Diabetes as an Independent Predictor for Extended Length of Hospital Stay and Increased Adverse Post-Operative Events in Patients Treated Surgically for Cervical Spondylotic Myelopathy

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Diabetes as an Independent Predictor for Extended Length of Hospital Stay and Increased Adverse Post-Operative Events in Patients Treated Surgically for Cervical Spondylotic Myelopathy

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Abstract

Background

Diabetes as an independent driver of peri-operative outcomes, and whether its severity impacts indications is conflicted in the research. The purpose of this study is to evaluate diabetes as a predictor for postoperative outcomes in cervical spondylotic myelopathy (CSM) patients.

Methods

A retrospective review was performed of patients treated surgically for CSM (ICD-9 721.1) from 2010-2012 in the prospectively-collected American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database. Outcome measures were length of stay, and the presence of complications. Diabetic patients were stratified based on whether or not their diabetes was insulin- or non-insulin-dependent.

Results

A total of 5,904 surgical CSM patients were included, 1101 (19%) had diabetes. 722 (65%) were non-insulin-dependent diabetics, and 381 (35%) were insulin-dependent diabetics. Diabetes was found to be an independent predictor of extended LOS (OR: 1.878[2.262-1.559], p<0.001) as well as of developing a complication (OR: 1.666[2.217-1.253], p<0.001) after controlling for associated variables like BMI. Type of diabetes (insulin- vs. non-insulin-dependent) showed little significant difference between the groups (p>0.05), however, patients with insulin-dependent diabetes were associated with an increased incidence of wound complications (p=0.027); severity of diabetes was not associated with any other individual complications.

Conclusions

Type and severity of diabetes is not a predictor for complication. Diabetes is associated with extended LOS and peri-operative morbidity. Level of evidence: Class 2b. Clinical relevance: Our findings support the view of many spine surgeons, who believe that diabetes has a negative impact on the outcome of surgery for CSM. Our findings support those cohort studies that found an association between diabetes and worst post-operative outcomes following surgical treatment of CSM. These findings lend support to the importance of monitoring preoperative serum glucose levels, as prevention of peri-operative hyperglycemia has been linked to improved postoperative outcomes in spine, joint and colon surgery.

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Introduction

Diabetes Mellitus (DM) is estimated to affect 439 million people worldwide by 2030, making it one of the most common comorbidities in the world.[1] Diabetes is a chronic systemic disease that can affect both the microvascular system and the peripheral nervous system. Previous studies have traditionally

focused on examining the impact of diabetes on patient outcomes following surgical treatment of thoracolumbar spinal pathologies.[2-5] Similarly, there is mounting evidence for an association between diabetes and poor patient outcomes following surgical deformity correction, including increased infection risk,[6] higher post-operative disability scores,[7] greater blood loss risk,[8] and elevated risk of peri-operative complications.[9]

Cervical spondylotic myelopathy (CSM) is one of the most prevalent neurological disorders, and decompression procedures for this condition are generally associated with excellent results.[10-12] Diabetes has been reported to occur in 13.3% of patients who undergo spine surgery for degenerative cervical pathology.[9,13] The studies investigating the correlation between DM and surgical CSM outcomes are few and limited primarily due to small cohorts of patients. Some are also limited by retrospectively collecting their data, having brief follow up periods, or failing to take into account the severity of diabetes. Some studies report that diabetes is associated with worse outcomes following the surgical treatment of CSM,[14,15,16-18] while others report no association.[16,19,20] DM is attributed with complications of microvasculature that can lead to cardiovascular, ophthalmic, renal, and peripheral vascular disease. In the context of surgical intervention, it may particularly lead to increased infection rates, and decreased long-term outcomes.[9,21] Systemic conditions such as DM can lead to impaired vascular flow, which ultimately leads to decreased tissue oxygenation. Tissue hypoxia due to decreased perfusion and insufficient angiogenesis leads to impairment of wound healing. Additionally, dysfunction in fibroblasts and epidermal cells, high levels of metalloproteinases, damage from reactive oxygen species and advanced glycation end products (AGEs), decreased host immune resistance, and neuropathy lead to impaired healing in diabetics.[22]

To our knowledge, no study has used a prospectively collected national database to examine the effect of diabetes on post-operative outcomes following surgical treatment of CSM. Specifically, few studies have analyzed the effect of diabetes on length of hospital stay in surgically treated CSM patients. Additionally, we sought to investigate whether the severity of DM, as measured insulin-dependent and non- status, escalates surgical risk. The purpose of this study was to perform a nationwide analysis of a large sample of patients treated surgically for CSM in order to evaluate diabetes as an independent predictor for suboptimal outcomes, including length of hospital stay, re-operation and per-operative complications, in CSM surgical patients.

Methods

Data Source

The American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database provides information based on patient medical charts that is risk-adjusted, case-mix-adjusted (allowing for it to take into consideration the complexity of procedures), and provides data for 30-day patient outcomes. The ACS-NSQIP draws its prospective data from more than 350 hospital centers in the US and consists of over 150 pre-operative, intra-operative, and 30-day post-operative data components.[23] Further details regarding the ACS NSQIP are available at https://www.facs.org/quality-programs/acs-nsqip/about. This study was a retrospective review of all CSM surgical patients identified in the ACS NSQIP database using ICD-9-CM coding (721.1) treated from 2005-2013.[23]

Data Collection and Analysis

Data collected included baseline patient demographics, complications, and surgical factors. Outcome measures included length of stay (defined according to the 75th percentile of the overall patient cohort; extended LOS ≥4 days), and the following complications: wound, deep incisional SSI, organ/space SSI, wound disruption, pneumonia, unplanned intubation, pulmonary embolism, use of ventilator >48 hours, progressive renal insufficiency, urinary tract infection, stroke/CVA, peripheral nerve injury, cardiac arrest requiring CPR, myocardial infarction, transfusions as a result of blood loss, graft/prosthesis/flap failure, DVT/thrombophlebitis, sepsis, and septic shock. Pulmonary comorbidities included severe chronic obstructive pulmonary disease, requirement of ventilator-assisted respiration within 48 hours of index surgery, and current pneumonia. Baseline cardiac comorbidities were defined as a his-

tory of congestive heart failure, myocardial infarction, cardiac surgery, or percutaneous coronary intervention.

Diabetes Grouping

According to the ACS-NSQIP database, diabetes is recorded and categorized based on the intensity of the treatment regimen of chronic, long-term management (i.e. greater than 2 weeks). The database distributes diabetes patients into three groups with respect to their disease treatment status: those with a diagnosis of diabetes requiring daily insulin-dependent therapy ('ID-DM' group), those who use a non-insulin anti-diabetic agent or manage by diet alone ('NI-DM' group), or neither ('NO-DM' group).

Statistical Analysis

Statistical analysis was performed using Statistical Package for the Social Sciences version 23.0 (SPSS Inc., Chicago, Illinois). Chi-squared tests for categorical factors and unpaired t-tests for continuous ones were utilized in order to evaluate differences in patient demographics, co-morbidities, and surgical variables between diabetic and non-diabetic patient groups. To determine whether or not diabetes presence was a risk factor for a given intra-operative and peri-operative complication, logistic regression was used. We controlled for age, BMI, smoking status, number of pulmonary comorbidities, and number of cardiac comorbidities. Diabetic patients were sub-stratified based on whether or not their diabetes was insulin- or non-insulin-dependent, and a sub-analysis was performed to compare these two groups to each other, with regard to complications presence and impact on outcomes. $P<0.05$ was determined to be statistically significant. Odds ratios are reported as (OR [95%CI], p-value).

Results

Study Sample

A total of 5,904 patients who underwent surgical treatment of cervical spondylotic myelopathy between 2010-2012 were identified from the ACS-NSQIP database. Of all patients undergoing surgical intervention for CSM, diabetes was the most prevalent baseline comorbidity (18.7%) represented in the ACS-NSQIP from 2010-2012 (Table 1). Of these patients, 381 (6.5%) were ID-DM, 722 (12.2%) were NI-DM, with the remainder of the population (N=4801, 81.3%) being NO-DM. For the overall cohort, the mean patient age was 61 years, average BMI was 29.37 kg/m^2 and 42.6% of the patients were female.

Baseline Comorbidity Burden

NI-DM were older than ID-DM (64.33 years vs 62.69, p=0.012) (Table 2). However, they otherwise presented with very similar comorbidity burdens for measured characteristics: BMI (p=0.472), BMI≥30 (p=0.239), BMI≥40 (p=0.215), smoking history (p=0.439), pulmonary comorbidites (p=0.062), and cardiac comorbidities (p=0.186). NO-DM were significantly younger/more morbid than diabetics for age (p<0.001), BMI (p<0.001), BMI≥30 (p<0.001), BMI ≥40(p<0.001), and cardiac comorbidities (p=0.001). Interestingly, NO-DM were more likely to smoke than NI-DM or ID-DM (30.1%, 19.9% p<0.001, and 19.7% p<0.001).

Surgical Invasiveness and Length of Stay

Intensity of surgery was not significantly different between diabetics and non-diabetics as measured by levels fused and decompressed, and operative time. With regards to extent of fusions, 17.5% of non-diabetics were fused over three levels, and 18.4% of diabetics (p=0.251). Operative time averaged 165 minutes for non-diabetics, and 167 for diabetics (p=0.522). Of patients who had diabetes, 340 (30.8%) had extended LOS. Diabetes was found to be an independent predictor of extended LOS (OR: 1.878[2.262-1.559] p<0.001) as well as of developing a complication (OR: 1.666[2.217-1.253] p<0.001) (Table 3).

Procedure-Related Complications

The total complication rate for diabetic patients in

this population was 12.1% (n=134). The most frequently-occurring complication among diabetic patients was the occurrence of transfusions as a result of blood loss (n=46, 4.2%, p=0.009)(Table 4), Other procedure-related complications present in the ACS-NSQIP database that were sustained in a significantly greater incidence among diabetic patients were as follows (Table 1): unplanned intubations (n=24, 2.2%, p=0.004), number of ventilator >48 hours occurrences (n=20, 1.8%, p<0.001), and UTI′s (n=26, 2.4%, p=0.030). Given BMI's relationship with hypoventilation syndrome and obstructive sleep apnea, morbid obesity patients (BMI >40) were removed from unplanned intubations and ventilator >48 hours occurrences. Statistically similar relationships were found: unplanned intubation (n=22, 2.3%, p=0.001) and ventilator > 48 hours occurrence (n=17, 1.8%, p=0.005). There was no difference in peripheral nerve injury between neither diabetics nor non-diabetics (p=1.0), nor NI- and ID-dependent diabetics (p=0.334). Many expected findings like cardiac complications were not significant due to their low frequency.

On multivariate analysis, controlling for BMI, smoking status, pulmonary comorbidities, and cardiac comorbidities, diabetes was an independent predictor for several complications: unplanned intubation (OR: 2.833[5.463-1.469], p=0.002), use of ventilator >48 hours (OR: 4.352[9.179-2.063], p<0.001), urinary tract infection (OR: 2.322[4.376-1.232], p=0.009), bleeding transfusions (OR: 1.602[2.496-1.029], p=0.037), and DVT/thrombophlebitis (OR: 2.880[6.443-1.287], p=0.10).

Sub-Analysis by Diabetes Type

Age (ID-DM 62.69, NI-DM 64.33, p=.012) was the only significantly different baseline characteristic between patients with ID-DM and NI-DM patients. Sub-analysis demonstrated that insulin-dependent diabetes predicted extended LOS (OR 1.961, p<0.001). Type of diabetes (insulin- vs. non-insulin-dependent) was not found to be a predictor of developing a complication (p>0.05)(Table 5), however, patients with insulin-dependent diabetes were associated with an increased incidence of wound complications (p=<0.001) (Table 2); Type of diabetes was not associated with any other individual complications. There was a trend towards insulin-dependent diabetics having at least one complication compared with

Table 1. Distribution of baseline comorbidities in the ACS-NSQIP database, comprising a modified CCI.[32]

CCI	CHF	Peripheral Vascular Disease	Cerebrovascular Injury	COPD	Diabetes	Hemiplegia	End-Stage Renal Failure	Ascites/ varices	Disseminated Cancer
N	21	27	140	373	1103	62	6	1	14
%	.4	0.5	2.4	6.3	18.7	1.1	0.1	.0	0.2

Table 2. Univariate associations for diabetes presence at baseline with individual procedure-related complications represented in the ACS-NSQIP database. "Yes" diabetes group includes both treatment regimens (insulin [ID-DM] and non-insulin [NI-DM]). Statistically significant differences at p<0.05 are bolded.

Variable	Diabetes Presence			P-values for Group Comparisons			
	NO-DM (n=4801)	NI-DM (n=722)	ID-DM (n=381)	NO-DM to NI-DM	NO-DM to ID-DM	NI-DM to ID-DM	NO-DM to DM
Age	59.42 (11.80)	64.33 (10.24)	62.69 (10.22)	**<0.001**	**<0.001**	**0.012**	**<0.001**
BMI (kg/m²)	28.66 (6.71)	32.37 (7.26)	32.72 (8.47)	**<0.001**	**<0.001**	0.472	**<0.001**
BMI≥30	1762 (36.7%)	428 (59.3%)	235 (61.7%)	**<0.001**	**<0.001**	.239	**<0.001**
BMI ≥40	234 (4.9%)	96 (13.3%)	58(15.2%)	**<0.001**	**<0.001**	.215	**<0.001**
Smoking Hx	1443 (30.1%)	144 (19.9%)	75 (19.7%)	**<0.001**	**<0.001**	.493	**<0.001**
Pulmonary Comorbidity	297 (6.2%)	48 (6.6%)	36 (9.4%)	0.341	**0.011**	0.062	**0.049**
Cardiac Comorbidity	168 (3.5%)	40 (5.5%)	27 (7.1%)	**0.007**	**0.001**	0.186	**<0.001**

non insulin-dependent diabetics (14.9% vs. 11.4%), although this was not statistically significant.

Discussion

Cervical spondylotic myelopathy is a common spinal disorder, and surgery for this condition has increased between twofold and sevenfold over the last 10 to 15 years.[24,25] Many spine surgeons practice on the assumption that diabetes mellitus (DM) has a major impact surgical outcomes and complications, however there is debate in the literature.[26] Machino et al in two different papers, one 505 patients, the other 105 patients that underwent double-door laminoplasty for CSM, found worse pre- and post-operative Japanese Orthopaedic Assocaition (JOA) scores, and slower, reduced improvement in patients with diabetes >10 years and HgbA1C>6.5%.[17,27] Dokai et al. reported that, among CSM patients treated with expansive laminoplasty, the diabetic cohort experienced poorer sensory and motor function recovery in lower extremities.[16] The diabetic cohort's recovery rate was negatively correlated with preoperative HgbA1C. In contrast, other trials on CSM have found non-different outcomes in diabetic patients. Kawaguchi et al. performed a retrospective review of 18 diabetic and 34 non-diabetic patients undergoing cervical laminoplasty for CSM, and found no differences between diabetic and non-diabetic patients in JOA outcome scores; however, there was a non-significant decrease in lower extremity recovery in diabetics.[20] Arnold et al. reported comparable surgical outcomes between diabetic and non-diabetic patients treated with surgical decompression for CSM.[19] The authors included that the outcome scores and the complication rates are non-different in patients with diabetes. Our study found that, controlling for baseline comorbidities like BMI, smoking status, and pulmonary and cardiac comorbidities, the presence of diabetes significantly increased the rate of experiencing any complication and having an extended length of stay. Specifically, diabetics experienced significantly increased rates of pneumonia, intubation, ventilation >48 hours, UTIs, and bleeding transfusions.

Surgeons agree diabetes has impacts on long-term

Table 3. Multivariate analysis for impact of diabetes on intra- and peri-operative patient outcomes.

	Outcome Measures (OR [95% CI], p-value)	
	Complication (Y/N)	LOS (Y/N)
ID-DM + ND-DM	1.67 (2.22-1.25) p<0.001	1.88 (2.26-1.88), p<0.001
ID-DM	0.492 (0.75-0.32), p=0.001	0.342 (0.46-0.25), p<0.001
ND-DM	0.73 (1.21-0.44), p=0.225	0.510 (0.72-0.36), p<0.001

Table 4. Association of Diabetes Presence (ID-DM and NI-DM) with Individual Complications (Non-insulin- vs. Insulin-Dependent Diabetes).

Complication	Diabetes Presence		p-value
	No (n=4801)	Yes (n=1103)	
Wound	0.6%	0.8%	0.194
Deep Incisional SSI	0.5%	0.3%	0.884
Organ/Space SSI	0.2%	0.3%	.212
Wound Disruption	0.2%	0.1%	0.762
Pneumonia	1.1%	12.1	0.014
Unplanned Intubation	0.9%	2.2%	0.004
Pulmonary Embolism	0.5%	0.6%	0.747
Ventilator > 48 Hours	0.7%	1.8	<0.001
Progressive Renal Insufficiency	0.1%	0.0%	0.788
Urinary Tract Infection	1.2%	2.4%	0.030
Stroke/CVA	0.1%	0.2%	0.958
Peripheral Nerve Injury	0.1%	0.1%	0.854
Cardiac Arrest Requiring CPR	0.3%	0.6%	0.348
Myocardial Infarction	0.2%	0.5%	0.150
Bleeding Transfusions	2.5%	4.2%	0.009
Graft/Prosthesis/Flap Failure	0.0%	0.1%	0.113
DVT/Thrombophlebitis	0.7%	1.5%	0.07
Sepsis	0.6%	0.8%	0.640
Septic Shock	0.2%	0.7%	0.081

Table 5. Association of Type of Diabetes with Individual Complications (Non-insulin- vs. Insulin-Dependent Diabetes).

Complication	NI-DM (n=722)	ID-DM (n=381)	p-value
Wound	0.5%	1.6%	<0.000
Deep Incisional SSI	0.3%	0.5%	1.000
Organ/Space SSI	0.0%	0.3%	0.334
Wound Disruption	0.3%	0.0%	1.000
Pneumonia	2.3%	2.9%	0.783
Unplanned Intubation	1.5%	3.1%	0.278
Pulmonary Embolism	0.9%	0.3%	0.307
Ventilator > 48 Hours	1.4%	2.7%	0.250
Urinary Tract Infection	2.0%	2.9%	0.588
Stroke/CVA	0.3%	0.0%	0.554
Peripheral Nerve Injury	0.0%	0.3%	0.334
Cardiac Arrest Requiring CPR	1.5%	2.1%	1.000
Myocardial Infarction	0.0%	0.3%	1.000
Bleeding Transfusions	4.7%	5.2%	0.838
Graft/Prosthesis/Flap Failure	0.3%	0.0%	1.000
DVT/Thrombophlebitis	1.8%	1.5%	1.000
Sepsis	1.0%	1.5%	0.692
Septic Shock	0.5%	0.5%	1.000

health. Surgical decision-making can be improved, however, in regards to DM severity. Differences between non- and insulin-dependent diabetics remain an understudied area of research. We saw the most pronounced increase in complications considering between non-diabetics and all diabetics. Our subanalysis on the type of diabetes revealed that only ID-DM CSM patients displayed an increased prevalence of wound complications (2.1% vs. 0.3%, p=0.045). In optimizing preoperative procedures regarding minimization of DM-related risk, our findings indicate that insulin dependence may not be significant. In that case, aggressive interventions trying to convert someone to noninsulin dependence or drastic medical (or surgical like bariatric surgery) measures to change type of diabetes would not impact CSM outcomes. An alternative explanation is that many patients in the NI-DM group do not have access to healthcare despite their diabetes status. Given the multifactorial pathophysiology of diabetes is very complicated, the dose-dependent relationship of DM is unclear and deserves further investigation.

To our knowledge, the present study is the first report using a prospectively-collected national database of patients undergoing surgical treatment of CSM. Our goal was to identify any increased complications or differences in hospital-related characteristics (length of hospital course, readmission) in patients with diabetes undergoing surgical treatment of CSM. From 2005-2013, we found that 19% of patients undergoing surgical treatment of CSM recorded in the ACS database presented with diabetes, a percentage even higher than previously reported.[12] The results of our study showed that there are a number of peri-operative complications associated with diabetes in patients undergoing surgical treatment of CSM including unplanned intubation, staying on a ventilator for more than 48 hours, urinary tract infection, transfusions secondary to blood loss, and DVT/thrombophlebitis.. This agrees with two recent works by Guzman et al on the National Inpatient Database on cervical and lumbar surgeries analyzing peri-operative complications. An increase was observed in the cervical spine for respiratory, cardiac, and genitourinary complications for uncontrolled diabetics (defined by ICD-9-CM code status). In the lumbar spine, Guzman et al observed an increase of cardiac, DVT, and shock complications for uncontrolled diabetics. A general increase was observed for peri-operative complications in controlled-diabetics in addition to longer LOS in both spine regions. Our analysis also observed significantly increased length of stay in DM patients. In efforts to avoid confounding effects of obesity, which has been shown to increase peri-operative complications, we analyzed ventilation and intubation-related complications with and without obese class III patients.[28,29] Surprisingly, there was no difference in the size of the effect without the highest-BMI cohort.

Unplanned and prolonged intubation puts the patient at a greater risk for further complications and mortality.[30] The loss of airway patency can be a life-threatening phenomenon, stressing the importance of identifying diabetes as an independent risk factor for postoperative airway complication, especially in surgery involving the cervical spine, even when controlling for obesity. It is not surprising that airway complications alone lead to greater 30-day complications and mortality rates. Surgeons should be aware that diabetic patients undergoing surgery for CSM may encounter complications related to airway and steps should be taken to minimize these complications.

The major advantage of our study compared to previous reports is the number of patients that we were able to study, and the broad distribution of centers from which patients were obtained. Using a prospectively-collected national database allowed us to utilize data from almost 6,000 patients to describe diabetes-mellitus' association with a number of post-operative complications and an increased length of stay. This held true even after controlling for demographic factors, as patients with diabetes were also found to be older, smoke more, and more likely to be overweight or obese. Another advantage of our study is the wide applicability of the findings. This study included patients from many medical centers, undergoing multiple types of procedures for CSM, by a vast number of different spinal surgeons.

Our study has several limitations, many of which are related to the use of the ACS-NSQIP database. The first is the reliance of the database on ICD-9 and

CPT coding, which allows for potential uncertainty regarding the accuracy of case assignment for the database. Second, the database only tracks patient complications for 30 days after their operation. Therefore, our collected information on complications is limited to these first 30 days, despite the fact that complications might be occurring after this time. We cannot collect information on functional outcomes after surgery, such as patient-reported functional scores or satisfaction surveys, which limits our results. Additionally, readmission rates were not collected as part of this database prior to 2013, so they could not be obtained for this study. Lastly, we are only able to identify the presence and type of diabetes from the database; we cannot collect any information regarding the severity of diabetes such as HgbA1C scores or end-organ damage. Despite these limitations, the large number of patients included for analysis allows us to draw conclusions regarding the data that was available.

Using a prospectively-collected national database, we have found that diabetes is associated with a longer length of stay, and a higher rate of complications in patients undergoing surgical treatment of CSM including unplanned intubation, use of a ventilator for more than 48 hours, urinary tract infection, transfusions secondary to blood loss, and DVT/thrombophlebitis. Our findings support the view of many spine surgeons, who believe that diabetes has a negative impact on the outcome of surgery for CSM.[26] Our findings support those cohort studies that found an association between diabetes and worst postoperative outcomes following surgical treatment of CSM. These findings lend support to the importance of monitoring preoperative serum glucose levels, as prevention of peri-operative hyperglycemia has been linked to improved postoperative outcomes in spine, joint and colon surgery.[31]

Conclusion

Diabetes was found to predict extended LOS as well the occurrence of complications. There was less difference between NI-DM and ID-DM than expected. The only observed increase in complications was an elevated rate of wound occurrences in ID-DM patients.

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