Title: A Model to Predict the Risk of AKI after Spine Surgery using the KDIGO Definition and Multicenter Perioperative Outcome Group Database

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Type of Study: Retrospective observational cohort study

Introduction

Major spine surgery is a common surgical procedure that was performed in 87 162 patients between 2009-11 in the United States alone.[1] The Medicare spending for lumbar spine surgery has increased 500% to $482 million dollars over the last decade.[2] With more complex spine procedures being performed in an increasing aging population, the risk of postoperative complications is increased. Deyo et al reported a major postoperative complication incidence of 3.1%, which increased to 5.3% when three, or more co-morbidities were present.[3] Furthermore, after adjusting for other risk factors, the odds ratio for life-threatening complications with complex spine fusions is 2.95 (95% confidence interval [CI], 2.50-3.49) compared to simple decompression.[3]

Multilevel spine surgery is associated with significant intraoperative hemodynamic and hemostatic perturbations, potentially increasing the risk of developing postoperative acute kidney injury (AKI). There are, however, limited studies reporting the incidence of AKI in spine surgery. Earlier studies reported an incidence of renal insufficiency that varied between 0.88-0.91%, utilizing a definition of a greater

than 2mg/dl increase in creatinine from baseline.[4,5] The latter definition however significantly under-estimates the milder, less severe forms of AKI. Naik et al reported an AKI rate of 3.9% in multilevel spine surgery based on the RIFLE classification with 3.2% falling in the RIFLE-Risk and 0.7% in the Injury category. (in print) Hypertension was the only perioperative risk factor associated with AKI with univariate analysis, but a small cohort of only 726 patients limited the strength of this study and motivates the investigation of AKI after major spine surgery in a large, multicenter population.

The importance of identifying the earlier stages of AKI is highlighted by the study of Bihorac et al. In a retrospective analysis of 10,518 patients undergoing major non-cardiac surgery, Bihorac and colleagues demonstrated a 10-year survival of 65% without perioperative AKI versus 50% and 44% for patients who developed RIFLE-risk and injury respectively.[6] Furthermore, even when complete renal recovery occurred there was an increased risk of mortality a decade after the sentinel event. Hobson et al demonstrated similar poor outcomes in a cohort of 2973 cardiothoracic surgery patients with the less severe forms of AKI.[7] Therefore, the identification and long-term follow-up of patients with perioperative stage I AKI is extremely important.

Currently there are no studies reporting the incidence of AKI in spine surgery from a large perioperative database. We propose using the Multicenter Perioperative Outcomes Group (MPOG) database for the following: 1) define the contemporary incidence of AKI in spine surgery using the Kidney Disease Improving Global Outcomes (KDIGO) classification, 2) define major independent predictors for AKI in spine surgery,

3) develop and validate a full pre-procedure risk model in addition to a simplified additive prediction tool that can be used by anesthesiologist and surgeons.

Material and Methods

Data Source

The MPOG database was utilized for this study. The MPOG database contains de-identified perioperative data relevant to this study. Institutional Review Board approval has already been obtained for all MPOG projects involving the University of Michigan, Ann Arbor, Michigan. Centers contributing preoperative history and physical data, intraoperative anesthesia records and postoperative laboratory result data were included for analysis. Procedures performed between the dates of January 1st 2007 and January 1st 2014 were reviewed.

Utilizing Current Procedural Terminology (CPT) codes, patients undergoing cervical, thoracic and/or lumbar spine surgery with and without osteotomy, fusion, correction of anomalous spinal vertebrae, instrumentation, artificial disc replacement and placement of bone grafts were identified. Demographic and preoperative data collected included age, sex, race, BMI, ASA physical status and the preoperative diagnosis of hypertension, diabetes mellitus, peripheral vascular disease and 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, cryoprecipitate transfused and the use of any antifibrinolytic. The need for intraoperative inotrope and/or vasopressor support, and the total dose of

drug infused were recorded. Both bolus and infusions of vasoactive agents was recorded. Lowest intraoperative hemoglobin, pH, bicarbonate and base deficit was obtained from intraoperative arterial blood gas determinations when available. Intraoperative hypotension was determined by a method previously described by Kheterpal et al. Each intraoperative anesthetic record was divided into consecutive ten-minute epochs. The median systolic blood pressure (SBP) and median mean arterial pressure (MAP) for each ten-minute epoch was calculated. The use of a median value over ten minutes decreases the impact of monitoring artifacts and transient hypotension with limited clinical significance [8]. These median values were compared to absolute hypotension cutoff points: SBP <80, < 70, < 60, and MAP < 60, < 50, and < 40. In addition, the median values were compared to the preoperative blood pressure documented in the history and physical to assess hypotension relative to this baseline blood pressure: SBP 30% decrease, 40%, 50% and MAP 30% decrease, 40%, and 50%. The number of epochs below these absolute and relative hypotension cutoff points was calculated for each case.

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 with no pre or postoperative creatinine value.

Definition of Acute Kidney Injury (AKI)

The KDIGO classification was used to identify the different stages of AKI. Stage 1 was

defined as an increase in serum creatinine by 0.3mg/dL or more within 48 hours **or** Increase in serum creatinine to 1.5 times baseline or more within 7 days of surgery **or** urine output less than 0.5 mL/kg/h for 6 hours. Stage 2 was an increase in creatinine 2-2.9 x the baseline (urine output < 0.5 ml/kg/h for 12 hours) while stage III was an increase in creatinine 3x baseline or an increase in creatinine > 4mg/dl or the initiation of renal replacement therapy.

The most recent preoperative serum creatinine was used as the baseline measurement to which postoperative elevations were referenced. The maximum postoperative creatinine during the first week after surgery was compared to the preoperative baseline creatinine. This limit of the first week after surgery was chosen to exclude other non-operative causes of renal dysfunction, which were deemed more likely to occur after this time period.

Statistical Analysis

Linear regression will be used to develop a predictive model for maximum post-op creatinine; this model will be used in conjunction with a residual bootstrap to estimate individual patient risk for AKI. The regression model will be developed on a subset of the data, assessed using standard linear regression diagnostics and validated by either 10-fold cross-validation or bootstrap model validation. After model validation, a final model using the already selected predictors will be fit to the entire data set. We will consider baseline patient and procedure characteristics as candidate predictors.

Patients will then be stratified based on pre-operative risk, based on this stratification we will evaluate the risk associated with intraoperative characteristics. We hypothesize

that intraoperative characteristics differently affect high and low risk patients. In addition summary statistics will be calculated describing the patient population.

Power Analysis

Naik et al reported 26 cases of AKI in a cohort of 726 patients **(3.6%)** based on the RIFLE definition in multi-level spine surgery (In print).

We have listed 25 predictor variables to model for post AKI with multi-level spine surgery. Based on the aforementioned incidence of AKI a logistic regression would need about 7,000 patient data to fit the model. By performing a validation to check the predictions, we double that estimate to 14,000 patients.

Since the database is expected to be limited to around 9,000 patients, we propose an alternative. We propose to analyze max post-op creatinine as a continuous variable and infer AKI from it; this leaves us estimating the impact of 25 predictor variables using a linear regression built on approximately 9,000 patients, which is more than sufficient.

*Justification for a separate AKI study*There is currently a project (PCRC-001) that is studying predictors and outcomes of postoperative acute kidney injury after non-cardiovascular surgery. This study does include a spine surgery cohort. There was some discussion amongst the primary and co-investigators about whether a separate study for spine surgery is justified. Listed below are specific issues that are unique to spine surgery and that would benefit from a separate study 1. Volume of blood loss. This can vary from trivial amounts to 2-3 x circulating blood volume with major deformity surgery.
2. Use of anti-fibrinolytics in major deformity surgery and its impact on blood conservation and ultimately AKI.3. The not uncommon practice of 'controlled hypotension' for these procedures and its impact on post-op AKI.4. The questions of high volume vs. low volume major spine centers and postoperative outcomes. 5. Differences between cervical vs. thoracic vs. lumbar surgery AKI risk 6. Primary vs. redo procedures.7. AKI risk with fusion vs. non-fusion cases. 8. Minimally invasive vs. open procedures.9. Anterior vs. posterior fusion.10. The high percentage of colloid use in spine surgery (as a result of the Postoperative Visual Loss Study In Anesthesiology last year) and its impact on AKI.

11. Finally a 'spine-specific' model for risk identification and stratification would be extremely valuable for perioperative team caring for these patients.

Questions for the Group/Limitations of the study

1. Lack of urine output data in order to make the dx of AKI
2. Pre-op vs. first post-op Cr value as a baseline
3. There may be issues with the use of CPT codes varying between centers. We will need to perform an analysis of which centers use which codes (or perform which procedures)
4. It is possible patients are censored (i.e. discharged before Cr peaks)
5. There is sampling bias against cases with longer LOS (and thus more opportunities for detection of AKI)

Candidate variables for the MPOG PCRC: AKI and Spine Surgery Study.

Demographic data	
Case ID	Aims_intraopcaseinfo.AIMS_Case_ID
Age	Aims_intraopcaseinfo.AIMS_patient_age_years
Sex	AIMS_Patients.AIMS_Sex
Race	AIMS_Patients.MPOG_Race_Concept_ID
ASA status	ASA_Class
Height	MPOG_Height_cm
Weight	MPOG_Weight_kg
BMI	AIMS_Body_Mass_Index
Surgery	
Surgery CPT codes (attached)	Charge_Capture_Primary_Surgery_Code
Preoperative Medical Conditions	
Hypertension	Cardiovascular - Hypertension MPOG Concept ID 70031 Cardiovascular - Pulmonary Hypertension MPOG Concept ID 70036
Diabetes	Endocrine - Diabetes MPOG Concept ID 7004
Chronic kidney disease	Renal / Urologic - Renal Failure MPOG Concept ID 7006
Peripheral Vascular disease	Cardiovascular - PVOD MPOG Concept ID 7003
Hemodialysis	AIMS_Preop.AIMS_Value_Text
Peritoneal dialysis	AIMS_Preop.AIMS_Value_Text
Preoperative Laboratory Values	
Most recent preoperative creatinine	Aims_labvalues, MPOG concept 5002
Most recent preoperative BUN	Aims_labvalues, MPOG concept 5012
Most recent preoperative hemoglobin	Aims_labvalues, Formal lab – Hemoglobin MPOG Concept ID 5005 Aims_labvalues, POC - Coulter counter - Hemoglobin MPOG Concept ID Aims_labvalues, Formal lab - Blood gas - Hemoglobin MPOG Concept ID Aims_labvalues, POC - Blood gas - Hemoglobin MPOG Concept ID 5081
Most recent preoperative white blood count	Aims_labvalues, MPOG Concept ID 5056
Most recent preoperative albumin	Aims_labvalues, MPOG Concept ID 5057

Procedure		
	Duration of anesthesia and surgery time	AIMS_BillingProcedures. AIMS_Total_Anesthesia_Units AIMS_BillingProcedures. AIMS_Date_Of_Service_Start_DT AIMS_BillingProcedures. AIMS_Date_Of_Service_End_DT
	Blood pressure measurements	BP Sys Non-invasive MPOG_Concept_ID 3015 BP Dias Non-invasive MPOG_Concept_ID 3020 BP Mean Non-invasive MPOG_Concept_ID 3025 BP Sys Arterial Line (Invasive, Peripheral) MPOG_Concept_ID3030 BP Dias Arterial Line (Invasive, Peripheral) MPOG_Concept_ID 3035 BP Mean Arterial Line (Invasive, Peripheral) MPOG_Concept_ID 3040
	Phenylephrine dose	AIMS_IntraopMedications, MPOG_Concept_ID 10354, 10355, 10356, 103 10358
	Norepinephrine dose	AIMS_IntraopMedications, MPOG_Concept_ID 10326
	Epinephrine dose	AIMS_IntraopMedications, MPOG_Concept_ID 10176, 10540, 10541
	Ephedrine dose	AIMS_IntraopMedications, MPOG_Concept_ID 10175
	Total Blood loss	AIMS_IntraopInputOutputTotals MPOG_Concept_ID 10499
	Total Cell saver volume	AIMS_IntraopInputOutputTotals MPOG_Concept_ID 10496
	Packed red blood cells	AIMS_IntraopInputOutputTotals Autologous - MPOG_Concept_ID 10489 Homologous - MPOG_Concept_ID 10490
	Fresh frozen plasma	AIMS_IntraopInputOutputTotals MPOG_Concept_ID 10493
	Cryoprecipitate	AIMS_IntraopInputOutputTotals MPOG_Concept_ID 10495
	Platelets	AIMS_IntraopInputOutputTotals MPOG_Concept_ID 10494
	Hydroxyethyl starch	AIMS_IntraopInputOutputTotals MPOG_Concept_ID 10601, 10605
	Lowest intraoperative hemoglobin	POC - Coulter counter - Hemoglobin MPOG Concept ID 3440 POC - Blood gas - Hemoglobin MPOG Concept ID 5081
	Lowest intraoperative pH	POC - Blood gas - pH (unknown sample type) - MPOG Concept ID 3370 POC - Blood gas - pH (arterial) - MPOG Concept ID 5022 POC - Blood gas - pH (venous) - MPOG Concept ID 5025
	Lowest intraoperative bicarbonate	MPOG Concept ID 10404
	Lowest intraoperative base deficit	MPOG Concept ID 90307
	Intraoperative tranexamic acid	MPOG Concept ID 10436
	Intraoperative aminocaproic acid	MPOG Concept ID 10024
	Intraoperative aprotinin	MPOG Concept ID 10036
Postoperative		
	Highest postoperative creatinine	Aims_labvalues, MPOG concept 5002
	Highest postoperative BUN	Aims_labvalues, MPOG concept 5012
	Lowest postoperative hemoglobin	Aims_labvalues, Formal lab – Hemoglobin MPOG Concept ID 5005 Aims_labvalues, POC - Coulter counter - Hemoglobin MPOG Concept ID Aims_labvalues, Formal lab - Blood gas - Hemoglobin MPOG Concept ID Aims_labvalues, POC - Blood gas - Hemoglobin MPOG Concept ID 5081
	Renal replacement therapy	MPOG Concept ID 50620, 50621

Primary and Additional CPT Codes

Primary CPT codes	Additional CPT Codes
63001	22206
63015	22207
63045	+22208
+63048	22210
63050	22212
63051	22214
63003	+22216
63016	22220
63046	22222
+63048	22224
63005	+22226
63012	22532
63017	22533
63047	+22534
+63048	22548
63020	22551
+63035	+22552
63040	22554
+63043	22556
63055	22558
+63057	+22585
63064	22586
+63066	22590

63077	22595
+63078	22600
63085	22610
+63086	22612
63087	+22614
+63088	22630
63090	+22632
+63091	22633
63101	+22634
+63103	22800
63030	22802
63042	22804
+63044	22808
63102	22810
+63103	22812
63056	22840
+63057	22841
	22842
	22843
	22844
	22845
	22846
	22847
	22848
	2294

	22850
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	22857
	22861
	22862
	22864
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	20930
	20931
	20936
	20937
	20938

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