Title
Factors Influencing Graft Choice in Revision Anterior Cruciate Ligament Reconstruction in the MARS Group

Author
Group, MARS

Peer reviewed

Factors Influencing Graft Choice in Revision ACL Reconstructions: A Propensity Analysis of the MARS Cohort

The MARS Group

Abstract

Background—It has not been known what drives revision ACL reconstruction graft choice in the past. We undertook this study to utilize the MARS (Multicenter ACL Revision Study) cohort and

Corresponding Author: Rick W. Wright, MD, Washington University Department of Orthopaedic Surgery, 660 S. Euclid Avenue, Campus Box 8233, St. Louis, MO 63110, Phone: 314-747-2639, Rwwright1@aol.com.

The following authors were a part of the MARS Group: Rick W. Wright, MD, Washington University, St. Louis; Laura J. Huston, MS, Vanderbilt University; Amanda K. Haas, MA, Washington University, St. Louis; Kurt P. Spindler, MD, Cleveland Clinic; Christina R. Allen, MD, University of California, San Francisco; Allen F. Anderson, MD, Tennessee Orthopaedic Alliance; Daniel E. Cooper, MD, W.B. Carrell Memorial Clinic; Thomas M. DeBerardino, MD, University of Connecticut Health Center; Brett A. Lantz, MD, Slocum Research and Education Foundation; Michael J. Stuart, MD, Mayo Clinic Rochester; Elizabeth A. Garofoli, Washington University, St. Louis; John P. Albright, MD, University of Iowa Hospitals and Clinics; Annunziato (Ned) Amendola, MD, University of Iowa Hospitals and Clinics; Jack T. Andrish, MD, Cleveland Clinic; Christopher C. Annunziata, MD, Commonwealth Orthopaedics & Rehab; Robert A. Arciero, MD, University of Connecticut Health Center; Bernard R. Bach Jr, MD, Rush University Medical Center; Champ L. Baker, III, MD, The Hughston Clinic; Arthur R. Bartolozzi, MD, 3B Orthopaedics, University of Pennsylvania Health System; Keith M. Baumgarten, MD,Orthopedic Institute; Jeffery R. Bechler, MD, University Orthopedic Associates, LLC; Jeffrey H. Berg, MD, Town Center Orthopaedic Associates; GeoffreyA. Bernas, MD, State University of New York at Buffalo; Stephen F. Brockmeier, MD, University of Virginia; Robert H. Brophy, MD, Washington University, St. Louis; Charles A. Bush-Joseph, MD, Rush University Medical Center; J. Brad Butler, V, MD, Orthopedic and Fracture Clinic; John D. Campbell, MD, Bridger Orthopaedic and Sports Medicine; James L. Carey, MD, MPH, University of Pennsylvania; James E. Carpenter, MD, University of Michigan; Brian J. Cole, MD, Rush University Medical Center; Jonathan M. Cooper, DO, HealthPartners Specialty Clinic; Charles L. Cox, MD, MPH, Vanderbilt University; R. Alexander Creighton, MD, University of North Carolina Medical Center; Diane L. Dahm, MD, Mayo Clinic Rochester; Tal S. David, MD, Arthroscopic and Orthopedic Sports MedicineAssociates; David C. Flanigan, MD, The Ohio State University; Robert W. Frederick, MD, The Rothman Institute/Thomas Jefferson University; Theodore J. Ganley, MD, Children's Hospital of Philadelphia; Charles J. Gatt, Jr., MD, University Orthopedic Associates, LLC; Steven R. Gecha, MD, Princeton Orthopaedic Associates; James Robert Giffin, MD, Fowler Kennedy Sports Medicine Clinic, University of Western Ontario; Sharon L. Hame, MD, David Geffen School of Medicine at UCLA; Jo A. Hannafin, MD, PhD, Hospital for Special Surgery; Christopher D. Harner, MD, University of Pittsburgh Medical Center; Norman Lindsay Harris, Jr., MD,Orthopaedic Associates of Aspen & Glenwood; Keith S. Hechtman, MD, UHZ Sports Medicine Institute; Elliott B. Hershman, MD,Lenox Hill Hospital; Rudolf G. Hoellrich, MD, Slocum Research and Education Foundation; Timothy M. Hosea, MD, University Orthopedic Associates, LLC; David C. Johnson, MD, National Sports Medicine Institute; Timothy S. Johnson, MD, National Sports Medicine Institute; Morgan H. Jones, MD, Cleveland Clinic; Christopher C. Kaeding, MD, The Ohio State University; Ganesh V. Kamath, MD, University of North Carolina Medical Center; Thomas E. Klootwyk, MD, Methodist Sports Medicine Center-The Orthopedic Specialists; Bruce A. Levy, MD, Mayo Clinic Rochester; C. Benjamin Ma, MD, University of California, San Francisco; G. Peter Maiers, II, MD, Methodist Sports Medicine Center-The Orthopedic Specialists; Robert G. Marx, MD, Hospital for Special Surgery; Matthew J. Matava, MD, Washington University, St. Louis; Gregory M. Mathien, MD, Knoxville Orthopedic Clinic; David R. McAllister, MD, David Geffen School of Medicine at UCLA; Eric C. McCarty, MD, University of Colorado Denver School of Medicine; Robert G. McCormack, MD, University of British Columbia; Bruce S. Miller, MD, MS, University of Michigan; Carl W. Nissen, MD, Connecticut Children's Medical Center; Daniel F. O'Neill, MD, EdD, Littleton Regional Hospital; LTC Brett D. Owens, MD, Keller Army Community Hospital-United States Military Academy; Richard D. Parker, MD, Cleveland Clinic; Mark L. Purnell, MD, Orthopaedic Associates of Aspen & Glenwood; Arun J. Ramappa, MD, Beth Israel Deaconess Medical Center; Michael A. Rauh, MD, State University of New York at Buffalo; Arthur C. Rettig, MD, Methodist Sports Medicine Center-The Orthopedic Specialists; Jon K. Sekiya, MD, University of Michigan; Kevin G. Shea, MD, Intermountain Orthopedics; Orrin H. Sherman, MD, NYU Hospital for Joint Diseases; James R. Slauterbeck, MD, University of Vermont College of Medicine; Matthew V. Smith, MD, Washington University, St. Louis; Jeffrey T. Spang, MD, University of North Carolina Medical Center; LTC Steven J. Svoboda, MD, Keller Army Community Hospital-United States Military Academy; Timothy N. Taft, MD, University of North Carolina Medical Center; Col. Joachim J. Tenuta, MD, Keller Army Community Hospital-United States Military Academy; Edwin M. Tingstad, MD, Inland Orthopaedics/Washington State University; Armando F. Vidal, MD, University of Colorado Denver School of Medicine; Darius G. Viskontas, MD, Royal Columbian Hospital; Richard A. White, MD, University of Missouri-Columbia; James S. Williams Jr, MD, Cleveland Clinic; Michelle L. Wolcott, MD, University of Colorado Denver School of Medicine; Brian R. Wolf, MD, University of Iowa Hospitals and Clinics; James J. York, MD, Chesapeake Orthopaedics & Sports Medicine Center; Warren R. Dunn, MD, MPH, University of Wisconsin.

Level of Evidence: Level II (prospective comparative study)

propensity score statistical analysis to determine the drivers of revision ACL reconstruction graft choice. We hypothesized that propensity analysis would demonstrate that individual surgeons still have significant impact on revision ACL reconstruction.

Methods—Twelve hundred patients were enrolled in this longitudinal revision cohort by 83 surgeons at 52 sites. The median age was 26 years and 505 (42%) were females. 1049 (87%) were undergoing their first ACL revision. Graft choice for revision ACL reconstruction for these patients was 48% autograft, 49% allograft, and 3% combination.

The independent variables of this model included gender, age, ethnicity, BMI, smoking status, sport, activity level, previous graft, revision number, surgeon, surgeon's opinion of failure, previous technical aspects, etc. Surgeon was defined as those who contributed more than 15 patients during the enrollment period. We calculated a propensity score for graft type based on the predicted probability of receiving an allograft from a logistic regression model.

Results—Propensity scores demonstrated that surgeon, prior graft choice, and patient age each had significant influence on which graft type was chosen for the revision ACL reconstruction ($p<0.0001$). The revising surgeon had the largest impact upon graft choice: approximately 5 times that of the second most important factor (prior graft). If the prior graft type was an autograft, then an allograft was 3.6 times more likely to be chosen for the revision.

Conclusions—This current study demonstrates that the individual surgeon is ultimately the most important factor in revision ACL reconstruction graft choice. Additional statistically significant influences of graft choice included age, gender, previous graft choice, ACL revision number, concurrent MCL/PM repair, and opinion of the previous failure. This demonstrates that if graft choice is determined to impact outcome then surgeons have the ability to change and determine the graft utilized.

INTRODUCTION

Revision ACL (anterior cruciate ligament) reconstruction remains a challenging clinical situation for patients and surgeons. A variety of studies have demonstrated that the outcome of revision ACL reconstruction is inferior to that of primary ACL reconstruction.[13,14] The Multicenter ACL Revision Study (MARS) was initiated to prospectively determine revision ACL reconstruction outcomes and the predictors for these results.[7] The overarching goal was to determine modifiable predictors of outcome so that surgeons could actively intervene to improve their revision patient's results.

Criticism of this approach has included a belief that the results of revision ACL reconstruction are predominantly preordained and that no true modifiable aspects of the care exist. Graft choice remains one factor that many surgeons believe significantly impacts outcome including graft rerupture and return to activity. Recently, the MARS group determined that use of autograft resulted in improved sports function and a 2.78 times reduction in graft rerupture.[6] It has not been known what drives revision ACL reconstruction graft choice in the past. Many surgeons believe that factors from the previous surgical reconstruction control and/or heavily impact graft choice in the revision setting. Thus, surgeons would have little control over graft choice issues. We undertook this study to utilize

the MARS (Multi-center ACL Revision Study) cohort and propensity score statistical analysis to determine the drivers of revision ACL reconstruction graft choice.

Propensity as originally described by Rosenbaum and Rubin in 1983 is the probability of a patient receiving a certain treatment in a nonrandomized setting as determined by a number of other variables.[1,10] The propensity score (PS) for a subject, is the conditional probability of the treatment choice given the individual's covariates. In a RCT treatment assignment is controlled. In an observational (cohort) study treatment is not controlled and thus factors impact decision making. Revision ACL reconstruction offers a rich environment of factors to assess. We hypothesized that propensity analysis would demonstrate that individual surgeons still have significant impact on revision ACL reconstruction despite the limits imposed by the patient's previous surgery.

METHODS

Study Group

MARS is an NIH-funded prospective longitudinal cohort of revision ACL reconstructions. It is supported by the American Orthopaedic Society of Sports Medicine with 83 surgeons at 52 sites who are currently active. Twelve hundred patients have enrolled (2006–2011) with median age 26 (20, 34 interquartiles). In the cohort 505 (42%) are females. 1049 (87%) were undergoing their first ACL revision. Graft choice for revision ACL reconstruction for these patients was 48% autograft, 49% allograft, and 3% combination.

Statistical Analysis

The independent variables of this model included gender, age, ethnicity, BMI, smoking status, sport, activity level, previous graft, revision number, surgeon, surgeon's opinion of failure, previous technical aspects including femoral and tibial fixation, etc (see Table 1). Surgeon was defined as those who contributed more than 15 patients during the enrollment period. All other surgeons with less than 15 patients in the cohort were lumped into "others". 28 surgeons contributed 71% of the patients. The "others" contributed 29%.

We calculated a PS for graft type based on the predicted probability of receiving an allograft from a logistic regression model. We included this as a covariate in the outcome models (not reported here) after taking the logit transformation, but removed it after observing that it had little effect on the estimated effect of using an allograft instead of an autograft. However, we felt the results of the propensity model would be a novel addition to the existing literature. Restricted cubic splines were used to allow for nonlinear relationships between continuous covariates and the response variable in the propensity model. We used multiple imputations via predictive mean matching to avoid casewise deletion of records that were missing any covariates.(9) We determined chi-squared (X^2) values with odds ratios (OR) to predict autograft/allograft choice. Statistical analysis was performed with free open source R statistical software.[4,12]

RESULTS

Propensity scores demonstrated that surgeon, prior graft choice, and patient age each had significant influence on which graft type was chosen for the revision ACL reconstruction (p<0.0001). The revising surgeon had the largest impact upon graft choice: approximately 5 times that of the second most important factor (prior graft). For example, Surgeon A was found to be 28.6 times more likely to choose an autograft for the ACL revision, while Surgeon B was 31.9 times more likely to choose an allograft. As a comparison, if the prior graft type was an autograft, then an allograft was 3.6 times more likely to be chosen for the revision. Similarly, the older the patient was, an allograft was also 3.6 times more likely chosen (Table 2).

Although not as influential, but still significant, were the variables of medial collateral ligament (MCL)/posteromedial (PM) repair, the surgeon's opinion of failure, the revision number, gender, and if the revision was the surgeon's own failure. Specifically, an allograft was more likely to be chosen for the following reasons: 1) if the patient had a concurrent MCL/PM repair, 2) if the opinion of failure was due to factors other than isolated biologic failure, 3) if it was the surgeon's own failure, 4) if it was the patient's 2nd revision (versus their first), and 5) if the patient was female (p<0.02; Table 2). All other variables were not statistically significant.

DISCUSSION

Propensity scores measure the probability of selecting a treatment dependent upon additional variables. In a RCT treatment assignment is controlled. In an observational (cohort) study treatment is not controlled and thus factors impact decision making. Propensity analysis has been shown to function best when a rich and diverse set of covariates exists. ACL revision reconstruction offers this with multiple factors that impact ACL decision making. Factors influencing ACL graft choice include age, sex, BMI, sport type, concomitant meniscal and chondral injury, and physician input. Surgeons believe graft choice matters, but that the ability to choose a graft is limited by outside factors in the revision setting. And thus, the ability to modify or impact outcome through treatment decisions is limited. This current study dramatically demonstrates that the individual surgeon is the most important factor in revision ACL reconstruction graft choice. (Table 2) If the surgeon desires to use an autograft then depending upon the original graft remaining options may include ipsilateral or contralateral hamstring, bone-patellar tendon-bone, or quadriceps tendon. If the surgeon's desire is to use allograft then obviously many options are available. Ultimately, though the surgeon is the largest driving force behind graft choice.

Observational studies occur frequently in our field and often are the preferred study design when the research question involves prognosis. However, in observational studies the investigators have no control over treatment assignments. Hence, differences between treatment groups on observed or unobserved covariates might exist, which can lead to biased estimates of treatment effects.[2] It has been shown that adjusting for a well-modeled PS (a single number) adjusts for the confounding due to all of the observed covariates that are included in the PS. Such adjustment effectively balances the covariates among treatment

groups, and consequently limits confounding bias (treatment by indication bias) to that caused by unmeasured covariates

In observational studies treatments are assigned to the patients without the benefit of randomization. This occurs in situations of retrospective analysis of cohorts or of prospective cohorts where randomization of treatment is neither practical nor possible. We sought in this study to determine what influences the given treatment in the area of graft choice.[3] Propensity analysis, which has not been frequently used in orthopedics, allows us to analyze this topic. Despite relatively infrequent use in orthopedics propensity scores have become popular especially in the area of the epidemiological analysis of treatment effects.[9] The generalized propensity score determines the probability of receiving a particular treatment based on a variety of variables.[5] Our hypothesis that surgeons can impact graft choice was confirmed.

Additionally, there were other issues that contributed to graft choice at a statistically significant level although at less than the impact of the revising surgeon. (Table 2). Prior graft choice obviously can impact future graft choices as the patient may want an autograft following failure of an allograft or desire an allograft to decrease the surgical insult from autograft harvest or may have reasons that they desire avoiding a different type of autograft. For example a patient may want to avoid a patellar tendon autograft after hamstring to avoid an increased risk of kneeling pain.[11]

Age is the third strongest factor in graft choice. Studies have demonstrated a higher allograft failure rate in young, high activity athletes with primary ACL reconstructions and a lower failure rate in older less active patients.[8] While it is not known that this will be true of failure rates in revision ACL reconstruction surgeons may be extrapolating this data to help with graft choice decisions. The surgeon's opinion of failure impacts choice. A belief that an allograft previously failed due to biological reasons strengthens the reasoning to revise with an autograft.

Allograft choice is more likely in the setting when a patient is undergoing a second or higher revision event. This is intuitive when you consider that with most second or higher revisions at least one if not two autografts may have been utilized thus limiting the ability to subsequently choose an autograft in the future.

Our study has several strengths and a few limitations. The strengths include the prospective nature of the cohort and the significant number of enrolled patients. This allows for a large number of variables to be included in the model, and a rich environment for analysis using propensity scores. An additional strength is the utilization of propensity score analysis to determine the influences of graft choice which is novel and will introduce this concept to a broader audience in orthopedics. This will encourage future use of these interesting statistics analyses. Limitations of our study include the inability to assess the "other" surgeon's impact on graft choice since they had contributed very few patients to the cohort. Based on the few patients enrolled (<15) these surgeons could not be included in the statistical analyses.

CONCLUSIONS

Propensity analysis determined that the most significant influence on allograft versus autograft choice for patients undergoing revision ACL reconstruction in the MARS cohort is surgeon. Additional statistically significant influences of graft choice included age, gender, previous graft choice, ACL revision number, concurrent MCL/PM repair, and opinion of the previous failure. This demonstrates that since graft choice impacts outcome and rerupture as demonstrated by the MARS cohort then surgeons have the ability to change and determine the graft utilized. This will allow the MARS cohort to impact revision ACL reconstruction outcomes through surgeon educational efforts in addition to the more difficult challenge of patient education.

Bibliography

1. Austin PC. Type I error rates, coverage of confidence intervals, and variance estimation in propensity-score matched analyses. The international journal of biostatistics. 2009; 5(1) Article 13.

2. D'Agostino RB Jr. Propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group. Statistics in medicine. Oct 15; 1998 17(19):2265–2281. [PubMed: 9802183]

3. Ertefaie A, Stephens DA. Comparing approaches to causal inference for longitudinal data: inverse probability weighting versus propensity scores. The international journal of biostatistics. 2010; 6(2) Article 14.

4. FE, H. rms: Regression Modeling Strategies. 2011. http://CRAN.R-project.org/package=rms

5. Feng P, Zhou XH, Zou QM, Fan MY, Li XS. Generalized propensity score for estimating the average treatment effect of multiple treatments. Statistics in medicine. Mar 30; 2012 31(7):681–697. [PubMed: 21351291]

6. MARS Group. Revision Anterior Cruciate Ligament Reconstruction Graft Choice Impact on Outcome in thie Multicenter Cohort. AJSM. Accepted–Pending Publication.

7. MARS Group. Wright RW, Huston LJ, et al. Descriptive epidemiology of the Multicenter ACL Revision Study (MARS) cohort. The American journal of sports medicine. Oct; 2010 38(10):1979–1986. [PubMed: 20889962]

8. Kaeding CC, Aros B, Pedroza A, et al. Allograft Versus Autograft Anterior Cruciate Ligament Reconstruction: Predictors of Failure From a MOON Prospective Longitudinal Cohort. Sports health. Jan; 2011 3(1):73–81. [PubMed: 23015994]

9. McCandless LC, Douglas IJ, Evans SJ, Smeeth L. Cutting feedback in Bayesian regression adjustment for the propensity score. The international journal of biostatistics. 2010; 6(2) Article 16.

10. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. Biometrika. 1983; 70(1):41–55.

11. Spindler KP, Kuhn JE, Freedman KB, Matthews CE, Dittus RS, Harrell FE Jr. Anterior cruciate ligament reconstruction autograft choice: bone-tendon-bone versus hamstring: does it really matter? A systematic review. The American journal of sports medicine. Dec; 2004 32(8):1986–1995. [PubMed: 15572332]

12. Team RDC. R: A Language and Environment for Statistical Computing. 2010. http://www.R-project.org/

13. Wright RW, Dunn WR, Amendola A, et al. Anterior cruciate ligament revision reconstruction: two-year results from the MOON cohort. The journal of knee surgery. Oct; 2007 20(4):308–311. [PubMed: 17993075]

14. Wright RW, Gill CS, Chen L, et al. Outcome of revision anterior cruciate ligament reconstruction: a systematic review. The Journal of bone and joint surgery. American volume. Mar 21; 2012 94(6):531–536. [PubMed: 22438002]

Table 1

List of Variables used in Model

Category	Variable	Levels
Patient Demographic Variables	Age (years)	continuous
	Gender	male, female
	Race/Ethnicity	asian, black, hispanic, white
	BMI	continuous
	Smoking status	never, quit, current
	Education level (years)	1 – 16
	Marital status	single, married, divorced/separated
	Work status	working full-time, part-time, student, other
	Sport (last 2 years)	baseball/softball, basketball, football, gymnastics, none, skiing, soccer, volleyball
	Sports level (last 2 years)	amateur (team or club), high school, non, recreational, semi-pro/pro
	Highest sport level achieved	amateur (team or club), high school, non, recreational, semi-pro/pro
	Baseline activity level (Marx)	continuous
Surgical Variables	Surgeon	individual
	Previous ACLR on contralateral knee	no, yes
	Revision number	1, 2, 3 or greater
	Surgeon's opinion of failure	biologic, biologic+technical, biologic+technical+traumatic, biologic+traumatic, other, technical, technical+traumatic, traumatic
	Surgeon's revision his/her own failure	no, yes
	Cause of technical failure	none, femoral tunnel malposition, tibial tunnel malposition, other, none
	Prior surgical technique	one incision, two incision, arthrotomy
	Prior graft type	autograft, allograft, other
	Prior graft source	BTB, soft tissue, combination/other/unknown
	Prior ACL Femoral tunnel	single tunnel, double tunnel
	Prior Femoral Fixation	interference screw, cross pin, endobutton, other/combination
	Prior Femoral Tunnel Position	ideal, ideal (both position and size)-but enlarged tunnel, compromised (position and/or size)
	Prior Tibial Fixation	interference screw (bioabsorbable), interference screw (nonbioabsorbable), other/combination
	Prior Tibial Tunnel Position	ideal, ideal (both position and size)-but enlarged tunnel, compromised (position and/or size)
	MCL or PM repair/reconstruction	no, yes
	LCL or PL repair/reconstruction	no, yes
	PCL repair/reconstruction	no, yes

Table 2

Significant Factors Driving Graft Type used for Revision ACL Reconstruction

Variable	Favors choice of ALLOGRAFT	Odds Ratio (lower 0.95, upper 0.95)	Chi-squared (X^2)	P value
Surgeon	Individual surgeon choice:		149.14	< 0.0001
	Favors Autograft	28.6 (7.2, 111.1)		
	Favors Allograft	31.9 (3.8, 272.0)		
Prior Graft Type	Autograft	3.6 (2.0, 6.2)	21.10	< 0.0001
Age	Older age	3.6 (1.6, 7.9)	20.28	< 0.0001
MCL/PM Repair	Concurrent MCL/PM repair	7.4 (2.4, 22.3)	12.36	0.0004
Surgeon Opinion of Failure	*	2.9 (1.1, 7.8)	16.85	0.0184
	**	6.6 (1.6, 27.6)		
	***	3.1 (1.6, 6.2)		
Revision Number	2nd time revisions	3.0 (1.6, 5.9)	11.40	0.0033
Gender	female	1.8 (1.3, 2.7)	10.12	0.0015
Surgeon Failure	Surgeon's own failure vs. not	2.0 (1.3, 3.2)	9.34	0.0022

Key:

*
(Biologic+Traumatic) vs. (Biologic only); where (Biologic+Traumatic) group favors allograft.

**
(Other) vs. (Biologic); where (Other) group favors allograft.

***
(Traumatic) vs. (Biologic); where (Traumatic) group favors allograft.