Risk Factors for Manipulation Under Anesthesia and/or Lysis of Adhesions After Anterior Cruciate Ligament Reconstruction

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Background: In the currently published literature, a higher risk for developing arthrofibrosis after anterior cruciate ligament (ACL) reconstruction has been reported for female patients, adolescents, early surgery or concomitant procedures, and the use of a patellar tendon autograft. There is a lack of evidence regarding other graft choices or factors.

Hypothesis: Multiple risk factors will play a significant role in the development of arthrofibrosis after ACL reconstruction. Specifically, we hypothesized that the risk of manipulation under anesthesia (MUA) and/or lysis of adhesions (LOA) would be affected by graft choice and patient demographic factors.

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

Methods: The charts of all patients who underwent ACL reconstruction over a 10-year period at a single academic institution were queried from an electronic medical record database and reviewed at a minimum of 6 months after ACL reconstruction, with the collection of demographic and surgical data. The relative risk for undergoing MUA and/or LOA was calculated for each analyzed risk factor.

Results: A total of 2424 ACL reconstructions were included, with a chart review at a mean of 56.7 months after surgery (range, 7.6-124.0 months). The rate of MUA and/or LOA for arthrofibrosis was 4.5%. A statistically significantly increased relative risk was found for infection (5.45), hematoma requiring evacuation (3.55), ACL reconstruction with meniscal repair (2.83), use of a quadriceps tendon autograft (2.68), age $<$18 years (2.39), multiple concomitant procedures (1.69), contact injury (1.62), female sex (1.60), and surgery within 28 days of injury (1.53), and a statistically significantly decreased relative risk was found for revision ACL reconstruction (0.30), age $>$25 years (0.34), and use of a tibialis anterior allograft (0.36). In the multivariate regression model, the use of a quadriceps tendon autograft ($P = .00007$), infection ($P = .00126$), and concomitant meniscal repair ($P = .00194$) were independent risk factors, whereas revision ACL reconstruction ($P = .0024$) was an independent protective factor.

Conclusion: Graft type, infection, concomitant meniscal repair, and primary reconstruction are significant risk factors for undergoing MUA or LOA after ACL reconstruction.

Keywords: ACL; knee; anterior cruciate ligament; physical therapy/rehabilitation

The anterior cruciate ligament (ACL) limits anterior translation and internal rotation of the knee joint, thus allowing a patient to better tolerate activities that require cutting and/or pivoting maneuvers. When the ACL is injured, leading to a loss of knee stability, reconstruction of the ligament can restore knee stability and allow a return to activities or sports. In the United States, ACL reconstruction was performed 134,421 times in 2006, up 37% per capita from 1994, with a 924% increased rate in patients younger than 15 years.[3]

Despite advancements in surgical techniques and rehabilitation protocols, approximately 5% of patients develop arthrofibrosis that impairs gait and athleticism, and they undergo a secondary procedure involving manipulation under anesthesia (MUA) and/or lysis of adhesions (LOA) of the knee to regain full knee range of motion.[7,10] Previous studies have reported on the possible risk factors associated with developing arthrofibrosis, including female sex,[5,15,17] the adolescent age group,[10,15,22] surgery within 3 to 4 weeks of the original injury date,[13,17,20] the use of a patellar tendon autograft,[15] and associated knee lesion(s) requiring concomitant procedures at the time of ACL reconstruction.[1,14,23] With the expanding demographics of patients undergoing ACL reconstruction, and evolving techniques,

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previously unrecognized risk factors for arthrofibrosis should be investigated.

One area of particular interest is the insurance status of the patient. We have noted that patients with government-sponsored insurance often have difficulty accessing physical therapy. A second area of interest is the use of a quadriceps tendon graft. This graft has become more popular in recent years, but its increased size and stiffness may predispose to arthrofibrosis.

The goal of this study was therefore to analyze a large series of ACL reconstructions to report on an array of patient and surgical factors that may influence the risk of undergoing MUA/LOA for arthrofibrosis. We hypothesized that there would be multiple significant independent risk factors.

METHODS

After institutional review board approval, a retrospective cohort study was performed via a chart review. Inclusion criteria were patients of any age who underwent ACL reconstruction between May 1, 2006, and April 30, 2016, at a single academic institution by any of 6 orthopaedic surgeons who were fellowship trained in sports medicine. Exclusion criteria were patients who either did not have the details of their ACL reconstruction documented in the current electronic medical record (EMR) system or did not have $\geq$2 postoperative follow-up visits documented. The patient charts were queried from an EMR database with the Current Procedural Terminology codes for "ACL Reconstruction" (29888), "Manipulation Under Anesthesia" (27570), and "Lysis of Adhesions" (29884). To allow for adequate time to pass for possible secondary surgery, all patients' EMR charts were reviewed at a minimum of 6 months after the date of ACL reconstruction. Demographic information at the time of surgery was collected and included age, sex, ethnicity, and insurance status. We categorized age as $<$18, 18-25, and $>$25 years based on previously reported age groups at risk for arthrofibrosis.[10,15,22] Details of the injury, surgical technique, clinical course, and any subsequent procedures were garnered from operative and clinical notes and included the date and mechanism of injury, previous ACL reconstructions, date of surgery, operative procedures performed, graft type, complications, failure of ACL reconstruction, diagnosis of arthrofibrosis, and subsequent performance of MUA and/or LOA.

The insurance status of each patient was categorized as private insurance (including commercial insurance and workers' compensation), government-sponsored health care program (Medicaid, Medicare, and Tricare), or no insurance. Each patient's EMR chart was manually assessed for his or her insurance status at the time of ACL reconstruction.

The typical rehabilitation protocol included a referral to physical therapy before ACL reconstruction to maximize range of motion and then a 4-phase, 6-month program after surgery. Patients were allowed immediate weightbearing as tolerated with crutches for the first 7 to 10 days, with knee range of motion from full extension to 90° of flexion allowed in the first 2 weeks. The majority of patients were prescribed a hinged knee brace that could be locked in extension to assist with early ambulation. Full knee range of motion was allowed with strengthening exercises initiated after the first 2 weeks.

Statistical analysis of the data was performed by calculating the relative risk, 95% CI, and P value for each analyzed risk factor using a chi-square test. A P value of $<.05$ was considered statistically significant. Multivariate logistic analysis was then performed using JMP Pro 12 Software (SAS Institute) to determine which risk factors were independent. As this was a retrospective chart review, we conducted a priori sample analysis and determined that we would need 30 ACL reconstructions with a given risk factor to determine a moderate effect size (Cohen efficient of 0.5 SDs) for requiring MUA and/or LOA when compared with patients without that risk factor.

RESULTS

Overall, 2558 ACL reconstructions in the 10-year study period were identified through the EMR query. Of these, 134 were excluded for insufficient follow-up, leaving 2424 ACL reconstructions that met the inclusion criteria. The mean time of chart review was 56.7 months (range, 7.6-124.0 months) after reconstruction. Table 1 lists the patient demographics, insurance status, type of injury, surgical factors, and complications for all included cases. Of the ACL reconstructions, 13.9% were revision ACL reconstruction, 49.8% were isolated ACL reconstruction, 27.7% involved meniscectomy, 6.2% included meniscal repair, 0.9% involved the repair or reconstruction of an additional knee ligament complex (medial collateral ligament, posterior cruciate ligament [PCL], or lateral collateral ligament/posterolateral corner), and 9.9% involved more than 1 concomitant procedure. Patients with private insurance made up 91.4% of the study population, while 8.0% were enrolled in a government-sponsored health care program, and 0.6% had no insurance. Postoperative hematomas requiring evacuation occurred in 1.1%, infections requiring irrigation

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Ethical approval for this study was obtained from Emory University.

TABLE 1
Characteristics of Patients and ACL Reconstructions (n = 2424)[a]

Characteristic	Value
Age, mean (range), y	27.2 (8-66)
Sex	
Female	1020 (42.1)
Male	1404 (57.9)
Ethnicity	
White	1850 (76.3)
Black	441 (18.2)
Hispanic	19 (0.8)
Asian	89 (3.7)
Native American	5 (0.2)
Middle Eastern	9 (0.4)
Other	10 (0.4)
Payer	
Private insurance	2216 (91.4)
Government-sponsored insurance	194 (8.0)
No insurance	14 (0.6)
Injury mechanism	
Contact	360 (14.9)
Noncontact	2023 (83.5)
Delay to surgery, median (range), d	52 (1-16,189)
Revision ACL reconstruction	336 (13.9)
Graft type	
Tibialis anterior allograft	822 (33.9)
Quadriceps tendon autograft	623 (25.7)
BPTB autograft	352 (14.5)
Hamstring autograft	369 (15.2)
BPTB allograft	90 (3.7)
Hamstring allograft	88 (3.6)
Concomitant procedures	
None (isolated ACL reconstruction)	1208 (49.8)
Meniscectomy	671 (27.7)
Meniscal repair	150 (6.2)
MCL, PCL, or LCL/PLC repair/reconstruction	23 (0.9)
Multiple procedures	241 (9.9)
Complications	
Arthrofibrosis treated with MUA and/or LOA	108 (4.5)
Hematoma	26 (1.1)
Infection	17 (0.7)
Graft failure	176 (7.3)

[a]Values are expressed as n (%) unless otherwise indicated. ACL, anterior cruciate ligament; BPTB, bone–patellar tendon–bone; LCL, lateral collateral ligament; LOA, lysis of adhesions; MCL, medial collateral ligament; MUA, manipulation under anesthesia; PCL, posterior cruciate ligament; PLC, posterolateral corner.

TABLE 2
Risk Factors for MUA and/or LOA After ACL Reconstruction[a]

Risk Factor	Rate of MUA/LOA, %	Relative Risk (95% CI)	*P* Value
Age			
<18 y	8.0	2.39 (1.65-3.46)	**<.0001**
18-25 y	5.1	1.24 (0.84-1.82)	.2846
>25 y	2.2	0.34 (0.22-0.53)	**<.0001**
Female sex	5.7	1.60 (1.10-2.31)	**.0131**
Payer			
Private insurance	4.3	0.69 (0.39-1.20)	.1885
Government-sponsored insurance	6.2	1.44 (0.80-2.57)	.2222
No insurance	7.1	1.61 (0.24-10.70)	.6234
Contact injury	6.7	1.62 (1.05-2.52)	**.0307**
Surgical factors			
Surgery within 28 d	6.1	1.53 (1.03-2.28)	**.0339**
Revision ACL reconstruction	1.5	0.30 (0.12-0.73)	**.0083**
Graft type			
Tibialis anterior allograft	2.1	0.36 (0.22-0.61)	**.0001**
Quadriceps tendon autograft	8.3	2.68 (1.86-3.87)	**<.0001**
BPTB autograft	6.0	1.42 (0.89-2.26)	.1370
Hamstring autograft	3.3	0.70 (0.39-1.26)	.2287
Concomitant procedures			
Isolated ACL reconstruction	3.7	0.72 (0.49-1.05)	.0840
Meniscectomy	3.3	0.67 (0.42-1.06)	.0858
Meniscal repair	11.3	2.83 (1.73-4.63)	**<.0001**
MCL, PCL, or LCL/PLC repair/reconstruction	8.7	1.97 (0.52-7.50)	.3205
Multiple procedures	7.1	1.69 (1.03-2.79)	**.0394**
Complications			
Hematoma	15.4	3.55 (1.41-8.91)	**.0070**
Infection	23.5	5.45 (2.26-13.10)	**.0002**
Graft failure	1.7	0.36 (0.12-1.14)	.0824

[a]Bolded *P* values indicate statistically significant association with MUA/LOA. ACL, anterior cruciate ligament; BPTB, bone–patellar tendon–bone; LCL, lateral collateral ligament; LOA, lysis of adhesions; MCL, medial collateral ligament; MUA, manipulation under anesthesia; PCL, posterior cruciate ligament; PLC, posterolateral corner.

and debridement in 0.7%, and graft failure in 7.3%. The surgeon with the highest volume of ACL reconstructions (J.X.) performed 67% of the cases, and the other 5 surgeons performed between 1% and 17% of cases each.

The rate of MUA and/or LOA for arthrofibrosis was 4.5% (n = 108), performed at a mean of 5.5 months after ACL reconstruction. The rate of arthrofibrosis for each risk factor is listed in Table 2. Over the 10-year study period, the rate of MUA and/or LOA fluctuated between 2.4% and 7.5%, without any strong trend (Figure 1).

Of the risk factors analyzed for an association with MUA/LOA after ACL reconstruction using a chi-square test (Table 2), a statistically significantly increased relative risk was found for infection (5.45), hematoma requiring evacuation (3.55), meniscal repair (2.83), use of a quadriceps tendon autograft (2.68), age <18 years (2.39), multiple concomitant procedures (1.69), contact injury (1.62), female sex (1.60), and surgery within 28 days of injury (1.53). A statistically significantly decreased relative risk was found for revision ACL reconstruction (0.30), age >25 years (0.34), and use of a tibialis anterior allograft (0.36) (Figure 2). Insurance status was not found to be a significant risk factor. In the multivariate regression model, only 4 statistically significant independent factors were identified: use of a quadriceps tendon autograft ($P = .00007$), infection ($P = .00126$), and meniscal repair ($P = .00194$) as risk

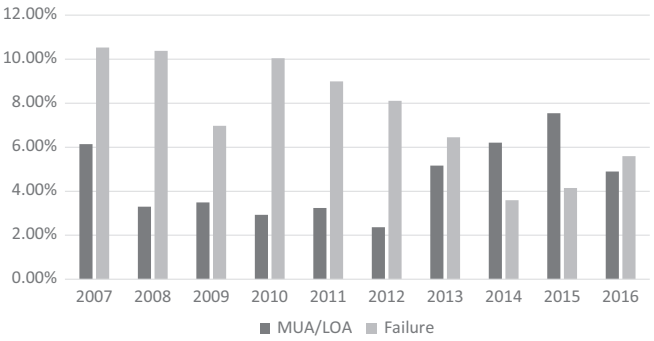

Figure 1. Chart demonstrating the rates of manipulation under anesthesia (MUA) and/or lysis of adhesions (LOA) and graft failure by year in which anterior cruciate ligament reconstruction was performed.

factors and revision ACL reconstruction as a protective factor ($P = .0024$).

Of the 108 patients who underwent MUA/LOA, 3 (2.8%) subsequently had graft failure. In comparison, the overall rate of graft failure after ACL reconstruction in this study was 7.3%. While this represents an almost 200% reduction in the risk of graft failure after MUA/LOA (risk ratio, 0.37), this study was not designed to analyze graft failure as an outcome, and this result was not statistically significant ($P = .0848$) (Table 3).

DISCUSSION

The results of this study confirmed the hypothesis that many variables are associated with the development of arthrofibrosis and the subsequent need for MUA/LOA after ACL reconstruction. The 9 risk factors of postoperative infection and hematoma, meniscal repair, use of a quadriceps tendon autograft, age <18 years, multiple concomitant procedures, a contact injury mechanism, female sex, and surgery performed within 4 weeks of injury, as well as the 3 protective factors of revision ACL reconstruction, age >25 years, and use of a tibialis anterior allograft, confirmed or expanded on previously identified factors.

The association of graft type with arthrofibrosis has been suggested in the previous literature. In a study on arthrofibrosis after ACL reconstruction in children and adolescents by Nwachukwu et al,[15] the use of a patellar tendon autograft was identified as a risk factor, with the authors surmising that its increased stiffness was influential. Sanders et al[17] reported that in 1355 ACL reconstructions, the use of an allograft was associated with a reduced risk of arthrofibrosis, but this finding did not reach statistical significance. The current study had similar results, with a tibialis anterior allograft having a lower risk of MUA/LOA and a bone–patellar tendon–bone (BPTB) autograft associated with a higher (although not statistically significant) rate of MUA/LOA. The novel finding of this study was the higher rate of MUA/LOA with the use of a quadriceps tendon autograft. This is an important finding because the quadriceps tendon is an increasingly popular autograft choice,[21] and it was used for 26% of the ACL reconstructions in this study. While recent studies have reported on the lower donor site morbidity of a quadriceps tendon autograft compared with a patellar tendon autograft[8,11,21] as well as potentially better stability and outcomes compared with a hamstring autograft,[4] this graft has also shown to be stiffer, with increased collagen quantity compared with an equivalently sized patellar tendon graft.[9,19] We surmise that this may increase the risk for arthrofibrosis.

The overall rate of graft failure in this study was 7.3%, but it was only 2.8% in patients who underwent MUA/LOA. This represents an almost 200% reduction in the risk and points to a possible inverse correlation between the risk of arthrofibrosis and graft failure. Considering that BPTB and quadriceps tendon autografts have low failure rates but seem to have a higher risk of arthrofibrosis, and that both are taken from the extensor mechanism of the knee, there may be an underlying mechanism. Yet, it is also possible that patients who undergo MUA/LOA for arthrofibrosis do not return to the same level of activity as other patients and therefore may not place themselves at the same risk for graft failure. Further studies will be necessary to investigate this correlation, especially as it relates to the increased utilization of a quadriceps tendon autograft for ACL reconstruction at our institution and others.

Concomitant procedures have been recognized as an important contributor to the development of arthrofibrosis after ACL reconstruction in prior published literature. For isolated ACL reconstruction, Freedman et al[7] reported a 5.4% incidence of MUA or LOA in a 2003 meta-analysis including 1804 ACL reconstructions. In 2015, Werner et al[23] reported a much lower 0.5% incidence of MUA and a 0.3% incidence of LOA within 6 months after isolated ACL reconstruction in a national sample of 48,631 patients. The incidence of MUA increased to 1.8%, 4.1%, and 8.0% with concomitant collateral ligament reconstruction, concomitant PCL reconstruction, and combined ACL, PCL, and collateral ligament reconstruction, respectively.[23] Austin and Sherman[1] reported a 10% incidence of arthrofibrosis after ACL reconstruction and meniscal repair. The present study demonstrated a similar trend, with a 3.7% rate of MUA/LOA after isolated arthroscopic ACL reconstruction in 1208 patients, increasing to 5.2% after ACL reconstruction with concomitant procedures in 1216 patients. More specifically, we found rates of MUA/LOA of 7.1% with multiple concomitant procedures, 8.7% with concomitant ligament repair/reconstruction, and 11.3% with meniscal repair. Increased trauma to the knee before surgery, a longer and more extensive surgical procedure, and a slower or more restricted rehabilitation program after surgery all likely contribute to the increased incidence of MUA/LOA after ACL reconstruction with concomitant procedures. Although meniscal repair has a reported higher success rate when performed at the same time as ACL reconstruction,[12] the increased incidence of arthrofibrosis and MUA/LOA should be kept in mind.

Other previously published risk factors associated with developing arthrofibrosis include female sex,[5,15,17] adolescent age group,[10,15,22] and timing of surgery.[13,17,20] Our study had concordant findings of an increased risk for

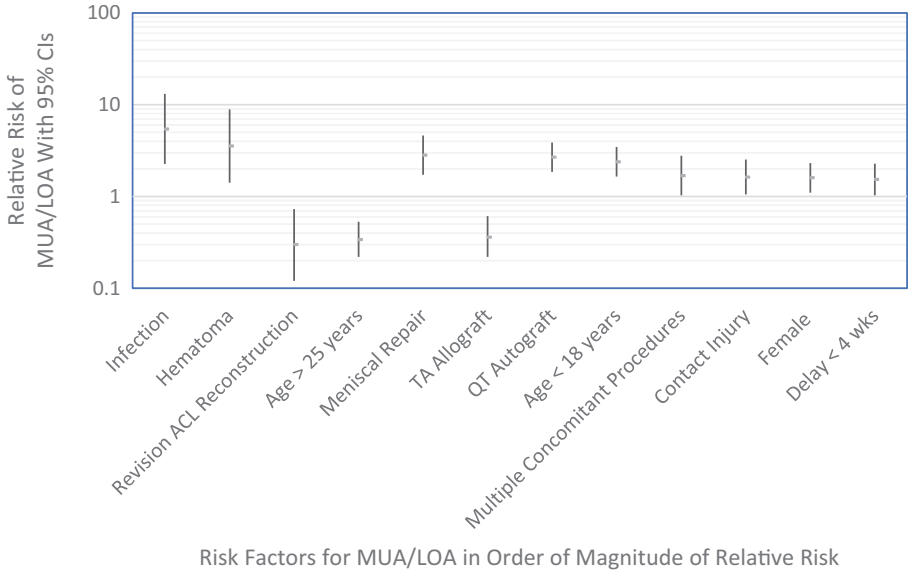

Figure 2. Statistically significant risk factors with univariate analysis for manipulation under anesthesia (MUA) and/or lysis of adhesions (LOA) after anterior cruciate ligament reconstruction. QT, quadriceps tendon; TA, tibialis anterior.

TABLE 3
Risk Factor for Graft Failure After ACL Reconstruction[a]

Risk Factor	Relative Risk (95% CI)	*P* Value
MUA and/or LOA	0.37 (0.12-1.15)	.0848

[a]ACL, anterior cruciate ligament; LOA, lysis of adhesions; MUA, manipulation under anesthesia.

female sex and age <18 years at the time of surgery. None of the previous studies identified reasons why female patients or adolescents are at an increased risk of developing arthrofibrosis, but it does appear to be noteworthy and likely involves a combination of social, psychological, musculoskeletal, and hormonal differences. In agreement with studies by Mayr et al[13] and Shelbourne et al,[20] our study found that patients undergoing ACL reconstruction within 4 weeks of injury had a higher rate of MUA/LOA. This is in contrast to a recent study by Sanders et al,[17] which reported the opposite to be true in a cohort of 1355 patients undergoing ACL reconstruction. Mayr et al[13] attributed the higher rate of arthrofibrosis with early surgery to increased swelling, effusion, and hyperthermia of the knee compared with a "less irritated" knee with delayed surgery. Sanders et al[17] surmised that the higher rate of arthrofibrosis observed in their delayed reconstruction group was in part due to the selective delay of patients who struggled to regain normal knee range of motion before surgery, these patients therefore being at a higher risk for stiffness after surgery as well. While our study did not identify the optimal timing for surgery, it supports the idea that knee inflammation and swelling should be allowed to dissipate and knee motion optimized with preoperative rehabilitation to reduce postoperative arthrofibrosis.[6]

The difference between primary and revision ACL reconstruction with regard to the need for subsequent MUA/LOA has not been well studied in the previous literature. Interestingly, this study found that patients undergoing revision ACL reconstruction had a statistically significant lower rate of MUA/LOA. It is possible that this finding is related to a tendency for ACL reconstruction failures to present after less traumatic events than primary ACL tears.

The current published literature has not addressed whether being enrolled in a government-sponsored health care program is associated with a higher MUA/LOA rate after ACL reconstruction. In the United States, a recent study reported that 14% of patients undergoing ACL reconstruction had Medicare, Medicaid, or other government-sponsored insurance, which is an almost 3-fold increase from 5% in 1996.[3] We hypothesized that government-sponsored health care would put patients at an increased risk of MUA/LOA, as numerous studies have reported a decrease or lag in access to care for this patient population,[2,16,24] and because we have noticed from our own experience that it is often more difficult for these patients to access physical therapy both preoperatively and postoperatively. The results of this study do not support this hypothesis, as the relative risk for undergoing MUA/LOA after ACL reconstruction for patients enrolled in government-sponsored health care was not found to be statistically significant. While there are many possible explanations for this, it is worth mentioning that adequate patient education and motivation may make up for decreased access to formal physical therapy. In a smaller study, Schenck et al[18] reported that arthrofibrosis was avoided in 22 patients with a home exercise program that involved fewer than 3 physical therapy visits on average. Thus, at this time, government-sponsored health care

should probably not be considered an important risk factor for requiring MUA and/or LOA after ACL reconstruction.

An important strength of the present study is the number of arthroscopic ACL reconstruction cases examined with a careful review of each patient's medical record. A total of 2424 ACL reconstructions were included and reviewed for postoperative MUA/LOA, with a minimum follow-up period of 7.6 months and mean follow-up period of 56.7 months. Yet, this retrospective study does have a number of limitations: (1) Our study included only patients who underwent ACL reconstruction by sports medicine fellowship–trained surgeons at a single academic institution in a large metropolitan area, with 1634 being performed by the highest volume surgeon. Patients with inadequate recovery of knee range of motion after surgery, impairing gait and athleticism, were indicated for MUA if they lacked desired flexion and LOA if they lacked desired extension. However, there was not a more clearly defined and standardized indication or time frame for pursuing MUA or LOA after ACL reconstruction for the purpose of this study. Therefore, the study results may be dependent on the included surgeons' preferences and may not be generalizable to other practices. The arthrofibrosis rate by surgeon was not analyzed.

Other limitations included the following: (2) Data regarding knee range of motion and compliance with prescribed physical therapy were not included in this study because these data were not accurately measured and recorded in a prospective fashion in the patient charts at follow-up visits. (3) Because of changes in the medical record system during the study period, not all ACL reconstructions performed by the designated surgeons during the study period were documented in the current EMR system, and this could have led to a sampling error. However, all patient charts that were identified through the code query of the database were reviewed for accuracy, and cases were omitted if they failed to meet the inclusion criteria. (4) Although the mean time to MUA/LOA after ACL reconstruction in our study was 5.5 months, and our mean follow-up was 56.7 months, we may be missing a small number of subsequent procedures by including patients with a follow-up as short as 7.6 months. (5) Another reason that this study may have underestimated the true rate of MUA/LOA is that patients who developed arthrofibrosis may have sought follow-up and undergone MUA/LOA with a provider outside of our academic institution without our knowledge. (6) Last, some of the data, such as the date or mechanism of injury, required subjective interpretation when these details were described in the medical record in imprecise terms. However, if there was insufficient information on which to base a rational judgment or estimation, those data were excluded from the analysis.

CONCLUSION

The development after ACL reconstruction of arthrofibrosis that requires MUA and/or LOA to improve functional range of motion is a common complication, occurring in approximately 5% of cases, and has many associated risk factors. Graft type, infection, concomitant meniscal repair, and primary reconstruction are significant independent risk factors, whereas hematoma, early surgery, age <18 years, female sex, a contact injury mechanism, and multiple concomitant procedures are also factors associated with a higher rate of MUA/LOA. Insurance status does not appear to be a significant risk factor.

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