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Background: Diabetes mellitus (DM) is risk factor for complications after orthopedic surgery.

Objectives: We tested the hypothesis that anesthesia preoperative clinic (APC) referral for elevated glycosylated hemoglobin (HbA1c) reduces complication rate after total joint arthroplasty (TJA).

Patients and Methods: Patients (n = 203) with and without DM were chosen from 1,237 patients undergoing TJA during 2006 - 12. Patients evaluated in the APC had surgery in 2006 - 8 regardless of HbA1c (uncontrolled). Those evaluated between in subsequent two-year intervals were referred to primary care for HbA1c $\geq 10\%$ and $\geq 8\%$, respectively, to improve DM control before surgery. Complications and mortality were quantified postoperatively and at three, six, and twelve months. Length of stay (LOS) and patients requiring a prolonged LOS (> 5 days) were recorded.

Results: Patients (197 men, 6 women) underwent 71, 131, and 1 total hip, knee, and shoulder replacements, respectively. Patients undergoing TJA with uncontrolled HbA1c and those with HbA1c $< 10\%$, but not those with HbA1c $< 8\%$, had a higher incidence of coronary disease and hypercholesterolemia than patients without DM. An increase in complication rate was observed in DM patients with uncontrolled HbA1c versus patients without DM ($P < 0.001$); the complication rate progressively decreased with tighter HbA1c control. More DM patients with preoperative HbA1c that was uncontrolled or $\geq 10\%$ required prolonged LOS versus those without DM ($P < 0.001$ and $P = 0.0404$, respectively).

Conclusions: APC referral for elevated HbA1c reduces complication rate and the incidence of prolonged hospitalization during the first year after surgery in diabetics undergoing TJA.

Keywords: Diabetes Mellitus; Glycosylated Hemoglobin; Orthopedic Surgery; Arthroplasty

1. Background

Diabetes mellitus is an important risk factor for postoperative complications after orthopedic surgery (1-5). Patients with diabetes undergoing primary or revision total joint arthroplasty had higher hospital costs, fewer routine discharges, and an increased risk of stroke, pneumonia, ileus, urinary tract infection, and transfusion than those without the disease (1, 5). Uncontrolled diabetes [as determined using patient self-reporting of blood glucose concentration, glycosylated hemoglobin (HbA1c) level, and end-organ damage] was shown to be particularly harmful, as the incidence of morbidity and mortality was greater in diabetic patients undergoing arthroplasty with poorly- versus well-controlled disease (4). Recent evidence further suggests that poor long-term control of diabetes may increase postoperative complications in orthopedic and other types of surgery (2, 3). A preoperative HbA1c $\geq 7.1\%$ was implicated as a major risk factor for all-cause complications in diabetic patients

undergoing total joint arthroplasty (2), whereas a HbA1c level $\leq 7.0\%$ may decrease the risk of perioperative and long-term complications in patients undergoing cardiac and noncardiac surgery (6-9). Anesthesia-directed preoperative clinics evaluation enhance operating room efficiency, improve patient education and satisfaction, reduce unnecessary testing and consultation, and decrease adverse perioperative events (10-13) in patients undergoing elective surgery, including those scheduled for orthopedic procedures (14). Whether the anesthesia preoperative evaluation clinic and referral to primary care are capable of reducing the adverse effects of diabetes by improving chronic control of blood glucose concentration is unknown.

2. Objectives

The authors tested the hypothesis that preoperative

evaluation clinic screening and referral of veterans with poorly controlled diabetes to their primary care physicians to obtain better long-term control of the disease before surgery reduces complication rate during the first year after elective total joint arthroplasty.

3. Patients and Methods

The Institutional Review Boards of Clement J. Zablocki Veterans Affairs Medical Center and Marquette University reviewed and approved the protocol. Written informed consent was waived because of the retrospective, observational study design. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. The electronic medical records of all patients undergoing total joint arthroplasty ($n = 1,237$) at the Zablocki Veterans Affairs Medical Center between January 1, 2006 and December 31, 2012 were identified using an orthopedic surgery database. Two hundred and three patients with and without diabetes ($n = 103$ and $n = 100$, respectively) undergoing elective joint arthroplasty were randomly chosen from this cohort. Patients undergoing revision arthroplasty and those with preexisting wound infections were excluded from analysis. All demographic and clinical outcome data for each patient were obtained from simultaneous review of the electronic medical record by three investigators (PJK, JN, AO) to assure consistency. Patients with diabetes were required to have a HbA1c level recorded in the medical record within six months before surgery. In January, 2009, based on emerging data about the possible importance of long-term control of blood glucose concentration on outcomes after surgery (4, 7, 8), the preoperative evaluation clinic director (PJK) began to recommend to his patients that those with HbA1c ≥ 10 should delay their procedures. These patients were counseled to return to their primary care physicians or the endocrinology clinic to obtain better long-term control of blood glucose concentration before proceeding with elective total joint arthroplasty. An analysis of pilot data conducted two years later suggested that this approach for patients with poorly controlled diabetes may be reducing the rate of complications. As a result, the threshold for referral was reduced to HbA1c $\geq 8\%$ during 2011 and 2012. We chose a threshold value HbA1c $\geq 8\%$ (rather than the 7% level recommended by the American Diabetes Association (15)) because aggressive compared with moderate glycemic control may inadvertently cause hypoglycemia and increase perioperative morbidity and mortality in high-risk patients (16, 17), such as elderly veterans undergoing total joint arthroplasty. Surgical site or urinary tract infections (verified with appropriate culture and sensitivity), delayed wound healing (including inflammation, dehiscence, and chronic drainage), requirement for transfusion of autologous blood products, unplanned prolonged hospitalization for inadequate pain control, chronic pain requiring long-term management, pneumonia, deep venous thrombosis with or with-

out pulmonary embolism, cardiovascular complications including myocardial ischemia or infarction and atrial or ventricular arrhythmias requiring medical treatment (antiarrhythmic medications, cardioversion, electrophysiology intervention, or device placement), cerebrovascular accident, and mortality were quantified during the immediate postoperative period and at the three, six, and twelve month orthopedic surgery follow-up appointments. Hospital length of stay and the number of patients requiring a prolonged length of stay (defined as greater than five days) after surgery were also recorded. Diabetic patients undergoing total joint arthroplasty in the current investigation were treated with either continuous infusions or sliding-scale bolus doses of insulin to maintain blood glucose concentration between 140 to 180 mg/dL during and after surgery regardless of preoperative HbA1c, (18, 19). "Tighter" control of blood glucose concentration was avoided because of the potential risk of hypoglycemia. Consultant internists or endocrinologists were responsible for postoperative diabetic care in these patients and used similar methods and goals for control of blood glucose concentration during hospitalization. Primary care physicians or endocrinologists managed blood glucose concentration using established American Diabetes Association guidelines (15) after the patients were discharged from the hospital.

3.1. Statistical Analysis

A power analysis conducted before beginning the study indicated that a group size ≥ 65 (patients with versus without diabetes) was required for a minimal difference of 20% in all-cause complication rate between patients with or without diabetes (alpha error < 0.05 ; beta error < 0.20) with a power of 95%. Continuous data between groups were analyzed using analysis of variance (ANOVA) followed by Bonferroni's test for differences between means. All continuous data are presented as mean \pm standard deviation. Differences in categorical variables were determined using chi-square analysis. Categorical variables are presented as raw numbers or percentages. Linear regression analysis was used to assess the correlation between the number of complications per patient and HbA1c. Stat Plus: Mac software (Analyst Soft, Alexandria, Virginia, USA) was used for statistical analysis. The null hypothesis was rejected when $P < 0.05$.

4. Results

Veterans (197 men and 6 women) underwent 71, 131, and 1 total hip, knee, and shoulder replacements, respectively (Table 1). The demographics in patients without diabetes were similar to those with diabetes irrespective of HbA1c control (Table 1). Serum creatinine was significantly greater in patients with uncontrolled diabetes undergoing elective surgery compared with patients who were not diabetic ($P = 0.00121$). Patients with diabetes with uncontrolled HbA1c and those with HbA1c $< 10\%$, but not

< 8%, had a higher incidence of coronary artery disease and hypercholesterolemia and were more likely to receive ACE inhibitors or ARB. An increase in complication rate was observed in diabetic patients with uncontrolled HbA1c versus patients without diabetes ($P < 0.0001$), but this elevated complication rate progressively declined with tighter HbA1c control (Tables 1 and 2). Diabetic patients with preoperative uncontrolled HbA1c or HbA1c <

10% also required prolonged length of stay, but the mean length of stay was similar between groups. There were no differences in the incidence of system-specific complications between diabetic patients regardless of HbA1c control compared with patients without diabetes (Table 3). A significant correlation was observed between the number (n) of complications per patient and HbA1c ($n = 0.339 \times \text{HbA1c} - 1.46$; $r = 0.32$, $P < 0.01$).

Table 1. Demographic, Historical, and Medication data for Patients With and Without Diabetes Based on A1c Control Before Elective total Joint Surgery ^{a, b}

Variables	-DM	+DM No Referral for A1c	+DM Referral for A1c <10%	+DM Referral for A1c <8%
Number	100	55	32	16
Surgery Type (Hip, Knee, Shoulder)	41/58/1	14/41/0	11/21/0	6/10/0
Gender				
Male	99	52	31	15
Female	1	3	1	1
Age, y	65 ± 9	66 ± 10	66 ± 8	66 ± 10
Weight, kg	102 ± 20	103 ± 21	113 ± 28	115 ± 26
Height, cm	178 ± 7	176 ± 9	177 ± 9	177 ± 10
Body Mass Index, kg/m²	32 ± 6	34 ± 7	36 ± 7 ^c	36 ± 7 ^c
A1c, %	5.7 ± 0.4	7.0 ± 1.0 ^c	6.9 ± 0.8 ^c	6.8 ± 0.6 ^c
Hematocrit, %	42 ± 4	42 ± 5	41 ± 4	41 ± 4
Creatinine, mg/dL	1.04 ± 0.25	1.24 ± 0.40 ^c	1.04 ± 0.31 ^d	0.88 ± 0.22 ^d
Potassium, mEq/L	4.1 ± 0.4	4.2 ± 0.4	4.1 ± 0.4	4.1 ± 0.4
Length of Stay, d	7.6 ± 6.4	10.2 ± 11.4	8.3 ± 5.7	8.3 ± 5.9
Prolonged Length of Stay	23	31 ^c	14 ^c	6
Complication Rate	0.36 ± 0.63	1.27 ± 1.18 ^c	0.78 ± 1.01	0.50 ± 0.89
Coronary Artery Disease	14	14 ^c	13 ^c	4
Hypertension	71	45	27	14
Hypercholesterolemia	42	33 ^c	23 ^c	9
Chronic Obstructive Pulmonary Disease	5	6	4	0
Peripheral Vascular Disease	4	3	1	1
Tobacco Use	29	16	8	2
Insulin	0	11	7	7
Oral Hypoglycemic Drug	0	21	23 ^d	10
Beta-Adrenoceptor Antagonist	34	24	17	6
Calcium Channel Blocker	23	7	7	3
Nitrate	1	6	5	2
ACE inhibitor or ATII blocker	32	32 ^c	22 ^c	8

^a Abbreviations: + and - DM, with and without diabetes mellitus, respectively; N, number; A1c, glycosylated hemoglobin concentration; ACE, angiotensin converting enzyme; ATII, angiotensin II.

^b Continuous data are mean ± standard deviation; categorical data are numbers.

^c Significantly ($P < 0.05$) different from - DM.

^d Significantly ($P < 0.05$) different from + DM No Control.

Table 2. P Values for Statistics in Table 1^{a,b}

Variables	-DM vs. +DM No Referral	-DM vs. +DM Referral for A1c <10%	-DM vs. +DM Referral for A1c <8%	+DM No Referral vs. +DM Referral for A1c <10%	+DM No Referral vs. +DM Referral for A1c <8%	+DM Referral for A1c <10% vs. Referral for A1c <8%
Type of Surgery	0.0783	0.647	1	0.522	-	0.920
Age	1	1	1	1	1	1
Weight	1	0.121	0.187	0.362	0.386	1
Height	0.667	1	1	1	1	1
Body Mass Index	1	0.00440	0.0142	0.100	0.116	0.791
A1c	<0.00001	<0.00001	<0.00001	1	1	1
Hematocrit	1	1	1	1	1	1
Creatinine	0.00121	1	0.317	0.0224	0.00038	0.592
Potassium	0.594	1	1	1	1	1
Length of Stay	0.332	1	1	1	1	1
Prolonged Length of Stay	<0.001	0.0404	-	0.362	0.296	0.920
Complication Rate	<0.0001	0.124	1	0.0826	0.152	1
Coronary Artery Disease	0.120	0.00272	-	0.218	-	0.313
Hypertension	0.196	0.203	0.764	1	-	-
Hypercholesterolemia	0.048	0.00617	0.427	0.377	1	0.450
Chronic Obstructive Pulmonary Disease	-	-	-	-	-	-
Peripheral Vascular Disease	-	-	-	-	-	-
Tobacco Use	0.863	0.823	-	0.863	-	-
Insulin	-	-	-	1	-	-
Oral Hypoglycemic Drug	-	-	-	0.00497	0.150	0.740
Beta-Adrenoceptor Antagonist	0.310	0.0843	1	0.527	0.888	0.476
Calcium Channel Blocker	0.181	0.920	-	0.413	-	-
Nitrate	-	-	-	-	-	-
ACE inhibitor or ATII blocker	0.00273	0.000512	0.262	0.454	0.764	0.343

^a Abbreviations: + and - DM, with and without diabetes mellitus, respectively; A1c, glycosylated hemoglobin concentration; ACE, angiotensin converting enzyme; ATII, angiotensin II.

^b Continuous data were analyzed using ANOVA followed by Bonferroni test for differences between means. Categorical data were analyzed using the Chi-square test (expected group size less than 5 were not analyzed).

Table 3. Incidence Proportion of Postoperative Complications in Patients With and Without Diabetes Based on A1c Control Before elective Total Joint Surgery^a

Variables	-DM	+DM No Referral	+DM Referral for A1c <10%	+DM Referral for A1c <8%
Number	100	55	32	16
Cardiac	0.06	0.11	0.13	0.06
Pulmonary	0.02	0.07	0.16	0.13
Neurologic	0.01	0.07	0	0
Urinary Tract Infection	0.02	0.07	0.06	0
Transfusion	0.11	0.27	0.19	0.06
Pain	0.04	0.27	0.19	0.06
Surgical Site Infection	0.05	0.15	0.19	0.06
Delayed Wound Healing	0.04	0.18	0	0.19
Mortality	0.01	0.07	0.03	0

^a Abbreviations: + and - DM, with and without diabetes mellitus, respectively; A1c, glycosylated hemoglobin concentration.

5. Discussion

The current results confirm the findings of several previous studies (1-5) indicating that is diabetes an important risk factor for postoperative complications. The results further demonstrate that more stringent long-term control of the disease directed by preoperative anesthesia clinic referral reduces the incidence of prolonged hospitalization and complication rate during the first year after surgery in patients undergoing elective total joint arthroplasty. Several previous large-scale clinical trials established a link between diabetes and major postoperative complications in orthopedic surgery patients. A study of 751,340 patients from the United States Nationwide Inpatient Sample undergoing primary or revision total knee or hip arthroplasty revealed that patients with diabetes were more likely to develop pneumonia, suffer cerebrovascular accidents, require autologous blood product transfusion, and have greater hospital costs than those without diabetes (1). Marchant et al. showed that the risk of stroke, urinary tract infection, ileus, postoperative hemorrhage, transfusion, prolonged hospitalization, and mortality was greater in patients with poorly controlled diabetes undergoing total joint arthroplasty compared with those whose diabetes was well controlled (4). Fewer infectious complications (particularly those involving the urinary tract), but not the risk of revision, deep venous thrombosis, pulmonary embolism, or prosthesis infection, were also observed in diabetic patients undergoing orthopedic surgery when HbA1c < compared with $\geq 7\%$ (3, 20, 21). When complicated by end-organ damage (presumably resulting from poor long-term control), diabetes was shown to be a strong predictor (odds ratio of 1.94) of 90-day overall complication risk in a ten-year study of 138,399 patients undergoing total hip arthroplasty in California (5). More recently, Harris et al. retrospectively examined 6,088 diabetic patients treated in the Veterans Health Administration system and showed that there was linear relationship between HbA1c and complications after total joint arthroplasty (2). Preoperative HbA1c ≥ 7 also increased the relative risk of complications and 90-day mortality after surgery. The current results demonstrating a significant correlation between the number of complications sustained per patient and long-term control of blood glucose concentration also verified the previously observed linear relationship between complication rate and HbA1c that was reported in veterans undergoing total joint arthroplasty (2). Other studies of diabetic patients undergoing cardiac (6-8, 22) and major noncardiac (23-26) have reached similar conclusions about the importance of long-term control of blood glucose concentration on complication rate and outcome. Identification and optimization of co-existing diseases, including diabetes, are important goals in the anesthesia preoperative clinic setting (27, 28). To date, short-term control of blood glucose concentration, most often entailing avoidance of hypoglycemia and profound

hyperglycemia, and management of the cardiovascular and renal sequelae of diabetes receive primary attention during preoperative assessment of patients with the disease (29), whereas attempts to gain tighter long-term control have generally not received emphasis. From this perspective, the objective of the current investigation was to examine whether preoperative clinic identification of veterans with poor long-term control of diabetes (as defined by HbA1c ≥ 10 in 2009-10 and ≥ 8 in 2011-12) and subsequent referral of these patients to primary care for improved control of their disease would reduce postoperative complications determined up to one year after elective total joint arthroplasty. Our results support this contention, as the simple decision to refer these patients with poorly controlled diabetes from the anesthesia preoperative clinic to primary care or endocrinology resulted in progressive reductions in complication rate and the number of patients requiring a prolonged hospital stay. Indeed, the rate of complications in diabetics when all patients with HbA1c ≥ 8 were referred to primary care (0.50 ± 0.89) was statistically indistinguishable from that observed in their healthy peers without the disease (0.36 ± 0.63 ; $P = 1$) when the current relatively small sample size was considered. Whether use of American Diabetes Association recommendations (HbA1c < 7%) (15) for chronic glycemic control would further reduce complication rate remains to be determined. However, the current data suggest that moderate, less rigorous long-term control of blood glucose concentration substantially improves outcome in the setting of elective total joint surgery by reducing complication rate to values similar to those observed in patients without diabetes. The current results in diabetic veterans support the general observations of Kamal et al. indicating that evaluation of patients scheduled to undergo complex orthopedic surgery in an anesthesia preoperative clinic reduces mortality, unplanned intensive care unit admissions, intensive care and high dependency unit lengths of stay, and cost (14). The current results should be interpreted within the constraints of several potential limitations. Almost all of patients enrolled in the study were men (97%) because of the Veterans Affairs population, and whether the current findings can also be extended to women is unknown. The sample size studied here was relatively small and was unable to distinguish differences in organ-specific complications between groups as a result. A larger study including women would be useful to determine such potential differences in end-organ complications and whether the observed complications are gender-specific. Nevertheless, it is clear, based on the observations of several large-scale clinical studies, that diabetes is a risk factor for cardiac, neurological, infectious, and wound healing complications after orthopedic surgery (1, 2, 4, 5). Veterans with uncontrolled or poorly controlled diabetes were significantly more likely to have coronary artery disease

and hypercholesterolemia than those in whom diabetic control was more rigorous. It is likely that the greater incidence of cardiovascular disease contributed to the higher complication rate in patients with poorly versus moderately controlled diabetes. The results also require qualification because patients with diabetes were required to have a HbA1c level recorded within six months before surgery. HbA1c most likely reflects chronic blood glucose control over a three-month interval (15), but many patients in our hospital often do not receive routine primary care to allow this frequency of HbA1c sampling. As a result, a six-month HbA1c sampling interval was chosen to indicate chronic preoperative control of blood glucose concentration. Whether the current results in patients undergoing elective orthopedic surgery are applicable in other surgical patients is unknown, but diabetes has been identified as a major risk factor for perioperative morbidity and mortality in noncardiac and cardiac surgery (6-8) and it seems likely that improved long-term glycemic control may also exert beneficial effects on outcome in other groups of surgery patients when approached prospectively. Finally, fewer total joint operations were performed in diabetic veterans with tighter chronic control of blood glucose concentration. The current investigation did not consider the benefits of delaying total joint replacement to obtain more stringent glycemic control in diabetic patients versus the relative risk of continued, often quite severe, functional limitations occurring as a result of primary chronic joint pathology. In summary, the current results demonstrate that anesthesia preoperative clinic referral of diabetic veterans to primary care for more rigorous glycemic control before elective total joint arthroplasty reduces the incidence of prolonged hospitalization and complication rate during the first year after surgery. These data support the contention that anesthesia preoperative clinic evaluation and intervention may be directly linked to improved patient outcome.

Authors' Contributions

Peter J. Kallio helped design the study, conducted the study, analyzed the data, and wrote drafts of and revisions the manuscript. This author has seen the original data, reviewed the analysis of the data, approved the final manuscript, and is the author responsible for archiving the data files. Jenea Nolan conducted the study, analyzed the data, and wrote drafts and revisions of the manuscript. This author has seen the original data, reviewed the analysis of the data, and approved the final manuscript. Amy C. Olsen conducted the study, analyzed the data, and wrote drafts and revisions of the manuscript. This author has seen the original data, reviewed the analysis of the data, and approved the final manuscript. Susan Breakwell helped design the study, analyzed the data, and edited the original and revised manuscript. This author has seen the original data, reviewed the analysis of the

data, and approved the final manuscript. Richard Topp helped design the study, analyzed the data, and edited the original and revised manuscript. This author has seen the original data, reviewed the analysis of the data, and approved the final manuscript. Paul S. Pagel analyzed the data and edited the original and revised manuscript. This author has seen the original data, reviewed the analysis of the data, and approved the final manuscript.

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