Incidence and risk factors for acute kidney injury after spine surgery using the RIFLE classification

Clinical article

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Object. Earlier definitions of acute renal failure are not sensitive in identifying milder forms of acute kidney injury (AKI). The authors hypothesized that by applying the RIFLE criteria for acute renal failure (Risk of renal dysfunction, Injury to the kidney, Failure of kidney function, Loss of kidney function, and End-stage kidney disease) to thoracic and lumbar spine surgery, there would be a higher incidence of AKI. They also developed a model to predict the postoperative glomerular filtration rate (GFR).

Methods. A hospital data repository was used to identify patients undergoing thoracic and/or lumbar spine surgery over a 5-year period (2006–2011). The lowest GFR in the first week after surgery was used to identify and categorize kidney injury if present. Risk factors were identified and a model was developed to predict postoperative GFR based on the defined risk factors.

Results. A total of 726 patients were identified over the study period. The incidence of AKI was 3.9% (n = 28) based on the RIFLE classification with 23 patients in the risk category and 5 in the injury category. No patient was classified into the failure category or required renal replacement therapy. The baseline GFR in the non-AKI and AKI groups was 80 and 79.8 ml/min, respectively. After univariate analysis, only hypertension was associated with postoperative AKI (p = 0.02). A model was developed to predict the postoperative GFR. This model accounted for 64.4% of the variation in the postoperative GFRs (r² = 0.644).

Conclusions. The incidence of AKI in spine surgery is higher than previously reported, with all of the patients classified into either the risk or injury RIFLE categories. Because these categories have previously been shown to be associated with poor long-term outcomes, early recognition, management, and follow-up of these patients is important.

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Key Words • acute kidney injury • RIFLE classification • thoracic • thoracolumbar spine • lumbar

With an aging population and advancement in diagnostic, anesthetic, and surgical techniques, an increasing number of patients with multiple comorbidities are undergoing surgical management for complex spine disorders. Deyo et al. reported a 15-fold increase in complex spine surgery in the Medicare population between 2002 and 2007. The incidence of major postoperative complications in their entire cohort was 3.1%; and this increased to 5.3% when 3 or more comorbidities were present. Furthermore, after adjusting for other risk factors, the odds ratio for life-threatening complications with complex spine fusions was 2.95 (95% CI 2.50–3.49) compared with decompression only.

Abbreviations used in this paper: AKI = acute kidney injury; GFR = glomerular filtration rate; RIFLE = Risk of renal dysfunction, Injury to the kidney, Failure of kidney function, Loss of kidney function, and End-stage kidney disease; SSII = Spine Surgery Invasiveness Index.

Multilevel spine surgery can be associated with significant intraoperative hemodynamic and hemostatic perturbations, potentially increasing the risk of developing postoperative acute kidney injury (AKI). There are, however, few studies reporting the incidence of AKI in spine surgery, and no studies that have defined the incidence of postoperative AKI based on the Acute Dialysis Quality Initiative RIFLE criteria for acute renal failure: Risk of renal dysfunction, Injury to the kidney, Failure of kidney function, Loss of kidney function, and End-stage kidney disease. This classification has 3 severity scores based on urine output, serum creatinine level, or estimated glomerular filtration rate (GFR), and 2 outcome groups (Table 1). The primary goal of this classification is to develop consensus regarding the definition of AKI. Multiple previous arbitrary definitions

This article contains some figures that are displayed in color online but in black-and-white in the print edition.
TABLE 1: RIFLE classification for acute renal failure

<table>
<thead>
<tr>
<th>Classification</th>
<th>GFR</th>
<th>Creatinine</th>
<th>Urine Output</th>
</tr>
</thead>
<tbody>
<tr>
<td>risk decrease &gt;25% of baseline</td>
<td></td>
<td>increase (\times 1.5) of baseline</td>
<td>&lt;0.5 ml/kg/hr (\times 6) hrs</td>
</tr>
<tr>
<td>injury decrease &gt;50% of baseline</td>
<td></td>
<td>increase (\times 2) of baseline</td>
<td>&lt;0.5 ml/kg/hr (\times 12) hrs</td>
</tr>
<tr>
<td>failure decrease &gt;75% of baseline</td>
<td></td>
<td>increase (\times 3) of baseline</td>
<td>anuria (\times 12) hrs, or &lt;0.3 ml/kg/hr (\times 24) hrs</td>
</tr>
<tr>
<td>loss</td>
<td></td>
<td>complete loss of renal function for &gt;4 wks</td>
<td></td>
</tr>
<tr>
<td>ESRD</td>
<td></td>
<td>end-stage renal disease</td>
<td></td>
</tr>
</tbody>
</table>

made it difficult to determine the true incidence of AKI in specific disease states. Furthermore, by utilizing clinically relevant metrics, a practical bedside scoring system has been developed. This system has relevance to surgeons, anesthesiologists, and intensivists caring for patients in the perioperative period. The RIFLE classification is sensitive in identifying earlier and milder forms of AKI, both of which are associated with both short- and long-term morbidity and mortality. These milder forms of AKI are associated with poorer long-term outcomes. Bihorac et al., in a retrospective study of 10,518 patients undergoing major noncardiac surgery, demonstrated a 10-year survival rate of 65% without perioperative AKI compared with 50% and 44% for patients who were classified as RIFLE risk and RIFLE injury, respectively. Furthermore, even when complete renal recovery occurred, there was an increased risk of death a decade after the sentinel event. Hobson et al. demonstrated similar poor outcomes in a cardiothoracic cohort of 2973 patients with the less severe forms of AKI. Therefore, the identification and long-term follow-up of patients with perioperative RIFLE risk and RIFLE injury classification is important.

We hypothesized that the incidence of renal injury in spine surgery, when assessed using the RIFLE criteria, would be increased compared with earlier studies. To test this hypothesis, we calculated the incidence of AKI by the estimated GFR and the RIFLE criteria. To identify patients at risk for AKI, risk factors were determined and a model developed to predict postoperative GFR based on the identified risk factors.

**Methods**

We performed a retrospective study of all patients undergoing elective thoracic and/or lumbar spine surgery during a 5-year period (June 2006 to July 2011). This study population included patients who underwent multilevel decompressions and more complex reconstructive surgery. The data set was limited to a 5-year period so that confounding changes in surgical and anesthesia practices would be limited.

**Data Sources**

The University of Virginia Institutional Review Board for Health Sciences Research approved the study. The requirement for obtaining informed consent was waived. The patients were identified using the University of Virginia Clinical Data Repository, which maintains demographic, financial, procedural, and length-of-stay data for all patients in the University of Virginia Health System. Utilizing Current Procedural Terminology (CPT) codes, patients undergoing thoracic and/or lumbar spine surgery with or without fusion were identified.

Included surgeries took place between June 2006 and July 2011. Demographic and preoperative data collected included included age, sex, race, and the presence of preoperative hypertension, diabetes mellitus, or chronic kidney disease. Intraoperative data included the anesthetic duration, total estimated intraoperative blood loss, volume of cell saver, crystalloid, colloid, packed red blood cells, fresh frozen plasma, and cryoprecipitate transfused. The need for intraoperative inotrope and/or vasopressor support and the total dose of drug infused were recorded. The base deficit was obtained from intraoperative arterial blood gas determinations when available.

**Exclusion Criteria**

Patients younger than 18 years of age and those with chronic kidney disease requiring renal replacement therapy were excluded. We also excluded patients who underwent cervical surgery, single-level decompressions, and those with no postoperative creatinine value.

**Spine Surgery Invasiveness Index**

Surgical complexity influences the incidence of perioperative complications. To standardize surgical complexity in spine surgery, Mirza et al. developed and validated a scoring system utilizing the 3 major components of spine surgery. The Spine Surgery Invasiveness Index (SSI) incorporates the number of levels decompressed, instrumented, and fused. Each operated vertebrae can be assigned a score between 0 and 6 based on the procedural elements described and whether an anterior and/or posterior approach was performed. A summative score was calculated that corresponded to the extent of the procedure performed. This score helped to determine the relationship between the extent of surgery and a predefined outcome.

**Definition of AKI**

The RIFLE classification was used to identify AKI. A baseline estimated GFR was calculated for all patients from the preoperative creatinine level. The Modified Diet in Renal Disease formula was used to calculate the estimated GFR. The Modified Diet in Renal Disease uses serum creatinine level, age, sex, and race to calculate the estimated GFR, adjusted for each 1.73 m² of body surface area. The maximum postoperative creatinine level dur-
Kidney injury, risk modeling, and spine surgery

ing the first week after surgery was used to determine the lowest estimated GFR. The frequency of creatinine measurements varied between patients and the frequency was determined by the primary service (attending neurosurgeon/orthopedic surgeon and his/her team). This limit of the first week after surgery was chosen to exclude other nonoperative causes of renal dysfunction, which we believed were more likely to occur after this time period. Patients were classified into RIFLE risk, RIFLE injury, and RIFLE failure if a 25%, 50%, or 75% decrease from their preoperative estimated GFR occurred, respectively. RIFLE loss was defined as complete loss of kidney function for greater than 4 weeks while RIFLE end stage was loss of function for greater than 3 months.

Statistical Analysis

Data analysis was performed with SPSS (IBM Corp.) and R (The R Project, version 2.15.1). Mean and median values of the parameters assessed, for the patients who did and did not experience kidney injury, were calculated. For continuous variables, normality was assessed using the Kolmogorov-Smirnov test. The Mann-Whitney U-test was used to compare nonnormal data, and normally distributed data were assessed by the Student t-test for equality of means. A linear regression model was used to predict postoperative AKI, defined as at least a 25% decrease in the estimated GFR. A p value < 0.05 was considered statistically significant.

To determine a model to predict AKI after spine surgery, the following parameters were included in the candidate model: baseline estimated GFR, SSII, age at procedure, blood loss (ml), hypertension, diabetes mellitus, chronic kidney disease, sex, race, and repeat surgery. Variables for the predictive model were based on previously recognized risk factors for AKI and sufficient numbers of observed outcomes. Thereafter, the entire dataset was divided into a training and validation set. Four hundred patients were used to form the training set, and the remaining 326 were used for the validation set.

The final predictors were chosen using the training set and an all-subsets model selection procedure using the Akaike information criterion as the selection criterion. The selected model was assessed for overfitting by comparing root mean square error on the training data with root mean square prediction error on the test data. After assessing the initial model for overfitting, the model was refit using the selected predictors and all 726 patients, producing a final model.

The final model was used to estimate the likelihood that individual patients’ estimated GFR would decrease by at least 25% from preoperative values. As the output value from the model represents the expected minimum postoperative estimated GFR, with individual patients exhibiting substantial variation around their expected minima (lowest value), this likelihood estimate requires modeling of both the expected minimum postoperative GFR and patients’ variability around their expected minima. Because the data were slightly more skewed toward adverse outcomes than would be expected under the classic normal error regression model, variability around the expected minima was modeled using the residual bootstrap procedure for prediction intervals described in Davison and Hinkley. Estimated probability curves were then created demonstrating the impact of hypertension, advancing age, and extent of surgery (by SSII) on the likelihood of renal injury across the range of baseline GFR values.

Results

In the 5-year period between June 2006 and July 2011, 888 patients underwent 989 procedures. Sixty-three patients were excluded because they underwent cervical surgery and were incorrectly coded or had a single-level decompression only. A complete data set with both preoperative and postoperative creatinine levels was identified in 726 patients. Demographic and perioperative parameters between AKI and non-AKI groups are described in Table 2. Of the 726 patients, 28 (3.86%) developed AKI as defined by the RIFLE classification. Of these 28 patients, 23 (3.17%) were classified in the RIFLE risk category, while 5 (0.69%) developed RIFLE injury based on a 25% and 50% diminution in the GFR, respectively (Fig. 1). No patient developed RIFLE failure or required renal replacement therapy.

The best predictive model was developed on the training set; the selected predictors were baseline GFR, SSII, age at procedure, and preoperative hypertension. The root mean square prediction error was 14.0 in the test data compared with a root mean square prediction error of 14.3 in the training set, suggesting that the model does not overfit the data. To produce the best possible predictions, we then refit the model using the complete data set of 726 patients. The resulting model was:

minimum postoperative GFR = 22.14 + 0.85(sbaseline GFR) + 0.16(SSII score) − 0.09(age at procedure) − 3.82(preoperative hypertension).

This model accounted for 64.4% of the variation in the postoperative GFRs (r² = 0.644). Based on the model above and the bootstrap prediction interval procedure, the likelihood of RIFLE risk is presented in Fig. 2.

Discussion

The aim of this study was to determine the incidence of AKI in patients undergoing major spine surgery, utilizing a more rigorous definition of renal dysfunction than historically applied. Our study supports the hypothesis that by applying the RIFLE criteria, the incidence of AKI is higher than previously reported. Previous studies report an incidence of renal insufficiency that varies between 0.88% and 0.91%, utilizing a definition of a greater than 2 mg/dl increase in creatinine from baseline. This definition, however, significantly underestimates the milder, less severe forms of AKI.

Our study demonstrated an AKI rate of 3.86%, of which the RIFLE risk and RIFLE injury categories were 3.17% and 0.69%, respectively. No patient developed RIFLE failure or required renal replacement therapy during the 5-year study period. Our reported incidence of AKI, although higher than previously reported in spine surgery, is much lower than that reported in major thoracic and general surgery procedures. Ishikawa et al and Kheterpal
et al.\textsuperscript{13} reported an incidence of 5.9\% and 21.4\% of AKI in major thoracic and general surgery, respectively.

A higher postoperative GFR compared with the baseline preoperative GFR noted in Fig. 1 is likely related to the effects of fluid resuscitation and creatinine dilution commonly observed after major surgery.

Using univariate comparison of the AKI and non-AKI groups, the only risk factor associated with developing AKI in our study was preoperative hypertension ($p = 0.02$). Chronic hypertension is known to increase the risk of perioperative blood pressure lability.\textsuperscript{9,21,22} Aronson et al.\textsuperscript{9} demonstrated the importance of perioperative blood

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**TABLE 2: Demographic parameters according to renal function status**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Non-AKI Group (n = 698)</th>
<th>AKI Group (n = 28)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>baseline (range)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male (%)</td>
<td>39.3</td>
<td>42.9</td>
<td>0.70</td>
</tr>
<tr>
<td>African American (%)</td>
<td>7.7</td>
<td>7.1</td>
<td>1.0</td>
</tr>
<tr>
<td>age in yrs</td>
<td>59.5 (18–90)</td>
<td>63 (40–82)</td>
<td>0.17</td>
</tr>
<tr>
<td>diabetes mellitus (%)</td>
<td>19</td>
<td>25</td>
<td>0.39</td>
</tr>
<tr>
<td>chronic kidney disease (%)</td>
<td>4</td>
<td>7</td>
<td>0.33</td>
</tr>
<tr>
<td>hypertension (%)</td>
<td>60</td>
<td>82</td>
<td>0.02</td>
</tr>
<tr>
<td>baseline estimated GFR (ml/min)</td>
<td>80 (27–165)</td>
<td>79.8 (45–173)</td>
<td>0.77</td>
</tr>
<tr>
<td>operative (range)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSII</td>
<td>15 (2–90)</td>
<td>12.5 (3–61)</td>
<td>0.06</td>
</tr>
<tr>
<td>spinal levels</td>
<td>4 (2–19)</td>
<td>3 (2–15)</td>
<td>0.10</td>
</tr>
<tr>
<td>case length (hrs)</td>
<td>6.2 (0.4–13.3)</td>
<td>5.66 (4.0–10.5)</td>
<td>0.69</td>
</tr>
<tr>
<td>blood loss (ml)</td>
<td>700 (10–12,200)</td>
<td>700 (0–5950)</td>
<td>0.95</td>
</tr>
<tr>
<td>packed red blood cells (units)</td>
<td>0 (0–19)</td>
<td>0 (0–19)</td>
<td>0.22</td>
</tr>
<tr>
<td>cell saver volume (ml)</td>
<td>100 (0–4900)</td>
<td>74.5 (0–1600)</td>
<td>0.67</td>
</tr>
<tr>
<td>ephedrine (mg)</td>
<td>10 (0–110)</td>
<td>15 (0–65)</td>
<td>0.18</td>
</tr>
<tr>
<td>phenylephrine (μg)</td>
<td>200 (0–53,945)</td>
<td>150 (0–27,115)</td>
<td>0.73</td>
</tr>
<tr>
<td>crystalloid (ml)</td>
<td>3550 (0–14,000)</td>
<td>3250 (1500–7000)</td>
<td>0.49</td>
</tr>
<tr>
<td>colloid (ml)</td>
<td>500 (0–15,000)</td>
<td>1000 (0–3000)</td>
<td>0.34</td>
</tr>
<tr>
<td>proportion of fluids as colloids (%)</td>
<td>11</td>
<td>16</td>
<td>0.30</td>
</tr>
<tr>
<td>base deficit</td>
<td>–2 (–16 to 5)</td>
<td>–1 (–14 to 3)</td>
<td>0.10</td>
</tr>
<tr>
<td>postop (range)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>min postop GFR</td>
<td>88 (27–165)</td>
<td>50 (44–173)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

**Fig. 1.** Minimal postoperative GFR compared with baseline GFR. The majority of patients demonstrated no AKI, with a small number classified into the risk and injury RIFLE categories.
pressure lability on outcome in their post hoc analysis of the ECLIPSE trial (Evaluation of Clevidipine in the Perioperative Treatment of Hypertension Assessing Safety Events). Systolic blood pressure variability outside a range of 75–135 mm Hg intraoperatively was associated with an increased odds ratio of death at 30 days (1.16, 95% CI 1.04–1.30). Furthermore, chronic hypertension shifts the renal autoregulatory range to the right on the pressure-flow curve. Therefore, a higher intraoperative mean arterial pressure is required to maintain an adequate renal perfusion pressure. This combination of intraoperative blood pressure lability and sustained digressions of the mean arterial pressure below the shifted autoregulatory range can increase the risk of postoperative AKI.

The near-significant association (p = 0.06) between a lower SSII and AKI is somewhat surprising. We postulate that this effect may be the result of our institutional practice of increased invasive hemodynamic and goal-directed fluid responsive therapy and aggressive postoperative intensive care unit management in the complex spine procedures than in patients undergoing less invasive surgery.

To quantify the risk of developing RIFLE risk with
age, preoperative hypertension, and SSII score, the residual bootstrap procedure was used. Estimated probability curves were generated for these parameters and are shown in Fig. 2. The probability curves highlight the increased risk of AKI with lower baseline GFR in all the aforementioned parameters. This is especially evident when the combination of a low baseline GFR and preexisting hypertension is present.

We evaluated the effect of hydroxyethyl starch use on the risk of postoperative AKI by studying the total volume and the proportion of total volume administered as colloids. The hydroxyethyl starch used during this study period included both Hespan (B Braun Medical Inc.) and Voluven (Fresenius Kabi). Although the volume (500 ml vs 1000 ml; \( p = 0.338 \)) and percentage of colloids (11.1% vs 15.6%; \( p = 0.299 \)) were higher in the AKI group than in the non-AKI group, this difference did not reach statistical significance. Recent prospective studies by the 6S and the Australian and New Zealand Intensive Care Society (ANZICS) study groups, and a meta-analysis by Zarzchanski et al., have highlighted the risk of AKI associated with hydroxyethyl starch use. However, their study populations included patients with multiorgan dysfunction and sepsis, which is different than the patients who all underwent elective spine surgery that were included in our analysis. Our data support the continued use of colloids in spine surgery. This is further highlighted by the recent postoperative visual loss study, which demonstrated a lower risk of ischemic optic neuropathy (OR 0.67, 95% CI 0.52–0.82; \( p < 0.001 \)) with a higher percent of colloid use.

The major limitation of our study is the small number of patients who developed AKI over the 5-year study period. This small number limited the number of variables that could be studied in a regression model. However, because AKI is defined in terms of postoperative GFR, a continuous variable, we were able to work around this limitation by modeling the continuous outcome. The variables chosen were based on investigator hypotheses, but other factors could have played a role. Another limitation of the study was that we used only estimated GFR in our definition of AKI. Urine output was not used because this metric was insufficiently recorded in the postoperative period. There may be a higher incidence of AKI if the urine output definition is applied.

By applying a more uniform definition of AKI, we have demonstrated a higher risk of postoperative renal dysfunction in multilevel spine surgery than previously described. Although no patients developed RIFLE failure or required renal replacement therapy, those patients who did develop RIFLE risk and injury warrant closer follow-up as they show increased mortality at 5 and 10 years. The process of risk identification, stratification, and modification begins during the preoperative evaluation of the patient by the surgeon. By using the risk model described above, the degree of postoperative estimated GFR decrement can be predicted. This prediction is of particular importance in our geriatric population with multiple comorbidities who present for extensive spine reconstructive procedures.

Patients at high risk of postoperative AKI, with poorly controlled hypertension, must have elective surgery delayed until normalization of the pressure is achieved. This is of particular importance in patients with a low baseline GFR and poorly controlled hypertension, as their risk of AKI is much higher (Fig. 2C). If difficulty is encountered with blood pressure management in patients with chronic kidney disease, consultation with a nephrologist is recommended. Upon normalization of the blood pressure, elective surgery can proceed with the goal of avoiding hypotension and hyperperfusion in the perioperative period. A hypertensive patient presenting for spine surgery may require invasive hemodynamic monitoring (arterial line and central venous monitoring) and goal-directed fluid and hemostatic therapy. This will involve the combined efforts of the perioperative team, who should be alerted to the high-risk patient presenting for surgery.

In the postoperative period, small decreases in the GFR must not be ignored. These decreases can be readily identified and classified by the RIFLE criteria. If patients do develop AKI postoperatively, secondary kidney injury must be avoided. These secondary injuries include sustained hypotension, hypovolemia, and the introduction of nephrotoxic agents. Early consultation with a nephrologist can aid in the management of these patients.

Conclusions

This study highlights the underappreciated risk of milder forms of AKI in patients undergoing spine surgery. We provide a risk-modeling tool that helps to identify these patients and present a practical solution to their perioperative management.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Naik, Durieux. Acquisition of data: McKinney, Smith, Titus. Analysis and interpretation of data: Naik, Colquhoun. Drafting the article: Naik, Raphael, Durieux. 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: Naik. Statistical analysis: McMurry.

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