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Postoperative Complications Following Orthopedic Spine Surgery: Is There a Difference Between Men and Women?

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ABSTRACT

Background: Patient sex is known to affect outcomes following surgery. Prior studies have not specifically examined sex-stratified outcomes following spine surgery. The objective is to determine the differences between men and women in terms of 30-day complications following spine surgery.

Methods: The National Surgical Quality Improvement Program database was queried for patients undergoing spine surgery from 2005 to 2014. Postoperative data were analyzed to determine the differences between men and women with regard to 30-day complications.

Results: A total of 41 315 patients (49.0% women, 51% men) were analyzed. Men were more likely to have diabetes ($P = .004$) and be active smokers ($P < .001$). Women were more likely to be taking steroids for chronic conditions ($P < .001$). Postoperatively, women were at increased risk for superficial surgical site infection, urinary tract infection, transfusions, and longer length of stay, whereas men were at increased risk of pneumonia and reintubation. On multivariate analysis, women were associated with urinary tract infections (odds ratio = 2.17) and transfusions (odds ratio = 1.63).

Conclusions: Differences in complications are evident between men and women following spine surgery. These differences should be considered during preoperative planning and when consenting patients for surgery.

Level of Evidence: 4

Other & Special Categories

Keywords: postoperative complications, sex, NSQIP, spine surgery, short-term outcomes

INTRODUCTION

The sex of a patient has previously been shown to have an impact on the outcome of a surgical intervention.[1–10] Women undergoing vascular surgery have been found to have higher mortality rates, more wound complications, greater need for blood transfusion, and increased length of stay.[1–5] In trauma surgery, male sex has been associated with increased mortality, length of stay, and complications.[7] In a broad study of patients undergoing orthopedic surgery, Molina et al[6] found that female sex was an independent risk factor for several complications, including urinary tract infection (UTI), pneumonia, deep surgical site infection (SSI), return to the operating room, and death.

There are very few data on the impact that patient sex has on postoperative outcomes following spine surgery. Schoenfeld et al,[11] in a systematic review of the influence of sex on mortality and morbidity following spine surgery, found that men have a higher risk of mortality following spine surgery. The authors found that sex-susceptibility to specific complications varied among papers, and there was inconsistency in risk factors for postoperative complications among studies. They did note that none of the studies included in their analysis were primarily investigating the impact of sex on postoperative outcomes and that their sex-related findings were secondarily imputed.

The National Surgical Quality Improvement Program (NSQIP) database is a surgeon-validated database maintained by the American College of Surgeons that contains preoperative data, operative data, and 30-day patient outcomes collected from more than 600 hospitals nationwide.[12] Using this database, some authors have reported on 30-day mortality and morbidity following individual spine surgical procedures.[9,10,13,14] Gruskay et al,[9] in a study of complications following anterior cervical discectomy and fusion, reported a secondary finding of male sex being a predictive factor for major complications such as mortality, venous thrombotic

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events, and return to the operating room. On the other hand, Kothari et al[10] reviewed a subset of patients who underwent spinal arthrodesis for spinal deformity and found that women were at higher risk for complications. Similarly conflicting data have been reported by other authors on the impact of sex on the incidence of complications, using the NSQIP and other databases.[10,11,13–19] These studies have not focused on sex as a primary variable. The aim of the current study was to use the NSQIP database and determine differences in short-term postoperative complications after spine surgery, when stratified by sex.

MATERIALS AND METHODS

A retrospective analysis of the NSQIP database from January 2005 to December 2014 was performed. The NSQIP database prospectively collects preoperative patient clinical characteristics and 30-day postoperative complication, readmission, and mortality rates for patients undergoing surgery from more than 600 participating hospitals throughout the United States.[12] The database has been extensively examined and validated by many prior studies in orthopedic surgery.[20–24] For the current analysis, we queried the NSQIP database for all patients who underwent spine surgery performed by an orthopedic surgeon between 2005 and 2014 using specific spine surgery–related Current Procedural Terminology (CPT) codes (Supplemental Table 1). Exclusion criteria that pertain to the database (eg, patient age less than 18 years old, cases meeting criteria of trauma, minor cases) have been previously published; we excluded all cases not performed by an orthopedic surgeon.[25] Entries missing the sex variable were excluded from analysis. This study was approved by the committee that maintains the Institutional Review Board approval for George Washington University Hospital's use of the NSQIP database.

Data on 23 specific postoperative complications were extracted from the NSQIP database and examined in the current study. Complications studied included superficial SSI, deep SSI, organ space SSI, wound disruption, pneumonia, unplanned intubation, pulmonary embolism, ventilator use for more than 48 hours, progressive renal insufficiency, acute renal failure, UTI, cerebral vascular accident or stroke with neurological deficits, coma for more than 24 hours, peripheral nerve injury, cardiac arrest requiring cardiopulmonary resuscitation, myocardial infarction, bleeding requiring transfusion, graft/prosthesis/flap failure, deep venous thrombosis, sepsis, septic shock, death, and readmission. Length of total hospital stay was also analyzed. Readmission data, data regarding whether the admission was unplanned, and data regarding whether the unplanned readmission was related to the index procedure were available in the NSQIP database from 2012 to 2014 and were obtained for this subset of our patients for analysis.

The influence of patient sex on postoperative complications, length of hospital stay, and readmission was evaluated using univariate analysis. P values were calculated using the Student t test for continuous variables and the Fisher exact test or chi-square test for categorical or binary variables. P value for length of stay was calculated using the Kruskal-Wallis test to account for possible outliers. Statistical significance was set at a P value of $<.05$. Logistic regression models were used to identify independent predictors for postoperative complications after controlling for all preoperative comorbidities and demographic variables. All analyses were conducted using statistical software R with a P value of $<.05$ defined as a significant variable.

RESULTS

A total of 3 071 317 patients were included in the NSQIP database between 2005 and 2014. Of those, 41 315 patients met inclusion criteria for analysis, identified by the CPT codes listed in Supplemental Table 1. Forty-nine percent (20 248) of the patients were women. Female patients were older than male patients (57.3 years vs 56.1, $P < .001$; Table 1). Male patients were more likely to have diabetes (15.4% vs 14.4%, $P = .004$), to be active smokers (23.1% vs 20.7%, $P < .001$), and to drink at least 2 alcoholic beverages a day (5.2% vs 1.1%, $P < .001$). Male patients were also more likely to have a history of prior cardiac surgery (5.6% vs 2.1%, $P < .001$), percutaneous coronary intervention (7.6% vs 3.0%, $P < .001$), and hypertension requiring medication (49.3% vs 48.0%, $P = .010$). On the other hand, women were more likely to be using steroids for a chronic medical condition (4.3 vs 3.0, $P < .001$). Women were more likely to have a lower American Society of Anesthesiologists classification ($P < .001$) but more likely to have shortness of breath and to be dependent on caregivers to perform activities of daily living (dependent functional status; $P < .001$ and $P = .019$, respectively).

Table 1. Patient demographics and preoperative characteristics.

Variable	Female (n = 20 248)	Male (n = 21 067)	*P* Value
Demographics			
Age, y	57.27	56.06	<.001
BMI	30.15	30.07	.227
Medical comorbidities, %			
Diabetes	14.4	15.4	.004
Smoking (current smoker within 1 y)	20.73	23.06	<.001
Alcohol use	1.09	5.18	<.001
History of severe COPD	3.91	3.82	.646
Hypertension requiring medication	47.97	49.25	.01
History of revascularization/ amputation for PVD[a]	0.57	1.23	.001
Disseminated cancer	0.69	0.91	.013
Steroid use for chronic condition	4.33	3	<.001
Preoperative transfusion required	0.49	0.35	.027
Bleeding disorder	1.3	2.02	<.001
Previous percutaneous coronary intervention[a]	3.02	7.58	<.001
Previous cardiac surgery[a]	2.08	5.67	<.001
ASA class, %[b]			<.001
1–No disturbance	4.62	6.61	
2–Mild disturbance	54.54	52.85	
3–Severe disturbance	38.83	37.96	
4–Life threatening	1.99	2.57	
5–Moribund	0.01	0.01	
Shortness of breath			<.001
At rest	0.31	0.22	
Moderate exertion	6.2	4.46	
No	93.49	95.32	
Functional status			.019
Independent	96.3	96.79	
Partially dependent	2.66	2.43	
Totally dependent	0.31	0.22	
Unknown	0.73	0.56	

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease.
[a]Female, n = 4234; male, n = 4074.
[b]Female, n = 20 224, male, n = 21 042.

Postoperatively, female patients were found to be at increased risk for superficial SSI (0.9% vs 0.7%, $P = .016$) and UTI (2.0% vs 0.9%, $P < .001$), whereas men were at increased risk for pneumonia (0.9% vs 0.7%, $P = .019$) and unplanned reintubation (0.6% vs 0.4%, $P = .008$; Table 2). Women more frequently required transfusions (12.7% vs 8.4%, $P < .001$) and had longer hospital lengths of stay (3.5 days vs 3.0 days, $P < .001$). There was no difference found in rate of pulmonary embolism, myocardial infarction, cardiac arrest requiring resuscitation, or 30-day readmission. Of 30-day readmissions, the majority were unplanned; 94.39% of women's 30-day readmissions were unplanned, whereas 96.11% of men's 30-day readmissions were unplanned. Of those unplanned readmissions, 66.21% of men's and 68.45% of women's were related to the index procedure (Table 2).

Table 2. Complication and 30-day readmission rate for men and women, univariate analysis.

Complications	Female (n = 20 248)	Male (n = 21 067)	*P* Value
Superficial surgical site infection, %	0.92	0.70	.016
Deep surgical site infection, %	0.74	0.63	.210
Pneumonia, %	0.71	0.92	.019
Pulmonary embolism, %	0.41	0.52	.114
Unplanned intubation, %	0.41	0.60	.008
Urinary tract infection, %	1.96	0.89	<.001
Requiring transfusion, %	12.74	8.39	<.001
Length of total hospital stay, d	3.47	3.01	<.001
30-day readmission, %[a,b]	3.81	3.73	.229
Readmissions that were unplanned, %[b]	94.39	96.11	
Unplanned readmissions that were related to index procedure, %[b]	68.45	66.21	

Abbreviation: CPR, cardiopulmonary resuscitation.
[a]These variables were only collected from 2012–2014. Female, n = 200 157; male, n = 160 890.
[b]N is larger for this variable than the complication variables owing to the increased input for this variable.
[c]Two men with incomplete data were excluded from this calculation.
[d]One man with incomplete data was excluded from this calculation.

Multivariate analysis allowed us to determine effects of specific risk factors on patient outcomes while eliminating the effects of confounding factors. Multivariate analysis showed that women have a two times greater likelihood of developing a UTI after adjusting for confounding variables (odds ratio [OR] = 2.17, $P < .001$; Table 3). Female sex was also predictive of requiring a transfusion (OR = 1.63, $P < .001$; Table 3), but protective against developing pneumonia (OR = 0.74, $P = .01$; Table 3) and requiring postoperative intubation (OR = 0.68, $P = .01$; Table 3). On multivariate analysis, female sex was not independently predictive of developing a superficial SSI (OR = 1.25, $P = .05$; Table 3).

Secondary findings were other risk factors that had effects on poor outcomes. Multivariate analysis also found that dependent functional status was an independent risk factor for developing a UTI, superficial SSI, and pneumonia, as well for requiring reintubation or postoperative transfusion. Elevated body mass index (BMI) was an independent risk factor for postoperative transfusion, UTI, and superficial SSI. Variables that were found to be independently predictive of superficial SSI, UTI, transfusion need, pneumonia, or postoperative intubation are noted in Table 3.

Table 3. Multivariate analysis.

Variables	Odds Ratio (95% CI)	*P* Value
Urinary tract infection		
Sex (female)	2.17 (1.81–2.60)	<.001
Age	1.03 (1.03–1.04)	<.001
Smoking (current smoker within 1 year)	0.63 (0.48–0.83)	<.001
Ventilator dependent	2.94 (1.04–8.32)	.04
Ascites	11.28 (1.07–119.44)	.04
Disseminated cancer	2.90 (1.67–5.05)	<.001
Partially dependent functional status	2.13 (1.53–2.98)	<.001
Totally dependent functional status	3.00 (1.22–7.39)	.02
BMI	1.02 (1.00–1.03)	.01
Postoperative transfusion		
Sex (female)	1.63 (1.52–1.74)	<.001
Age	1.02 (1.02–1.02)	<.001
Smoking (current smoker within 1 year)	0.80 (0.72–0.87)	<.001
Chronic steroid use	1.17 (1.01–1.36)	.04
Preoperative transfusion	4.66 (3.30–6.59)	<.001
Independent functional status	0.02 (0.01–0.04)	<.001
Partially dependent functional status	1.53 (1.29–1.81)	<.001
Totally dependent functional status	3.07 (1.87–5.05)	<.001
BMI	0.99 (0.98–0.99)	<.001
Pneumonia		
Sex (female)	0.74 (0.59–0.92)	.01
Age	1.03 (1.02–1.04)	<.001
Ventilator dependent	7.74 (3.73–16.09)	<.001
History of COPD	1.89 (1.33–2.70)	<.001
History of CHF	3.39 (1.51–7.60)	<.001
Dialysis	2.53 (1.11–5.77)	.03
Chronic steroid use	1.71 (1.17–2.51)	.01
Partially dependent functional status	2.48 (1.69–3.62)	<.001
Totally dependent functional status	5.91 (2.55–13.69)	<.001
Postoperative intubation		
Sex (female)	0.68 (0.51–0.90)	.01
Age	1.02 (1.01–1.04)	<.001
Alcohol use	3.48 (1.19–10.15)	.02
Ventilator dependent	5.61 (2.23–14.11)	<.001
History of COPD	1.83 (1.16–2.88)	.01
Partially dependent functional status	2.03 (1.23–3.34)	.01
Totally dependent functional status	7.21 (2.83–18.36)	<.001
Superficial surgical site infection		
Sex (female)	1.25 (1.00–1.57)	.05
History of bleeding disorder	2.03 (1.11–3.71)	.02
Preoperative transfusion	3.28 (1.12–9.61)	.03
Partially dependent functional status	6.78 (1.72–26.75)	.01
BMI	1.04 (1.03–1.06)	<.001

Abbreviations: BMI, body mass index; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident.

DISCUSSION

The National Institutes of Health Revitalization Act of 1993 first acknowledged that men and women may respond differently to medical treatments, and it mandated that both sexes had to be included in a study in order to comment on treatment efficacy for either sex.[26] A subsequent report issued by the Institute of Medicine explored the differences between men and women.[27] The report noted that patient sex can influence everything from how patients interact with their environment to how they respond to disease or medications on a cellular level; they noted that the basic cellular biochemistries of men and women are different, and encouraged researchers to further explore the differences in patient outcome by sex.

This has been verified in some aspects of medicine. In patients undergoing endovascular aortic repair, Abedi et al[1] found that female sex was an independent risk factor for wound complications, postoperative transfusions, and increased length of stay, and Arnaoutakis et al[2] found that women had increased length of stay, transfusion risk, operative time, and mortality after thoracic endovascular aortic repair. Liu et al[7] performed a systematic review to examine the influence of sex on outcomes for trauma patients; they found that male sex was associated with increased risk of complications, mortality, and longer hospital stay. A 2014 Academic Emergency Medicine consensus report identified several research areas across several fields in the emergency setting that deserved more attention in order to improve patient outcomes.[28–30]

There are limited data on the role of sex in patients undergoing orthopedic surgery and, more specifically, in patients undergoing spine surgery. Molina et al[6] used the NSQIP database to compare outcome differences between men and women undergoing a wide spectrum of orthopedic procedures. Women were found to be at increased risk for both major and minor complications. Bekelis et al[13] used the NSQIP database in an attempt to create a model to identify risk in patients undergoing surgery and found that female sex was an independent risk factor for UTI and stroke but was protective for pulmonary embolism, myocardial infarction, and death.[13] On the other hand, Schoenfeld et al,[11] in a systematic review on the impact of sex on spinal surgery outcomes, found no differences between men and women in the odds for complications (OR = 1.04) and, in fact, found increased odds of mortality (OR = 1.63) in men. The pooled OR for SSI for men was 0.92 and ranged from 0.44 to 7.64 throughout the studies. Current information on sex-related complications following spinal surgery is culled from studies that simultaneously assess multiple variables. We were unable to find studies that had a primary goal of determining differences in clinical outcomes after orthopedic spine surgery, when stratifying by sex. This is important because these studies probably did not control for all relevant confounds, given that sex was not their primary predictor of interest. Moreover, it is possible that inconsistencies across previous studies

in which covariates were controlled for may possibly explain their inconsistent results.

Our study found that female sex was a risk factor for superficial site infection in the univariate analysis but was not an independent risk factor in the multivariate analysis. Current spine studies have mixed results regarding the impact of sex on infection. Lieber et al,[14] in a study of preoperative predictors of infection following spine surgery using the NSQIP database, found that female sex was an independent risk factor for superficial SSI (OR = 1.25) in the multivariate analysis; this study was restricted to data from 2006 to 2012 and included a different series of surgical procedures, which may account for the difference in outcomes. Kothari et al[10] found no differences in sex for wound complications across all NSQIP spinal fusion cases. Other case-control and retrospective case series have also reported that patient sex was not a strong risk factor for infection.[14,18,19,31,32] A retrospective case-control study on posterior spinal fusions by Rao et al[33] found that male sex was an independent risk factor for superficial site infection (OR = 2.7). However, when they reperformed the analysis only on fusions indicated for degenerative changes (excluding trauma/emergent procedures), sex was no longer a risk factor for infection. Whereas sex was not found to be an independent risk factor for superficial SSI, we did find that the need for postoperative blood transfusion, BMI, and partially dependent functional status are independent risk factors for superficial SSI. Although a secondary finding, it is worth noting that these risk factors are modifiable and a patient's BMI, anemia, and functional status can and should be optimized prior to undergoing an elective spinal procedure.

Postoperative blood transfusion increases risk to the patient, increases system costs, and depletes a supply of blood products that is in high demand. There have been worldwide efforts in cardiovascular and orthopedic surgery to reduce blood transfusion. Our study found that female sex was an independent risk factor for postoperative transfusion (OR = 1.63). Other studies have also found female sex associated with an increased risk for transfusion. McCutcheon et al[21] and Kothari et al[10] found female sex was associated with increased risk for transfusion (OR = 1.19 and 1.6, respectively). Basques et al[24] specifically looked at blood transfusion in patients undergoing posterior spinal fusions. Female sex had an increased risk of transfusion, and receiving a transfusion was associated with poorer outcomes: complication, sepsis, return to the operating room, deep SSI, and pulmonary embolism. Preoperative testing should include a complete blood count, and any anemia should be corrected prior to surgery. Our study also found that smoking status, elevated BMI, having an infected wound, and being an active recipient of radiation were risk factors for postoperative blood transfusion. These risk factors should all be addressed at preoperative visits to reduce the likelihood of postoperative blood transfusion and to improve patient outcomes.

The present study found that female sex was a risk factor for UTI. Both Kothari et al[10] and Bekelis et al[13] found female sex to be a risk factor for postoperative UTI. The condition can lead to increased length of stay and increased cost of stay due to need for antibiotics. Catheter-associated UTI results is a quality measure that results in reduced hospital reimbursement. The incidence of asymptomatic bacteriuria increases with age in women, with a prevalence of 6% to 16% in women aged 65 to 90 years, with prevalence increasing with increased disability.[34–36] The association between asymptomatic bacteriuria and UTI is not clear. The higher prevalence of UTI in the NSQIP female postoperative patient may be attributed to patients with asymptomatic bacteriuria who were treated regardless of symptoms. It may be cost-effective to obtain a urinary analysis at preoperative testing and treat symptomatic patients prior to surgery. Postoperatively, restricting urinary analysis to symptomatic patients can help reduce unnecessary antibiotic treatment in patients who may have asymptomatic bacteriuria.

Length of stay following surgical intervention is an important variable that affects the cost of health care. In our study, women had a longer length of hospital stay by nearly half a day (3.47 vs 3.01 days). This was also found in other NSQIP database studies of patients undergoing spine surgery. Bekelis et al[13] found women to be at increased risk for length of stay greater than 3 days (OR = 1.39) across all spine surgeries and Kothari et al[10] showed that women had an increased risk for length of stay greater than 5 days (OR = 1.3). In a retrospective cohort study of patients undergoing anterior cervical decompression and fusion at their own institution, Arnold et al[17] similarly found that female sex was an independent risk factor for increased hospital length of stay.[17] On the other hand, a

study by Alosh et al[16] of the Nationwide Inpatient Sample database on patients undergoing anterior cervical spine procedures found that female patients stayed 0.25 fewer days and their stays cost $4000 less than those of men. These authors did not examine if there were differences between the male and female cohorts in patient comorbidities or in the numbers of levels operated on. Whereas hospital length of stay can be affected by several factors, we hypothesize that the greater length of stay our study found in female patients undergoing spine surgery may result from a variety of reasons: their need for blood transfusions, which can take several house to infuse, a higher incidence of UTIs, or need for discharge to nursing or rehabilitation facilities due to more dependent statuses preoperatively, which can take more time to arrange.

The present study found no difference between sexes in risk for cardiac arrest, myocardial infarction, or pulmonary embolism, whereas male sex was a risk factor for reintubation and pneumonia. Kothari et al[10] also found female sex to be protective of pulmonary and cardiac compilations in the univariate analysis, but not in the multivariate analysis. Schoenfeld et al[8] looked at spinal arthrodesis patients in NSQIP and found men to be at lower risk for minor complications. Gruskay et al[9] looked at patients with anterior cervical discectomy and fusion in the NSQIP database and found that male sex was a predictor for major complications. Our study combines all forms of orthopedic procedures into one analysis, which likely obscures the differences in complications found between different types of spinal procedures. Nevertheless, a similar set of modifiable risk factors for these complications emerge: dependent functional status, elevated BMI, smoking, and alcohol use.

The present study is limited by the inherent nature of the NSQIP database. Morbidity and mortality that results following the 30-day window but stems in part from complications within this window will not be recorded by the database. Furthermore, the NSQIP database represents a sample from only those hospitals that participate in the database; it is unclear whether this can be extrapolated to all hospitals nationally. Another limitation is that we kept our focus broad by including all orthopedic spine procedures in the database. This prevents readers from drawing conclusions about specific types of spine procedures. The goal of the study was to be able to draw broad conclusions regarding the impact of sex, in order to help guide preoperative optimization, and postoperative expectations.

The present study confirms that patient sex is an independent risk factor for several different complications following spine surgery. When considering surgery in patients, one should keep in mind the sex-associated risks of postoperative blood transfusion, UTI, pneumonia and reintubation, and work on optimizing patient health prior to the procedure. Weight loss, smoking cessation, physical therapy for improving functional status and shortness of breath, and an anemia work-up should all be carried out to improve patient outcomes and decrease hospital length of stay. Men and women should also be counseled appropriately regarding their risk for specific short-term postoperative complications. A medical approach tailored by sex will help further optimize clinical outcomes in spine surgeries.

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