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Association of Preoperative Hemoglobin A1c and Body Mass Index with Wound Infection Rate in Spinal Surgery

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ABSTRACT

Background: The deleterious effect of diabetes mellitus on surgical outcomes is well documented for joint replacement surgery. We analyzed the large national US Department of Veterans Affairs (VA) database for patients who had undergone elective spinal surgery.

Methods: We retrospectively searched the VA database and identified 174 520 spine cases.

Results: There were 7766 (4.5%) wound infections and 49 271 (28%) had hemoglobin A1c (HbA1c) testing (range: 3.0–17.8) prior to surgery. In the preoperative HbA1c–checked group, there were 2941 (6.0% of 49 271) infections and in the without–preoperative HbA1c group, there were 4825 (3.9% of 125 249) infections. The distribution of infections was significantly different ($\chi^2 = 372.577$, $P < .0001$) and suggests a 2.12% increase in the absolute risk of infection based on the presence of preoperative HbA1c testing, regardless of the result. Logistic regression revealed a preoperative HbA1c test was associated with an odds ratio of 1.435 for infection (confidence interval 1.367–1.505, $P <$ .0001). In a separate model based on HbA1c levels, we found that HbA1c is a significant predictor of infection with an odds ratio of 1.042 (confidence interval 1.017–1.068, $P = .0009$) for each 1% increase in the test result. This analysis differs from using a strict cutoff value of HbA1c of 6.5%. Similar testing for body mass index and age yielded an odds ratio of 1.027 for each increase of 1 kg/m^2 and an odds ratio of 1.009 for each 1-year increase in age respectively.

Conclusions: Hemoglobin A1c testing, HgA1c value, body mass index, and age all contribute to the risk of wound infection after elective spine surgery in a large national VA population. These data can be used to estimate surgical risks and to aid in patient counseling about proposed spine surgery.

Level of Evidence: 4.

Other & Special Categories

Keywords: veterans, spine, BMI, hemoglobin A1c, wound infection

INTRODUCTION

In recent years, diabetes mellitus has emerged as a common and significant comorbidity in the United States. The latest compiled statistics from the Centers for Disease Control and Prevention estimate that 30.2 million US adults, (12.2% of the adult population) have diabetes, including 7.2 million who are undiagnosed.[1]A further 84.1 million adults (33.9%) had prediabetes in 2015, including 48.3% of all adults aged 65 or older.[2] Notably, evidence also shows that the prevalence of diabetic patients undergoing spinal surgery is on the increase.[3,4]

The deleterious effect of uncontrolled diabetes on surgical outcomes is well documented in the literature,[5] particularly with respect to joint replacement surgery[6–11] and peripheral nerve surgery.[12] Less well described is the relationship between diabetes and outcomes in spinal surgery.[13,14] In this study, we undertake a national retrospective database review to model any risk relationship between preoperative obesity and glycemic control (as approximated by body mass index [BMI] and hemoglobin A1c [HbA1c], respectively) and postsurgical wound infection in patients undergoing surgery for degenerative spine conditions.

METHODS

With the consent of the Institutional Review Board, a request was made of the US Department of Veterans Affairs (VA) corporate data warehouse for access to the national VA database in Austin, Texas, using the VA Informatics and Computing Infrastructure. A request was made for information on all VA patients undergoing elective spinal surgery for degenerative spine conditions from years 2007 to 2016. Spine surgeries were included based on common procedure terminology (CPT) codes. The operations included laminectomies (CPT 63005, 63017, 63042, 63045, 63047), discectomies (63030), foraminotomies (63045, 63047, 63048), anterior cervical discectomies and fusions (63075, 22551, 22845), cervical arthroplasties (22856), cervical laminoplasties (63050), posterior cervical fusions (22590, 22595, 22600, 22614), anterior lumbar fusions (22558, 22585, 22845, 22851), and posterior lumbar fusions (22612, 22630, 22840, 22842, 22843). Surgeries for trauma, infection, or neoplasms were excluded. Information was extracted including patient age, date of surgery, weight and height of the patients as recorded in the 3 months prior to surgery, HbA1c levels measured in the 3 months prior to surgery, and complications of surgery. Complications were identified by ICD codes 996.66 (infection due to internal implant or prosthesis), 996.67 (infection due to other orthopedic device, implant, or graft), 998.59 (other postoperative infection), 998.83 (nonhealing surgical wound), 998.89 (other complications of procedures), and T81.4XXA (infection following a procedure), which were recorded in the 6 months following the index procedure. These were combined into a single primary outcome: presence of an infectious complication.

Statistical analysis and modeling were performed using the SAS 9.2 statistical package (2008, SAS Institute, Cary, NC). Based upon the dichotomous nature of the outcome variable infection and the continuous nature of predictor variables of HbA1c, age, and BMI, we selected logistical regression analysis a priori. STROBE guidelines for reporting observational studies[15] were used in the design and reporting of this study. Data are presented as mean ± SD.

RESULTS

The initial query resulted in 430 000 individual CPT codes. Following removal of redundant entries with multiple CPT codes for the same procedure, and procedures not meeting criteria, there were 191 320 unique procedures. Of these patients, 175 895 had sufficiently recorded height and weight to calculate BMI prior to surgery. We elected to exclude patients with BMI < 15 and BMI > 50 to prevent the inclusion of significant outliers and decimal point errors in the model. The decision to exclude BMI outliers was based on a preliminary analysis showing significant positive skew of the distribution of BMI that corrected after application of these boundaries. This ultimately excluded 0.78% of cases and resulted in a final population of 174 520 patient cases for analysis. A summary of patient characteristics is provided in Table 1. Using the text descriptors of the procedures performed, we tabulated the types of operations these patients received and grouped them by approach (anterior, posterior, lateral, or unspecified), by spinal segment (cervical, thoracic, lumbar, multiple, or unspecified), and by whether the surgery involved decompression alone or the placement of hardware; a summary is provided in Table 2. Many of the surgeries could not be precisely characterized due to the nonspecific text titles of the procedures supplied.

The mean age at surgery was 59 years (±13 years). In the analyzed population, 49 271 patients (28%) had their HbA1c tested prior to surgery. Values of HbA1c in this group ranged from 3.0 to 17.8. We suspected that many patients in this

Table 1. Patient characteristics.

Characteristic	n (%)
Sex	
Male	163 473 (92.94)
Female	12 422 (7.06)
Race	
White	126 110 (71.70)
Black	30 128 (17.13)
Native American	1821 (1.04)
Hawaiian or Pacific Islander	1711 (0.97)
Asian	723 (0.41)
Unknown/declined to state	15 402 (8.76)
Ethnicity	
Hispanic/Latino	7223 (4.11)
Non-Hispanic/Latino	168 672 (95.89)

Table 2. Spine surgeries.

Surgical Details	n (%)
Approach	
Anterior	20 583 (11.79)
Posterior	56 269 (32.24)
Lateral	126 (0.07)
Unspecified	97 542 (55.89)
Segment	
Cervical	11 905 (6.82)
Thoracic	1059 (0.61)
Lumbar	34 408 (19.72)
Multiple or unspecified	127 148 (72.86)
Type	
Decompression alone	65 042 (37.27)
Fusion and/or instrumentation	48 828 (27.98)
Unspecified	6 650 (34.75)

Table 3. Predictors of infection.

Models	Odds Ratio	Confidence Interval	*P* Value
Model 1: continuous HbA1c			
Age	1.009	1.006–1.012	< .0001
BMI	1.027	1.020–1.034	< .0001
HbA1c	1.042	1.017–1.068	.0009
Model 2: presence vs absence of HbA1c			
Age	1.015	1.013–1.017	< .0001
BMI	1.030	1.025–1.034	< .0001
HbA1c presence	1.435	1.367–1.505	< .0001

Abbreviations: BMI, body mass index; HbA1c, hemoglobin A1c.

population were being screened for preclinical diabetes by HbA1c sampling; therefore, we examined differences in age and BMI, stratified by whether HbA1c had been tested. We found that BMI was significantly greater in the tested group (30 vs 28 in the untested group, $P < .0001$). Likewise, the patients who had HbA1c testing were significantly older than those who were untested (62 vs 58 years, $P < .0001$). Given these findings, we elected to include age as well as BMI in our regression model.

Of 174 520 patients, there were 7766 postoperative infections (4.5%). In the group that had a preoperative HbA1c checked, there were 2941 such infections (6.0% of 49 271), while in the group without a preoperative HbA1c, there were 4825 infections (3.9% of 125 249). The distribution of infections in these 2 groups was significantly different from their expected proportions ($\chi^2 = 372.577$, $P < .0001$) and suggests a 2.12% increase in the absolute risk of infection based on the mere presence of preoperative HbA1c testing, regardless of the result.

Due to the nature of the coding of the procedures in our database, extraction of approach and spinal level is available for a minority of the patients, and many of these have one or the other only specified. This is a known drawback of large database analysis based upon the coding acumen and heterogeneous coding practices of many institutions. A subset analysis of a sample of the first 4000 patients in the database yielded the following: Among the surgeries with resulting infections, 34.6% were cervical, 1% were thoracic, 35.6% were lumbar (59.5% fusions), 25% were at an unknown spinal level, and 3.8% involved a stimulator or pump device; 68.3% of infections involved a fusion or an implanted stimulator or pump. Infected procedures were 9.6% anterior without fusion, 22.1% posterior without fusion, 38.5% posterior with fusion, 19.2% anterior with fusion, and 6.7% with fusion of unknown approach. This is consistent with published data of wound infections in spinal surgery.[13,14]

Infection rates were also reviewed by race/ethnicity. In the Veterans Administration, Hispanic or Latino is an ethnicity attached to either White or Black races, so patients are counted in both groups. Therefore, the total numbers differ from the total population as noted above. The infection rates of the entire population with HbA1 values were 4.7% among Whites, 3.5% among Blacks, 4.0% among Hispanics, 4.3% among Hawaiian and other Pacific Islanders, 2.5% among Asians, and 4.7% among Native Americans and Alaska Natives. Black veterans constituted 17.13% of our population, but only 14.5% of the infections; therefore, there did not seem to be a predisposition to infection among Black veterans (see "Discussion," below).

Logistic regression models were constructed using the following as possible predictors for infectious complications: age at surgery, BMI, HbA1c level, and the dichotomized presence vs absence of HbA1c testing in the patient's chart. We used both HbA1c as a continuous variable and as a dichotomized variable (tested for or not tested for) in separate analyses. Odds ratios and *P* values for these models are summarized in Table 3. Due to high covariance, HbA1c level and the categorical variable for the presence of preoperative HbA1c testing were not included in the same regression model. In its own model, the presence of a preoperative HbA1c test was associated with an odds ratio of 1.435 for infection (confidence interval 1.367–1.505, $P < .0001$). In a separate model based on HbA1c levels, we found that HbA1c is a significant predictor of infection with an odds ratio of 1.042 (confidence interval 1.017–1.068, $P = .0009$) for each 1% increase in the test result. Similar testing for BMI and age yielded an odds ratio of 1.027 for each increase of 1 kg/m^2 and an odds ratio of 1.009 for each 1-year increase in age.

DISCUSSION

Diabetes mellitus is a known risk factor for adverse surgical outcomes.[5,7,8] In a study of 7565 elective and emergency surgeries requiring at least 1 night of hospitalization (including 724 neurosurgical and 1000 orthopedic procedures), Yong et al[5] found that diabetes mellitus, defined as HbA1c $\geq$6.5%, was associated with increased 6-month mortality, major complications, intensive care unit admission, mechanical ventilation, and hospital length of stay, even after adjustment for age, Charlson comorbidity index, glomerular filtration rate, and length of surgery. In total hip arthroplasty, elevated HbA1c levels have been correlated with increased cost of care.[7] In reviewing the current evidence about diabetes mellitus and risk of arthroplasty, Lopez et al[8] concluded that while diabetes increases the risk for postoperative complications, there is no evidence to determine if this risk is related to glycemic control as measured by HbA1c.

Prior findings in the spinal surgery literature have been mixed regarding the contribution of diabetes mellitus to the risk of postoperative wound infection and the role of HbA1c in predicting this risk, though there is a broad consensus that glycemic control must play some role. In a retrospective review of 165 patients, Takahashi et al[16] found that while factors related to diabetes predict poor recovery from lumbar spinal surgery for criteria such as improvement in back pain or lower extremity numbness, there was no significant difference in the incidence of infection or reoperation between their diabetic and nondiabetic patients. However, their study may have been underpowered for detecting this endpoint.

A large database analysis of 423 050 diabetic patients undergoing degenerative lumbar surgery by Guzman et al[3] in 2014 found increased odds of medical complications and postoperative infection in uncontrolled diabetics relative to controlled diabetics. Uncontrolled and controlled diabetes were defined by diagnosis codes and not by HbA1c. The odds ratio for postoperative infection of any type was 2.61 for uncontrolled diabetes and 1.36 for controlled diabetes. The same group also looked at cervical spinal surgery, reporting that patients with uncontrolled diabetes had higher risks for postoperative infection (odds ratio 4.90), pulmonary embolism, inpatient mortality, and length of stay than patients with either controlled diabetes (for infection: odds ratio 1.91) or no diabetes.[4] However, the same group in a subsequent study detected no significant difference in the odds of infection based on diabetic status after adult scoliosis surgery,[17] though they did observe that diabetic status is a predictive factor of other known postoperative complications such as acute renal failure and hemorrhage.

A more recent study[18] examined a cohort of 523 diabetic patients who underwent posterior lumbar surgery with a wound infection rate of 7.1%. They found that HbA1c $\geq$7.50 increased the odds of a wound infection significantly, but did not find a correlation between age or BMI and wound infection risk. Notably, their analysis only included HbA1c dichotomized at the level of 7.5%, which may have affected these conclusions.

Other studies have found correlation of diabetes with postoperative spinal wound infection, but did not document the criteria for the diagnosis of diabetes, for inclusion in the control group, or for the degree of glycemic control[13] or used medical record criteria or nonrandom, nonfasting serum glucose levels during hospitalization or at a preoperative clinic visit for some patients in the study.[14]

Our study examines a large cohort and establishes a dose-response relationship between BMI or HbA1c and the odds of infection. Given an overall incidence of wound infection of 4.45% in our study population, it is reasonable under the rare disease assumption to consider the odds ratios generated by our model as approximating the relative risk of infection. The units of HbA1c are percent and the units of BMI are kg/m^2. As such, we can state that in this population, a 1% increase in HbA1c is associated with an increase of 4.2% in relative risk and 0.19% in absolute risk of postoperative infection. A 1 kg/m^2 increase in BMI in the same population was associated with an increase of 2.7% in relative risk and 0.12% in absolute risk of infection. In comparison, a 1-year increase in age was associated with an increase of 0.9% in relative risk or 0.04% in absolute risk of infection, which indicates that both BMI and HbA1c are stronger predictors of infection.

The presence of preoperative HbA1c testing, regardless of the resultant HbA1c level, was associated with a 43.5% increase in the relative risk of infection, corresponding to a 2.12% increase in the absolute risk of infection in the study population. As preoperative diabetes screening is uncommon in elective spinal surgery at our institution in patients not documented to have diabetes mellitus, we assume that the majority of the HbA1c tests in our study were ordered by primary care providers, either based on a history of diabetes mellitus or strong suspicion of an underlying diagnosis. Preoperative HbA1c testing has become standard practice in other surgical environments. A recent study by Shohat et al[10] in 2018 found that 8% of patients (123/1461) undergoing joint arthroplasty were found to have undiagnosed diabetes via preoperative HbA1c measurement, thus suggesting that diabetes screening performed prior to surgical care can provide important information to an operating team. In our experience, preoperative diabetes screening is not standard practice in spinal surgery. As our data suggest that risk of postoperative infection significantly increases with suspicion of diabetes and that the possibility exists of diabetes being undiagnosed before surgical referral, we recommend that preoperative testing of HbA1c prior to spinal surgery be incorporated in presurgical screening moving forward. Furthermore, as the aforementioned increase in relative risk of infection associated with preoperative HbA1c testing includes patients with HbA1c levels <6.5 (no diabetes or controlled diabetes), we strongly believe that obesity and other features of metabolic syndrome may also predispose spine surgical patients to infection. Thus, future directions for investigation may include evaluation of broader metabolic syndrome as it contributes to the risk of postoperative spine infection, including risk factors such as hypertension and hyperlipidemia that have not previously been studied in this context.

Attainment of optimal preoperative glycemic control is presumed to reduce the risk of postoperative infection. While the results of our study corroborate this by suggesting that lower HbA1c levels are associated with reduced risk of infection, this finding is somewhat diminished by the large additional risk associated with the presence of HbA1c testing preoperatively. Nonetheless, emerging evidence in the evaluation of glycemic control is promising with respect to further clarifying preoperative optimization for diabetic patients. Shohat et al[19] in 2017 related an emerging marker, serum fructosamine, to the incidence of periprosthetic joint infection. Fructosamine levels $\geq$292 μmol/L had a significant association with deep wound infection, but HbA1c level $\geq$7% did not. Ngaage et al[20] provide an excellent review of fructosamine and 2 other serum biomarkers (glycosylated albumin and 1,5-anhydroglucitol) and propose further investigation into their use as predictors of outcomes in spinal surgery. It is possible that similar evaluation of these newer markers of glycemic control will shed light on the exact relationship between diabetes, its management, and the risks associated with spinal surgery.

Infection rates among various ethnicities in our group cannot be attributed strictly to their ethnic origin, as ethnicity may be a surrogate for where the patient lives (such as Pacific Islanders in Hawaii), poverty, or other factors. The dataset we analyzed is overwhelmingly White, so the results of a subgroup analysis by race are not generalizable. Infections after instrumented fusions have been previously reported to be more common than in surgeries without implants[3] and more likely in posterior fusions than anterior fusions.[4]

\We did not review our cohort for cardiopulmonary disease or other confounding medical factors that have been reported to influence readmission rates and complications of spinal surgery. In a study looking at 111 892 spine surgery patients in the National Surgical Quality Improvement Project database and using 68 preoperative characteristics, diabetes mellitus did not seem to correlate with readmission or reoperation, although age, African American (Black) race, recent weight loss, chronic steroid use, dialysis, blood transfusion, American Society of Anesthesiologists classification $\geq$3, contaminated wound, and operative time >3 hours did correlate.[21] We did not find a risk associated with African-American race. In another similar study in 18 602 patients undergoing spinal fusion surgery, diabetes mellitus was not shown to correlate with readmission and major perioperative complications (P = .097).[22] In 7016 patients undergoing lumbar decompression, diabetes mellitus did correlate in a univariate, but not a multivariate analysis, with unplanned readmission.[23] In 4793 patients undergoing lumbar decompression without or with fusion, diabetes mellitus was not associated with readmission in a multivariate analysis.[24]

Other study limitations include the retrospective, nonrandomized nature. We cannot verify a diagnosis of diabetes in patients having HbA1c tested preoperatively, but as discussed above, the mere fact that patients were tested suggests either a diagnosis of diabetes or a strong suspicion of the same. Identification of the types of surgeries and the presence of infections relied upon CPT and ICD ontologies. While this is a common methodology in large-scale retrospective database studies, there are potential risks of miscoding and incomplete coding that bias our analysis.[25] The infection rates may therefore represent a low estimate. The biologic plausibility of the associations we describe and similar findings reported in other clinical scenarios bolster the validity of this study. The postoperative infection rate we report is similar to that in other studies,[18] suggesting that the inclusion of a large number of miscoded infections seems less likely. Finally, it is important to note that the veteran population profiled in this study is overwhelmingly male and Caucasian (White), which reduces the external validity of our findings to some degree. The strengths of this study include the large size of the patient population, the non–self-reported nature of the weight and BMI data, the actual HbA1c values, and the heterogeneous nature of the procedures and surgeons at multiple institutions, which aids in broad applicability.

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