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# Predictors of Clinical Outcome Following Revision Anterior Cruciate Ligament Reconstruction

MARS Group

# BACKGROUND

Anterior cruciate ligament (ACL) reconstruction remains the treatment of choice for ACL deficient active individuals involved with sports or activities that involve quick start/stop, cutting, jumping and abrupt change of direction activities. Based on insurance, industry and implant evidence there are approximately 200,000 ACL reconstructions per year in the United States.<sup>1</sup> Fortunately, primary reconstructions typically do well, but can fail at a low but significant rate.<sup>2–4</sup> While highly successful in the short term there can be problems with primary reconstructions including loss of motion, extensor dysfunction with certain grafts, arthritis and graft failure. This treatise will address graft failure and the multicenter, multi-surgeon group (Multicenter ACL Revision Study – MARS) assembled to study the issues surrounding revision ACL reconstruction.

A variety of studies have evaluated graft failure in the primary ACL reconstruction setting and have found the failure rates to range from ~1–8% in the standard patient and graft setting.<sup>2, 4, 5</sup> In the Multicenter Orthopaedic Outcomes Network (MOON) the graft failure rate in primary reconstructions was 3% in the ipsilateral knee and 3% in the contralateral knee at 2-year follow-up.<sup>4</sup> In a systematic review evaluating hamstring vs. patellar tendon autografts, Spindler et al. reported a 3.7% overall failure rate.<sup>3</sup> Wright et al. in a systematic review of minimum 5-year follow-up of ACL reconstructions found an ipsilateral ACL graft failure rate of 5.8% and a contralateral native ACL failure rate of 11.8%.<sup>2</sup>

These are reasonably low levels of failure, but the question confronting us was what happens in cases of failure. What expectations of current and future knee health should these patients have? Can they return once again to the activities that resulted in ACL failure? A better understanding of revision results would allow us to better counsel patients as to expected outcomes.

Defining the outcomes patients can expect and the outcomes that truly matter in the ACL revision setting was the impetus for the development of the Multicenter ACL Revision Study (MARS) Group. There was consensus amongst the MARS surgeons that revision ACL reconstruction typically resulted in worse outcomes compared to primary reconstructions.

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<sup>&</sup>lt;sup>†</sup>We express our appreciation to the late Barton Mann, PHD (AOSSM, Rosemont, IL USA), Timothy M. Hosea, MD (University Orthopaedic Associates LLC, Princeton, NJ USA), and Allen F. Anderson, MD (Tennessee Orthopaedic Alliance, Nashville, TN) whose contribution to this work was of great significance.

Revision ACL reconstruction was the strongest predictor for worse KOOS scores in a mixed ACL reconstruction cohort early in the MOON experience.<sup>6</sup> In a series of ACL reconstructions reported at minimum 5-year follow-up, revision was the strongest predictor for worse outcome across the board, but in the editing process the journal reviewers and Editor requested that the revision ACL reconstructions be removed from the published manuscript due to the small number and percentage of revision reconstructions.<sup>6</sup>

Unfortunately, little Level 1 or 2 evidence existed at the time to help us confirm this discrepancy in outcomes that we observed between primary and revision ACL reconstructed patients. In a mixed model meta-analysis of 21 studies with minimum 2-year follow-up after revision reconstruction these worse results were demonstrated after revision reconstruction.<sup>7</sup> Of the 21 studies, however, only 4 were Level 1 or 2, while 1 was Level 3 and 16 were Level 4 studies. Objective failure (defined as a re-revision, KT-1000 side-to-side difference of >5 mm, or a positive pivot shift) occurred in  $13.7\pm2.7\%$  -- a much higher rate of failure than typically reported in primary ACL reconstruction. Patient-reported outcomes were worse than expected compared with primary ACL results and usually exceeded the known clinically important difference for these outcome scores.

Based upon these findings, the MOON Group reviewed their prospectively collected cohort which began as a mixed primary and revision patient ACL reconstruction cohort.<sup>8, 9</sup> Their working hypothesis was that revision ACL reconstruction results in worse outcome compared to primary reconstruction, as measured by validated patient-based outcome measures, including the Marx activity rating scale, Knee injury and Osteoarthritis Outcome Score (KOOS), and International Knee Documentation Committee Subjective form (IKDC). 408/487 (84%) were available at minimum 2-year follow-up with 39/47 (83%) revisions available at 2-year follow-up. At 2 years, median Marx activity level scores had dropped from 12 to 9 points in the primary reconstructions vs. 10 to 6 points in revisions (p=0.009). While the minimally clinically important difference (MCID) is not known for the Marx score, it is assumed on a 16-point scale that 2 points (representing more than a 10% change or difference) would be clinically significant. The IKDC at 2 years was 85.6 for primary ACL reconstructions and 79.6 for revisions, which was statistically different (p=0.005), but not clinically significant (MCID: 11.5 points).<sup>10, 11</sup> For the 5 KOOS subscales a difference of 8–10 points is clinically significant. In this study, the KOOS knee-related quality of life (KRQOL) subscale was lower in revisions at 2 years (75 vs. 62.5; p<0.001). The KOOS sports and recreation subscale also was worse for revisions at 2 years (85 vs. 75; p=0.004). KOOS Pain was lower in revisions and potentially clinically significant (91.7 vs. 83.3). KOOS Symptoms (85.7 vs. 78.6) and ADLs (98.7 vs. 97.1) did not demonstrate a clinically significant difference between primary and revision reconstructions.

Thus, the data represented a prospectively collected cohort of primary and revision ACL reconstructions that used identical validated patient-reported outcome measures. While worse scores across the board were observed for revisions, the factors contributing to these worse outcomes were unknown. Unfortunately, revisions represented only 10% of the cohort. We sought to identify predictors for these worse results. To identify predictors, multi-variable analysis requires ~10–15 subjects per variable assessed and with the multiple factors (50–75 or more) potentially contributing to revision ACL reconstruction outcomes,

we realized that a comprehensive assessment of important factors in revision ACL outcomes would require a cohort with 750–1000 patients. It became apparent that the MOON Group, with less than 20 members, could not enroll an adequate number of patients quickly enough for this type of study. A simple moon could not get it done, as we needed a planet. With this in mind we set out to establish a larger group of interested sports medicine surgeons.

## METHODS

### Study Design

We felt the basic approach utilized by the MOON Group would be appropriate for evaluating the revision patient but realized there were different factors involved in revision surgeries that would need to be captured. A small group developed a Standard Operating Procedure (SOP) manual that outlined rules of engagement for surgeons and patients. Very early on, we engaged the American Orthopaedic Society for Sports Medicine (AOSSM), through Bart Mann, the AOSSM research director. He, the AOSSM Research Committee, and the AOSSM society were enthusiastic about the opportunity to engage their members in an important research question. Based on this collaboration, we had access to the AOSSM website and email systems and were able to solicit broad surgeon participation. Interested AOSSM members participated in three training meetings to learn how the study would proceed. Participants were also engaged in designing forms and determining the variables that would be collected and analyzed. Over 100 members originally expressed interest and we currently have 83 surgeons participating at 52 IRB approved sites. The surgeons are a near 50/50 mix of academic and private practice surgeons, adding to the generalizability of our results.<sup>12</sup>

In determining study design, we debated over a prospective cohort design versus a randomized trial. Ultimately, we believed we did not know a single critical variable to randomize and felt a cohort to determine predictors would best serve a revision series with its rich number of potential factors. We thus chose a prospective longitudinal cohort similar to the classic Framingham study for cardiovascular disease many years ago.<sup>13</sup>

#### Surgeon Involvement

Surgeon inclusion was based on AOSSM membership, attendance at one of our training meetings, and a willingness to follow the procedural issues identified in the SOP. This included utilizing a Musculoskeletal Transplant Foundation (MTF) graft if an allograft was chosen for the subsequent revision. Training videos were reviewed for consensus on meniscal and chondral injury classification and treatment and were based upon similar studies performed by members of the group.<sup>14, 15</sup> We studied the group's ability to agree on etiology of failure for ACL reconstructions utilizing intra-articular videos and radiographs and found fair agreement on most items measured.<sup>16</sup>

#### Study Logistics

After obtaining informed consent, the patient filled out a 13-page questionnaire prior to their revision ACL surgery that included questions regarding demographics, sports participation, injury mechanism, comorbidities and knee injury history. Within this questionnaire, each

participant also completed the Knee injury and Osteoarthritis Outcome Score (KOOS), the International Knee Documentation Committee Subjective form (IKDC) and the Marx activity rating scale. Contained within the KOOS was the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Surgeons filled out a 49-page questionnaire at the time of the revision surgery that included the impression of the etiology of the previous failure, physical exam findings, surgical technique utilized, the intra-articular findings and surgical management of meniscal and chondral damage.

Patient follow-up was completed by mail with re-administration of the same questionnaire as the one they completed at baseline. Patients were also contacted by phone or email to determine whether any subsequent surgery had occurred to either knee since their initial revision ACL reconstruction. If so, operative reports were obtained, whenever possible, in order to document pathology and treatment.

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<sup>TM</sup> software (OpenText, Waterloo, Ontario, Canada) utilizing optical character recognition, and the scanned data was verified and exported to a master database.

Teleform<sup>™</sup> paper forms were utilized so data was available in real time. If starting today we would utilize electronic data capture, but in 2006 this was best practice for us and our coordinating center. Data was housed at Vanderbilt. Our data capture was outstanding; greater than 99% of all patient and surgeon data points were completed when assessed on our first 900 patients (Table 1).

Once 2-year follow-up began we added a full-time central follow-up coordinator whose responsibility was to contact all patients to send out and obtain questionnaires and perform phone/email follow-up. Each site manages their site with their personal health care personnel or research personnel. An electronic newsletter (Figure 1) was developed that arrived monthly to all surgeons and coordinators and acted as an impetus to stimulate patient enrollment listing total and monthly enrollment figures for surgeons. Participating surgeons all had the goal of appearing on the Top 10 list.

Keys that helped us early on were frequently based on our experience with MOON and included the use of conference calls and the ability to communicate by email. The group's experience with IRB helped new sites get approval and the knowledge regarding grants helped immensely in obtaining funding.

We developed a Scientific Advisory Board for advice. This eight-member Board meets at least annually and provides advice and oversight for the study. This has included what studies should be performed via an application form by members. This has been critical for governance issues. The makeup is balanced by geography, gender and practice type.

## **Unique Aspects of MARS**

The MARS Group and study offer many unique aspects for orthopaedics and even for medical research in general. The recruitment of surgeon participants from the broad population of the AOSSM allowed private practice surgeons to participate and make

intellectual contributions that might otherwise not be possible in their practice setting. In fact, the final MARS study surgeon breakdown included more private than academic surgeons (55% vs. 45%). Moreover, the inclusion of private practice surgeons improves the generalizability of the results for the entire orthopaedic surgeon population. We were able to accomplish this broad demographic of participants by leveraging the strength of the coordinating center personnel and minimizing local site and surgeon burden. This included assistance with IRB preparation and submission with no central site multicenter IRB available in 2006 when this study was initiated. Additionally, central coordinating site control of phone and questionnaire follow-up provided outstanding follow-up for a population that is sometimes difficult to follow due to changing patient locations. The 52 sites represent the largest number of sites utilized for a single orthopaedic surgery research study and one of the largest number of sites involved in any multicenter medical studies.

The size and prospective nature of our study is unique for this topic. As we designed the study, we were uncertain of the critical factors leading to the worse outcome observed following revision ACL reconstructions. Thus, we felt a randomized controlled trial of one or two variables might be misguided and inappropriate. We believed a prospective longitudinal cohort design would allow us to recruit adequate subjects and allow leeway for the surgeons to appropriately manage what can be challenging technical cases. This has been borne out by examining one key issue – graft choice for the revision reconstruction. This was the most critical issue for many surgeons performing these reconstructions. Our study design allowed accumulation of a large number of subjects that ended up (unintentionally) equally divided between the four main graft options with ~25% for each choice (BPTB autograft, soft tissue autograft, BPTB allograft, soft tissue allograft). More detail of the graft choice study is discussed in the results section.

The size of this study dwarfs all previous revision ACL reconstruction studies. We performed a meta-analysis of the 21 previous studies with minimum 2-year follow-up. In that meta-analysis it was noted that the 21 studies involved follow-up results for 863 patients in total with predominantly Level 4 retrospective case series represented. Thus, in one study (with over 1200 enrolled patients) we have eclipsed the entirety of the previous result reporting for this important orthopaedic problem. The strength of the size of our cohort becomes even more apparent when moving beyond 2-year follow-up. Recently we performed a systematic review of minimum 5-year follow-up of revision ACL reconstructions.<sup>17</sup> Wright et al. demonstrated there are only four studies involving 148 patients with 121 followed. We have completed minimum six-year follow-up and have more than 800 patients followed at that time point. We have begun analysis (see Results) of our six-year results and will have information for surgeons that no other cohort can accomplish. Using this approach, we have simultaneously collected the largest cohort ever assembled prospectively of the multiply revised ACL patient: 150 patients (157/1234; 13%) of the cohort had two or more revisions of their ACL reconstructions.

We performed an analysis that represents a unique approach for orthopaedic research. A propensity analysis was performed after our graft choice analysis demonstrated improved results and decreased failure rates if an autograft was utilized.<sup>18</sup> Propensity analysis can determine factors that predict decision making for factors when they are not controlled by

study design. Propensity analyses flourish when there are more variables so a study of revision ACL reconstructions is a rich milieu to perform this in and would address the concern that graft choice is a fait accompli and that it is predetermined by patient age, sport, previous graft etc. and cannot be impacted by the surgeon choice. Our propensity analysis proved this belief wrong as surgeon was by five times the strongest determinant of the graft utilized for the patient (Figure 2).

Thus, if the surgeon wanted to use an autograft they could typically find a way to accomplish this. We were encouraged by this that our study actually has impact because educating surgeons through manuscripts, reviews and podium presentations is an easier, cheaper approach than any other approach for broadcasting these results i.e. educating patients.

## RESULTS

#### Epidemiology

Follow-up has been very successful despite the challenge of coordinating 52 sites. Our use of central follow-up for this study has been a successful model and provides consistency across the study. The demographics and epidemiology of our cohort was first described in our original MARS publication as well as subsequent publications.<sup>12, 19</sup> 1234 patients have been enrolled in the study. Median age was 26 with a range from 12–63 years. 518 (42%) were female. For 87% it was their first revision,<sup>12</sup> while 13% were undergoing their 2<sup>nd</sup> or higher revision ACL reconstruction. 73% were injured while playing a sport. The most common sports involved both genders and were soccer and basketball. Associated surgeries included high tibial osteotomies (n=21), medial meniscus transplants (n=34), and lateral meniscus transplants (n=10).

Modern ACL reconstruction with appropriate grafts and well positioned tunnels realistically began in the 1980s. In the 1990s, case series of revision ACL surgery began to appear. In the vast majority of these cases it was felt the etiology of the original ACL graft failure was due to technical issues.<sup>20–22</sup> However, in the MARS cohort trauma was more commonly reported as a cause of graft failure (Table 2, Figure 3). This reflects two potential considerations for this finding: 1) improved technical ability with improved training and education; and 2) surgeons self-reporting on their own failures in this cohort: 30% (367/1234) of the patients were the surgeons' own failures.

The cause of technical failure in the MARS study was most commonly felt to be due to femoral tunnel malposition (Table 3) with the tibial tunnel the 2nd most common cause. Varus and valgus malalignment were seldom felt to be an issue. (Table 3).

Prior graft utilized was autograft 68% of the time, allograft 29% and a combination (autograft + allograft) 3%. The most common previous autograft was patellar tendon, utilized 52% of the time. Patellar tendon was the most common allograft utilized previously for the primary ACL reconstruction (11%). Current graft utilized was 26% patellar tendon autograft, 20% soft tissue autograft, 23% patellar tendon allograft and 25% soft tissue allograft.

Radiographs were obtained for enrolled patients. MARS had required (bilateral standing Anterior-Posterior, full extension lateral) and recommended (Rosenberg, sunrise/merchant, and bilateral long leg standing alignment) radiographs. These radiographs were analyzed for the group and findings collated.<sup>23, 24</sup> Sagittal views of the femur demonstrated 42% of femoral tunnels were more than 40% anterior to the posterior cortex. On the tibia sagittal view 49% demonstrated some form of roof impingement on full extension. On longstanding alignment films the average limb alignment was 43% from the medial edge of the tibia.

An interesting use of the cohort involved assessment of osteoarthritis rating scales utilizing the radiographs obtained as part of the study.<sup>25</sup> Reliability of different radiographic views as correlated with arthroscopic findings were analyzed. In addition, a multirater osteoarthritis scale study was performed analyzing the Kellgren-Lawrence, IKDC, Albrecht, Fairbank, Brandt and Jäger-Wirth grading scales. 45° flexion posterior-anterior weightbearing radiographs demonstrated the best interobserver reliability as compared to anteroposterior straight standing radiographs. The IKDC grading scale correlated best with the arthroscopic findings of cartilage damage.

### **Graft Choice**

The choice of graft is a major issue for revision ACL reconstructions. Obviously, the patient's previous graft will alter and potentially bias future choices. Many surgeons prefer allograft due to the complexity of the revision ACL reconstructions. Previous studies in the last few years have demonstrated failure rates for allograft in primary ACL reconstructions to be higher than those noted for autograft reconstructions.<sup>26, 27</sup>This is especially true in the young active patient. Despite these findings there was no evidence that these higher failure rates would be present in the different clinical situation of a revision ACL reconstruction. Additionally, many surgeons believed that processing was the key to the higher failure rates in allograft reconstructions and that a fresh frozen allograft with no irradiation would perform similarly to an autograft. For that reason, we knew that controlling the source and preparation for our allografts was key. We limited our allograft source to MTF and were able to track the demographics and preparation history for each individual graft utilized in the MARS study. This has given increased validity to our findings outlined later in this review.

We analyzed graft choice as a predictor for outcome as one of the specific aims of our NIHfunded grant.<sup>11</sup> The demographics of patients that received autograft and allograft can be seen in Table 4. Allografts were placed in older, less active patients on average.

The form of treatment was known for each allograft and included no radiation (aseptic), light total whole-body irradiation (<1.8 mrad), or rarely terminal radiation (Table 5).

The overall re-rupture rate at two years was 3.3% (37/1112): 2.2% (12/545) in autografts, 4.5% (24/534) in allografts, and 3% (1/33) in combination autograft+allografts. Autograft use was 2.78 times less likely to re-rupture (p=0.047; 95% CI=1.01, 7.69). No difference in re-rupture rate was found in soft tissue vs. BTB in either autograft or allograft. IKDC scores improved with autograft reconstruction with an odds ratio (OR) of 1.33 (95% CI: 1.01–1.7; p=0.045). KOOS Sports and Recreation subscale significantly improved with autograft

(OR=1.33; CI: 1.02–1.73; p=0.037), as did the KOOS Quality of Life (OR=1.33; CI: 1.03–1.73; p=0.031). The KOOS ADL and Symptoms subscales were not affected by graft choice.

Many people believed that graft choice was a predetermined fate in a revision setting and that the surgeon truly had no choice in determining what graft the patient obtained. To analyze this belief we performed a propensity analysis for graft choice (Figure 2).<sup>18</sup> Our analysis demonstrated that the surgeon performing the procedure was far and away the biggest factor on what graft type was chosen for the revision reconstruction, approximately 5 times more impactful than the 2nd most common predictor (which was prior graft). Thus, surgeons truly did have a choice in what graft they utilized. This allows us to modify clinical practice by educating surgeons through publications and podium presentations at major meetings such as the American Academy of Orthopedic Surgeons (AAOS) or AOSSM.

Subsequent 6-year follow-up for the MARS Group has strengthened the graft choice conclusions.<sup>28</sup> In an analysis presented at the 2019 AAOS Annual Meeting and currently in manuscript preparation we noted the following. Questionnaire follow-up was obtained on 810 subjects (65%), while phone follow-up was obtained on 949 subjects (76%). Graft choice proved to be a significant predictor of 6-year Marx activity level scores (p=0.024). Specifically, the use of a BTB (bone-patellar tendon-bone) autograft for revision reconstruction predicted improved activity levels compared to a BTB allograft [Odds Ratio (OR)=1.92; 95% confidence intervals (CI)=1.25, 2.94]. Graft choice was not significant in predicting 6-year IKDC, WOMAC, or KOOS outcome scores.

Graft rerupture was reported in 5.8% (55/949) of patients by their 6-year follow-up: 3.4% (16/472) in autografts, 8.3% (37/448) in allografts, and 6.9% (2/29) in combination allograft + autografts. Use of a BTB autograft for revision resulted in patients 4.2 times less likely to sustain a subsequent graft rupture than if a BTB allograft was utilized (p=0.011; 95% CI=1.56, 11.27). Thus, graft choice has increased in significance in predicting re-rupture and sports performance.

## Meniscus and Articular Cartilage

Compared to primary reconstructions the revision patient has a much higher chance of having meniscus or articular cartilage damage at the time of revision reconstruction. In our cohort, only 9% of the patients did not have a meniscus tear or grade 2 or worse articular cartilage damage, 90% had at least meniscus or articular cartilage damage and 59% had both at the time of revision (Table 6).

We analyzed the impact of these meniscus tears and articular cartilage damage on patient outcomes at 2 years.<sup>29</sup> Previous lateral meniscectomy prior to the time of revision significantly resulted in worse patient reported outcomes (Table 7); previous medial meniscectomy less so. Interestingly, current meniscal pathology variables documented at the time of the index revision surgery had no significant predictor effect on any 2-year patient outcome measure (Table 7).

Grade 2 or worse articular cartilage damage grade negatively impacted patient-reported outcomes at 2 years. The most significant finding was the consistent negative impact of trochlear groove chondrosis across outcome measures (Table 8).

MARS analyzed the impact of previous meniscectomy on the presence of chondral damage noted at the time of revision ACL reconstruction. Previous partial meniscectomy was associated with chondral damage (p<0.0001). Meniscus repair appeared to be chondral protective as there was no statistically significant increase in chondral damage noted in the setting of meniscus repair. There was no difference between knees that had not had previous meniscus surgery and those with repair.<sup>30</sup>

The association of meniscus status, lower extremity alignment and body mass index (BMI) with chondrosis at the time of revision ACL reconstruction was also analyzed.<sup>31</sup> The medial compartment had more chondrosis than the lateral compartment (grade 2/3, 42% versus lateral grade 2/3, 26%). The mean weight-bearing line was 0.43 as measured from the medial edge of the tibia. Medial compartment chondrosis was associated with higher BMI (p=0.025), alignment (p=0.002), and "disrupted" medial meniscus status (i.e. a tear that required a repair or a partial meniscectomy; p=0.001). No patient with a weight-bearing line greater than or lateral to 0.625 had grade 4 medial compartment chondrosis. Lateral compartment chondrosis was significantly associated with higher age (p=0.013) and "disrupted" lateral meniscus status (i.e., a tear which required a repair or a partial meniscus status (i.e., a tear which required a repair or a partial meniscus status (i.e., a tear which required a repair or a partial meniscus status (i.e., a tear which required a repair or a partial meniscus status (i.e., a tear which required a repair or a partial meniscus status (i.e., a tear which required a repair or a partial meniscus status (i.e., a tear which required a repair or a partial meniscus status (i.e., a tear which required a repair or a partial meniscus status (i.e., a tear which required a repair or a partial meniscus status (i.e., a tear which required a repair or a partial meniscus status (i.e., a tear which required a repair or a partial meniscus status of associated chondrosis by 64% to 84%.<sup>31</sup>

Predictors of significant chondral surface damage from primary reconstruction to revision reconstruction were analyzed utilizing the MARS and MOON databases.<sup>32</sup> One hundred thirty four patients had been enrolled in the MOON cohort and subsequently underwent revision and were enrolled in MARS. Progression of articular cartilage damage was noted in 25.4% (34/134) of patients in the lateral compartment, 23.9% (32/134) in the medial compartment and 23.1% (31/134) in the patellofemoral compartment. For the lateral compartment, patients who had undergone a greater than 33% partial lateral meniscectomy at the time of primary ACL reconstruction had a 16.9 times greater odds of progression of articular cartilage injury than those with an intact lateral meniscus (p=0.001). Patients that underwent a less than 33% partial medial meniscectomy at the time of primary ACL reconstruction had a 4.8 times greater odds of progression of articular cartilage injury then those with an intact medial meniscus at the time of primary reconstruction (p=0.02). For each increase in age by one year there was a 6% increase in the onset of significant chondral damage in the medial compartment and 5% in the lateral compartment (p 0.02). For the patellofemoral compartment use of an allograft reconstruction at the time of primary ACL reconstruction resulted in a 15 times increase in the risk of progression of articular cartilage injury as compared to a patellar tendon autograft (p < 0.001). At the time of revision ACL reconstruction, a 1 unit increase in BMI was associated with a 10% increase in the risk of progression of articular cartilage damage (p=0.046).

Meniscus repair success at two years was analyzed for the cohort.<sup>33</sup> In total, 218 patients from 1205 revision ACL reconstructions underwent concurrent meniscal repairs (18% of the

cohort). There were 235 repairs performed: 153 medial, 48 lateral and 17 medial + lateral. The vast majority of these repairs (n=178; 76%) were performed with all-inside techniques. Two-year surgical follow-up was obtained on 90% (197/218) of the cohort. Overall, the meniscal repair failure rate was 8.6% (17/197) at 2 years. Of the 17 failures, 15 were medial (13 all-inside, 2 outside-in) and 2 were lateral (both all-inside). Four of the medial failures were treated in conjunction with a subsequent repeat revision reconstruction. Thus, meniscus repair is overall very successful in the revision setting approaching that of repair results in isolated or primary ACL reconstruction settings.

#### Surgical Factors

Surgical factors were analyzed to determine the impact on patient-reported outcome measures at 2 years.<sup>34</sup> A variety of factors were analyzed and in many cases it is difficult to determine intuitively why certain factors impacted outcome. With regards to surgical approach, having undergone a prior arthrotomy decreased IKDC scores (p=0.037, OR=2.43) and decreased all KOOS subscales (p<0.05, OR range =2.38–4.35). A double femoral tunnel resulted in worse KOOS QOL scores (p=0.027, OR=3.13). An ideal tibial position that was not enlarged resulted in worse KOOS, WOMAC, and IKDC scores (p=0.001–0.03, OR range=1.19–2.68). Using a femoral tunnel declared "optimum" vs. drilling an entirely new femoral tunnel resulted in worse KOOS QOL scores (p=0.025, OR=1.79). Undergoing a notchplasty decreased KOOS, IKDC, and WOMAC scores (p=0.013–0.034, OR range=1.40–1.49). Factors that did not impact outcome included blended tunnels and knee position at time of graft fixation.

Graft fixation as a surgical factor impacting outcome was also analyzed. Femoral fixation with a metal screw had better 2-year outcomes in KOOS and WOMAC scores (p=0.01-0.05, OR range=1.41–1.96) when compared to using a bioabsorbable screw, cross-pin or combination. Tibial fixation other than metal screw resulted in worse IKDC (p=0.017, OR=1.67) and WOMAC stiffness (p=0.013, OR=1.72) scores.

Use of biologics and bone grafting was analyzed. Use of biologic enhancement in the revision setting resulted in lower 2-year MARX activity level scores (p=0.025, OR=1.79). Utilizing femoral bone grafts resulted in lower MARX activity scores at 2 years (p=0.048, OR=2.04). Conversely, not bone grafting the tibia resulted in worse KOOS Pain scores (p=0.046, OR=1.95) and WOMAC Pain scores (p=0.004, OR=3.31).

Reoperations following revision ACL reconstruction were analyzed.<sup>35</sup> 11% of patients underwent subsequent reoperation by 2-year follow-up: 27% were meniscal procedures (69% meniscectomy, 26% repair), 19% were revision ACL reconstructions, 17% were cartilage procedures (61% chondroplasty, 17% microfracture, 13% osteochondral autograft), 11% hardware removal and 9% were performed for arthrofibrosis reasons. Multivariate analysis demonstrated that age less than 20 years old resulted in a doubling of the risk for reoperation as compared to patient's age range between 20–29 years old. Use of an allograft at the time of revision was a significant predictor for the need for reoperation within 2 years (OR=1.79; p=0.007). Patients with grade 4 chondral damage noted at the time of revision ACL reconstruction were 78% less likely to undergo a reoperation within 2 years. Gender,

body mass index, smoking history, Marx activity scale and meniscal treatment (repair, meniscectomy) did not impact the need for reoperation within two years.

## **Rehabilitation Factors**

Rehabilitation factors were analyzed regarding their potential impact on revision ACL reconstruction outcomes. <sup>36</sup> Two rehabilitation factors predicted outcome: 1) use of an ACL derotation brace for return-to-sport had better KOOS sports/rec scores at 2 years (odds ratio=1.50; 95% CI=1.07–2.11; p=0.019), and 2) use of an ACL derotation brace for post-operative rehabilitation period were 2.3 times more likely to have a subsequent surgery by 2 years (OR=2.26; 95% CI=1.11–4.60; p=0.024). Use of an ACL derotation brace at the time of return to sport could not be determined to improve or decrease the graft re-rupture rate. Restricting or allowing of all other factors did not predict outcome including active range of motion, passive range of motion, immediate weight-bearing, and the use of rehabilitative postoperative bracing.

#### **Patient-Reported Outcomes**

Predictors both positive and negative for patient reported outcomes measured at 2 years were studied.<sup>37</sup> Patient reported outcomes for 2 and 6 years remained stable except steadily decreasing Marx activity level scores (Table 9). Scores for KOOS Quality of Life and Sports/Recreation and IKDC were 15–20 points below those for the same time point in historical primary ACL reconstruction series (Table 9, Figure 4).

The most significant positive predictors of 2-year IKDC scores were having a high baseline IKDC score, high baseline Marx activity level, male gender, and having a longer time between a patient's last ACL reconstruction, while negative predictors included having a previous lateral meniscectomy, Grades 3/4 trochlear groove or medial tibial plateau (MTP) chondrosis. For KOOS, having a high baseline score and having a longer time between their last ACL reconstruction were significant positive predictors for having better (i.e. higher) 2-year KOOS scores, while having a previous lateral meniscectomy prior to the revision ACL reconstruction was a consistent predictor for having significantly worse (i.e. lower) 2-year KOOS scores. Statistically significant positive predictors for 2-year Marx activity levels included higher baseline Marx activity levels, younger age, male gender, and being a non-smoker. Negative 2-year activity level predictors included having an allograft and a biologic enhancement.

#### **Other Databases**

The size and strength of this cohort has encouraged comparison to other registries and cohorts. Our first analysis in this area was to compare it to a prospectively collected primary cohort. During identical enrollment times using a similar collection approach we compared MARS and MOON intra-articular findings.<sup>38</sup> Demographics were similar for both populations. Prevalence of medial meniscus tears were fundamentally equivocal (40%) in both populations. New untreated lateral meniscus tears were less common in the revision setting (46% in primaries vs. 34% in revisions; odds ratio (OR)=0.54; p< 0.01). Outerbridge Grade 3 and 4 chondrosis was more common in the patellofemoral joint of revision ACL reconstructions (3–7% in primaries vs. 11–13% in revisions; OR=1.70; p=0.04) and the

lateral femoral condyle (5% in primaries vs. 11% in revisions; OR=1.73; p=0.04). No other compartments demonstrated statistically significant differences between revision and primary ACL reconstructions. Both revision and primary ACL reconstructions demonstrated an increased risk of medial and lateral femoral condyle and medial and lateral tibial plateau Grade 3 and 4 chondrosis in the setting of a previous medial or lateral meniscectomy respectively.

The MARS cohort was compared to the Norwegian revision registry and a revision database for the French Arthroscopic Society.<sup>39</sup> Patient demographics were very similar. Allograft was more frequently chosen in the United States MARS cohort (29% vs. <1%). Hamstring autograft was most commonly used in Norway (74%) and the most common French graft was a bone patellar tendon bone autograft (70%). Significant articular cartilage injuries were most commonly noted in the MARS cohort. Patient-reported outcomes at baseline were statistically significantly different for KOOS and IKDC for the different patient groups but was only clinically significantly different for the KOOS sports and recreation sub scale where the MARS Group was more than 8 points better at baseline.

## CONCLUSIONS

The MARS group was formed over 10 years ago, with the aim of assessing both the short and long-term progression of outcomes following revision ACL reconstruction, and to determine how the initial factors at the time of revision surgery may influence and predict disease progression. This consortium is unique in its size, scope and demographics. The MARS group comprises the most sites involved in a single orthopaedic study with 83 members at 52 sites, covering both academic (44%) and private practice (56%) settings. The study design involves a longitudinal prospective cohort of over 1,200 patients, for whom we have baseline, 2-year and 6-year follow-up on, and which has allowed us to assess modifiable surgical factors in a fashion never before contemplated. While there have been multiple challenges encountered in the MARS study they have for the most part been surmountable. The level of research and the questions that can be asked and answered in a cohort of this size and type is unmatched by any other approach. We believe the study design and scaffolding we have developed for this type of truly multi-surgeon, multicenter research can be a model for future orthopaedic research groups.

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# The Rover

#### <u>What's New?</u>

- This newsletter! The new MARS newsletter will be sent out on the first working day of each month. We are still in the process of working on content and layout, so comments and suggestions will be velcomed at the AOSSM MARS meeting. For those of you who will not be in attendance, please submit any comments or suggestions using the hyper-link at the bottom of the page.
- Dr. Bob Giffin and Dr. Matt Matava are developing a study to determine our ability to agree on modes and mechanisms of failure of ACL reconstruction at the time of ACL revision reconstruction. Dr. Matava will be presenting a short presentation about this study at the MARS meeting in July.
- Please welcome newly IRB approved MARS surgeons: Robert Arciero, Keith Baumgarten, Jeffery Bechler, J. Brad Butler, Brian Cole, Charles Gatt, Tim Hossa, G. Peter Maiers II, Arun Ramappa, Arthur Rettig, and Orrin Sherman.

#### Upcoming Events

AOSSM MARS Meeting Saturday July 12th, 12:30-2:30 Mediterranean Ball room of the JW Marriott. Lunch will be provided. Please RSVP to haasa#/wudosis.wustl.edu if you have not already done so.

We are in the planning stages of organizing research coordinator phone conferences. More details to come.





- <u>XRAYS</u>
   As a reminder, everyone should be obtaining x-rays <u>Pre-OP</u> for MARS patients.
   The following views are <u>required</u>:
   1) Standing bilateral AP in full extension
   2) Lateral view in maximum extension
  - The following views are <u>recommended</u> and would allow additional analysis for predictors of outcome:

Bright Blue Newly Formed Stars, (NASA)

Vermont IRB– Expires 7/5/08 HSS IRB– Expires 7/15/08

Lenox Hill IRB- Expires 7/22/08

Colorado IRB- Expires 8/1/08 Connecticut Children's IRB- Expires 8/31/08

COR-Arlington, VA University of North Carolina Case Western

Need New IRB Approval Letters From:

Upcoming IRB Renewals

Booth, Bartolozzi, Balderston Ortho. IRB- Expires 7/31/08

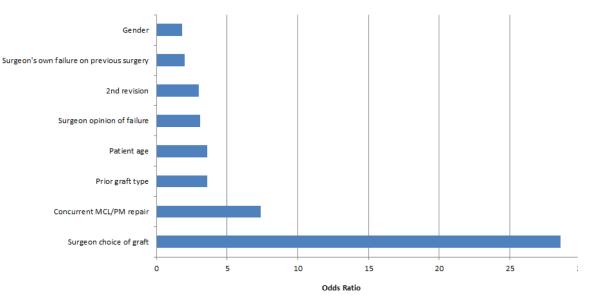
- 3) Bilateral flexion weightbearing views at 45° (Rosenberg) 4) Bilateral 45° Merchant views 5) Standing Alignment (hip-knee-ankle)
- New Surgeons

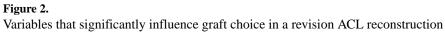
Continue to work on getting your IRB approval. It is all downhill from there!

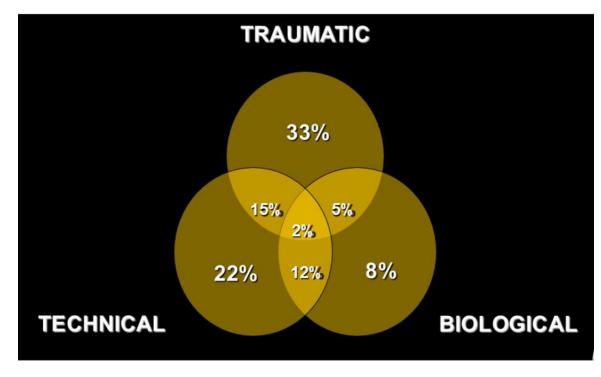
Questions or Comments? E-mail us at haasa@wudosis.wustl.edu or call (314) 362-3768

**Figure 1:** Electronic Newsletter

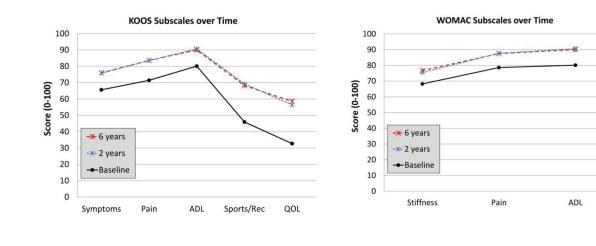


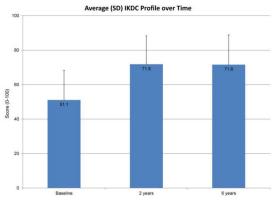


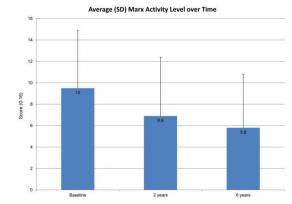




**Figure 3.** Cause of Failure Venn Diagram







**Figure 4.** Global Patient-Reported Outcomes over Time

## Table 1.

Data completeness within a subset of variables (n=900 cases)

Outcome Variable	Questionnaire Source Form	# Variables	# Missing / Observations (%)	% Complete
Marx Activity Level	Patient	4	23 / 3,600 (0.6%)	99.4%
IKDC	Patient	19	38 / 17,100 (0.2%)	99.8%
KOOS	Patient	42	259 / 37,800 (0.7%)	99.3%
Current graft type	Surgeon	1	1 / 900 (0.1%)	99.9%
Surgical technique	Surgeon	1	2 / 900 (0.2%)	99.8%
Rehabilitation factors	Surgeon	6	35 / 5,400 (0.7%)	99.3%

### Table 2.

Cause of Failure in the MARS Cohort

	#	%*
Traumatic	697	56%
Technical	616	50%
Biologic	329	27%
Other	35	3%
Blank	2	<1%

\_

\* the denominator is >100% due to multiple choice option of this question (surgeons were instructed to 'check all that apply').

Note: n=426 (35%) of these responses listed a combination of these components as the reason for failure.

## Table 3.

## Cause of Technical Failure

	#
Femoral tunnel malposition	595
Tibial tunnel malposition	228
Varus / Valgus malalignment	23
Femoral fixation	38
Tibial fixation	18
Autograft source	17
Allograft source	66
Posteromedial laxity	16
Posterolateral laxity	4

#### Table 4.

	Autograft Group (n=598)	Allograft Group (n=599)	Auto+Allo Group (n=37)
Age	24 (19, 32)	28 (21, 36)	21 (18, 28)
Gender			
• males (%)	361 (60%)	338 (56%)	17 (47%)
• females (%)	237 (40%)	261 (44%)	19 (53%)
Marx Activity Level			
Baseline	12 (5, 16)	10 (3, 15)	12 (8, 16)
• 2 year follow-up	8 (2, 12)	5 (1, 11)	10 (3, 13)
<ul> <li>6 year follow-up</li> </ul>	6 (2, 10)	4 (0, 8)	8 (3, 10)

Key: continuous variables are reported as medians (25%, 75% interquartiles). Frequencies are reported as number (percentage).

Graft Choice Demographics

## Table 5.

# Allograft Treatment

Sterilization Method	Allograft Cohort (n=636)	Allograft Failure Cohort at 6 years		
Aseptic	257 (40%)	15 (42%)		
Whole Body (1.2-1.8 mRad)	343 (54%)	18 (50%)		
Terminal (0.7–1.0 mRad)	36 (6%)	3 (8%)		

## Table 6.

Overall Meniscal and Articular Cartilage Integrity in the MARS Cohort at the time of Enrollment

		Articular	Articular Cartilage Pathology			
		Normal	Abnormal	Total		
Meniscal Pathology	Normal	9%	12%	21%		
	Abnormal	19%	59%	78%		
	Total	28%	71%			

### Table 7.

Meniscus Impact on 2-Year Patient-Reported Outcomes (significant p values only)

	KOOS					WOMAC				
Structure	Marx	Symptoms	Pain	ADL	Sports / Rec	QOL	IKDC	Stiffness	Pain	ADL
Previous Meniscal Pathology										
• medial			0.002				0.035			
• lateral		0.008	0.042			< 0.001	0.038	0.03	0.032	
Current Meniscal Pathology										
• medial										
• lateral										

Key: Wald Chi-Squared Test used to compute overall predictor variable significance. Blank cells indicate non-significant p values of > 0.05. ADL=activities of daily living; Rec=recreation; QOL=quality of life.

#### Table 8.

Articular Cartilage Impact on 2-Year Patient-Reported Outcomes (significant p values only)

Structure	Marx			KOOS			IKDC	v	VOMAC	
		Symptoms	Pain	ADL	Sports/Rec	QOL		Stiffness	Pain	ADL
Previous AC Pathology										
• Yes/no										
Current AC Pathology										
• MFC			0.018						0.012	
• LFC				0.048						0.048
• MTP					0.004					
• LTP										
• Patella										
• Trochlea			0.034	< 0.001	0.011		0.01			< 0.001

Key: Wald Chi-Squared Test used to compute overall predictor variable significance. Blank cells indicate non-significant p values of > 0.05. ADL=activities of daily living; Rec=recreation; QOL=quality of life; AC=articular cartilage; MFC=medial femoral condyle; LFC=lateral femoral condyle; MTP=medial tibial plateau; LTP=lateral tibial plateau.

## Table 9.

Median (IQR) of KOOS, IKDC, and Marx Outcomes over Time of the MARS Cohort

	Score Range	Baseline	2 Years	6 Years
IKDC	0-100	52 (38, 63)	77 (60, 86)	75 (60, 87)
KOOS				
• symptoms	0-100	68 (54, 82)	79 (64, 89)	79 (64, 89)
• pain	0-100	75 (58, 86)	89 (75, 94)	89 (75, 97)
<ul> <li>activities of daily living</li> </ul>	0-100	87 (69, 96)	97 (88, 100)	97 (87, 100)
<ul> <li>sports &amp; recreation</li> </ul>	0-100	45 (25, 65)	75 (55, 90)	75 (50, 90)
• quality of life	0-100	31 (19, 44)	56 (38, 75)	62 (44, 75)
WOMAC				
• stiffness	0-100	75 (50, 88)	75 (62, 100)	75 (63, 100)
• pain	0-100	85 (70, 95)	95 (80, 100)	95 (80, 100)
<ul> <li>activities of daily living</li> </ul>	0-100	87 (69, 96)	97 (88, 100)	97 (87, 100)
Marx Activity Level	0–16	11 (4, 16)	7 (2, 12)	5 (1, 9)