Original Article

Hemoglobin A1c Levels >6.6% Are Associated With Higher Postoperative Complications After Anterior Cruciate Ligament Reconstruction

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Purpose: To investigate the relation between hemoglobin A1c (HbA1c) levels and postoperative complications after primary anterior cruciate ligament reconstruction (ACLR). **Methods:** A retrospective review was performed of consecutive patients with an isolated anterior cruciate ligament tear, preoperative diagnosis of diabetes, and documented HbA1c within 90 days of primary ACLR between 2000 and 2019. Data collected included demographic and surgical characteristics, 90-day medical complications, and subsequent surgeries on the ipsilateral knee. A receiver operating curve was constructed for each HbA1c level in relation to postoperative complications and the optimal cutoff identified via Youden's *J* statistic. Multivariable logistic regression was performed to assess the relation between postoperative complications and age, sex, graft type, diabetes subtype, and HbA1c. **Results:** Nineteen patients (7 females, 12 males) fulfilled inclusion criteria with preoperative HbA1c ranging from 5.5 to 10. Complications included septic knee (n = 1) and cyclops lesions requiring arthroscopic lysis (n = 3). Patients with HbA1c of 6.7% or higher were 25 times more likely to experience any postoperative complication ($P = .04$) and 16 times more likely to require lysis of adhesions ($P = .08$). On multivariable regression, HbA1c remained significantly associated with any complication ($P = .005$) and developing arthrofibrosis ($P = .02$) independent of age, sex, graft type, and diabetes subtype. **Conclusions:** Diabetic patients undergoing primary ACLR with a preoperative HbA1c of 6.7% or higher were 25 times more likely to require repeat surgical intervention for a postoperative complication. These complications included arthrofibrosis and infection. Strict glycemic control may help minimize the risk of postoperative complications after ACLR. **Level of Evidence:** Level III, retrospective cohort study.

Diabetes has been associated with a higher risk of perioperative complications, readmission, and reoperation in both trauma and elective settings.[1-5] Studies specifically focused on investigating the association between diabetes and postoperative outcomes following primary anterior cruciate ligament reconstruction (ACLR) have reported a broad range of associated risks in patients with diabetes, including an almost tripled risk of 30-day hospital readmission,[6] a 19 times higher risk of postoperative infection requiring surgical intervention,[7] increased risk of severe postoperative complications,[8] lower patient-reported outcome measures (PROMs) at 2-year follow-up,[9] and higher total postoperative charges as compared to patients undergoing ACLR without diabetes.[8]

The Multicenter Orthopaedic Outcomes Network (MOON) Group has largely led efforts in investigating the potential associations between preoperative diabetes and perioperative outcomes in the setting of elective primary ACLR.[9] While the MOON cohort includes 2-year postoperative outcomes, conclusions are limited by the small sample size of 22 patients and self-reporting of preoperative diabetes.[7,9,10] Retrospective studies with much larger sample sizes, from several hundred to ~100,000, investigating patients with confirmed diagnoses of preoperative diabetes have reported lower risks of postoperative infection (odds ratio [OR], 2.3-2.7) than observed within the MOON cohort.[8,11,12] While these retrospective studies include larger sample sizes, the follow-up period is limited to the 30- to 90-day period captured by these databases. Furthermore, both the MOON and retrospective cohort investigations categorize diabetes into variations of

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absence vs controlled/uncontrolled diabetes in analyses, effectively obviating the pertinent consideration of the spectrum of disease that can exist within each of these categories. The preoperative hemoglobin A1c (HbA1c) goal for patients planning to undergo elective arthroscopic knee surgery is not well understood.

HbA1c is a well-established serous marker of subacute diabetes control. The American College of Physicians recently updated clinical practice guidelines for long-term HbA1c goals advocating for deintensification of regimens achieving HbA1c levels <6.5%.[13] Currently, HbA1c levels between 7% and 8% are generally accepted as the goal range for chronic management to balance death and macrovascular complications while minimizing harm and financial burdens of strict diabetes control.[13] The American Diabetes Association does recommend preoperative optimization diabetes control, but specific glycemic goals remain surgeon dependent.[14,15] In arthroplasty, there is a stepwise increase in postoperative complications and total charges as preoperative HbA1c levels increase within the accepted 6.5% to 8% range.[16] In patients undergoing elective spine surgery, preoperative HbA1c levels <6.8% were associated with a lower risk of reoperation while HbA1c levels <6.1%, well below current internal medicine guidelines for chronic management, were associated with a higher likelihood of achieving minimal clinically important differences in PROMs postoperatively.[17] As the prevalence of diabetes continues to rise,[18] it has become imperative for orthopaedic surgeons to understand the association of preoperative diabetes management with perioperative outcomes to provide realistic informed consent discussions and advocate for preoperative disease optimization. The purpose of this study was to investigate the relation between HbA1c levels and postoperative complications after primary ACLR. We hypothesized there would be a HbA1c threshold within the long-term management goal of 6.5% to 8% over which the risk of postoperative complications would be higher.

Methods

Patient Cohort

Following institutional review board approval (ORA 2019P003181), consecutive patients between 2000 and 2019 were identified who fulfilled the following inclusion criteria: ACLR performed at our institution, a preoperative diagnosis of diabetes, and documented HbA1c within 90 days of primary ACLR. Patients without a clinical diagnosis of diabetes (prediabetes, gestational diabetes) were excluded from the study. Patients who underwent additional or complex procedures at the time of ACLR were excluded: revision ACLR, multiligamentous reconstruction, osteotomy, and/or arthroplasty (Fig 1).

Indications for ACLR at the institution were functional knee instability (supported by physical examination findings including laxity on Lachman test and a grade 2 pivot shift) as well as preoperative magnetic resonance imaging confirmation of an anterior cruciate ligament (ACL) tear. Clinical stability of the remaining knee ligaments was confirmed preoperatively and again with examination under anesthesia. Patients underwent elective arthroscopic ACLR at a median 26 weeks after injury (range, 10 weeks to 5 years; interquartile range, 16 to 104 weeks). Graft type determination was a shared decision between surgeon and patient. All patients underwent physical therapy prehabilitation to regain full range of motion preoperatively. All patients received interference screw fixation for the tibial portion of the graft. For femoral fixation, 4 patients had suture suspension fixation, and the remaining 15 patients had interference screw fixation. Thirteen patients had 10-mm tunnels, 3 patients had 11-mm tunnels, 2 patients had 9-mm tunnels, and 1 patient had an 8-mm tunnel due to hamstring autograft limitations.

Electronic medical records were reviewed to collect the following data: demographic characteristics, including age and sex; medical characteristics include diabetes subtype and preoperative HbA1c values. Surgical characteristics, including graft type and concurrent surgeries, were evaluated. Records were assessed for 90-day medical complications, including venous thromboembolism, pulmonary embolism, pneumonia, cardiac event, infection, or sepsis. Surgical complications were defined as subsequent surgery performed on the ipsilateral knee related to ACLR, including debridement, irrigation, revision, and lysis of adhesions. Diagnoses associated with repeat ipsilateral surgery were documented.

Statistical Analysis

Cohort characteristics were summarized as means and standard deviations (SDs) for continuous variables and count/percentages for categorical variables. A receiver operating characteristic (ROC) curve analysis was performed for each 0.1% increment in HbA1c level from 5.6 to 9.9 and the optimal HbA1c cutoff to minimize postoperative complications identified via Youden's J statistic. Fisher exact, Kruskal-Wallis, and Wilcoxon rank-sum tests were used when appropriate to identify associations between patient demographic and surgical characteristics with preoperative HbA1c and postoperative complications. Multivariable analysis was performed via logistic regressions for postoperative complications, and a separate regression was constructed for the development of localized anterior arthrofibrosis requiring surgical lysis. All pertinent patient characteristics were included in each regression, and the Pearson goodness-of-fit (GOF) statistic was computed to assess model fit with high P values

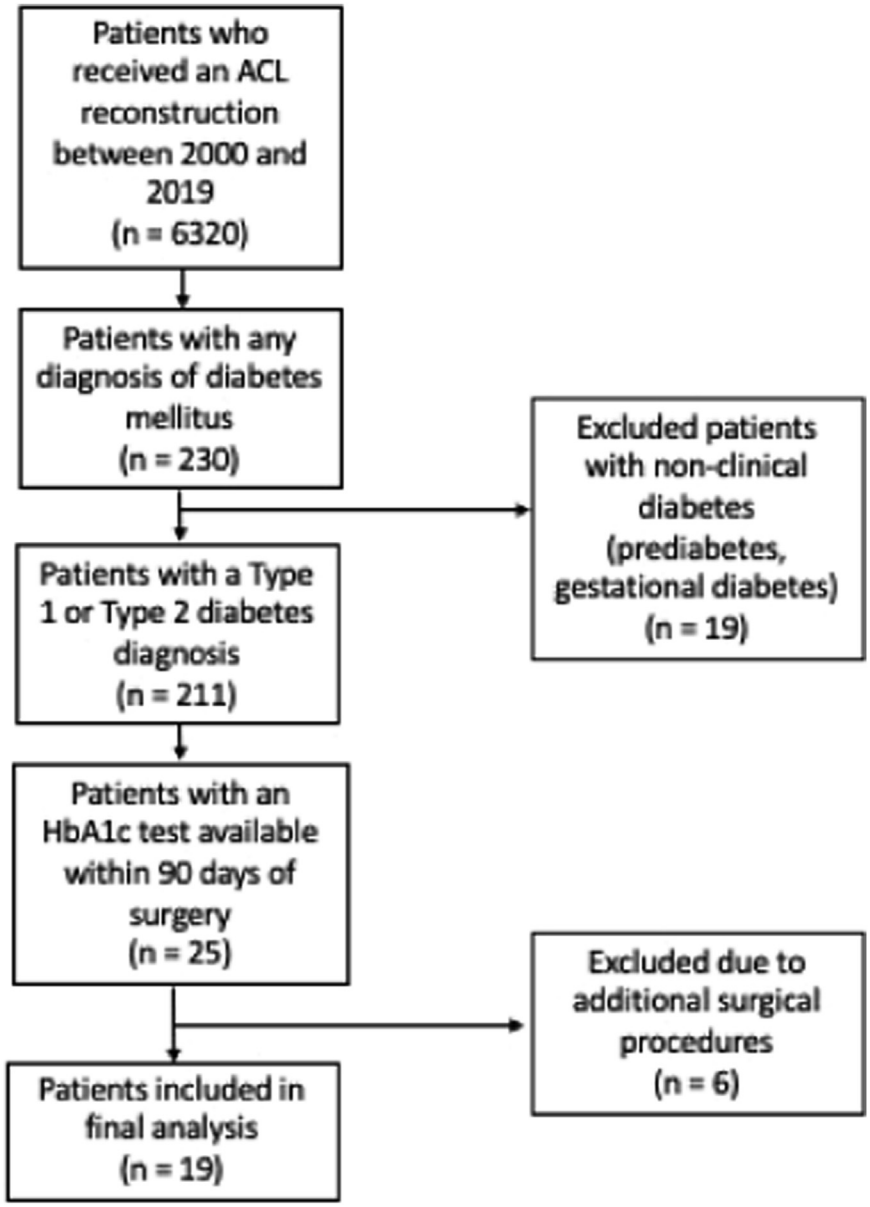

Fig 1. STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) diagram of patient selection.

indicating good fit. Alpha was set to 0.05 and all analyses were conducted in RStudio software version 4.1.3 (R Foundation for Statistical Computing).

Results

After application of inclusion criteria, a total of 19 patients (7 female, 12 male) were included in the final analysis with a median age of 45 years (range, 15 to 60), median preoperative HbA1c of 6.6 (range, 5.5 to 10), and minimum follow-up ranging from 13 months to 20 years. Four patients were former smokers, and there were no active smokers at the time of surgery. The characteristics of patients included in this study are listed in Table 1. After ACLR, there were no patients who experienced medical complications. Four patients experienced a surgical complication. One patient developed a septic knee 3 days postoperatively, confirmed with a white blood cell count of 59,000 on aspiration and no crystals, and required arthroscopic irrigation and debridement. Three patients developed localized anterior arthrofibrosis with progressive loss of full extension requiring arthroscopic lysis 3, 7, and 19 months after ACLR. Two of 3 patients with arthrofibrosis had preoperative magnetic resonance imaging confirmation of a cyclops lesion. All patients had intraoperative confirmation of postsurgical adhesions in the anterior compartment. There were no patients with superficial wound infections.

The HbA1c level with the maximized Youden's index was at 6.7%. There were no significant differences in

Table 1. Demographic and Clinical Characteristics of Patients by Hemoglobin A1c Groups

Characteristic	HbA1c <6.7% (n = 11)	HbA1c ≥6.7% (n = 8)	*P* Value
Age, y	44 [32, 48]	48 [38, 57]	.48
Sex			1.00
Male	7 (64)	5 (63)	
Female	4 (36)	3 (37)	
Graft type			.57
BTB	4 (36)	1 (13)	
Hamstring	1 (9)	2 (25)	
Allograft	6 (55)	5 (63)	
Diabetes			1.00
Type 1	2 (18)	2 (35)	
Type 2	9 (82)	6 (65)	
A1c	6.0 [5.8, 6.4]	7.5 [7.2, 8.3]	<.001
Medical complications	0	0	—
Surgical complications	0	4 (50)	.018
Follow-up, mo	59 [35, 195]	89 [69, 159]	.39

NOTE. Values are presented as number (%) or median [interquartile range].

BTB, bone patellar tendon bone; HbA1c, hemoglobin A1c.

Table 2. Demographic and Clinical Characteristics of Patients by Any Complication Requiring Reoperation

Characteristic	No Complication (n = 15)	Surgical Complication (n = 4)	*P* Value
Age, y	47 [38, 55]	38 [32, 41]	.25
Sex			1.00
Male	9 (60)	3 (75)	
Female	6 (40)	1 (25)	
Graft type			.14
BTB	5 (33)	0 (0)	
Hamstring	1 (7)	2 (50)	
Allograft	9 (60)	2 (50)	
Diabetes			1.00
Type 1	3 (20)	1 (25)	
Type 2	12 (80)	3 (75)	
A1c	6.3 [5.9, 6.6]	8.1 [7.2, 9.1]	.016
Follow-up, mo	68 [40, 154]	146 [71, 219]	.34

NOTE. Values are presented as number (%) or median [interquartile range].

BTB, bone patellar tendon bone.

age, sex, graft type, or diabetes subtype between groups (Table 1). Univariate analysis revealed HbA1c level was associated with a 25 greater odds of developing any postoperative complication ($P = .04$) and a 15.9 greater odds of arthrofibrosis ($P = .08$), whereas age, sex, graft type, or diabetes subtype showed no association (Table 2). Multivariable analysis of the association between patient characteristics and HbA1c revealed HbA1c of 6.7% or higher was independently associated with a 66% increased likelihood of experiencing any postoperative complication (OR, 1.66; 95% confidence interval [CI], 1.23-2.25; $P = .007$; Pearson GOF = 1.00) (Table 3). Similarly, patients with HbA1c of 6.7% or greater had a 45% increased likelihood of experiencing localized anterior arthrofibrosis requiring surgical lysis (OR, 1.45; 95% CI, 1.09-1.92; $P = .020$; Pearson GOF = 1.00) (Table 4).

Discussion

The most important findings of this cross-sectional investigation are as follows: (1) in patients with documented diabetes, a preoperative HbA1c level of 6.7% or higher is associated with a 25-fold increased risk of developing a postoperative complication requiring repeat surgical intervention; (2) when accounting for age, sex, graft type, and diabetes subtype, preoperative HbA1c levels 6.7% or higher remain significantly associated with a greater risk of postoperative complications; and (3) preoperative HbA1c levels 6.7% or higher are associated with an approximately 16-fold increased risk of developing localized anterior arthrofibrosis requiring surgical lysis.

The MOON group has reported on the association of diabetes and postoperative outcomes. Patient cohorts with diabetes in the MOON database range from 16 patients undergoing revision ACLR[7] to 23 pooled patients undergoing primary and revision ACLR.[9] Medical record confirmation of self-reported diabetes diagnosis ranged from 50% to 95.6%, and no MOON investigations considered preoperative glycemic control.[7,9,10] Similarities in methodology between prior MOON investigations and the present investigation include similar sample sizes of diabetic patients undergoing ACLR, consideration of graft type in multivariable analyses, and long-term follow-up of included patients. On the other hand, pertinent methodologic strength of the present investigation includes numeric consideration of preoperative glycemic control, identification of diabetic patients via established laboratory markers for diabetes diagnosis rather than self-reported disease, and stratification of diabetes by pathophysiology (i.e., type 1 diabetes vs type 2 diabetes). While the sample size in this study is limited, findings from this investigation add to prior investigations through the MOON group due to both inclusion of patients with serum marker–confirmed preoperative diagnosis of diabetes and treatment of diabetes in analyses as a continuous disease state rather than a categorical presence vs absence of disease. The use of HbA1c as a proxy for the broad range of disease states within a diagnosis of diabetes is much closer to the clinical considerations during preoperative medical clearance discussions. Furthermore, the consistency of results throughout analyses (higher HbA1c in cohort experiencing a postoperative complication on bivariate analysis followed by persistent statistical significance on multivariable analysis of complications with a low probability of type I error) as

Table 3. Multivariable Analysis of Any Surgical Complication

Characteristic	Odds Ratio	95% Confidence Interval	*P* Value
Age, y	0.98	0.97-1.00	.046
Sex			.25
Male	Reference	Reference	
Female	0.82	0.60-1.13	
Graft type			
BTB	Reference	Reference	.11
Hamstring	1.52	0.94-2.44	.15
Allograft	1.39	0.92-2.11	
Diabetes			.32
Type 1	Reference	Reference	
Type 2	1.24	0.83-1.85	
A1c			**.005**
<6.7%	Reference	Reference	
≥6.7%	1.66	1.23-2.25	

NOTE. Bold values indicate statistical significance.
BTB, bone patellar tendon bone.

Table 4. Multivariable analysis of arthrofibrosis

Characteristic	Odds Ratio	95% Confidence Interval	*P* Value
Age, y	0.99	0.97-1.00	.07
Sex			.76
Male	Reference	Reference	
Female	0.95	0.71-1.28	
Graft Type			
BTB	Reference	Reference	.07
Hamstring	1.56	1.00-2.44	.38
Allograft	1.20	0.81-1.77	
Diabetes			.50
Type 1	Reference	Reference	
Type 2	1.14	0.79-1.67	
A1c			**.02**
<6.7%	Reference	Reference	
≥6.7%	1.45	1.09-1.92	

NOTE. Bold values indicate statistical significance.
BTB, bone patellar tendon bone.

well as with prior literature increased the confidence of the validity of the present results despite the limited sample size.

Diabetic patients have a greater risk of postoperative infections and have been observed to have a higher incidence of postoperative arthrofibrosis.[19-21] Rates of infection in diabetic patients undergoing ACLR in the MOON database have been reported to be 8.6% (n = 2) in primary ACLR[9] as compared to 12.5% (n = 2) in revision ACLR.[10] When examining 2-year outcomes of patients with diabetes undergoing either primary or revision ACLR, Brophy et al.[7] reported an 18.8 ($P <$ .001) greater risk of infection for diabetic patients undergoing either primary or revision ACLR. Brophy et al.[7] subsequently reported a 28.6 (P = .004) increased risk of infection for diabetic patients undergoing revision ACLR.[10] These previously reported rates of infection are higher than the rate of 5% (n = 1) observed in the present study. While a prior investigation using the National Surgical Quality Improvement Program database conducted further multivariable analyses with a diabetic patient cohort that similarly included only a single case of infection,[22] further multivariable analyses specific to postoperative infection were deferred in the present study to minimize risk of β errors in the setting of unbalanced data.

As compared to prior investigations that have not found a greater risk of reoperation in diabetic patients,[7,9,10] the present investigation found a subgroup within diabetic patients that has a significantly higher risk of reoperation after ACLR. Excluding reoperation for infection, Brophy et al.[9] reported 13% (n = 3) of diabetic patients who underwent ipsilateral reoperation as compared to 15% (n = 304) in patients without diabetes. Reoperation procedures included revision ACLR and debridement/manipulation for loss of motion. Based on these results, Brophy et al.[9] concluded that patients with diabetes should be counseled on an increased risk of infection but could be reassured they do not face an elevated risk of subsequent surgery. The results of the present study contradict these previously reported findings. When stratified by preoperative glycemic control, patients with diabetes and with HbA1c >6.7% or higher were 25 (P = .04) times more likely to experience any postoperative complication requiring surgical intervention and 16 (P = .08) times more likely to experience postoperative stiffness requiring surgical intervention. The risk of any reoperation remained statistically significant even when accounting for age, sex, graft type, and diabetes subtype. In contrast to current studies in the literature that have been limited by the absence of glycemic control in analyses,[7,9-11,22] the present investigation reports on a previously unknown association between preoperative glycemic control and postoperative outcomes. These results support further investigation on the role of preoperative screening for diabetes and glycemic control to optimize perioperative outcomes in patients planning to undergo primary ACLR.

Musculoskeletal conditions such as adhesive capsulitis, idiopathic postoperative knee stiffness, and post-arthroscopic shoulder stiffness[19] have all been associated with diabetes. Both the systemic and localized inflammation observed in diabetic patients may contribute to the greater risk of postoperative stiffness after ACLR.[20,21,23-25] Patients with diabetes may additionally have independent risk for delayed recovery speed and lower responsiveness to closed manipulation of arthrofibrosis.[26] In the present study, patients with a HbA1c of 6.7% or higher had a 44% increased risk of experiencing arthrofibrosis requiring surgical intervention. For long-term HbA1c management, the American Diabetes Association and the American College of Physicians recommend HbA1c goals between 7% and

8%. However, the balance of glycemic control against risks of perioperative complications may weigh more toward strict perioperative HbA1c goals to optimize outcomes and minimize the burden of repeat surgical intervention within an episode of care for diabetic patients. As such, orthopaedic surgeons may thus consider stricter preoperative optimization of glycemic control (HbA1c <6.7%) for patients undergoing elective primary ACLR. Further studies are needed to better understand the pathophysiology behind arthrofibrosis in the setting of diabetes.

Limitations

This study is not without limitations. As a retrospective study, patient-reported outcome measures were not prospectively collected and thus long-term functional outcomes were not investigated. Second, the relatively small cohort of diabetic patients included in this investigation limits the statistical power of analyses. A post hoc power analysis of detecting a difference in any postoperative complication as a function of diabetes control was conducted. A total of 87 cases would be required to detect a difference with 80% power and α of 0.05. This was minimized by using nonparametric statistical tests valid for application in small sample sizes as appropriate.

Conclusions

Diabetic patients undergoing primary ACLR with a preoperative HbA1c of 6.7% or higher were 25 times more likely to require repeat surgical intervention for a postoperative complication. These complications included arthrofibrosis and infection. Strict glycemic control may help minimize the risk of postoperative complications after ACLR.

Disclosures

The authors report no conflicts of interest in the authorship and publication of this article. Full ICMJE author disclosure forms are available for this article online, as supplementary material.

References

1. Charles SJ, Chen SR, Mittwede P, et al. Risk factors for complications and reoperation following operative management of displaced midshaft clavicle fractures. *J Shoulder Elbow Surg* 2022;31:e498-e506.
2. Mcdonald CL, Cohen BH, Medina Pérez G, Modest JM, Kuris EO, Born C. Pre-operative medications as a predictor for post-operative complications following geriatric hip fracture surgery. *Geriatr Orthop Surg Rehabil* 2022;13:215145932210910.
3. Miller EM, McAllister BD. Increased risk of postoperative wound complications among obesity classes II & III after ALIF in 10-year ACS-NSQIP analysis of 10,934 cases. *Spine J* 2022;22:587-594.
4. Danilkowicz R, Levin JM, Crook B, Long JS, Vap A. Analysis of risk factors, complications, reoperations, and demographics associated with open and arthroscopic rotator cuff repair: An analysis of a large national database. *Arthroscopy* 2022;38:737-742.
5. Tracy BM, Kravets V, Staley C, Wilson JM, Schwartz AM, Schenker ML. The metabolic syndrome paradox: Increased morbidity and decreased mortality in operative orthopedic trauma. *Orthopedics* 2022;45:103-108.
6. Best MJ, Harris AB, Marrache M, Martin SD, Rue JH, Wilckens JH. Risk factors for readmission following anterior cruciate ligament reconstruction. *J Knee Surg* 2023;36:459-464.
7. Brophy RH, Wright RW, Huston LJ, Nwosu SK, Spindler KP. Factors associated with infection following anterior cruciate ligament reconstruction. *J Bone Joint Surg* 2015;97:450-454.
8. Marchant MH Jr, Viens NA, Cook C, Vail TP, Bolognesi MP. The impact of glycemic control and diabetes mellitus on perioperative outcomes after total joint arthroplasty. *J Bone Joint Surg Am* 2009;91:1621-1629.
9. Brophy RH, Huston LJ, Wright RW, et al. Outcomes of ACL reconstruction in patients with diabetes. *Med Sci Sports Exerc* 2016;48:969-973.
10. Brophy RH, Wright RW, Huston LJ, et al. Rate of infection following revision anterior cruciate ligament reconstruction and associated patient- and surgeon-dependent risk factors: Retrospective results from MOON and MARS data collected from 2002 to 2011. *J Orthop Res* 2021;39:274-280.
11. Kawata M, Sasabuchi Y, Taketomi S, et al. Atopic dermatitis is a novel demographic risk factor for surgical site infection after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2018;26:3699-3705.
12. Westermann R, Anthony CA, Duchman KR, et al. Infection following anterior cruciate ligament reconstruction: An analysis of 6,389 cases. *J Knee Surg* 2017;30:535-543.
13. Qaseem A, Wilt TJ, Kansagara D, et al. Hemoglobin A1c targets for glycemic control with pharmacologic therapy for nonpregnant adults with type 2 diabetes mellitus: A guidance statement update from the American College of Physicians. *Ann Intern Med* 2018;168:569-576.
14. Draznin B, Aroda VR, Bakris G, et al. Glycemic targets: Standards of medical care in diabetes—2022. *Diabetes Care* 2022;45:S83-S96.
15. Diaz R, Dejesus J. Managing patients undergoing orthopedic surgery to improve glycemic outcomes. *Curr Diabetes Rep* 2021;21:68.
16. Kavin M, Yayac M, Grosso MJ, Courtney PM. Preoperative hemoglobin A1c >7.5 is associated with increased bundled payment costs in total hip and knee arthroplasties. *J Am Acad Orthop Surg* 2021;29:970-976.
17. Roth SG, Chanbour H, Gupta R, et al. Optimal hemoglobin A1C target in diabetics undergoing elective cervical spine surgery. *Spine J* 2022;22:1149-1159.
18. Centers for Disease Control and Prevention. National Diabetes Statistics Report. 2022. https://www.cdc.gov/diabetes/data/statistics-report/index.html. Accessed October 16, 2022.

19. Vezeridis PS, Goel DP, Shah AA, Sung SY, Warner JJ. Postarthroscopic arthrofibrosis of the shoulder. *Sports Med Arthrosc Rev* 2010;18:198-206.
20. Owen AR, Tibbo ME, van Wijnen AJ, Pagnano MW, Berry DJ, Abdel MP. Acquired idiopathic stiffness after contemporary total knee arthroplasty: Incidence, risk factors, and results over 25 years. *J Arthroplasty* 2021;36: 2980-2985.
21. Pfefferle KJ, Shemory ST, Dilisio MF, Fening SD, Gradisar IM. Risk factors for manipulation after total knee arthroplasty: A pooled electronic health record database study. *J Arthroplasty* 2014;29:2036-2038.
22. Manzi JE, Quan T, Cantu N, et al. The association between diabetes status and postoperative complications for patients receiving ACL reconstruction. *Eur J Orthop Surg Traumatol* 2023;33:1607-1612.
23. Poolsri W, Jutabha P, Chavasiri W, Muanprasat C. A novel compound AD021 attenuates renal fibrosis by inhibiting transforming growth factor-β1 in renal proximal tubule epithelial cells. *Faseb J* 2022;36(suppl 1). doi:10.1096/fasebj.2022.36.S1.R2316.
24. Sarasua SM, Floyd S, Bridges WC, Pill SG. The epidemiology and etiology of adhesive capsulitis in the U.S. Medicare population. *BMC Musculoskelet Disord* 2021;22:828.
25. Ma Y, Cai F, Huang X, et al. Mannose-binding lectin activates the nuclear factor-κB and renal inflammation in the progression of diabetic nephropathy. *Faseb J* 2022;36: e22227.
26. Ko YW, Park JH, Youn SM, Rhee YG, Rhee SM. Effects of comorbidities on the outcomes of manipulation under anesthesia for primary stiff shoulder. *J Shoulder Elbow Surg* 2021;30:e482-e492.