CLIN CARE/EDUCATION/NUTRITION/PSYCHOSOCIAL

Preoperative A1C and Clinical Outcomes in Patients With Diabetes Undergoing Major Noncardiac Surgical Procedures

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OBJECTIVE

To evaluate the relationship between preoperative A1C and clinical outcomes in individuals with diabetes mellitus undergoing noncardiac surgery.

RESEARCH DESIGN AND METHODS

Data were obtained from the National Surgical Quality Improvement Program database and the Research Patient Data Registry of the Brigham and Women's Hospital. Patients admitted to the hospital for ≥1 day after undergoing noncardiac surgery from 2005 to 2010 were included in the study.

RESULTS

Of 1,775 patients with diabetes, 622 patients (35%) had an A1C value available within 3 months before surgery. After excluding same-day surgeries, patients with diabetes were divided into four groups (A1C ≤6.5% [*N* = 109]; >6.5–8% [*N* = 202]; >8–10% [*N* = 91]; >10% [*N* = 47]) and compared with age-, sex-, and BMI-matched nondiabetic control subjects (*N* = 888). Individuals with A1C values between 6.5 and 8% had a hospital length of stay (LOS) similar to the matched control group (*P* = 0.5). However, in individuals with A1C values ≤6.5 or >8%, the hospital LOS was significantly longer compared with the control group (*P* < 0.05). Multivariate regression analysis demonstrated that a higher A1C value was associated with increased hospital LOS after adjustments for age, sex, BMI, race, type of surgery, Charlson Comordity Index, smoking status, and glucose level on the day of surgery (*P* = 0.02). There were too few events to meaningfully evaluate for death, infections, or readmission rate.

CONCLUSIONS

Our study suggests that chronic hyperglycemia (A1C >8%) is associated with poor surgical outcomes (longer hospital LOS). Providing a preoperative intervention to improve glycemic control in individuals with A1C values >8% may improve surgical outcomes, but prospective studies are needed.

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Diabetes mellitus is a known risk factor for postoperative complications including infection and mortality (1,2). Acute hyperglycemia during the perioperative period is also associated with poor clinical outcomes in patients with and without diabetes (3). This relationship is well established for hyperglycemia on the day of surgery, within 24–48 h of surgery and during the entire hospital stay (4,5). Further, insulin infusion protocols designed to prevent hyperglycemia in the perioperative and postoperative period demonstrate improved surgical outcomes (6). However, few studies have examined the relationship between preoperative A1C level and surgical outcomes. A study in patients undergoing coronary artery bypass surgery showed an association between high A1C values and surgical complications, including mortality, cerebrovascular accidents, and deep sternal wound infection (7). However, high A1C values in cardiac surgery patients may be associated with more severe primary cardiac disease; therefore, these data are probably not applicable to noncardiac surgery patients.

Chronic hyperglycemia (high A1C) is clearly a predictor of long-term complications of diabetes and is the main target for glycemic control in diabetes (8). It remains unclear whether chronic hyperglycemia has an adverse effect on surgical outcomes over and above acute perioperative hyperglycemia and whether standards of care that address elevated A1C levels prior to surgery would improve clinical outcomes. Because of a lack of data, arbitrary A1C cutoffs are used by surgeons, anesthesiologists, internists, and endocrinologists. This study was conducted to evaluate whether A1C has an impact on noncardiac surgery outcomes independent of perioperative blood glucose levels in patients with diabetes.

RESEARCH DESIGN AND METHODS

Data for this retrospective study were obtained from National Surgical Quality Improvement Program (NSQIP) database (9). The NSQIP database includes preoperative, intraoperative, and postoperative variables in a randomly selected sample of patients (20% of all surgeries at our institute) who undergo a general (including gastrointestinal, endocrine, thoracic, or oncologic) or vascular surgical procedure. Cardiac surgery cases are not included.

Patients included in this analysis were admitted to the Brigham and Women's Hospital between 2005 and 2010. Individuals undergoing same-day surgeries were excluded. If an individual underwent multiple surgeries, only the first surgery was taken into account. The NSQIP database provided information on demographics, principle operative procedure, diabetes status, surgery type (vascular or general surgery), and surgical outcomes including deep surgical wound infection, other infections, cardiac arrest, unplanned intubation, postoperative sepsis, renal failure, death during hospitalization, death within 30 days after hospitalization, rehospitalization within 30 days, and hospital length of stay (LOS). Because the NSQIP database does not include A1C level, blood glucose level, and other diagnoses, these data were obtained from the Research Patient Data Registry. The Research Patient Data Registry is a data warehouse that serves as a central clinical data repository for participating hospitals and clinics within the Partners Healthcare System, an integrated health-care delivery network in Eastern Massachusetts that includes Massachusetts General Hospital and Brigham and Women's Hospital. All study data were obtained after the Partners Healthcare Human Research Committee approved the protocol and waived the requirement for written informed consent.

Diabetes was defined as any individual identified as having diabetes in the NSQIP database, a physician diagnosis in records, or an ICD-9 Clinical Modification code. All individuals with a diagnosis of diabetes and an A1C measurement within 90 days before surgery were included in the analysis as the diabetic group. A nondiabetic control group admitted to the hospital during the same time period and matched for age (±5 years in the following groups: 18–24, 25–34, 35–44, 45–54, 55–64, 65–74, and 75–84 years), sex, and BMI ($<$18, ≥18 and $<$25, ≥25–30, and $>$30 kg/m^2) were selected, with two control subjects matched for every one case patient wherever possible. The number of control subjects was less than twice the number of patients with diabetes due to limited availability. Charlson Comorbidity Score (CCI) was calculated from ICD-9 codes and used as an indicator of the severity of illness (10).

Statistical Analyses

We designated hospital LOS as our primary outcome. The event rates for other surgical outcomes (infection, mortality, renal failure, and rehospitalization within 30 days) were too small in this data set for comprehensive analyses.

Population characteristics are presented as the mean ± SD. Two group comparisons were analyzed using a Pearson's χ^2 test for categorical variables and a *t* test (normal distribution) or Wilcoxon rank sum test (non-normal distribution) for continuous variables.

We compared clinical outcomes in the following five categories of patients: *1*) healthy individuals (no diabetes); *2*) diabetes with A1C ≤6.5%; *3*) diabetes with A1C $>$6.5–8%; *4*) diabetes with A1C $>$8–10%; and *5*) diabetes with A1C $>$10%. Categories were based on health-care effectiveness data (11) and our own team's clinical judgment on the classification of diabetes severity. The main analytic approach was ANCOVA. A Dunnett test was used to account for multiple comparisons when comparing A1C groups to the control group. Since it is well known that low A1C values are associated with a higher risk of hypoglycemia (12) and patients with hypoglycemia have different hospital outcomes compared with those without hypoglycemia (13), we also evaluated the relationship between A1C and LOS after removing individuals with A1C ≤6.5% and using A1C as a continuous variable.

Linear regression analyses were performed to evaluate *1*) the effect of diabetes status on LOS and *2*) the effect of A1C on LOS. Covariates included in the linear regression models comprise age, sex, BMI, race (Caucasian, African

American, and other), surgery type (vascular/nonvascular), CCI, smoking status, and glucose level on the day of surgery, and were chosen based on initial bivariate analyses that demonstrated their possible relationship with hospital LOS. Statistical analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC).

RESULTS

There were 19,159 surgeries included in the NSQIP database during the specified period (Fig. 1). Of these, 2,395 surgeries were performed on 1,775 unique patients with diabetes. Only 622 patients (35%) with diabetes undergoing a first surgery had an A1C level available within the 90 days before surgery. The distribution of individuals with missing A1C values was almost equal across racial groups. Among Caucasians, 73% had a missing A1C values, and among African Americans 71% had missing A1C values. After excluding patients who underwent same-day surgery, 449 were included in the final analysis.

Baseline characteristics of the diabetes group and the control group are shown in Table 1. Patients with diabetes were more likely to be nonwhite and smokers, and to have undergone vascular surgery more often than subjects in the control group. As expected, patients with diabetes had a significantly greater number of surgical complications including death, infections, and hospital LOS. Regression analysis demonstrated that individuals with diabetes had significantly increased hospital LOS ($P < 0.0001$) even after adjustments for age, sex, BMI, race, smoking status, type of surgery (vascular vs. general surgery), CCI, and glucose level on the day of surgery.

Comparisons among A1C categories and the control group are shown in Table 2. Individuals with A1C levels >6.5–8% had hospital LOS similar to the control group ($P = 0.5$). However, hospital LOS in individuals with A1C levels ≤6.5%, A1C >8–10%, and A1C >10% was significantly longer compared with the control subjects ($P < 0.0001$, $P < 0.0001$, and $P = 0.02$, respectively) and compared with individuals in the A1C >6.5–8% group ($P < 0.001$, $P < 0.0.008$, and $P = 0.06$, respectively). Individuals with A1C levels ≤6.5 and >8% (combined group of A1C >8–10% and A1C >10%) were associated with a significantly longer hospital LOS compared with control subjects and the A1C group >6.5–8% after accounting for multiple testing. There were no significant differences among other surgical outcomes (wound class, infections, renal failure, death within 30 days, and hospital readmission).

After removing high-risk individuals with A1C levels ≤6.5%, univariate regression analysis demonstrated that higher A1C values in patients with diabetes were associated with increased hospital LOS ($P = 0.002$). This relationship remained significant in multivariate regression analysis after adjustments for age, sex, BMI, race, smoking status, type of surgery, CCI, and glucose level on the day of surgery ($P = 0.02$) . Further, these relationships remained significant after removing individuals who died during hospitalization ($P = 0.02$). Higher A1C level was significantly associated with LOS when the analysis was conducted in Caucasians only ($P = 0.04$).

CONCLUSIONS

We conclude that A1C level >8% is associated with increased hospital LOS after surgery and that A1C is a predictor of hospital LOS independent of plasma glucose on the day of surgery. A1C level ≤6.5% is also associated with increased LOS. It is possible that the increase in LOS in the population with A1C levels ≤6.5% was related to the greater severity of their underlying illness, as suggested by their relatively higher CCI. They may also have had a higher incidence of hypoglycemia before hospital admission, but we do not have these data. This analysis is the first to demonstrate an independent relationship between chronic glycemic control and noncardiac surgery outcome in patients with diabetes. Hyperglycemia is associated with impaired neutrophil phagocytic activity, increased inflammation and oxidative stress, and poor endothelial function, factors that can potentially affect the healing process after surgical procedures (14–16). More severe and prolonged hyperglycemia is likely to cause more severe damage than acute hyperglycemia alone. One previous study (7) has shown poor clinical outcomes in relation to A1C levels in cardiac surgery patients. A study (17) in noncardiac surgery patients did not find a relationship between A1C level and surgical infections, but confirmed the relation between hyperglycemia

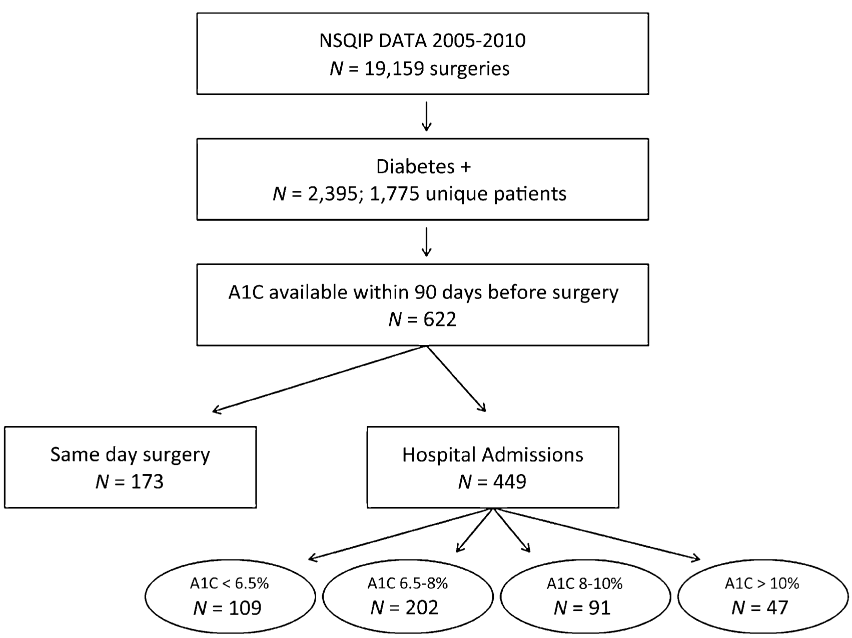

Figure 1—NSQIP data and inclusion of patients with diabetes.

Table 1—Baseline characteristics and surgical outcomes of individuals with diabetes and age-, sex-, and BMI-matched control subjects

Characteristics	Control subjects (*N* = 888)	DM patients (*N* = 449)	*P* value
Age (years)	59.1 ± 13.9	59.1 ± 14.1	0.9
Female sex	465 (52)	229 (51)	0.6
Caucasian	757 (85)	310 (69)	<0.0001
BMI (kg/m^2)	34.8 ± 9.9	35.6 ± 10.7	0.2
Current smoker (%)	118 (13)	80 (18)	<0.0001
Blood glucose level on day of surgery (mg/dL)	127.9 ± 29.7	153.8 ± 59.8	<0.0001
A1C level (%)	—	7.7 ± 1.8	—
CCI score	1.36 ± 2.24	1.29 ± 1.15	0.6
Surgery (vascular)	128 (14)	114 (25)	<0.0001
Hospital LOS (days)	5.2 ± 5.3	6.7 ± 6.6	<0.0001
Postoperative acute renal failure	3 (0.3)	1 (0.2)	0.7
Death within 30 days	0 (0)	19 (4)	<0.0001
Wound class (dirty)	0 (0)	44 (10)	<0.0001

Data are *n* (%) or mean ± SD, unless otherwise stated.

and increased risk of infections. Other studies, focused on specific surgical procedures, demonstrate conflicting results. For example, high A1C level was shown to be associated with increased risk for wound infection and acute renal failure after gastric bypass surgery (18); however, no association between A1C level and any clinical outcomes was found in a smaller population of patients undergoing gastric sleeve surgery (19). Among patients admitted to the hospital for wound closure, a high A1C level was associated with increased risk of wound dehiscence (20). High A1C level has also been shown to be associated with increased morbidity after spine surgery (21), joint replacement (22), and vascular surgery (23). However, in these studies, data were not controlled for important factors like severity of illness and perioperative glycemic control; further, many studies did not evaluate the relationship between A1C and hospital LOS. Our study is different because we control for multiple risk factors, including blood glucose level on the day of surgery, and demonstrate a threshold A1C level above which the risk of complications increases.

As expected, patients with diabetes had poor clinical outcomes compared with the nondiabetic control group. The effect of diabetes on surgical outcomes has been shown in several studies (2,24–26). Higher rates of postoperative complications in patients with diabetes lead to increased resource utilization by this population and higher health-care costs. Thus, interventions targeted toward decreasing postoperative complications in individuals with diabetes may lead to improved surgical outcomes, more efficient utilization of health-care resources, and decreased health-care costs. However, it remains unclear whether these interventions should be targeted to all individuals with diabetes or focused on a subset of patients with poor glycemic control before surgery. Our study is of particular importance for clinical decision making in patients with diabetes undergoing elective surgery. Currently, focus is placed on single blood glucose measurements on the day of surgery or perioperative glucose control, because a clear relationship exists between acute elevations in blood glucose during and after surgery and surgical outcomes (3,4). Our results suggest that long-term glycemic control is a stronger predictor of hospital LOS, and this result is independent of blood glucose measurements on the day of surgery. Currently, there are no standards of care for optimal A1C level before surgery.

Table 2—Patient characteristics and surgical outcomes by A1C category

Characteristics	Control subjects (*N* = 888)	A1C ≤6.5% (*N* = 109)	A1C >6.5–8% (*N* = 202)	A1C >8–10% (*N* = 91)	A1C >10% (*N* = 47)
Age (years)	59.1 ± 13.9	60.2 ± 18.8	60.2 ± 13.7	58.10 ± 13.4	53.9 ± 12.1
Female sex	465 (52)	55 (50)	108 (54)	113 (64)	23 (55)
Caucasian	757 (85)	83 (76)*	143 (71)*	58 (64)*	26 (55)*
BMI (kg/m^2)	34.8 ± 9.9	33.8 ± 11.1	36.2 ± 10.7	35.7 ± 10.4	37.1 ± 10.4
Current smoker (%)	118 (13)	20 (18)	32 (16)	17 (19)	11 (23)
Blood glucose on day of surgery (mg/dL)	127.9 ± 29.7	141.6 ± 77.3	156.2 ± 77.3*	153.5 ± 70.7*	196.0 ± 83.5*
A1C level (%)	—	5.98 ± 0.48	7.23 ± 0.37	8.79 ± 0.58	11.65 ± 1.73
CCI score	1.36 ± 2.24	1.44 ± 2.10	1.16 ± 1.80	1.28 ± 1.99	1.50 ± 2.30
Surgery (vascular)	128 (14)	30 (28)*	41 (20)	29 (32)*	14 (30)
Hospital LOS (days)	5.2 ± 5.3	8.3 ± 7.4*	5.3 ± 5.6	7.9 ± 7.0*	6.8 ± 6.7
Postoperative acute renal failure	3 (0.3)	1 (0.9)	0 (0)	0 (0)	0 (0)
Death within 30 days	0 (0)	9 (8)	6 (3)	3 (3)	1 (2)
Wound class (dirty)	0 (0)	12 (11)	18 (9)	11 (12)	3 (6)

Data are mean ± SEM or *n* (%). *Comparison with control $P < 0.05$ after accounting for multiple testing using the Dunnett test.

As a result, arbitrary cutoffs are used by various professionals. Some surgeons consider it important to lower A1C levels to the goals recommended by the American Diabetes Association (<7% for most patients) before elective surgery, while others consider it unnecessary because current evidence exists only for acute hyperglycemia. Our study suggests that an A1C level >8% may have an effect on surgical outcomes, specifically, increased hospital LOS, which represents increased morbidity and higher health-care costs. In our study, A1C >10% seemed to have less significance because of the smaller number of individuals in this group. We think that an A1C level >8% can be used as a threshold for increased risk of complications after surgery until more data are available. The criterion for same-day surgery is expected hospital LOS <24 h. Because hospital LOS was our primary outcome, we excluded subjects undergoing same-day surgery. However, A1C level <8% may be appropriate for outpatient or same-day surgeries because of similar pathophysiological changes.

Our study also demonstrates that almost 65% patients with diabetes mellitus did not have an A1C measurement that was available within 3 months before surgery. This was surprising to us, but it highlights the issue, raised by others (27), that glycemic control is inadequately addressed in the hospital setting in general. Apathetic attitudes toward diabetes may be the result of inadequate evidence on the benefits of glycemic control, lack of ownership, and/or nonavailability of diabetes care providers in most hospital settings. Incorporating algorithms to remind surgeons and anesthesiologists about A1C testing and targeted interventions by diabetes specialists to improve glycemic control in those individuals with A1C levels >8% could help to ensure that patients at high risk are identified, and are appropriately treated preoperatively and perioperatively.

Because of its retrospective nature, our study has several limitations. Our data were collected from a single site and our sample size was small, limiting the number of outcomes that we could evaluate. Further, because A1C levels or fasting plasma glucose levels for the nondiabetic group were unavailable, some of the control subjects may have had unidentified diabetes. However, if true, these individuals are likely increasing the mean hospital LOS of the control group, and removing these individuals would have increased the difference between the diabetes and control groups, demonstrating the robustness of our findings. Another limitation includes the use of blood glucose levels on the day of surgery as a surrogate for perioperative hyperglycemia. Blood glucose levels after the day of surgery instead of the day of surgery may alter the regression equation, and the relationship between A1C and LOS; however, since similar results for other surgical outcomes have been found with glucose measurements for both time periods (4), we doubt that our results would have differed. Moreover, most of our patients with diabetes are seen by the diabetes management team after surgery, and their glycemic control is fairly good and equivalent, irrespective of the preoperative glycemic control and A1C level. We did not study factors like socioeconomic status, level of education, or treatment adherence that can affect not only the A1C level but also surgical outcomes. Last, our study does not provide insight into whether lowering A1C levels before surgery will improve clinical outcomes over and above the control of hyperglycemia during hospitalization. It may be impractical for some patients to wait for the lowering of their A1C level before undergoing elective surgery, and, moreover, the required duration of lower A1C levels before surgery is unknown. Despite all of these limitations, we think these data are important because they provide guidance for the management of diabetes when patients can wait for elective surgery. Based on these data, our hospital has implemented changes in the preoperative evaluation protocol so that all patients with diabetes have their A1C level measured before elective surgery; if it is >8%, our diabetes team gets involved in the preoperative care of the patient. However, we are not recommending delaying surgery until more data are available.

In conclusion, this retrospective data analysis demonstrates that poor glycemic control with A1C levels >8% is associated with longer hospital LOS in individuals with diabetes who are undergoing noncardiac surgery. Larger multisite studies are required to evaluate other surgical outcomes (mortality, infections, renal failure, and rehospitalization). Further, prospective intervention studies are required to evaluate whether improving A1C levels prior to surgery decreases hospital LOS, improves surgical outcomes, and decreases health-care costs.

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