Depression as an independent predictor of postoperative delirium in spine deformity patients undergoing elective spine surgery

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OBJECTIVE Depression is the most prevalent affective disorder in the US, and patients with spinal deformity are at increased risk. Postoperative delirium has been associated with inferior surgical outcomes, including morbidity and mortality. The relationship between depression and postoperative delirium in patients undergoing spine surgery is relatively unknown. The aim of this study was to determine if depression is an independent risk factor for the development of postoperative delirium in patients undergoing decompression and fusion for deformity.

METHODS The medical records of 923 adult patients (age ≥ 18 years) undergoing elective spine surgery at a single major academic institution from 2005 through 2015 were reviewed. Of these patients, 255 (27.6%) patients had been diagnosed with depression by a board-certified psychiatrist and constituted the Depression group; the remaining 668 patients constituted the No-Depression group. Patient demographics, comorbidities, and intra- and postoperative complication rates were collected for each patient and compared between groups. The primary outcome investigated in this study was rate of postoperative delirium, according to DSM-V criteria, during initial hospital stay after surgery. The association between depression and postoperative delirium rate was assessed via multivariate logistic regression analysis.

RESULTS Patient demographics and comorbidities other than depression were similar in the 2 groups. In the Depression group, 85.1% of the patients were taking an antidepressant prior to surgery. There were no significant between-group differences in intraoperative variables and rates of complications other than delirium. Postoperative complication rates were also similar between the cohorts, including rates of urinary tract infection, fever, deep and superficial surgical site infection, pulmonary embolism, deep vein thrombosis, urinary retention, and proportion of patients transferred to the intensive care unit. In total, 66 patients (7.15%) had an episode of postoperative delirium, with depressed patients experiencing approximately a 2-fold higher rate of delirium (10.59% vs 5.84%). In a multivariate logistic regression analysis, depression was an independent predictor of postoperative delirium after spine surgery in spinal deformity patients ($p = 0.01$).

CONCLUSIONS The results of this study suggest that depression is an independent risk factor for postoperative delirium after elective spine surgery. Further studies are necessary to understand the effects of affective disorders on postoperative delirium, in hopes to better identify patients at risk.

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KEY WORDS depression; delirium; spine; deformity; surgery; outcomes

ABBREVIATIONS A-fib = atrial fibrillation; BMI = body mass index; CABG = coronary artery bypass graft; CAD = coronary artery disease; CHF = congestive heart failure; DVT = deep vein thrombosis; EBL = estimated blood loss; ICU = intensive care unit; MI = myocardial infarction; PE = pulmonary embolism; PRBC = packed red blood cell; PVD = peripheral vascular disease; SNRI = serotonin-norepinephrine reuptake inhibitor; SSI = surgical site infection; SSRI = selective serotonin reuptake inhibitor; UTI = urinary tract infection.

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DEPRESSION is the most common affective disorder in the United States, with 16.6% of the population experiencing at least 1 major depressive episode in their lifetime.⁸ Patients with spinal deformity in particular have been shown to be at an increased risk for depression when compared with the general population.^{12,21} Spinal deformities can cause body image dissatisfaction, physical disability, and chronic pain, all of which may limit psychosocial functioning and increase the risk of depression.¹⁸ In addition, depression has been shown to be a significant risk factor for poor surgical outcomes after spine surgery, such as increased pain and postoperative disability.^{15,17}

In particular, postoperative delirium has also been associated with increases in complication rates, hospital length of stay, in-hospital mortality, and overall health care costs.^{3,14} Due to the quality of care and economic implications of postoperative delirium, previous studies have attempted to determine independent associations and risk factors for postoperative delirium. In a retrospective study of 549 patients who underwent spinal surgery, Gao et al.⁴ found several preoperative risk factors for the development of postoperative delirium, including older age, number of medications, diabetes mellitus, and central nervous system disorders. However, the relationship between depression and postoperative delirium in spine surgery remains relatively unknown.

The aim of this study is to determine whether depression is an independent risk factor for postoperative delirium in spine deformity patients after spinal surgery.

Methods

In this retrospective analysis, the medical records of 923 adult (age ≥ 18 years) spine deformity patients who had undergone elective spine surgery at Duke University Medical Center from 2005 through 2015 were reviewed. Institutional review board approval was obtained prior to study initiation. We included adult patients (age ≥ 18 years) who met the following criteria: 1) diagnosis of spinal deformity, such as scoliosis and kyphosis, with radiographic evidence of degenerative scoliosis or spondylolisthesis; 2) undergoing elective corrective spinal surgery for spinal deformity; and 3) documented intra- and postoperative hospital course. Patients who had undergone spinal surgery previously or had any preexisting spinal pathology, including primary osseous pathology that might impair fusion, tumor, and infection, were excluded. We identified 255 patients (27.6% of the overall group) who had a known history of depression and had received a diagnosis of depression from a board-certified psychiatrist prior to surgery (Depression cohort). The remaining 668 patients (72.4%) made up the No-Depression cohort. The primary outcome of this study was the incidence of postoperative delirium.

Demographic variables evaluated included age, sex, and body mass index (BMI). Comorbidities included congestive heart failure (CHF), coronary artery disease (CAD), atrial fibrillation (A-fib), peripheral vascular disease (PVD), myocardial infarction (MI), hypertension, diabetes, deep vein thrombosis (DVT), hyperlipidemia,

and pulmonary embolism (PE). Baseline alcohol use was recorded as well. For the Depression cohort, preoperative antidepressants were assessed and classified as selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and/or other antidepressants, including tricyclic antidepressants, atypical antidepressants, and monoamine oxidase inhibitors.

Intraoperative variables and complications included number of vertebral levels involved, operative time, estimated blood loss (EBL), percent of patients requiring a blood transfusion, number of packed red blood cell (PRBC) transfusions, spinal cord injury, nerve root injury, and durotomy. Postoperative variables included length of hospital stay, intensive care unit (ICU) admission and length of stay, urinary tract infection (UTI), fever, ileus, deep and superficial surgical site infections (SSIs), hypertension, hypotension, hematoma, myocardial infarction (MI), pulmonary embolism (PE), deep vein thrombosis (DVT), sepsis, weakness, sensory deficit, urinary retention, and whether the patient was discharged with a Foley catheter. Data on postoperative neural deficits were also collected.

Parametric data were expressed as means (with standard deviations) and compared using the Student t-test. Nonparametric data were expressed as medians (with interquartile ranges) and compared via the Mann-Whitney U-test. Nominal data were compared with the chi-square test. The relationship between independent variables and postoperative delirium was assessed using a multivariate logistic regression model. All tests were 2-sided, and results were considered statistically significant if the p value was less than 0.05. Statistical analysis was performed using JMP, Version 12 (SAS Institute Inc.).

Results

A total of 923 adult patients (age ≥ 18 years) were included in this study—668 in the No-Depression cohort and 255 patients in the Depression cohort. There were no significant between-group differences in demographic characteristics, with similar proportions of men and similar mean age and BMI (Table 1). There were also no significant differences between the groups with respect to comorbidities, including CHF, CAD, A-fib, PVD, MI, hypertension, diabetes, DVT, hyperlipidemia, and PE, or alcohol consumption. In the Depression cohort, 85.1% of the patients were taking at least 1 antidepressant prior to surgery; 53.3% of the patients in this cohort were taking an SSRI, 22.0% were taking an SNRI, and 9.8% were taking other types of antidepressants (Table 1).

The median number of vertebral levels involved in the procedure was similar in the No-Depression and Depression groups, as was the operative time, EBL, urine output (768.07 ± 737.52 ml vs 680.94 ± 595.84 ml, $p = 0.07$), and number of PRBC transfusions (Table 2). The rate of incidental durotomy was similar in the 2 cohorts, and neither group had any direct intraoperative spinal cord or nerve root injuries.

Postoperative Hospital Stay and Complication Profile

Postoperative hospital stays were similar in the No-

TABLE 1. Preoperative variables

Variable	No Depression (n = 668)	Depression (n = 255)	p Value
Preop variables			
Male	36.53%	34.90%	0.70
Age in yrs (mean)	61.00 ± 15.84	61.87 ± 11.59	0.36
BMI in kg/m ² (mean)	28.39 ± 6.84	29.08 ± 5.90	0.14
CHF	1.05%	0.00%	0.20
CAD	11.08%	10.20%	0.81
A-fib	5.69%	4.71%	0.63
PVD	1.65%	1.96%	0.78
MI	2.99%	1.96%	0.50
HTN	55.24%	61.57%	0.09
DM	14.82%	13.33%	0.60
DVT	3.29%	4.31%	0.43
HLD	37.28%	38.82%	0.70
PE	1.80%	3.53%	0.14
Alcohol use	29.64%	29.02%	0.87
Treatment of depression			
Treated		85.1%	
SSRI		53.3%	
SNRI		22.0%	
Other		9.8%	

DM = diabetes mellitus; HLD = hyperlipidemia; HTN = hypertension.
Mean values are given with SDs.

Depression and Depression groups, including mean overall length of stay, ICU admission rates, and mean length of stay in the ICU for patients admitted to the ICU. The prevalence of postoperative complications was also similar in the 2 cohorts. Details are given in Table 3. A few patients had postoperative neurological deficits, but all of these deficits appeared to have resolved at 6 months after surgery.

There was a significant difference between the No-Depression and Depression groups with respect to postoperative delirium. In total, 66 patients (7.15%) experienced an episode of postoperative delirium. Patients with depression had nearly a 2-fold higher incidence of postoperative delirium (5.84% in the No-Depression group vs 10.59% in the Depression group, $p = 0.015$) (Table 3). When we examined types of delirious episodes in the 2 patient groups, we found no significant differences between groups with respect to the prevalence of hyperactive, hypoactive, or mixed delirious episodes. In the Depression group, among patients who experienced delirious episodes, 33.3% of episodes were hyperactive, 18.5% were hypoactive, and 33.3% were mixed delirious episodes; and in the No-Depression group, among patients who experienced delirious episodes, 23.1% of episodes were hyperactive, 10.3% were hypoactive, and 23.1% were mixed delirious episodes. Between-patient group comparisons of hyperactive, hypoactive, and mixed delirium episodes yielded $p = 0.36$, $p = 0.34$, and $p = 0.36$, respectively. Furthermore, within the Depression cohort, there was no significant difference in the incidence of de-

TABLE 2. Intraoperative variables and complications

Variable	No Depression (n = 668)	Depression (n = 255)	p Value
No. of levels			
Median	4	4	0.61
IQR	2–7	2–6	
Operative time in minutes (mean)	274.33 ± 138.67	294.19 ± 132.34	0.054
EBL in ml (mean)	798.90 ± 1153.80	959.33 ± 1342.45	0.09
No. of PRBC transfusions (mean)*	0.73 ± 1.55	0.89 ± 1.59	0.15
Spinal cord injury	0%	0%	1.00
Nerve root injury	0%	0%	1.00
Incidental durotomy	5.84%	7.84%	0.29

* 1 unit = 350 ml.

lirium between the patients who were receiving treatment for depression and those who were not (11.1% vs 7.9%, respectively, $p = 0.56$).

The complication profile was compared between patients who did and did not have delirium. There was a significant difference in the mean length of hospital stay (8.4 ± 3.9 days for patients with delirium vs 5.1 ± 3.7 days for those without, $p < 0.001$). Moreover, the proportion of patients transferred to the ICU was significantly greater in the group with delirium than in the group without delirium (33.9% vs 18.1%, $p = 0.025$), as was the percentage of patients with UTI (19.7% vs 3.5%, $p < 0.0001$), ileus (12.1% vs 4.7%, $p = 0.017$), and readmission within 30 days (18.2% vs 9.7%, $p = 0.036$). All other complication rates were similar in the 2 cohorts.

Postoperative Delirium Independent Predictors

In a multivariate binary logistic regression analysis, depression ($p = 0.01$), patient age ($p < 0.001$), operative time ($p = 0.03$), and postoperative UTI ($p < 0.001$) were independent predictors of postoperative delirium (Table 4). Other patient variables, including sex, BMI, CHF, CAD, hypertension, PVD, diabetes mellitus, hyperlipidemia, and alcohol consumption, were not statistically significant independent predictors of postoperative delirium. Other operative variables and postoperative complications, including fusion levels, fever, deep SSI, superficial SSI, hypotension, UTI, and urinary retention, were also not statistically significant predictors.

Discussion

In this retrospective study of 923 adult patients (age ≥ 18 years) undergoing elective spinal surgery, depression emerged as an independent risk factor for the development of postoperative delirium.

Prior studies in various surgical fields have associated depression with an increased incidence of postoperative delirium. In a prospective study of 109 elderly patients (age ≥ 65 years) undergoing surgery for acute hip fracture, Koskderelioglu et al.⁷ demonstrated that depressive mood,

TABLE 3. Postoperative complications

Variable	No Depression (n = 668)	Depression (n = 255)	p Value
LOS in days (mean)	5.19 ± 3.79	5.70 ± 3.89	0.07
ICU	20.36%	16.46%	0.21
Length of ICU stay in days (mean)	3.09 ± 19.33	3.05 ± 16.42	0.98
Delirium	5.84%	10.59%	0.015*
UTI	4.04%	6.27%	0.16
Fever	3.44%	2.75%	0.68
Ileus	5.84%	3.53%	0.19
Deep SSI	0.60%	1.57%	0.23
Superficial SSI	0.75%	1.18%	0.69
HTN	2.84%	2.35%	0.82
Hypotension	5.34%	7.06%	0.34
Hematoma	1.05%	1.18%	0.87
MI	0.45%	1.18%	0.36
PE	0.75%	1.57%	0.27
DVT	0.30%	0.78%	0.31
Sepsis	1.66%	0.39%	0.20
Weakness	5.09%	5.88%	0.62
Sensory deficit	2.40%	2.75%	0.81
Urinary retention	7.78%	9.02%	0.59
D/C w/ Foley catheter	2.70%	1.57%	0.47

D/C = discharge; LOS = length of stay.

* Statistically significant.

as assessed by the Beck Depression Inventory, correlated with the occurrence of postoperative delirium. In another prospective study of 485 elderly men undergoing transurethral prostatectomy for benign prostatic hyperplasia, Tai et al.¹⁶ showed that patients with a higher Geriatric Depression Scale (GDS) score were significantly more likely to develop postoperative delirium. Similarly, in a retrospective study of 224,060 patients undergoing elective total shoulder arthroplasty between 2002 and 2012, Mollon et al.¹⁰ showed depression to be an independent risk factor for postoperative delirium. In another retrospective analysis of 91 patients (age ≥ 75 years) who underwent esophagectomy for the treatment of esophageal cancer, Yamamoto et al.²⁰ showed that GDS score was independently associated with postoperative delirium. Analogous to these studies, our study demonstrated that adult patients with a diagnosis of depression prior to surgery were more likely to develop postoperative delirium than patients without a history of depression.

Previous studies have been conducted to elucidate the pathophysiology connecting depression and postoperative delirium. In a prospective cohort study of 113 patients undergoing coronary artery bypass graft (CABG) surgery, Kazmierski et al.⁵ found 2 factors that correlated with postoperative delirium: depression and elevated pre-operative cortisol levels. However, once depression was controlled for, the association between cortisol levels and postoperative delirium lost its statistical significance.⁵ Therefore, this study hypothesized that depression is cor-

TABLE 4. Independent predictors of postoperative delirium

Variable	Coefficient	p Value
Sex	0.057	0.72
Age	0.083	<0.0001*
Depression	0.398	0.01*
BMI	0.022	0.43
CHF	0.385	0.56
CAD	0.128	0.98
HTN	0.049	0.64
PVD	0.093	0.07
DM	-0.006	0.65
HLD	0.084	0.95
Alcohol	0.011	0.41
Fusion levels	-0.622	0.31
Operative time	-0.673	0.03*
Postop fever	0.549	0.20
Postop deep SSI	0.856	0.30
Postop superficial SSI	0.320	0.44
Postop hypotension	0.165	0.49
Postop UTI	0.769	<0.001*
Postop urinary retention	0.002	0.11

* Statistically significant (p < 0.05).

related with higher cortisol levels, and the elevated levels of stress hormones increase the risk of postoperative delirium.⁵ This conclusion is supported by other studies in the literature that have shown depression to be linked with increased cortisol levels, in both humans and nonhuman primates.^{13,19} Additionally, in a prospective study of 243 patients undergoing elective CABG surgery, Mu et al.¹¹ found high cortisol levels to be linked with postoperative delirium. These elevated glucocorticoid levels have been hypothesized to cause structural changes in hippocampal neurons and to perturb the hypothalamic-pituitary axis, which may predispose the brain to episodes of delirium.⁶ In sum, this group of studies supports a potential link between depression, cortisol, and the development of postoperative delirium, lending a biological basis to this present research.

Postoperative delirium constitutes a significant financial burden on our health care system. In a study of 500 patients undergoing esophagectomy for malignancy, Markar et al.⁹ found that delirium was associated with a longer hospital stay (14 vs 10.9 days), longer ICU stay (3.6 vs 2.7 days), and increased cost (\$28,222.80 vs \$22,702.20). Similarly, in a retrospective study of 242 elderly patients (age ≥ 65 years) who underwent surgical treatment for hip fracture in Canada, Zywił et al.²² found that delirium increased the hospital stay following surgery by a mean length of 7.4 days and increased the cost of care by \$8286 (Canadian dollars). Furthermore, this study extrapolated that a 50% reduction in postoperative delirium rates could decrease health care costs by \$50,708,000 (Canadian dollars) each year in Canada, assuming that their results were generalizable across the entire country.²² These studies therefore suggest that utilization of preventive measures

to reduce the incidence of postoperative delirium could significantly lessen the health care costs that have been soaring across the world.

Previous studies have identified possible preventive measures to improve postoperative outcomes in patients with depression. In a retrospective study of 140 adults who had undergone anterior cervical discectomy and fusion, Elsamadicy et al.² found that patients with a history of depression that were pretreated with an antidepressant for at least 6 months prior to surgery had similar self-reported surgical outcomes to the control group that had no prior history of depression. Similarly, in a randomized control trial of 100 depressed patients who underwent CABG surgery, Dao et al.¹ found that brief preoperative cognitive behavioral therapy reduced in-hospital length of stay (7.9 vs 9.2 days) in addition to improving depressive symptoms and quality of life. However, further studies are necessary to better understand the effects of depression on surgical outcomes.

The study has several limitations that may impact its interpretation. The variables were collected retrospectively and analyzed; therefore, this study is subject to the weaknesses of retrospective analysis, including reliance on record keeping of others, difficulty in determining temporal relationships, and selection and information bias. The chart review for this study involved only a single institution and may not reflect areas with different patient populations. Furthermore, data regarding the severity of the depressive symptoms and the duration of treatment were not collected for all patients and therefore these variables may have been subject to selection bias for the cohorts. Similarly, postoperative narcotic use and complete metabolic panels were not collected and assessed in all patients, which may have implications on our analysis (not accounting for potentially confounding factors and isolated metabolic differences between the cohorts). Despite these limitations, this study has shown that depression is an independent risk factor for the development of postoperative delirium in our patient population.

Conclusions

The results of this study suggest that depression is an independent risk factor for postoperative delirium after elective spine surgery. Further studies are necessary to understand the effects of affective disorders on postoperative delirium, in the hope of better identifying at-risk patients and improving patient care.

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Disclosures

Dr. Karikari reports a consultant relationship with NuVasive.

Author Contributions

Conception and design: Adogwa, Elsamadicy. Acquisition of data: Elsamadicy, Lydon, Sergesketter, Kaakati. Analysis and interpretation of data: Adogwa, Elsamadicy. Drafting the article: Adogwa, Elsamadicy, Lydon, Sergesketter, Kaakati. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Adogwa. Statistical analysis: Adogwa, Elsamadicy. Administrative/technical/material support: Mehta, Vasquez, Cheng, Bagley, Karikari. Study supervision: Mehta, Vasquez, Cheng, Bagley, Karikari.

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