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## Risk factors and clinical impact of perioperative neurological deficits following thoracolumbar arthrodesis<sup>★</sup>

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### Abstract

**Objectives:** The rates of arthrodesis performed in the United States and globally have increased tremendously in the last 10–15 years. Amongst the most devastating complications are neurological deficits including spinal cord injury, nerve root irritation, and cauda equine syndrome. The primary purpose of this study is to understand the risk factors for perioperative neurological deficits in patients undergoing thoracolumbar fusion.

**Patients and methods:** Data from the Nationwide Inpatient Sample between the years of 1999–2011 was analyzed. Patients were between the ages of 18 and 80 who had thoracolumbar fusion. Excluded were patients who underwent the procedure as a result of trauma or a malignancy. A list of covariates, including demographic variables, preoperative and postoperative variables that are known to increase the risk of perioperative neurological deficits were compiled. Statistical analysis utilized univariate and multivariate logistic regression for comparisons between these covariates and the proposed outcomes.

**Results:** The analysis of 37,899 patients yielded an overall rate of perioperative neurological deficits and mortality of 1.20% and 0.27%, respectively. Risk factors for perioperative neurological deficits included increasing age (OR 1.023 95% CI 1.018–1.029), Van Walraven 5–14 (OR 1.535 95% CI 1.054–2.235), and preoperative paralysis (OR 2.551 95% CI 1.674–3.886). Furthermore, the data showed that being 65 years old or older doubled the risk for perioperative deficit (OR 1.655, CI 1.248–2.194,  $p < 0.001$ ).

**Conclusions:** This population based study found that increasing age, higher comorbid burden, and preoperative paralysis increased the risk of perioperative neurological deficits while female gender and hypertension were found to be protective.

### Keywords

Thoracolumbar fusion; Arthrodesis; Spine; Neurological deficits; Mortality; National Inpatient Sample; Outcomes; Complications

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## 1. Introduction

Arthrodesis remains one of the most viable options for the treatment of a variety of spinal pathologies that have proved refractory to conservative management [1]. Since the earliest reports of spine fusion in the early 20th century by Hibbs and Albee, fusions have revolutionized the way in which patients with back pain, radiculopathy, and deformities are managed [2]. Due to a number of technological advancements, the rates of arthrodesis performed in the United States and globally have increased tremendously in the last 10–15 years, with a 220% increase in the 1990's and a subsequent 135% increase in the early 2000's [1,3,4]. Additionally, the proportion of health resources allocated to these procedures has increased substantially from \$10 billion in 2001 to \$46.8 billion in 2010 [5]. The indications for this technically evolving operation include but are not limited to trauma, congenital or idiopathic spinal deformity, degenerative spine disease, vascular malformations, and malignancy [6]. However, these procedures are not without their risks [7–9]; previous studies have yielded complication rates ranging from 2 to 3%. Amongst the most devastating complications following spinal fusion are perioperative neurological deficits [10]. Injuries most commonly include spinal cord injury (contusion and/or transection), nerve root irritation or damage, and cauda equine syndrome [11,12].

These injuries can be debilitating for any patient, especially for those who were functionally independent prior to the procedure. There is an abundance of literature detailing the impact of spinal cord injury, nerve irritation, and cauda equine syndrome on mortality, morbidity, decreased quality of life, and increased cost of healthcare [13–18]. However, the literature lacks data on what characteristics put patients at risk for these deficits and it also lacks information on the effect of these deficits on in-hospital outcomes (i.e., mortality). These are important data points, as in-hospital outcomes occur in a time period during which intervention is possible and are metrics of the quality of hospital care [19]. It is important to understand the outcomes associated with perioperative neurological deficits, as increased length of stay has been associated with significantly increased health care costs, and an increased risk of hospital acquired infections, which are subsequently associated with their own increase risk of in-patient mortality, and increased cost of hospitalization [20–23].

With the advancement of neuromonitoring with somatosensory evoked potentials and motor evoked potentials it is possible to identify intraoperative signal changes indicative of possible injury. The identification of patients who have either suffered a neurological deficit or are at a high risk for suffering one will allow providers to adopt more aggressive rehabilitative strategies after the event, and offers the opportunity to develop and employ intraoperative neuroprotective therapies.

The primary and secondary aims of our study are to investigate the risk factors for perioperative neurological deficits in patients undergoing thoracolumbar arthrodesis and to understand the effects of these deficits on in-hospital mortality and morbidity, respectively. Although, based on data, approximately 95–97% of patient who undergo thoracolumbar fusion do not develop neurological deficits postoperatively [7–9], it is still paramount to understand why the small subset of patients do in fact experience neurological deficits. We

will also evaluate trends of procedure utilization based on patient characteristics, as well as trends in the early outcomes of thoracolumbar fusion.

## 2. Patient and methods

### 2.1. Data source

The investigational data was procured from the National Inpatient Sample (NIS) Health Cost Utilization Project (HCUP) between the years 1999 to 2011 as it related to the particular patient subset we were interested in. The NIS represents a 20% stratified sample of discharges from community hospitals. Unweighted, the NIS contains between 7 and 8 million hospital stays each year, and when weighted, provides an estimate of > 35 million hospitalizations each year, which makes it the biggest all-payer health care database that is publically available [24]. We extracted the data using the International Classification of Diseases, Ninth Revision–Clinical Modification (ICD-9-CM) procedure codes and diagnosis codes. This study did not require IRB approval, as no identifying information is included in the database.

### 2.2. Patient population

The study included patients who underwent thoracolumbar fusion as their primary procedure (ICD-9). However, excluded were patients below the age of 18 and above the age of 80. Additionally, excluded were patients who underwent the operation as a result of trauma or malignancy.

### 2.3. Covariates

An extensive list of covariates, including demographic variables such as age and gender, pre-operative and post-operative variables that are known to increase the risk of perioperative neurological deficits were analyzed. We additionally used the van Walraven score, a weighted numerical surrogate for the Elixhauser comorbidity index as a covariate to assess comorbidities that have been associated with in-hospital mortality after thoracolumbar fusion. Table 1 depicts the van Walraven (VWR) score stratified into patient risk categories, illustrated as low risk (VWR < 5), medium risk [5–14], and high-risk categories (14+). Studies have shown the van Walraven score to be equally effective at predicting mortality as other established methods (Charlson-Deyo index) [22]. Also, the van Walraven score has been shown to be superior than using purely comorbidity counts [23]. We performed univariate comparisons between covariates and our primary and secondary outcome. We also ran a multivariable logistic regression, adjusting for many of the aforementioned covariates. Finally, we conducted trend analyses via univariate logistic regression.

### 2.4. Outcomes

The primary outcome is perioperative neurological deficits with secondary being in-hospital mortality. Our primary independent variable is a perioperative neurological deficit. We defined perioperative neurologic deficits as any injury to the spinal cord without evidence of spinal bone injury. In addition, if the patient suffered a nervous system complication such as a CNS complication like anoxic brain damage or cerebral hypoxia or a postoperative

cerebrovascular complication, or any unspecified or other nervous system complications, the patient was considered to have suffered a perioperative neurological deficit.

## 2.5. Statistical analysis

We initially extracted our data using SAS version 9.3 (SAS Institute, Inc., Cary, NC). We accounted for each hospital at least once using the Hospital Weight files provided by the NIS and aggregated each individual year's data into a common database for all years. We generated the Elixhauser Comorbidity Index and the van Walraven scores using SAS, using the "Comorbidity Software" (available at HCUP website) and the van Walraven macro (available at the Cleveland Clinic website) [24,26]. All analyses were conducted in Stata version 14 (StataCorp, College Station, TX). We conducted all analyses using Stata's survey command, which allowed us to group by hospital ID, weigh the data using the "Trend Weights" provided by HCUP. We used the unpaired *t*-test and the survey-adjusted Wald test to make univariate comparisons for continuous and categorical variables, respectively. Finally, we generated a number of multivariable logistic regression models for the outcomes of mortality and morbidity. We used the van Walraven score as a surrogate for all Elixhauser comorbidities and included the individual comorbidities that we felt were relevant to our analysis as supported by existing literature.

## 3. Results

### 3.1. Patient characteristics

The average age of our cohort ( $n = 37,899$ ) was 33.32 years of age, with 32.20% of our population between the ages of 18–44, 18.35% between the ages of 45–54, 21.90% between the ages of 55–64, 19.38% between the ages of 65–74, and 8.17% above the age of 75. The majority of patients were white (75.77%) and Female (65.14%). Most of our patients underwent the procedure on an elective basis (90.89%). The average van Walraven score of our population was 1.65, with the majority of our patients falling in the VWR < 5 category, 79.64% (Table 1). The average age of our population trended linearly upwards from 1999 to 2011 ( $p = 0.001$ ) as did the average van Walraven score ( $p < 0.001$ ). The proportion of patients in the low risk category (VWR < 5) decreased linearly from the years 1999–2011 ( $p < 0.0001$ , Fig. 1), while the proportion of patients in the medium risk category (VWR 5–14) increased linearly ( $p < 0.0001$ ), and the proportion of patients in the high risk category (VWR 14+) increased linearly as well ( $p < 0.0001$ ) (Figs. 2 and 3).

### 3.2. Incidence and trends of perioperative neurological deficits

Neurological deficits following thoracolumbar fusion occurred in 1.2% (455) of patients. While the rates of perioperative neurological deficits seem to be increasing each year (Fig. 1, Table 4), the trend is not statistically significant ( $p = 0.073$ ).

### 3.3. Factors associated with neurological deficits following TLF

Table 2 and Fig. 1 show the results of our multivariate analysis of the various predictors of perioperative neurological deficits. These included increasing age (OR 1.023 95% CI 1.018–1.029), VWR 5–14 (OR 1.535 95% CI 1.054–2.235), and pre-operative paralysis (OR 2.551

95% CI 1.674–3.886). Hypertension was also found to be protective (OR 0.604 95% CI 0.467–0.780), as was female gender (OR 0.789 95% CI 0.653–0.9),

### 3.4. Perioperative neurological deficits independently predict in-hospital mortality

In our multivariable analysis, perioperative neurological deficits were found to be independent predictors of in-hospital mortality following thoracolumbar fusion (OR 3.467, 95% CI 1.473–8.158). Other statistically significant predictors of mortality (Table 3) included Age (OR 1.013 95% CI 1.003–1.022), a VWR score of 5–14 (OR 2.872, 95% CI 1.382–5.601), Pulmonary Circulatory Disorders (OR 4.593, 95% CI 1.732–12.18), Coagulopathy (OR 2.091, 95% CI 1.112–3.932), and Cardiac Arrhythmias (OR 1.863, 95% CI 1.065–3.259). Female gender was associated with a decreased risk of in-hospital mortality following TLF (OR 0.532, 95% CI 0.350–0.810).

## 4. Discussion

In our large, longitudinal, and population-based dataset, we found that increasing age (OR 1.023), more specifically > 65 years old, VWR 5–14 (OR 1.535), and preoperative paralysis (OR 2.551) were statistically significant predictors of neurological deficits following TLF, while female gender (OR 0.789) and hypertension (OR 0.604) were found to be protective factors (Table 2). Hypertension is thought to be neuroprotective given the high blood loss during these procedures, baseline high blood pressure helps to auto perfuse the spinal cord to decrease incidence of ischemia. However, the female gender being protective is a quite interesting. The authors postulate that is likely related to hormonal up regulation in women during heighten period of stress, such as surgery. In the trauma literature, there were some early studies which showed hormone like progesterone to be neuroprotective. Perioperative neurological deficits were found to be statistically significant predictors of mortality (OR 3.467, OR 4.084, Table 3). Our analysis also confirmed an increasing national trend in spinal arthrodesis being performed each year ( $p < 0.001$ ), with an estimated 10,383 thoracolumbar fusions performed in 1999 and 20,007 in 2011 (Fig. 4) [5]. We noted that the average age of patients undergoing thoracolumbar fusion is also increasing ( $p < 0.001$ ). Moreover, due to health trends in the United States, this operation is being performed on patients with more substantial medical comorbidities, as evidenced by the increasing van Walraven score each year (Table 4), as well as the proportional increase in “high risk” (VWR > 14) patients (Fig. 1). This is consistent with the aging of the U.S. population; it is estimated that the number of patients above the age of 65 will double by the year 2050 [27]. This is also significant as our multivariable regression analysis found that both age and increasing VWR score are independently associated with a higher risk of mortality (Table 3). Interestingly, while the average VWR score and age of our cohort increased from 1999 to 2011, both the prevalence of neurological deficits as well as the overall mortality from the procedure has not changed (Table 4).

Although not specifically addressed, this study makes a case for why iatrogenic neurological deficits, specifically in the setting of thoracolumbar fusion, should be carefully monitored, as we may be able to appropriately stratify this at risk patient populations. The use of intraoperative neuromonitoring provides an avenue to predict these perioperative

neurological deficits and to improve the care of patients, as its use has been associated with improved clinical outcomes in noncomplex spine surgeries [28–31]. Additionally, a number of studies have found intraoperative neurophysiological monitoring to be cost-saving [32–35].

Our study is subject to a number of limitations. First, the NIS relies on claims data that is subject to inaccurate billing and potential underestimation of certain covariables including delirium and perioperative neurological deficits. Additionally, there was a substantial amount of missing data in our dataset and this prevented us from including variables such as race in the multivariable regression model. Lastly, the NIS only provides in-hospital data, and therefore we were not able to provide rates of neurological deficits in either a 30-day postoperative period or any information with regards to the long term sequelae of these neurological deficits.

Future directions should be geared at prevention and intervention in the preoperative, intraoperative, and postoperative time frames. Our study provides valuable data that can be used to develop preoperative risk stratification tools which will allow us to identify patients at a high risk of suffering from perioperative neurological deficits. Understanding who is at high risk will provide a platform for preventative efforts to the patients who will most likely benefit from them. More studies directed towards understanding the utility and cost-effectiveness of intraoperative neurophysiological monitoring should be conducted. Perioperative injury increases patient morbidity and mortality thus increasing hospital stay and overall medical cost. Any change in intraoperative electrophysiological monitoring during such thoracolumbar fusion could alter a surgeon's decision in real time to halt a transient event from becoming permanent. Additionally, we should focus efforts on developing intraoperative and/or perioperative neuroprotective therapies that will allow us to mitigate intraoperative damage. Together, informed preoperative risk stratification, intraoperative monitoring, and timely post-operative intervention will be a strong first step in decreasing the incidence and damage caused by perioperative neurological deficits.

## 5. Conclusions

In this large, longitudinal, and population based study, we found that age, higher comorbid burden, and pre-operative paralysis increased the risk of perioperative neurological deficits while female gender and hypertension were found to be protective. Additionally, we found that perioperative neurological deficits are in fact independent risk factors for in-hospital mortality after thoracolumbar fusion. The identification of risk factors associated with perioperative deficits presents an opportunity to facilitate patient stratification, increase patient safety, and decrease healthcare cost.

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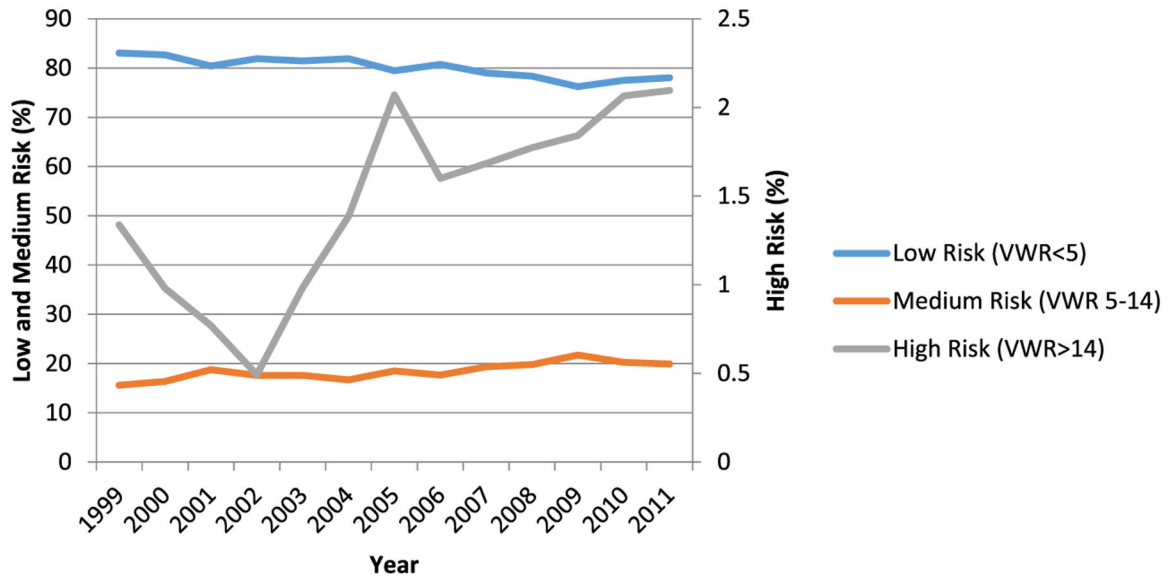
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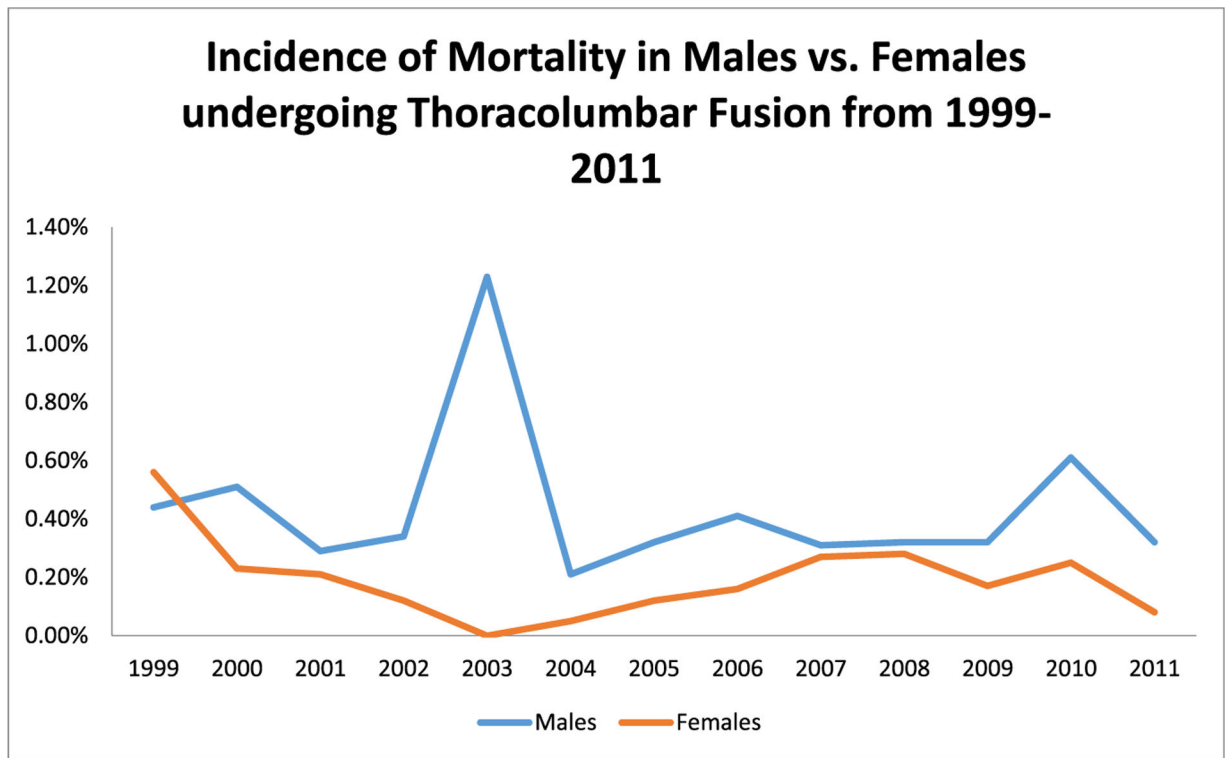


## Proportions of low, medium, and high risk patients undergoing Thoracolumbar Fusion from 1999-2011



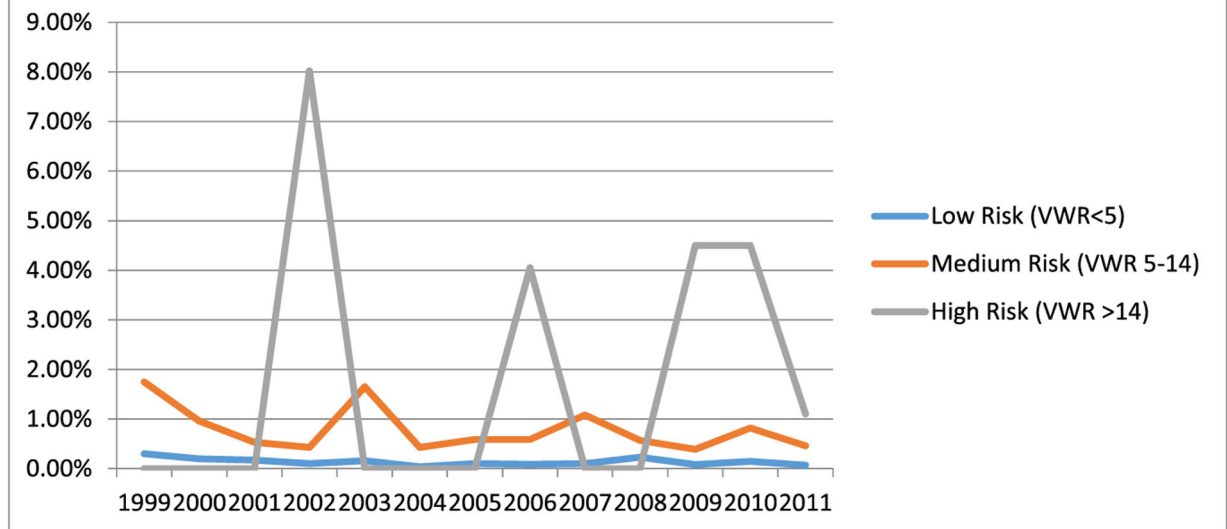
**Fig. 1.**

The proportion of patients in the low-risk (VWR < 5) population has decreased linearly, while the proportion of patients in medium-risk (VWR 5–14) and high-risk (VWR > 14) populations have both increased linearly from the years 1999–2011.



**Fig. 2.** Males overall have a higher rate of in-hospital mortality than females following thoracolumbar fusion. This phenomena held constant from 1999 to 2011.

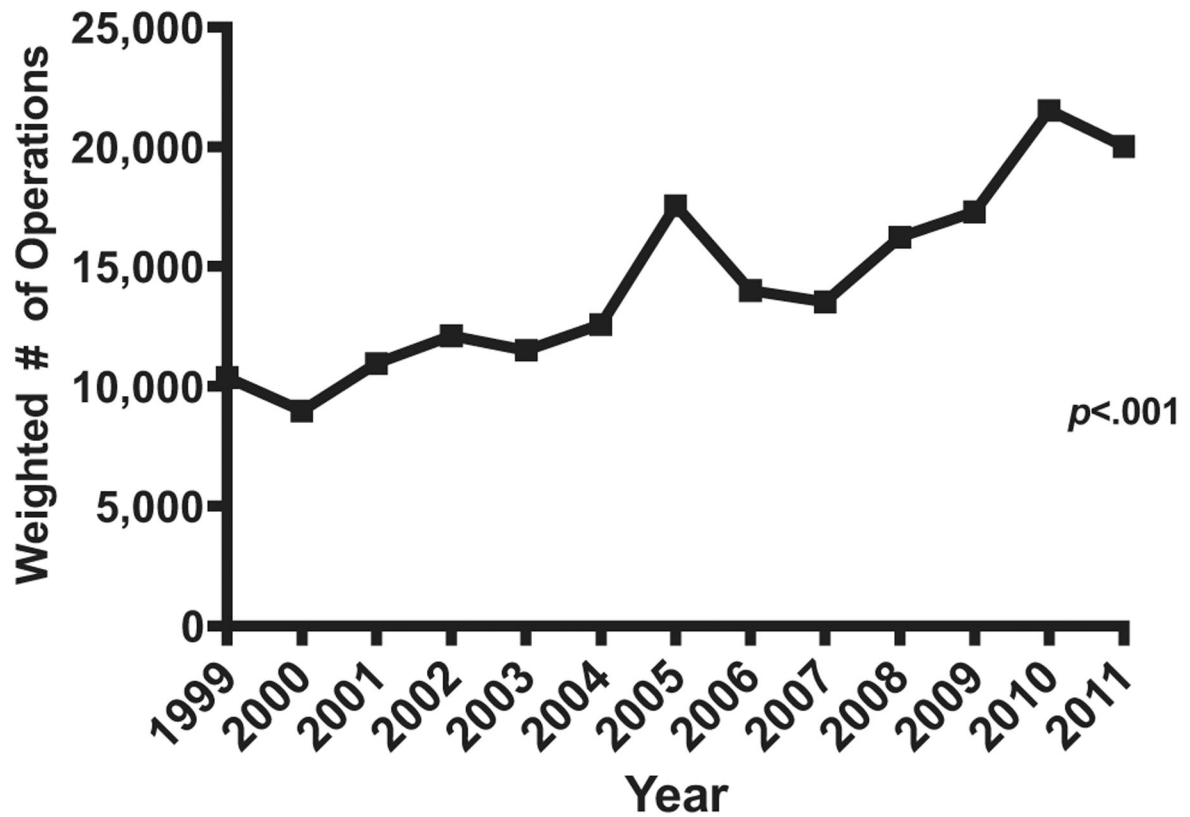
### Incidence of Mortality in patients undergoing Thoracolumbar fusion from 1999-2011, stratified by VWR score



**Fig. 3.**

Patients in the medium risk van Walraven group (VWR 5–14) suffered from higher rates of mortality than patients in the low risk (VWR < 5) group. The rates of mortality in the high (VWR > 14) group were much higher in some years (2002, 2006, 2009–2010), but the trend was not as clear as the one between medium and low VWR score groups.

## TLF Procedures Performed from 1999-2011



**Fig. 4.** shows the increase in thoracolumbar fusion procedures performed between 1999 and 2011. The number of procedures performed went from a weighted 10,000 in 1999 to a peak of 22,000 in 2010, more than doubling in the time period covered by this study.

**Table 1**

## Patient demographics.

Variables	% of patients (n = 37,899)
Average age ( $\pm$ SD)	33.32
Age group	
18 to 44	32.20%
45 to 54	18.35%
55 to 64	21.90%
65 to 74	19.38%
75+	8.17%
Gender	
Female	65.14%
Male	34.86%
Race/ethnicity	
White	75.77%
Black	9.91%
Hispanic	8.15%
Asian	1.91%
Native American	0.50%
Other/missing	3.76%
Admission status	
Emergent	3.36%
Urgent	5.71%
Elective	90.89%
Risk factors and comorbidities	
Average Van Walraven score	1.65
Risk category	
Low risk (VWR < 5)	79.64%
Moderate risk (VWR 5 to 14)	18.78%
High risk (VWR > 14)	1.58%
Comorbidities	
1. Congestive heart failure	1.21%
2. Valvular disease	2.68%
3. Pulmonary circulation disorders	0.58%
4. Peripheral vascular disease	0.85%
5. Hypertension	20.96%
6. Paralysis	8.75%
7. Other neurological disorders	6.27%
8. Chronic pulmonary disease	12.20%
9. Diabetes without chronic complications	5.30%
10. Diabetes with chronic complications	0.69%
11. Hypothyroidism	5.45%

Variables	% of patients (n = 37,899)
12. Renal failure	0.90%
13. Liver disease	0.51%
14. Chronic peptic ulcer disease	0.10%
15. HIV/AIDS	0.02%
16. Lymphoma	0.01%
17. Metastatic cancer	0%
18. Solid tumor without metastases	0.27%
19. Rheumatoid arthritis/collagen vascular diseases	1.91%
20. Coagulation deficiency	4.09%
21. Obesity	5.36%
22. Weight loss	1.12%
23. Fluid and electrolyte disorders	11.80%
24. Blood loss anemia	1.07%
25. Deficiency anemias	9.35%
26. Alcohol abuse	0.63%
27. Drug abuse	0.90%
28. Psychoses	1.57%
29. Depression	7.14%
Other risk factors	
Cardiac Arrhythmias	7.11%
Delirium	0.79%
Perioperative neurological deficits	1.20%

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**Table 2**

Risk factors for perioperative neurological deficits following thoracolumbar arthrodesis.

Variables	Perioperative neurological deficits N = 37,899		
	Odds ratio	95%CI	p-Value
Age	1.023	1.018–1.029	< 0.001 *
Age > 65	1.655	1.248–2.194	< 0.001 *
Female gender	0.789	0.653–0.952	0.013 *
VWR 5–14	1.535	1.054–2.235	0.025 *
VWR > 14	1.398	0.631–3.098	0.409
Congestive heart failure	1.001	0.536–1.870	0.996
Pulmonary Circulatory Disorders	1.032	0.420–2.533	0.946
Paralysis	2.551	1.674–3.886	< 0.001 *
Coagulopathy	1.204	0.825–1.756	0.335
Electrolyte disorder	1.233	0.899–1.689	0.193
Cardiac Arrhythmias	1.324	0.929–1.887	0.121
Hypertension	0.604	0.467–0.780	< 0.001 *
Rheumatoid arthritis/collagen vascular diseases	1.399	0.869–2.250	0.167

\*p-Value < 0.05 indicates statistical significance.

**Table 3**

Multivariate analyses for mortality after thoracolumbar fusion.

Variables	In-hospital mortality N = 37,863		
	Odds ratio	95%CI	p-Value
Age	1.013	1.003–1.022	0.009*
Female	0.532	0.350–0.810	0.003*
VWR 5–14	2.782	1.382–5.601	0.004*
VWR > 14	2.381	0.733–7.735	0.149
Perioperative neurological deficits	3.467	1.473–8.158	0.004*
Congestive heart failure	1.954	0.880–4.340	0.100
Pulmonary Circulatory Disorders	4.593	1.732–12.18	0.002*
Paralysis	1.440	0.730–2.839	0.293
Coagulopathy	2.091	1.112–3.932	0.022*
Electrolyte disorder	0.910	0.497–1.667	0.760
Cardiac Arrhythmias	1.863	1.065–3.259	0.029*

\*p-Value < 0.05 indicates statistical significance.

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**Table 4**

Analysis of trends in variables after thoracolumbar fusion, organized by year.

Calendar year	Perioperative neurological deficits (%)	Died during hospitalization (%)	Average Van Walraven score	Average age
1999	1.4	0.52	1.537	23.471
2000	0.61	0.32	1.378	26.364
2001	1.03	0.24	1.513	26.109
2002	1.06	0.2	1.376	27.571
2003	0.89	0.41	1.526	31.479
2004	1.14	0.11	1.440	30.761
2005	1.03	0.19	1.748	28.300
2006	1.1	0.24	1.633	34.298
2007	1.55	0.28	1.742	34.616
2008	1.53	0.3	1.685	38.284
2009	1.31	0.23	1.872	38.801
2010	1.13	0.38	1.779	39.227
2011	1.39	0.17	1.734	39.389
Total	1.2	0.27	1.65	33.32
p-Value	0.073	0.420	< 0.0001 *	0.001 *

\* p-Value < 0.05 indicates statistical significance.

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