft was used in 590 (49%), and both types were used in 32 (3%). Questionnaire follow-up was obtained for 989 subjects (82%), while telephone follow-up was obtained for 1112 (92%). The IKDC, KOOS, and WOMAC scores (with the exception of the WOMAC stiffness subscale) all significantly improved at 2-year follow-up ($P < .001$). In contrast, the 2-year Marx activity score demonstrated a significant decrease from the initial score at enrollment ($P < .001$). Graft choice proved to be a significant predictor of 2-year IKDC scores ($P = .017$). Specifically, the use of an autograft for revision reconstruction predicted improved score on the IKDC ($P = .045$; odds ratio [OR] = 1.31; 95% CI, 1.01-1.70). The use of an autograft predicted an improved score on the KOOS sports and recreation subscale ($P = .037$; OR = 1.33; 95% CI, 1.02-1.73). Use of an autograft also predicted improved scores on the KOOS quality of life subscale ($P = .031$; OR = 1.33; 95% CI, 1.03-1.73). For the KOOS symptoms and KOOS activities of daily living subscales, graft choice did not predict outcome score. Graft choice was a significant predictor of 2-year Marx activity level scores ($P = .012$). Graft rerupture was reported in 37 of 1112 patients (3.3%) by their 2-year follow-up: 24 allografts, 12 autografts, and 1 allograft and autograft. Use of an autograft for revision resulted in patients being 2.78 times less likely to sustain a subsequent graft rupture compared with allograft ($P = .047$; 95% CI, 1.01-7.69).

Conclusion: Improved sports function and patient-reported outcome measures are obtained when an autograft is used. Additionally, use of an autograft shows a decreased risk in graft rerupture at 2-year follow-up. No differences were noted in rerupture or patient-reported outcomes between soft tissue and bone–patellar tendon–bone grafts. Surgeon education regarding the findings of this study has the potential to improve the results of revision ACL reconstruction.

Keywords: anterior cruciate ligament; ACL revision; graft; outcomes

Revision anterior cruciate ligament (ACL) reconstruction remains challenging for patients and surgeons. Multiple studies have demonstrated worse clinical outcomes for revision reconstructions compared with primary

reconstructions.[5,11,24,25] These outcomes, combined with the beliefs of orthopaedic sports medicine surgeons, resulted in the development of the Multicenter ACL Revision Study (MARS) group. The goal was to establish a prospective longitudinal cohort to evaluate the predictors of outcome in revision ACL reconstruction.

Most surgeons believe that graft choice for ACL reconstruction is an important factor related to outcome. Less outcome evidence is available for revisions compared with primary ACL reconstructions, but most surgeons believe that graft choice remains important. Graft choice for revision surgery may be limited by previously used grafts. Thus, surgeons are interested in the effect of both allograft versus autograft and soft tissue versus bone–patellar tendon–bone choices to determine how important it is to pursue different grafts for revision surgery. Previous prospective cohorts have demonstrated an increased failure rate of allografts in young, high-activity patients.[10] One of the goals of our prospective MARS cohort was to determine whether this remained true in the revision setting or whether more modern allograft processing and other factors would result in a similar allograft/autograft failure rate for revision surgery.

The purpose of this study was to determine whether graft choice predicts outcomes related to sports function, activity level, osteoarthritis symptoms, graft rerupture, and reoperation at 2 years after revision ACL reconstruction. We hypothesized that autograft use would result in increased sports function, increased activity level, and decreased osteoarthritis symptoms (as measured by validated patient-reported outcome instruments). Additionally, we hypothesized that autograft use would result in decreased graft failure and reoperation rate 2 years after revision ACL reconstruction.

METHODS AND MATERIALS

Setting and Study Population

The MARS group is composed of 83 surgeons at 52 sites. Surgeons are a 50:50 mix of academic and private practitioners who are all sports medicine fellowship–trained. Enrollment began in 2006 and ended June 30, 2011, during which 1205 revision ACL reconstruction patients were enrolled in this prospective longitudinal cohort (Figure 1). The study included any patients undergoing revision of a previously failed ACL reconstruction who agreed to participate and filled out an informed consent and a series of patient-reported outcome instruments. Multiligament reconstructions were excluded. Surgeon inclusion criteria included completion of a training session that integrated articular cartilage and meniscus agreement studies,
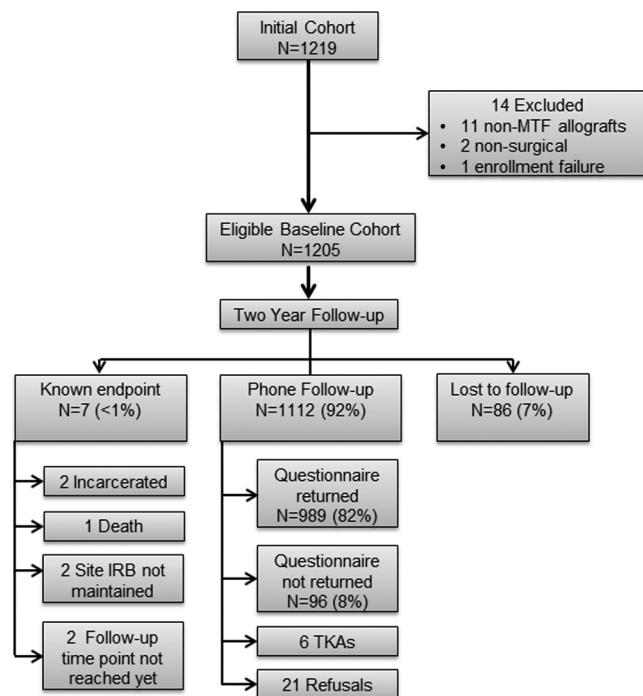
Figure 1. Patient enrollment flow diagram. IRB, institutional review board; MTF, Musculoskeletal Transplant Foundation; TKA, total knee arthroplasty.

review of study design and patient inclusion criteria, and a review of the surgeon questionnaire. Surgeons performed the surgery as they desired with the only stipulation that if an allograft was used it must be supplied by the Musculoskeletal Transplant Foundation (MTF). This was a stipulation to control and make consistent the source and processing of allografts, given the importance of the issue of allograft versus autograft use. Processing of the allografts was as follows: MTF used a technique for evaluating the incoming tissue called the VanGuard Method. MTF took actual samples of bone and soft tissue from every area that was to be used for transplantable grafts and destructively tested them, which indicated potential organism and bioburden. From these results the tissue had 4 potential pathways: (1) the tissue was solely processed aseptically; (2) depending on the type of organism and level, the tissue was discarded entirely; (3) the whole donor underwent a bulk tissue gamma radiation treatment of 1.2 to 1.8 mrad as a pretreatment step before processing; or (4) in a small number of cases at the surgeon's request, terminal irradiation of 0.7 to 1.0 mrad was delivered. Of the patients who received allografts, 247 (42%)

were processed aseptically, 313 (53%) received low-dose whole-body irradiation, and 31 (5%) received terminal irradiation. This study was registered at ClinicalTrials .gov (NCT00625885).

Data Sources and Measurement

After informed consent was obtained, each participant completed a 13-page questionnaire (see Appendix 1, available online at http://ajsm.sagepub.com/supplemental) that encompassed baseline demographics, injury descriptors, sports participation level, comorbidities, knee surgical history, and patient-reported outcome measures that included the International Knee Documentation Committee (IKDC) questionnaire,[8] the 5 subscales of the Knee injury and Osteoarthritis Outcome Score (KOOS; symptoms, pain, activities of daily living [ADL], sports and recreation, and knee-related quality of life [QoL]),[17-19] the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC),[1,2,6] and the Marx activity rating scale.[14] Their validity, reliability, responsiveness to clinical change, and minimal clinically meaningful differences have been previously documented.[22,23] All questionnaires were completed before the procedure.

Immediately after the surgical procedure, each surgeon completed a 49-page questionnaire (see Appendix 2, available online) that documented the results of the examination under anesthesia, the surgical technique, and the arthroscopic findings and treatment of concomitant meniscal and cartilage injury.[13] Surgeon documentation of articular cartilage injury was recorded based on the modified Outerbridge classification.[15] Meniscus injuries were classified by size, location, and partial versus complete tears, while treatment was recorded as no treatment, repair, or extent of resection.

Completed data forms were mailed from each participating site to the data coordinating center. Data from both the patient and surgeon questionnaires were scanned with TeleForm software (Cardiff Software Inc) using optical character recognition, and the scanned data were verified and exported to a master database. A series of logical error and quality control checks were subsequently performed before data analysis.

Patient Follow-up

The 2-year follow-up was completed by mail with readministration of the same questionnaire to each patient, which included the same outcome measures as completed at baseline (IKDC, KOOS, WOMAC, and Marx activity scale). Patients were also contacted by telephone to determine whether graft failure and any subsequent surgeries had occurred since their initial revision ACL reconstruction.

Quantitative Variables and Statistical Methods

Multivariable regression models were used to examine the independent (risk factor) variables and incidence of graft failure, reoperation rate, and sports function at 2 years after ACL revision surgery. For the ordinal outcome measures, analysis was performed using a proportional odds logistic regression model. Binary outcome measures analysis was

performed using a logistic regression model. Parameter estimates were exponentiated to obtain odds ratios (ORs) along with their corresponding 95% confidence intervals. The dependent variables were treated as either categorical or continuous and consisted of graft failure (yes/no), reoperation (yes/no), IKDC (0 [worst] to 100 [best]), KOOS (0 [worst] to 100 [best]), WOMAC (0 [worst] to 100 [best]), and the Marx activity scale (0 [low activity] to 16 [highest activity]). Independent patient-related covariates controlled for in the model included age at the time of surgery, sex, body mass index (BMI), smoking status, education level, activity level as assessed with the Marx activity rating scale, and baseline measure of the outcome (IKDC, KOOS, WOMAC, and Marx) (Table 1). All continuous covariates were modeled using a 3-knot restricted cubic spline to allow for a nonlinear relationship with the outcomes measures.

Independent surgical-related covariates controlled for in the model encompassed previous surgical characteristics and findings as well as surgical characteristics and findings at the time of revision (Table 1). Previous surgical characteristics included the revision number, previous ACL reconstruction on the contralateral knee (yes/no), previous meniscal injury, surgeon's opinion of cause of failure, and prior graft type. Time from previous ACL reconstruction (calculated as the time from the patient's previous ACL surgery to the date that the patient had the revision ACL surgery) was included in the model and was treated as a continuous variable. Current surgical characteristics included individual surgeon, mechanism of injury, current revision graft type (autograft, allograft, both), graft source (bone-tendon-bone [BTB], soft tissue, other), surgical technique, meniscal and articular cartilage injury, and treatment.

Regarding minimal clinically important difference (MCID) change in score, we used 11 points for the IKDC,[9] 8-10 points for the 5 subscales of the KOOS,[16] 8-10 points for the WOMAC,[22,23] and 2 points for the Marx activity scale. To avoid casewise deletion of records with missing covariates, we used multiple imputation via prediction mean matching. Statistical analysis was performed with the open source R statistical software using the Hmisc and rms packages (http://www.r-project.org).[7]

RESULTS

Study Population

Table 2 provides a synopsis of the baseline patient and surgical characteristics of our cohort. A total of 1205 patients (697 [58%] males) were enrolled. The median age was 26 years. In 88% of patients this was their first revision; 341 patients (28%) were undergoing revision by the surgeon who had performed their previous reconstruction. The median time since the patients' last ACL reconstruction was 3.4 years. Fifty percent of the surgeons were in private practice, while 50% were involved in academic practice. An autograft was used for revision in 583 patients (48%), allograft was used in 590 (49%), and both types were used in 32 (3%). A 2-stage procedure for bone grafting of tunnels was performed for the femur in 7% of patients and for the tibia in 8% of patients.

TABLE 1
List of Independent Modeling Variables[a]

Category	Variable	df^b	Levels
Baseline outcome score	IKDC, KOOS (5 subscales), WOMAC (3 subscales), or Marx	1	Continuous
Patient demographics	Age, y	1	Continuous
	Sex	1	Male, female
	Body mass index	1	Continuous
	Smoking status	2	Never, quit, current
	Education level, y	1	Continuous (range, 1-16)
	Baseline activity level (Marx)	1	Continuous
Previous surgical information	Revision number	2	1, 2, 3, or more
	Time since last ACLR, y	1	Continuous
	Previous ACLR on contralateral knee	1	No, yes
	Previous meniscal surgery type		
	Medial	3	No, yes (repair healed/stable), yes (repair not healed/unstable), yes (excision)
	Lateral	3	No, yes (repair healed/stable), yes (repair not healed/unstable), yes (excision)
	No. of previous articular cartilage surgeries	1	No, yes
	Surgeon's opinion of failure	4	Traumatic, technical, biological, other, combination
	Surgeon's revision his/her own failure	1	No, yes
	Cause of technical failure	4	Femoral tunnel malposition, tibial tunnel malposition, femoral + tibial malposition, other, none
	Prior graft type	3	Autograft, allograft, both autograft + allograft, unknown
	Prior graft source	3	BTB, soft tissue, BTB + soft tissue, other/unknown
Current surgical technique and findings	Mechanism of injury	3	Nontraumatic gradual onset, nontraumatic sudden onset, traumatic noncontact, traumatic contact
	Current graft type	2	Autograft, allograft, both
	Current graft source	2	BTB, soft tissue, other
	Interaction, current graft type × current graft source	4	2 × 2
	Current surgical exposure/technique	3	1 incision (transtibial), 1 incision (anteromedial portal), 2 incisions, arthrotomy/other
	Current femoral tunnel aperture position	5	Optimum position, same tunnel but compromised position, blended new tunnel, entirely new tunnel, added a second tunnel, OTT
	Current tibial tunnel aperture position	4	Optimum position, same tunnel but compromised position, blended new tunnel, entirely new tunnel, added a second tunnel
	Current femoral fixation	4	Interference screw, suture + button/endo, cross pin, other, combination
	Current tibial fixation	4	Interference screw, Intrafix (DePuy Synthes), suture + button/Endobutton (Smith & Nephew) or post, other, combination
	Biological enhancement	1	No, yes
	Meniscal injury		
	Medial	4	Normal, no treatment for tear, repair, excision, other
	Lateral	4	Normal, no treatment for tear, repair, excision, other
	Articular cartilage injury		
	Medial femoral condyle	3	Normal/grade 1, grade 2, grade 3, grade 4
	Lateral femoral condyle	3	Normal/grade 1, grade 2, grade 3, grade 4
	Medial tibial plateau	2	Normal/grade 1, grade 2, grades 3/4
	Lateral tibial plateau	2	Normal/grade 1, grade 2, grades 3/4
	Patella	2	Normal/grade 1, grade 2, grades 3/4
	Trochlea	2	Normal/grade 1, grade 2, grades 3/4
	Surgeon years of experience	1	Continuous

[a]ACLR, anterior cruciate ligament reconstruction; BTB, bone-tendon-bone; *df*, degrees of freedom; IKDC, International Knee Documentation Committee; KOOS, Knee injury and Osteoarthritis Outcome Score; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

[b]Total number of *df* = 88.

TABLE 2
Baseline Patient and Surgical Characteristics (N = 1205)[a]

Patient demographics		Previous surgical information (continued)	
Sex		Prior graft source	
Male	697 (58)	Autograft	639 (53)
Female	508 (42)	Allograft	459 (38)
Age, y	20, 26, 34	Both autograft + allograft	14 (1)
Body mass index	22.6, 25.1, 28.5	Other/unknown	93 (8)
Education, y	12, 15, 16	**Current surgical information**	
Baseline activity level (Marx)	4, 11, 16	Surgeon years of experience	8, 13, 18
Smoking status		Mechanism of injury	
Never	923 (77)	Nontraumatic, gradual	339 (28)
Quit	154 (13)	Nontraumatic, sudden onset	84 (7)
Current	109 (9)	Traumatic, noncontact	636 (53
Previous surgical information		Traumatic, contact	144 (12)
Time since last ACLR, y	1.4, 3.4, 8.3	Current graft type	
No. of revisions		Autograft	583 (48)
1	1055 (88)	BTB	318
2	125 (10)	Quad-bone	18
3+	25 (2)	Hamstring (SG+G)	224
Previous ACLR on contralateral knee		Hamstring (ST)	20
No	1083 (90)	Combination of 2 soft tissue grafts	1
Yes	122 (10)	BTB + soft tissue	1
Previous medial meniscus surgery		Other	1
No	743 (62)	Allograft	590 (49)
Yes, repair healed/stable	31 (3)	BTB	285
Yes, repair not healed/unstable	68 (6)	Quad-bone	3
Yes, excision	362 (30)	Tibialis anterior	133
Previous lateral meniscus surgery		Tibialis posterior	53
No	958 (80)	Achilles tendon	83
Yes, repair healed/stable	28 (2)	Hamstring (ST)	17
Yes, repair not healed/unstable	23 (2)	Hamstring (SG+G)	4
Yes, excision	195 (16)	Combination of 2 soft tissue grafts	8
Previous articular cartilage surgeries		BTB + soft tissue	2
No	1059 (88)	Other	2
Yes	146 (12)	Both autograft + allograft	32 (3)
Surgeon's opinion of failure		Hamstring (ST)	3
Traumatic	405 (34)	Hamstring (ST) + hamstring (ST+G)	2
Technical	265 (22)	Hamstring (ST) + tibialis anterior/posterior	3
Biological	108 (9)	Hamstring (ST) + quad-bone	1
Other	27 (2)	Hamstring (ST+G)	3
Combination	398 (33)	Hamstring (ST+G) + tibialis anterior/posterior	8
Surgeon's revision of his/her own failure		Hamstring (ST+G) + other	7
No	859 (71)	Tibialis anterior	1
Yes	341 (28)	Second-time revisions with serial single grafts used	4
Prior graft type		Current graft source	
Autograft	816 (68)	BTB	625 (52)
Allograft	348 (29)	Soft tissue	566 (47)
Both autograft + allograft	29 (2)	Both BTB + soft tissue/other	14 (<1)
Other/unknown	12 (<1)		

[a]Values are represented as n (%); as lower, median, and upper quartiles for continuous variables; and as n for individual types of allograft or autograft. ACLR, anterior cruciate ligament reconstruction; BTB, bone-tendon-bone; G, gracilis; quad-bone, quadriceps tendon–patellar bone; ST, semitendinosus.

2-Year Follow-up

Questionnaire follow-up was obtained on 989 subjects (82%), while follow-up by telephone was obtained on 1112 subjects (92%). Six subjects had undergone a total knee arthroplasty by the 2-year follow-up, and no follow-up questionnaire was required from these subjects.

Patient-Reported Outcomes
(IKDC, KOOS, WOMAC, and Marx Activity Level)

Table 3 summarizes and compares the median patient-reported outcome scores between baseline and 2 years. The IKDC, KOOS, and WOMAC scores (with the exception of the WOMAC stiffness subscale) all significantly improved at the 2-year follow-up ($P < .001$). These

TABLE 3
Median (25%, 75% quartile) Outcome Scores Over Time[a]

Outcome Measure	Scale	Baseline Score	2-Year Follow-up Score
IKDC	0-100	52 (38, 63)	77 (61, 86)[b]
KOOS			
Symptoms	0-100	68 (54, 82)	79 (64, 89)[b]
Pain	0-100	75 (58, 86)	89 (75, 94)[b]
Activities of daily living	0-100	87 (69, 96)	97 (88, 100)[b]
Sports and recreation	0-100	45 (25, 65)	75 (55, 90)[b]
Quality of life	0-100	31 (19, 44)	56 (38, 75)[b]
WOMAC			
Stiffness	0-100	75 (50, 88)	75 (62, 100)
Pain	0-100	85 (70, 95)	95 (80, 100)[b]
Activities of daily living	0-100	87 (69, 96)	97 (88, 100)[b]
Marx activity score	0-16	11 (4, 16)	7 (2, 12)[b]

[a]IKDC, International Knee Documentation Committee; KOOS, Knee injury and Osteoarthritis Outcome Score; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

[b]Significant difference in outcome score compared with baseline score ($P < .001$).

improvements all surpassed their respective MCIDs, illustrating that revision ACL surgery was beneficial to this cohort. However, the 2-year KOOS QoL subscale, although showing significant improvement at the 2-year mark (31 vs 56), fell well below the previously reported primary ACL score of 75 at the same 2-year follow-up time.[20]

In contrast to the IKDC, KOOS, and WOMAC scores, the 2-year Marx activity scale demonstrated a significant decrease from the initial score at enrollment ($P < .001$). At baseline, the median score was 11 (on a 16-point scale), with a 75th percentile score of 16. At 2 years, the median dropped to 7 and the 75th percentile dropped to 12. To illustrate this point, we calculated the number of patients who scored either 0 (lowest) or 16 (highest) at baseline and compared it with the number of patients who rated themselves as either 0 or 16 at 2 years. Only patients in whom we had both baseline and 2-year Marx scores were included (n = 980). There were 124 patients (12.7%) who rated themselves 0 at baseline, increasing to 165 patients (16.8%; an increase of 4 percentage points) at 2-year follow-up. Similarly, 281 patients (28.7%) rated themselves 16 at baseline, which decreased to 109 (11.1%; a decrease of nearly 18 percentage points) at 2 years. This reflects a substantial number of subjects who decreased their frequency of playing high-level sports (172 patients) or essentially dropped their activity to sedentary levels (41 patients).

Influence of Graft Choice on 2-Year Patient-Reported Outcomes

IKDC Score. Graft choice proved to be a significant predictor of 2-year IKDC scores ($P = .017$). Specifically, the use of an autograft for revision reconstruction predicted improved score on the IKDC ($P = .045$; OR, 1.31; 95% CI, 1.01-1.70). Subjects who had a combination autograft plus allograft (at the time of revision surgery, 32 patients)

also had improved IKDC outcomes at 2 years ($P = .022$; OR, 2.77; 95% CI, 1.16-6.64). Additional factors that predicted an improved IKDC score included a higher baseline IKDC score ($P < .001$; OR, 3.06; 95% CI, 2.50-3.74), male sex ($P < .001$; OR, 1.64; 95% CI, 1.25-2.13), a longer time since the last ACL reconstruction ($P = .010$; OR, 1.92; 95% CI, 1.30-2.82), and a higher baseline Marx activity score ($P = .023$; OR, 2.21; 95% CI, 1.55-3.15).

KOOS Results. The KOOS sports and recreation subscale demonstrated higher scores in the setting of an autograft compared with allograft for revision reconstruction ($P = .037$; OR, 1.33; 95% CI, 1.02-1.73). Other factors that predicted improved KOOS were similar to those that predicted improved IKDC score, including a higher baseline KOOS sports and recreation score ($P < .001$; OR, 2.97; 95% CI, 2.42-3.63), higher baseline Marx score ($P = .001$; OR, 1.81; 95% CI, 1.26-2.59), and a longer time since previous reconstruction ($P = .008$; OR, 2.03; 95% CI, 1.38-2.99). Autograft also predicted improved scores on the KOOS QoL subscale ($P = .031$; OR, 1.33; 95% CI, 1.03-1.73). For the KOOS symptoms and ADL subscales, graft choice did not predict outcome score.

WOMAC Score. The stiffness subscale on the WOMAC demonstrated higher scores in subjects who had a combination BTB with soft tissue graft (n = 14; $P = .029$; OR, 6.48; 95% CI, 1.22-34.57). Additional factors that predicted less knee stiffness via the WOMAC were better baseline WOMAC stiffness scores ($P < .001$; OR, 4.34; 95% CI, 3.39-5.56) and a longer time since previous reconstruction ($P = .003$; OR, 1.77; 95% CI, 1.19-2.63).

MARX Activity Score. Graft choice was a significant predictor of 2-year Marx activity scores ($P = .012$). Specifically, the use of a combination autograft plus allograft for revision reconstruction predicted improved scores on the Marx ($P = .005$; OR, 3.33; 95% CI, 1.43-7.78). Additional factors that predicted an improved 2-year Marx activity score included a higher baseline Marx score ($P < .001$; OR, 5.79; 95% CI, 4.01-8.35), male sex ($P < .001$; OR, 1.79; 95% CI, 1.39-2.33), younger age ($P < .001$; OR, 2.17; 95% CI, 1.41-3.23), and whether the revision involved the surgeon's own failure ($P = .017$; OR, 1.54; 95% CI, 1.08-2.19). Factors that predicted a lower activity level at 2 years included current smoking at the time of revision surgery ($P = .018$; OR, 1.72; 95% CI, 1.10-2.70), a previous ACL reconstruction on the contralateral leg ($P = .047$; OR, 1.49; 95% CI, 1.01-2.22), and a biological enhancement at the time of revision surgery ($P = .019$; OR, 1.82; 95% CI, 1.11-3.03).

Influence of Graft Choice on Predicting Graft Rerupture and Reoperation at 2 Years

Graft Rerupture. Graft rerupture was reported in 37 of 1112 patients (3.3%) by their 2-year follow-up: 24 of 540 (4.4%) allografts, 12 of 542 (2.2%) autografts, and 1 of 29 (3.4%) allograft + autograft. Subjects with an autograft revision were found to be 2.78 times less likely of sustaining a subsequent graft rupture compared with subjects who received an allograft ($P = .047$; 95% CI, 1.01-7.69).

The 25 patients who had rerupture with an allograft included 13 (52%) treated aseptically, 11 (44%) treated with whole body irradiation, and 1 (3%) treated with terminal irradiation. The use of BTB versus soft tissue grafts did not affect graft rerupture rate for either allograft or autograft use. Analysis of additional predictors for graft rerupture demonstrated that the number of previous revisions significantly predicted risk for future graft rupture. Specifically, patients undergoing revision number 3 or higher were 25.8 times more likely to sustain a subsequent graft rerupture by 2 years after their enrollment surgery (*P* = .021; 95% CI, 1.65-400).

Reoperation. A total of 150 of 1112 patients (13.5%) underwent reoperation in the 2 years since their revision reconstruction. For this specific analysis, we eliminated reoperations that included meniscal transplant (n = 4), high tibial osteotomy (n = 6), or knee replacement (n = 6) because we believed that these were not related to graft choice. The included reoperations in the analysis were chondroplasty and other articular cartilage treatment procedures, meniscectomy, meniscal repair, and hardware removal. Analysis demonstrated that graft choice was not a predictor of incidence of subsequent reoperations at 2 years after revision surgery. However, patients undergoing their third revision or higher were 4.7 times more likely to incur subsequent surgeries (*P* = .016; 95% CI, 1.34-16.4).

DISCUSSION

This study, which demonstrates the ability of the MARS group to prospectively collect and analyze a large cohort of patients with revision ACL reconstruction, has many strengths. To our knowledge, this is the largest cohort of patients undergoing revision ACL reconstruction ever studied. The 21 studies with minimum 2-year follow-up analyzed by systematic review included a collective total of 863 patients.[25] This current cohort, with follow-up of more than 1000 patients, eclipses the collective previous patients documented in the medical literature. The large cohort (N = 1205) allows for inclusion of a large number of variables (88) to be controlled for in the modeling, while keeping within statistical rules requiring 10 subjects per variable for multivariate analysis. Based on the 50:50 mix of academic and private practice surgeons, our results are generalizable to the sports medicine community. Our findings support our hypothesis that graft choice was a predictor of 2-year revision ACL reconstruction outcomes. Specifically, the use of autograft resulted in improved sports function and activity level as measured by patient-reported outcome measures. Also consistent with our hypothesis was that the use of autograft decreased the likelihood of subsequent graft rupture.

The findings that autograft use predicted higher sports function and activity level and decreased graft rerupture at 2 years will require continued surveillance. In our study, those who had an autograft were 2.78 times less likely to incur an additional revision ACL reconstruction compared with patients with an allograft. But given the few number

of events in this category, the power to detect a difference is low. As such, these findings should be approached with caution. Additionally, the effect of BTB versus soft tissue grafts, while not a predictor for the current study, will require additional review with longer follow-up.

Reoperation after revision ACL reconstruction is not uncommon, as reflected by the rate of 13.5% that we found. This has not been a common focus in previous studies.[25] It does reflect an occurrence that should be discussed with patients preoperatively since 1 patient in 8 may require further surgery after revision. Analyzing the predictors for reoperation does not lend itself to issues that are modifiable from a surgeon's standpoint and thus will remain a future issue despite our study.

The debate regarding the indications for and outcomes of allograft versus autograft ACL reconstruction has existed for several years. Graft choice remains a topic of high interest for surgeons performing primary and revision ACL reconstructions.[3,4,12] The key factors appear to be mode of processing of the allograft and the age and activity of the patient receiving the graft.[3,10] We chose to standardize the source and processing of the allografts in this cohort. The MTF grafts were all fresh-frozen and had undergone minimal (≤1.8 mrad) to no irradiation. This is thought to represent the best-case scenario for allografts. Different processing approaches by other allograft sources may be better, but the evidence regarding this is unavailable. An additional factor that affects graft choice for revision reconstruction is whether an autograft was used previously; if so, that specific graft is not a choice for future revision reconstruction. A previous study analyzed graft choice propensity and determined surgeon choice to have the strongest effect on graft choice (5 times stronger than any other factor; MARS Group, unpublished data, 2013). Thus, surgeons typically can use the graft they determine to be best for their patient, which underscores the importance of the current study.

Previous studies, when subjects are not stratified by age or activity, have not identified a difference in graft failure rates. Kaeding et al,[10] when using age and activity as part of their analysis, demonstrated a 4-fold increase in graft failure for allograft in a primary cohort that included some irradiated grafts. In the current revision cohort, autograft predicted improved sports function as measured by the IKDC score and the KOOS sports and recreation and QoL subscale scores. Graft type did not predict Marx activity scales except in the small number of patients receiving combined allograft and autograft. The clinical significance of this finding may be small, as few patients undergo a revision with this graft combination. A previous analysis of IKDC scores and KOOS at 6 years in a primary prospective cohort demonstrated that the use of allograft was a significant predictor of lower IKDC score and KOOS sports and recreation and QoL subscale scores.[20]

The IKDC scores in the MARS revision cohort demonstrated levels similar to those seen in previous primary settings. Spindler et al[20] reported 2- and 6-year primary ACL reconstruction median IKDC scores of 75 and 77, respectively, which was similar to our score of 77 at 2 years. Wright et al,[25] in a systematic review of revision ACL

reconstructions with minimum 2-year follow-up, reported a pooled IKDC of 74.8 in 202 patients. However, unlike the IKDC score, the KOOS results in the MARS revision cohort were noted to be lower to an extent that was clinically important. The 2-year median KOOS sports and recreation score was 75, compared with 85 and 90 at 2 and 6 years after primary ACL reconstruction as reported by Spindler et al.[20] The KOOS QoL was 56 for the MARS cohort versus 75 and 81 (2 and 6 years) in the Spindler et al[20] primary cohort. The MCID is 8 to 10 points for the KOOS.[16]

The Marx activity scores demonstrated dramatic decreases over the 2 years after revision ACL reconstruction. This occurred in a cohort that was older than the typical primary ACL reconstruction cohort and should have already had a natural decline in activity that we have noted every 2 years in a primary series.[20,21] The typical activity progression is a decrease from a high-activity high school sports athlete, to a college intramural/recreational athlete, and then to full-time employment and family obligations. At a median age of 26 years in this study, most of these patients have already gone through many of the lifestyle changes that would decrease their activity naturally. This decrease in activity at 2-year follow-up more closely resembles the decrease in activity levels noted at 6-year follow-up in a previous cohort of patients with primary ACL reconstruction cohort.[20] It is unclear whether the reduction in activity level of subjects in the current study occurred because they cannot be active due to the condition of their knee or because they have chosen to decrease their activity to lower the risk of future injury.

The baseline Marx score acted as a very strong predictor for our 2-year patient-reported measures. It predicted 2-year IKDC as well as 4 of the 5 KOOS subscales (symptoms score excepted), and it may be a simple tool to help counsel patients (ie, if you were not previously active with your knee in the year before revision, there is a strong chance you will not be active or highly satisfied with your knee after 2 years). Another common predictor was time since last reconstruction. It appears that patients for whom several years had elapsed since their last reconstruction did well after revision. While it cannot be known why this occurs, it is possible that patients who coped and functioned for several years previously are more likely to do well again.

Our study has many strengths and a few limitations. This is the largest prospective longitudinal cohort to analyze the outcomes of revision ACL reconstructions. The 50:50 mix of academic and private practice surgeons makes the results generalizable to the sports medicine fellowship–trained community. The use of validated patient-reported outcome measures allowed us to compare this with future and previous studies that have used these measures in other settings. The large number of patients enrolled allowed us to perform sophisticated statistical analyses controlling for a large number of variables to understand the predictors of inferior outcomes noted in revision ACL reconstructions. Our cohort study design resulted in an even split of autograft and allograft patients, with high numbers to allow analysis to control for multiple variables without the

need for randomization of graft choice, which would have added significant challenges in conducting the study. Our study design is limited in that it currently precludes on-site follow-up and is limited to 2-year follow-up. For this reason we may have underestimated the incidence of revision ACL graft rupture. Previous studies have demonstrated higher failure rates at minimum 2-year follow-up.[25] This decreased rate may reflect improved results, as many of the previous studies were more than 10 years old, or it may reflect a lack of rupture detection in our study design. Future follow-up will address this with on-site clinical assessments.

CONCLUSION

Optimal graft choice for revision reconstruction was not known before this study. Improved sports function and patient-reported outcome measures were obtained when an autograft was used. Additionally, use of an autograft showed a decreased risk in graft rerupture at 2-year follow-up.

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