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Relations between Long-term Glycemic Control and Postoperative Wound and Infectious Complications after Total Knee Arthroplasty in Type 2 Diabetics

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Background: The authors examined whether poor preoperative glucose control, as indicated by the hemoglobin A1c (HbA1c) level of more than 8%, is associated with postoperative wound and infectious complications in diabetic patients that have undergone total knee arthroplasty (TKA).

Methods: One hundred and sixty-seven TKAs performed in 115 patients with type 2 diabetes mellitus, from January 2001 through March 2007, were retrospectively reviewed. Logistic regression was used to identify the variables that had a significant effect on the risk of wound complications or early deep infection. The variables considered were age, gender, body mass index, comorbidities, operation time, antibiotic-impregnated cement use, amount of blood transfusion, close suction drain use, duration of diabetes, method of diabetes treatment, diabetes complications, and preoperative HbA1c level.

Results: The overall incidence of wound complications was 6.6% (n = 11) and there were seven cases (4.2%) of early postoperative deep infection. Logistic regression revealed that the independent risk factors of wound complications were preoperative HbA1C ≥ 8% (odds ratio [OR], 6.07; 95% confidence interval [CI], 1.12 to 33.0) and operation time (OR, 1.01; 95% CI, 1.00 to 1.03). No variable examined was found to be significantly associated with the risk of early postoperative deep infection.

Conclusions: Poorly controlled hyperglycemia before surgery may increase the incidence of wound complications among diabetic patients after TKA.

Keywords: *Total knee replacements, Wound complication, Early deep infection, Type 2 diabetes mellitus*

Postoperative wound and infectious complications after total knee arthroplasty (TKA) cause poor overall outcomes and increase health care costs, particularly among patients with diabetes mellitus, who have greater risks of infection.[1,2] In particular, recent evidence suggests that hyperglycemia plays a significant role in the development of postoperative infections,[3,4] and it has also been reported to delay collagen synthesis[5] and impair phagocytosis.[6] These factors translate into higher risk of various infections and poorer wound healing after any surgical procedure in diabetic patients. Furthermore, strategies aimed at reducing postoperative morbidity by tightly controlling blood glucose levels in the postoperative setting have been highly successful, in both diabetic and nondiabetic patients.[7,8]

Poor long-term glucose control, as determined by hemoglobin A1c (HbA1c), greatly increases the incidence and severity of many chronic complications, such as nephropathy, neuropathy, and retinopathy, associated directly with diabetes.[9-11] However, it has not been established whether long-term metabolic control also helps reduce acute infectious complications during the postoperative

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period. The purpose of this study is to determine whether poor preoperative glucose control, as indicated by HbA1c level of more than 8%[12-14] is associated with postoperative wound and infectious complications in diabetic patients after TKA. Our hypothesis is that glycated hemoglobin, since it reflects long-term regulation of blood glucose, might be associated with incidence of wound complications and early postoperative deep infection after TKA in diabetic patients.

METHODS

In this retrospective cohort study, we analyzed data contained in the electronic medical records from January 2001 through March 2007. All type 2 diabetic patients, who underwent TKA performed by a senior surgeon (SBK) during this period with HbA1c levels recorded within 30 days prior to surgery, were eligible for this study. Only the first case for patients undergoing serial bilateral TKA within 90 days was included. Patients who were considered to be septic preoperatively were excluded, as were patients with rheumatoid arthritis, psoriasis, or a malignant tumor, and those undergoing immunosuppressive treatment.

All operations were performed in standard operating rooms with laminar airflow. Isolation suits were not worn. All procedures were undertaken using a midline incision and a mid-vastus approach. Prostheses were cemented in all cases with either Simplex P (Stryker, New Brunswick, NJ, USA; 103 knees) or Antibiotic Simplex (erythromycin and colistin impregnated; Howmedica International, Limerick, Ireland; 64 knees). We used closed suction drains even when there was substantial bleeding after meticulous hemostasis; drains were retained for less than 48 hours. Each patient received intravenous antibiotics (cephalosporin) at induction of anesthesia preoperatively, and for 5 to 7 days postoperatively if there was no specific wound problem. Patients were maintained on bed rest for the first day after the operation, quadriceps exercises and continuous passive motion were started on the second postoperative day. Weight-bearing was allowed immediately with crutches as needed. Perioperative diabetic evaluation and management were after consultation with an endocrinologist. HbA1c levels were measured by high pressure liquid chromatography (coefficient of variation < 1%).

Demographic and clinical information were obtained from electronic patient records. In terms of the analysis, age and gender were viewed as demographic variables, and obesity, which was determined using body mass indices (BMI), hypertension, dyslipidemia, and cardiovascular disease, as comorbidities.[13] Types of diabetic therapy (oral or insulin) were included to determine whether they affected the outcome. The duration of diabetes and presence of complications associated directly with diabetes, such as nephropathy, neuropathy and retinopathy, were also included. In addition to these patient characteristics and HbA1c levels, several procedure-related variables were selected because of known associations with postoperative infections. These included closed suction drain use, amount of blood transfused postoperatively, antibiotic-impregnated cement use, and operation time.

Age, BMI, operative time, and transfusion amount were treated as continuous variables, and gender, comorbidities, diabetic therapy (none, oral, insulin), antibiotic-impregnated cement use, and HbA1c level (< 8% vs. ≥ 8%) as categorical variables, though HbA1c levels were also analyzed as a continuous variable.

The primary outcomes were wound complications (hematoma, bulla, drainage or superficial infection) and early postoperative deep infection. Superficial wound infections were defined as infections with purulent drainage that occurred at the incision sites with positive or negative bacteriological cultures within 30 days of surgery. Early postoperative deep infections were defined as clinically diagnosed infections involving the knee joint with persistent wound discharge or joint pain, with positive or negative cultures from deep tissues within 3 months of TKA.[14,15]

Descriptive analyses were performed to quantify the relationships between each independent variable and wound and infectious complications. Logistic regression was then used to determine the unadjusted association between each variable and outcome. Logistic regression, including the factors that were found to be statistically significant at the $p < 0.05$ level by unadjusted analyses, was also used to determine the independent impacts of variables on outcome. Odds ratios and their corresponding confidence intervals and p-values are reported. Data analysis was performed using the SPSS ver. 11.5 (SPSS Inc., Chicago, IL, USA).

RESULTS

During the study period, 136 type 2 diabetic patients underwent TKAs. Of these, 21 patients were excluded because of incomplete data or a previous septic condition. A total of 115 patients (167 knees) were included in the final analysis. Patient characteristics are described in Tables 1 and 2. Patients were predominantly female with the mean overall age of 68 years (range, 49 to 82 years). One hundred and thirty-eight knees (82.6%) belonged to over-

Table 1. Demographic Data

Characteristic	Values (%)
Age (yr), mean (range)	68 (49–82)
Gender	
Male	15 (9.0)
Female	152 (91.0)
Body mass index (kg/m^2)	
< 25	29 (17.4)
25 to 29.9	87 (52.1)
≥ 30	51 (30.5)
Co-morbidity	
Hypertension	116 (69.5)
Dyslipidemia	21 (12.6)
Cardiovascular disease	12 (7.2)

Table 2. Clinical Data

Characteristic in diabetes	Value
Duration of diabetes (yr)	7 (0–30)
Diabetes therapy	
None	30 (18.0)
Oral medicines	105 (62.9)
Insulin treatment	32 (19.1)
Hemoglobin A1c level	7.5 (5.0–15.2)
Complications of diabetes	55 (32.9)

Values are presented as mean (range) or number (%).

Table 3. Logistic Regression Analysis of Preoperative Variables with Wound Complications

Factor	Adjusted odds ratio (95% CI)
Body mass index	0.89 (0.35–1.28)
Hypertension	1.00 (0.94–1.05)
Volume of blood transfusion	0.99 (0.97–1.01)
Antibiotics-impregnated cement	0.70 (0.00–181.86)
Operation time	1.01 (1.00–1.03)
Hemoglobin A1c ≥ 8%	6.07 (1.12–33.0)

CI: confidence interval.

weight or obese patients,[16] and most (73.7%) were associated with one or more other medical comorbidities. Oral treatment was the main form of diabetic therapy (62.9%). The range of recorded HbA1c levels was from 5.0% to 15.2% (mean, 7.5%). A closed suction drain and antibiotic-impregnated cement were used in 66.5% and 38.3% of knees, respectively. The mean volume of blood transfusion and operative time was 796 mL (range, 0 to 1,800 mL) and 100 minutes (range, 60 to 175 minutes), respectively.

The overall incidence of wound complications was 6.6% (n = 11), and these included superficial infection in 1.8% (n = 3), hematoma or bullae in 3.6% (n = 6), and drainage in 1.2% (n = 2). There were seven cases (4.2%) of early postoperative deep infection. Wound cultures from superficial infection in two patients grew methicillin-sensitive *Staphylococcus aureus* (MSSA), and were treated with intravenous cefazoline. One patient developed a methicillin-resistant *S. aureus* (MRSA) wound infection without any sign of deep infection, and despite aggressive antibiotic therapy and wound debridement, the infection progressed to soft tissue necrosis and a deep joint infection 6 weeks later. This case was not counted as early deep infection. Of the 7 early deep infections, wound cultures grew MSSA in one patient, MRSA in another, methicillin-resistant *S. epidermidis* in two, and no bacteria in 3. Infections were controlled in 2 of the 7 infections by aggressive antibiotic therapy and open joint debridement. Five patients underwent successful 2-stage revision TKA. No recurrence of infection has occurred in these 7 patients to date. Unadjusted analyses showed that the following factors were associated ($p < 0.05$) with higher risk of wound complications; BMI, hypertension, volume of blood transfusion, antibiotic-impregnated cement use, operation time, and a HbA1c level ≥ 8%. However, no variables were found to have a statistically significant effect on the risk of early postoperative deep infection. These variables were then entered into a multiple logistic regression model, and BMI, hypertension, volume of blood transfusion, and antibiotic-impregnated cement were above the threshold of $p > 0.05$; whereas, the operation time and HbA1c levels continued to be significant (odds ratio [OR], 1.01 and 6.07; 95% confidence interval [CI], 1.00 to 1.03 and 1.12 to 33.0) (Table 3).

DISCUSSION

Our data show that poor preoperative glycemic control, defined as HbA1c level of more than 8%, is associated with a significantly higher risk of a postoperative wound

complication after TKA, after adjusting for other factors known to influence this outcome. Our results also show that operative time is associated with the risk of a wound complication. However, the presence of a comorbidity and type of diabetic treatment were not found to significantly increase the risk. In terms of the risk of deep infection, none of the factors examined was found to be significant. Several authors have sought to determine whether long-term blood glucose control affects the occurrences of postoperative wound complications and surgical site infections related to non-orthopedic operations.[4,17-19] Bishop et al.[18] recommended denying penile prosthesis operations basis on their definition of poor diabetes control (HbA1c ≥ 11.5%). However, Wilson et al.[20] found no association between HbA1c level ≥ 11.5% and the risk of surgical site infection. Had we used the same level to define poor control, all patients with HbA1c levels between 7% and 11.5% would have been assigned to the well-controlled group, and in our study of 115 patients, only 2 (1.7%) would have been allocated to the poorly-controlled group. In another prospective study on the association between HbA1c levels and wound infections in patients undergoing cardiac surgery, the threshold of HbA1c level used was ≥ 8%.[4] In this previous study, twice as many infections occurred in the high HbA1c group than in the low HbA1c group (8% vs. 4%), though this failed to reach a level of statistical significance. In the present study, we used the American Diabetes Association target HgA1c level of ≥ 8% to define the poor control.

Several studies in the orthopedic literature suggest that the presence of comorbidities, particularly diabetes, has a negative effect on surgical outcome. For predisposing factors of surgical site infections, male sex, insulin-dependent diabetes, steroid use, wound classification, and operative time were suggested.[21] However, limited research has been performed on the influence of glycemic control on the prevention of wound complications or infections in total knee replacement patients.[1,13,22,23] The superficial wound infection rate for diabetic TKA patients has been reported to be 6% to 12%[22,23] and for the general population to be 1.7% to 10.5%.[14,24,25] These figures confirm that diabetics are more susceptible to postoperative wound infections, even with adequate antibiotic prophylaxis. Similarly, diabetics had a higher risk of deep joint infections when compared with the general population (0.34% to 2%).[14,15,23] In a study by England et al.,[22] wound complication and deep infection rates after TKA were found to be 12% and 7%, respectively, in those with diabetes. The outcomes of our diabetic patients appear to be substantially better; that is, only 6% developed a wound complication in the present study. Another previous review reported higher infection rates in TKA in diabetics compared with nondiabetics.[23] An overall wound infection rate of 7.3% during the early postoperative period (≤ 1 month) and the risk of deep joint infection was 5.5%. In the present study, the risk of deep joint infection was found to be independent of age, gender, BMI, presence of comorbidity, HbA1c, and other diabetes-related variables. Many types of factors have been suggested to contribute to the risk of deep joint infection, such as, patient factors, operative factors (operating environment, operation course, operation suits, etc), surgical technique (implant selection, antibiotic usage, postoperative wound care, etc.), and postoperative factors. Chiu et al.[26] found that blood sugar levels alone did not contribute to the development of deep infection, and suggested that higher rates of deep infection might be due to a combination of poorly controlled blood sugar and an inappropriate operating environment. Dronge et al.[27] suggested two explanations for why the preoperative glycemic control is associated with postoperative infections. The first concerned the likelihood of better postoperative glucose control in patients with good preoperative control, as tight glucose control during the postoperative period reduces complications, including infections, and mortality in both diabetic and non-diabetic patients.[7,28] In diabetic patients, the association between hyperglycemia and susceptibility to infection has been well established.[29] Several factors, such as genetic susceptibility to infection, altered cellular and humoral immune defense mechanisms, local factors, including poor blood supply and nerve damage, and the defective regulation of collagen synthesis could predispose diabetic patients to infections.[5,6] Another explanation is that the overall general health and metabolic milieu are better in well-controlled diabetic patients.

The present study has several limitations. First, it is intrinsically limited by its retrospective nature, and thus, a prospective study focused on levels of glycemic control prior to surgery is likely to provide additional information regarding the treatments necessary to help avert postoperative wound complications or deep infections. Second, this study was conducted at a single hospital. Third, the patient population was predominantly female, and thus, our findings may not be generalizable. Forth, we defined early postoperative deep infections as clinically diagnosed infections involving the knee joint within 3 months of TKA. This study was not designed to know the result of infected TKA in diabetic patients, but to determine whether poor preoperative glucose control is associated with postoperative wound and infectious complications in diabetic patients after TKA. Therefore, we did not follow Tsukayama's

classification.[30] Finally, although we adjusted for several factors known to be associated with postoperative wound complications and infections, we did not control for other innumerable factors, such as local skin condition, systemic medical condition, and prior surgery, which may also have affected the results.

Poorly controlled hyperglycemia before surgery may increase the incidence of wound complications among diabetic patients after TKA. Due to the increased risk of wound complications in poorly controlled diabetics, we recommend that caution be exercised during patient selection and surgical timing. Furthermore, strategies aimed at improving glycemic control prior to TKA could be employed to reduce the risk of wound complications and improve the overall outcomes.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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