

Transtibial ACL Femoral Tunnel Preparation Increases Odds of Repeat Ipsilateral Knee Surgery

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Background: Recent efforts to improve the results of anterior cruciate ligament (ACL) reconstruction have focused on placing the femoral tunnel anatomically. Medial portal femoral tunnel techniques facilitate drilling of femoral tunnels that are more anatomic than those made with transtibial techniques. Few studies have compared the clinical outcomes of these two femoral tunnel techniques. We hypothesized that the transtibial technique is associated with decreased Knee injury and Osteoarthritis Outcome Scores (KOOS) and an increased risk of repeat surgery in the ipsilateral knee when compared with the anteromedial portal technique.

Methods: Four hundred and thirty-six patients who had undergone primary isolated autograft ACL reconstruction with a transtibial (229 patients) or anteromedial portal (207 patients) technique in 2002 or 2003 were identified in a prospective multicenter cohort. A multiple linear regression model was used to determine whether surgical technique (transtibial or anteromedial portal) was a significant predictor of KOOS at six years postoperatively, after controlling for preoperative KOOS, patient age, sex, activity level, body mass index (BMI), smoking status, graft type, and the presence of meniscal and chondral pathology at the time of reconstruction. A multiple logistic regression model was used to determine whether surgical technique was a significant predictor of repeat ipsilateral knee surgery, after controlling for patient age and activity level, graft type, and meniscal pathology at the time of reconstruction.

Results: Postoperative KOOS were available for 387 patients (88.8%). Femoral tunnel drilling technique was not a predictor of the KOOS Quality of Life subscore ($p = 0.72$) or KOOS Function, Sports and Recreational Activities subscore ($p = 0.36$) at the six-year follow-up evaluation. Data regarding the prevalence of repeat surgery were available for 380 patients. Femoral tunnel technique was a significant predictor of subsequent ipsilateral knee surgery (odds ratio [OR] = 2.49, 95% confidence interval [CI] = 1.30 to 4.78, $p = 0.006$).

Conclusions: Patients who underwent ACL reconstruction with a transtibial technique had significantly higher odds of undergoing repeat ipsilateral knee surgery relative to those who underwent reconstruction with an anteromedial portal technique.

Level of Evidence: Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

Anterior cruciate ligament (ACL) reconstruction is often successful in enabling athletes to return to the playing field; however, relatively high reinjury and reoperation

rates and suboptimal functional outcome scores have been noted in some populations¹⁻³. As surgeons' understanding of the anatomy and function of the ACL and its role in knee kinematics

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continues to improve, reconstructive techniques continue to evolve. Recent efforts have focused on the restoration of native ligament anatomy, with a trend away from placement of the femoral tunnel in the traditionally defined over-the-top position^{4,5}.

Two commonly employed techniques for drilling the femoral tunnel are transtibial drilling and drilling via an anteromedial portal. While the transtibial technique has been used for years with good clinical outcomes, some investigators have shown that it cannot reliably place the femoral tunnel in its anatomic footprint⁶⁻¹⁰. The tunnels produced with use of transtibial methods have been shown by numerous authors to be, on average, located in an anatomically more anterior position (commonly referred to as more vertical in the notch) relative to those placed with the anteromedial portal technique⁶⁻¹⁴. Biomechanical studies have demonstrated that grafts placed in this nonanatomic position are subjected to less load than those placed anatomically¹⁵ and result in poorer rotational control^{11,16-21}. Decreased rotational control and increased loading of other intra-articular structures such as menisci and articular cartilage would be expected to result in decreased patient-reported outcome scores and increased risk of subsequent ipsilateral knee surgery.

While biomechanical data increasingly demonstrate differences between the results of reconstructions with transtibial

techniques and those of procedures done with anteromedial portal techniques, clinical differences have not been clearly demonstrated. The few studies comparing the outcomes of different tunnel positions²²⁻²⁴ and different femoral tunnel preparation techniques²⁵⁻³¹ demonstrated mixed results regarding clinical outcomes. A recently published study of prospectively collected data from the Danish ACL registry demonstrated increased risk of revision ACL reconstruction when the anteromedial portal technique was compared with the transtibial technique but did not address the odds of repeat surgery other than revision ACL reconstruction³². The purpose of the present study was to compare, with use of a prospectively collected database, the clinical outcomes of patients in whom the ACL femoral tunnel had been drilled via the transtibial technique with those of patients in whom the tunnel had been drilled via the anteromedial portal technique. We hypothesized that the transtibial technique was associated with decreased Knee Injury and Osteoarthritis Outcome Scores (KOOS) and increased risk of repeat surgery in the ipsilateral knee in the first six years following the index surgery.

Materials and Methods

Patient Selection

The study was performed with use of the 2002 to 2003 Multicenter Orthopaedic Outcomes Network (MOON) data set, which is a prospective

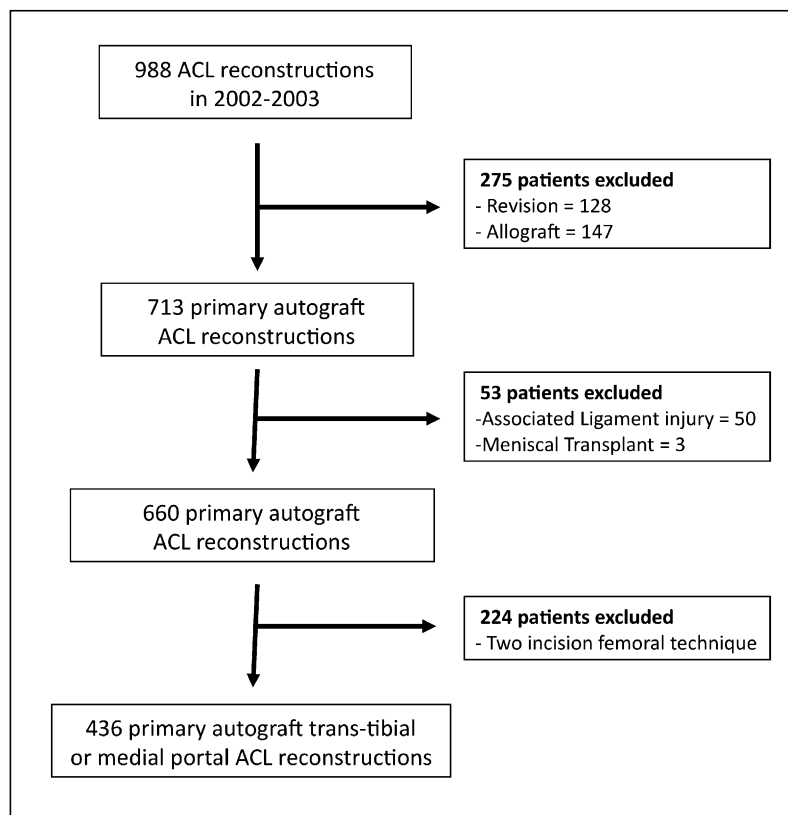


Fig. 1

Flow diagram demonstrating the selection of eligible patients for the analysis. Exclusion criteria included revision reconstruction, reconstruction with allograft tissue, the presence of associated ligament injury of grade II or higher, the performance of a meniscal transplant, or the use of a two-incision technique for femoral tunnel ACL reconstruction.

TABLE I Preoperative Characteristics of Patients According to Femoral Tunnel Technique

| | Transtibial (N = 229) | Anteromedial Portal (N = 207) | P Value for Difference Between Groups |
|--------------------------------------|-----------------------|-------------------------------|---------------------------------------|
| Male (no. [%]) | 119 (52.0%) | 102 (49.3%) | 0.63 |
| Age* (yr) | 25.6 ± 10.3 | 27.0 ± 12.1 | 0.18 |
| Smokers (%) | 26 (11.4%) | 17 (8.2%) | 0.33 |
| BMI at surgery* (kg/m ²) | 25.3 ± 4.3 | 25.2 ± 4.3 | 0.84 |
| Graft type (no. [%]) | | | 0.001 |
| Hamstring tendon | 172 (75.1%) | 112 (54.1%) | |
| Bone-tendon-bone | 57 (24.9%) | 95 (45.9%) | |
| Cartilage damage (no. [%]) | | | |
| Lateral compartment | 27 (11.8%) | 29 (14.0%) | 0.57 |
| Medial compartment | 42 (18.3%) | 36 (17.4%) | 0.80 |
| Patellofemoral | 33 (14.4%) | 30 (14.5%) | 1.00 |
| Medial meniscus (no. [%]) | | | 0.001 |
| Normal | 145 (63.3%) | 129 (62.3%) | |
| Partial meniscectomy | 60 (26.2%) | 33 (15.9%) | |
| Meniscus repair | 19 (8.3%) | 29 (14.0%) | |
| Tear not addressed | 5 (2.2%) | 16 (7.7%) | |
| Lateral meniscus (no. [%]) | | | 0.004 |
| Normal | 143 (62.4%) | 109 (52.7%) | |
| Partial meniscectomy | 62 (27.1%) | 52 (25.1%) | |
| Meniscus repair | 12 (5.2%) | 15 (7.2%) | |
| Tear not addressed | 12 (5.2%) | 31 (15.0%) | |
| Preop. KOOS-QOL* | 35.9 ± 20.1 | 35.0 ± 19.9 | 0.65 |
| Preop. KOOS Sports/Rec* | 47.3 ± 29.5 | 48.5 ± 29.6 | 0.69 |
| Preinjury Marx score* | 11.0 ± 5.3 | 12.0 ± 4.9 | 0.048 |

*The values are given as the mean and standard deviation.

longitudinal cohort including preoperative and six-year follow-up data on 988 patients treated with ACL reconstruction by experienced surgeons. Available data include patient demographic information, surgical technique and graft choice, prevalence of associated chondral and meniscal injuries, patient-reported outcome scores (KOOS) and activity level, and prevalence of repeat surgery including revision ACL reconstruction. Patients eligible for inclusion in this study had undergone unilateral primary ACL reconstruction with autograft tissue, with the femoral tunnel created by either a transtibial or an anteromedial portal technique. Patients who had undergone primary ACL reconstruction with allograft, revision reconstruction, or a concurrent meniscal transplant and those who had an associated posterior cruciate or collateral ligament injury of grade II or higher were excluded. Additionally, patients were excluded if the femoral tunnel had been created with a method other than the transtibial or the anteromedial portal technique. The 436 patients who met all inclusion and exclusion criteria formed the study group (Fig. 1).

Data Collection

Data extracted from the prospective database for analysis included patient sex; age at the time of the ACL reconstruction; graft type (hamstring or patellar tendon); body mass index (BMI) at the time of the reconstruction; smoking status; presence and treatment of meniscal and cartilage injuries; KOOS knee-related Quality of Life subscale (KOOS-QOL) and KOOS Function, Sports and Recreational Activities subscale (KOOS-Sports/Rec) preoperatively and at the six-year follow-up evaluation³³; Marx activity score³⁴ preoperatively and at the

six-year follow-up evaluation; and the prevalence of subsequent ipsilateral knee surgery. The technique by which the femoral tunnel was drilled is not a variable initially recorded in the database. This variable was thus determined retrospectively by contacting the surgeons directly and querying them regarding their surgical technique during the data collection period. Three of six surgeons performed exclusively transtibial reconstructions, two performed exclusively anteromedial portal reconstructions, and one performed reconstructions utilizing both techniques. Chart review was utilized to identify the technique used for each patient by the surgeon who utilized both techniques. The surgical technique was unambiguously identified in all 436 cases.

Outcome Variables

The patient-reported outcome scores chosen for this analysis were the KOOS-QOL and KOOS-Sports/Rec subscales on the basis of prior evidence that questions from these subscales are the most responsive to patients' symptoms and limitations following ACL reconstruction³⁵. Subsequent surgery on the ipsilateral knee was utilized as the secondary outcome measure. Data regarding repeat surgery were obtained by telephone interviews with each patient and include surgical procedures performed at the index institution and elsewhere.

Statistical Methods

A multiple linear regression model was utilized to determine whether femoral tunnel technique (transtibial versus anteromedial portal) was a significant

TABLE II Subsequent Knee Surgery by Femoral Tunnel Technique

| | Transtibial* (N = 203) | Anteromedial Portal* (N = 177) |
|--------------------------------|------------------------|--------------------------------|
| Total procedures† | 71 | 29 |
| Anterior debridement | 16 (7.9%) | 4 (2.3%) |
| Manipulation under anesthesia | 1 (0.5%) | 2 (1.0%) |
| Partial medial meniscectomy | 11 (5.4%) | 5 (2.8%) |
| Partial lateral meniscectomy | 9 (4.4%) | 5 (2.8%) |
| Articular cartilage procedures | 7 (3.4%) | 2 (1.0%) |
| Revision ACL reconstruction | 9 (4.4%) | 5 (2.8%) |
| Other procedures | 13 (6.4%) | 2 (1.0%) |
| No operative report | 5 (2.5%) | 5 (2.8%) |

*The values are given as the number (percentage) of patients. †Some patients underwent multiple repeat operations.

predictor of KOOS-QOL or KOOS-Sports/Rec subscale scores at six years postoperatively, after controlling for the respective preoperative KOOS, graft type, patient sex, patient age and BMI at the time of the reconstruction, smoking status, and the presence and treatment of associated intra-articular pathology. Cartilage injury was modeled with use of one variable for each compartment (medial, lateral, and patellofemoral) denoting the presence or absence of cartilage damage of at least grade II in that compartment. Meniscal injury and treatment were modeled separately for the medial and lateral menisci. Each compartment was coded as normal or no treatment rendered, partial meniscectomy performed, or meniscal repair performed. A power analysis based on the anticipated thirteen degrees of freedom in the model indicated that data from at least 101 patients were required to achieve a power of 80% with α set at 0.05.

A multiple logistic regression model was utilized to determine whether the femoral tunnel drilling technique was a significant predictor of repeat ipsilateral knee surgery. The a priori model used the occurrence of at least one subsequent ipsilateral knee surgery as the outcome variable and included the following predictors: femoral tunnel technique, graft type, patient age and activity level at the time of follow-up, and meniscal injury and treatment. Meniscal injury and treatment were modeled separately for the medial and lateral menisci. Each compartment was coded as normal or no treatment rendered, partial meniscectomy performed, or meniscal repair performed. Because of collinearity between the surgeon performing the surgery and the femoral tunnel technique utilized, the variable "surgeon" could not be included in the logistic regression model. To ensure that no one surgeon's data had excessive influence on the result, a sensitivity analysis was performed. The logistic regression model was run six additional times, excluding one surgeon from the analysis each time, and the variability of the resulting odds ratio (OR) describing the relationship between femoral tunnel technique and revision was noted.

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Results

Of the 436 patients eligible for study inclusion, 229 (52.5%) underwent transtibial ACL reconstruction and 207 (47.5%) underwent anteromedial portal ACL reconstruction. The base-

line characteristics of the patients in the two drilling-technique groups were similar except for an increased frequency of meniscal repair and patellar tendon grafts in the anteromedial portal group (Table I). One postoperative infection requiring debridement was reported in the transtibial group.

Patient-reported outcome data were available preoperatively and at six years postoperatively for 387 (88.8%) of the 436 eligible patients. Multiple linear regression analysis revealed no significant association between femoral tunnel technique and the KOOS-QOL subscore ($\beta = -0.83$, 95% confidence interval [CI] = -5.43 to 3.77 , $p = 0.72$) or KOOS-Sports/Rec subscore ($\beta = 2.15$, 95% CI = -2.43 to 6.71 , $p = 0.36$) at six years postoperatively, after controlling for the respective preoperative KOOS subscale score, patient age, sex, BMI, smoking status, and meniscal and cartilage pathology. No significant changes in the findings were noted with the use of BMI and smoking status at the time of follow-up rather than BMI and smoking status at the time of reconstruction.

Data regarding repeat surgery, femoral tunnel technique, meniscal pathology, and activity level at six years postoperatively were available for 380 (87.2%) of the 436 eligible patients. Seventy-one subsequent ipsilateral knee operations were performed in forty-four of the 203 patients in the transtibial group and twenty-nine subsequent ipsilateral knee operations were performed in twenty-three of the 177 patients in the anteromedial portal group. The specific procedures performed in each group are described in Table II and stratified by surgeon in Table III. Multiple logistic regression analysis demonstrated a significantly higher odds of undergoing repeat surgery on the ipsilateral knee in the transtibial group relative to the anteromedial portal group (OR = 2.49, 95% CI = 1.30 to 4.78, $p = 0.006$), after controlling for graft type, patient age and activity level at the time of follow-up, and meniscal status at the time of the reconstruction. The results of the sensitivity analysis of the effect of surgeon demonstrated that the correlation of transtibial drilling with increased odds of repeat surgery was not dependent on any one surgeon's data. The odds ratio describing this relationship ranged from 2.04 to 3.31 and in each case remained

TABLE III Subsequent Surgical Procedures Performed by Each Surgeon

| Surgeon | No. of Procedures | Anterior Debridement | Manipulation Under Anesthesia | Partial Medial Meniscectomy | Partial Lateral Meniscectomy | Articular Cartilage | Revision ACL | Other | No Report |
|---------------------|-------------------|----------------------|-------------------------------|-----------------------------|------------------------------|---------------------|--------------|-------|-----------|
| Transtibial | | | | | | | | | |
| 1 | 51 | 2 | | 2 | 2 | 1 | 2 | 2 | 2 |
| 2 | 111 | 12 | 1 | 8 | 5 | 4 | 5 | 5 | 3 |
| 3 | 42 | 1 | | | 1 | | 2 | 2 | |
| 5 | 25 | 1 | | 1 | 1 | 2 | | 4 | |
| Anteromedial portal | | | | | | | | | |
| 3 | 5 | | | | | | | | |
| 4 | 56 | | 1 | 3 | | | | 1 | |
| 6 | 146 | 4 | 1 | 2 | 5 | 2 | 5 | 1 | 5 |

significant ($p < 0.05$). Because most of the anterior debridement procedures were performed by one surgeon, the multiple logistic regression analysis was repeated with repeat surgery other than anterior debridement as the end point. This analysis again demonstrated significantly higher odds of undergoing repeat surgery on the ipsilateral knee in the transtibial group relative to the anteromedial portal group (OR = 2.08, 95% CI = 1.05 to 4.10, $p = 0.035$).

Discussion

The most important finding of this study is that patients who underwent ACL reconstruction with a transtibial technique to drill the femoral tunnel had significantly higher odds of undergoing repeat ipsilateral knee surgery relative to those in whom the femoral tunnel had been drilled with an anteromedial portal technique. Although we did not explore the reason for this association, it is possible that decreased loading of a nonanatomic graft and decreased rotational control in patients who underwent transtibial ACL reconstruction resulted in higher forces on the meniscus and altered pressure distribution on the articular cartilage^{15,16}, increasing the risk of subsequent injury. Furthermore, the anatomically more anterior tunnel position (more vertical in the notch) that often results from a transtibial technique may predispose to graft impingement and an increased prevalence of anterior debridement surgery to address subsequent cyclops lesions³⁶. Interestingly, no significant differences in patient-reported outcome scores were noted between the two groups. One might expect that, if decreased rotational control in the transtibial group is a contributor to the increased risk of repeat ipsilateral knee surgery, these patients would have poorer patient-reported outcome scores as well. Additional research is necessary to investigate the relationship between rotational control and patient-reported outcomes.

One must consider that tunnel position was not evaluated in this study and thus the more vertical tunnel position in the transtibial group cannot be confirmed; however, numerous studies have demonstrated that a transtibial technique generally results in femoral tunnels that are located anterior to the

anatomic femoral footprint of the ACL^{6-14,37}. While modifications of the transtibial technique have been reported to reproduce a normal femoral ACL footprint^{12,13}, there is very little margin for error with use of such techniques.

Several authors have examined whether it is even possible to place a femoral tunnel within the anatomic femoral footprint via a traditional transtibial approach. In 2001, Arnold et al. investigated this question by performing arthroscopic transtibial ACL reconstruction on five cadaveric specimens⁷. Following open dissection, it was determined that it was not possible to place a transtibial femoral guide pin within the femoral ACL footprint. The closest position achievable was at the margin of the femoral attachment. Strauss et al. also investigated this topic in a cadaveric model³⁷. They hypothesized that the constraint from an 8-mm tibial tunnel would preclude transtibial placement of the femoral tunnel in an anatomic position. The percent overlap with the native ACL femoral insertion averaged only 30%. Similarly, McConkey et al. demonstrated in cadavers that the transtibial technique is more likely to produce a more anterior femoral tunnel and less likely to be rated as anatomically placed by independent observers³⁸. It is therefore highly likely that the femoral tunnels in the current study created with the transtibial approach were located in a more nonanatomic position than those created with an anteromedial portal technique.

Biomechanical evidence from both cadaveric and in vivo studies has demonstrated superior rotational control in anatomic single-bundle reconstructions relative to reconstructions with more anterior graft positions from transtibial techniques. Kondo et al., in a controlled laboratory study, tested tibiofemoral kinematics in eight cadaveric knees mounted in a six degrees of freedom setup¹⁸. Rotational laxity with internal tibial torque and anterior laxity in a simulated pivot shift were significantly less in anatomic single-bundle reconstructions compared with nonanatomic single-bundle reconstructions. Steiner et al. performed ACL reconstruction on ten pairs of cadaveric knees using either a transtibial drilling method or an independent drilling method¹⁴. The independent drilling method produced more horizontal grafts and a more central

location of the femoral tunnel within the footprint. Biomechanically, the independent drilling was superior, with anterior translation and internal rotation restored under all loading conditions.

In vivo, Schairer et al. used magnetic resonance imaging (MRI) to evaluate knee kinematics following ACL reconstruction with either an anteromedial portal or a transtibial femoral tunnel technique³⁹. MRIs were acquired with 125 N of simulated load at full extension and at 30° to 40° of flexion. ACL reconstructions performed with the anteromedial portal technique restored knee kinematics that were closer to normal than those resulting from the transtibial technique. In a similar study, Abebe et al. used MRI and biplanar fluoroscopy to evaluate in vivo knee kinematics following ACL reconstruction¹⁶. Patients were grouped on the basis of the location of their femoral tunnel as “anteroproximal” or central (anatomic) relative to the native ACL footprint. Patients were asked to perform a quasi-static lunge maneuver, and data were collected. Grafts placed more centrally in the ACL footprint restored normal knee kinematics more completely than those placed anteroproximally.

While the anatomic and biomechanical consequences of transtibial ACL reconstruction have been closely investigated, data are less consistent regarding the impact of surgical technique on clinical outcomes following ACL reconstruction. Alentorn-Geli et al. compared the results of transtibial and anteromedial portal techniques in a population of active soccer players²⁵. Significantly larger improvements in International Knee Documentation Committee (IKDC) scores were noted in the anteromedial portal group compared with the transtibial group. Karlsson et al. compared single-incision and two-incision techniques for ACL reconstruction, with the two groups having similar age, sex distribution, and activity level²⁸. They found significantly lower Lysholm scores in the single-incision group after a mean of forty-seven months of follow-up but the IKDC scores did not differ between the groups. Seon et al. compared patients with a more anatomic femoral tunnel with those with a more anterior (vertical) femoral tunnel²⁴. Neither the Tegner nor the Lysholm scores differed between the groups. In a study in which recently published data from the Danish registry was used to compare revision risk and clinical outcomes (KOOS) between patients treated with the anteromedial technique and those treated with the transtibial technique³², an increased revision risk was noted in the anteromedial portal group. However, with findings similar to those of the current study, the authors noted no difference in KOOS between the groups. The current study did not demonstrate a difference in the risk of revision ACL reconstruction on the basis of femoral tunnel technique, but it was underpowered to detect such a difference.

The current study has several weaknesses. First, as a result of the design of the prospective database and follow-up, the exact three-dimensional position of each patient's tunnel is not known. Unfortunately, we found no studies in the literature that included three-dimensional tunnel position and had sufficient power to perform multiple linear regression analysis to

determine the impact of tunnel position along with other factors on outcome. Another weakness of our study is that we lacked physical examination data with which to detect any difference in rotational or anteroposterior laxity between the two groups. In addition, the relatively small number of revision ACL reconstructions performed in patients in this cohort limits the power to analyze the relationship between surgical technique and the odds of undergoing revision ACL reconstruction. Furthermore, the follow-up time of six years and lack of radiographs preclude detection and assessment of the influence of degenerative changes. Longer follow-up that includes radiographic evaluation may yield useful information in this cohort regarding the effect of femoral tunnel technique on outcome.

Another weakness is that the number of predictors that could be included in the multiple logistic regression model was limited by the number of patients who underwent repeat surgery on the ipsilateral knee (sixty-seven). The desired a priori model contained eight degrees of freedom, slightly in excess of those allowed by the traditional rule requiring $n/10$ predictors, where n is the number of events (in this case, repeat operations)⁴⁰. However, recent work has demonstrated that this rule can be relaxed without compromising the model, particularly in cases (such as the current case) in which the predictor of interest is a binary variable⁴¹. The use of a composite outcome variable for repeat surgery (combining all procedures into a simple “yes/no”) is a simplification of the data that was necessary for analysis but does introduce possible bias if the prevalence of a single procedure drove the results. The finding that the results remained consistent even after removal of anterior debridement from the analysis (see above) demonstrates that this situation is unlikely.

A final, and perhaps the most important, limitation of this study is that nearly all of the surgeons performed only one surgical technique. Only one of the six surgeons performed two different techniques during the study. The resultant collinearity precluded the inclusion of “surgeon” as a potential predictor in the multiple logistic regression model. Although numerous potential confounders were controlled for in the analysis and we performed a sensitivity analysis to ensure that no one surgeon's results unduly influenced the data, it is possible that additional, unidentified differences between the patient populations of the different surgeons contributed to the differences in repeat-surgery rates. Such differences could be explored only through evaluation of patients operated on by the same surgeon randomized to different techniques. Until such data are available, the current study represents the best available evidence regarding the effect of femoral tunnel drilling technique on the odds of repeat ipsilateral knee surgery.

In conclusion, patients undergoing ACL reconstruction with use of a transtibial technique to drill the femoral tunnel have increased odds of undergoing repeat ipsilateral knee surgery within the first six postoperative years compared with those who undergo reconstruction with an anteromedial portal

technique. No differences in patient-reported outcome scores were noted. ■

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Update

This article was updated on January 13, 2015, because one of the members of the MOON Group (Warren R. Dunn, MD, MPH) was not listed in the footnote. The footnote now reads: “*MOON contributing authors: Kurt P. Spindler, MD, and Laura J. Huston, MS (Vanderbilt University School of Medicine); Rick W. Wright, MD, Matthew J. Matava, MD, and Robert H. Brophy, MD (Washington University School of Medicine at Barnes-Jewish Hospital); Eric C. McCarty, MD (University of Colorado School of Medicine); Robert G. Marx, MD, MSc (Hospital for Special Surgery); Richard D. Parker, MD, Jack T. Andrich, MD, and Morgan H. Jones, MD, MPH (Cleveland Clinic); Annunziato Amendola, MD, and Brian R. Wolf, MD, MS (University of Iowa); James L. Carey, MD, MPH (University of Pennsylvania); and Warren R. Dunn, MD, MPH (University of Wisconsin).”