The Use of Intraoperative Dexmedetomidine Is Not Associated With a Reduction in Acute Kidney Injury After Lung Cancer Surgery

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Objective: **To evaluate whether the use of intraoperative dexmedetomidine (DEX) during lung cancer surgery may reduce the incidence of acute kidney injury (AKI).**

Design: **A retrospective study.**

Setting: **An academic hospital.**

Participants: **Data were collected from 1,207 adult patients who underwent resection for non-small-cell lung cancer between January 2004 and December 2012.**

Interventions: **None.**

Measurements and Main Results: **All patients had a general balanced anesthetic technique, and dexmedetomidine use was at the discretion of the anesthesiologist. Data analysis was done utilizing the Wilcoxon rank sum tests and Chi-square tests to compare continuous variables and categoric variables between the 2 groups, respectively. Multivariate logistic analysis with backward selection was fitted to find out factors for AKI incidence. Overall, 8.1% of the patients developed AKI during their hospital stay. There were no statistically significant differences in demographic, perioperative variables, and the incidence of AKI between patients who did and did not receive DEX. A logistic regression model was fitted to determine factors independently associated with AKI. Factors that were independently associated with AKI included body mass index, American Society of Anesthesiologists 3-4, hypertension, smoking status, and thoracotomy procedure.**

Discussion: **The authors hypothesized that DEX use would be associated with a decreased incidence of AKI in thoracic surgery; however, they were unable to prove this hypothesis. Their results did demonstrate that there are 5 factors independently associated with AKI.**

KEY WORDS: acute kidney injury, lung neoplasms, thoracic surgery, dexmedetomidine

ACUTE KIDNEY INJURY (AKI, formerly acute renal failure) is used to describe a rapid deterioration in renal excretory function.[1] AKI is associated with complications that may lead to multiorgan dysfunction and potentially to multiorgan failure in critically ill patients.[2] AKI accounts for 5% after general surgery to 45% after cardiac surgery of AKI acquired during hospital stays and tends to be associated with increased length of hospital stay as well as increased morbidity and mortality.[3,4] Even slight increases in postoperative serum creatinine concentrations, defined as stage 1 by Kidney Disease: Improving Global Outcome (KDIGO) criteria, have been associated with almost 5-fold increases in mortality.[5] Despite recovery from AKI, these patients have increased long-term morbidity.[6,7]

Dexmedetomidine is a potent and highly selective alpha (2)-adrenoreceptor that has analgesic, sedative, anxiolytic, and sympatholytic effects.[8] In the context of cardiac surgery, the use of dexmedetomidine has been associated with improvement in survival and reduced postoperative complications, although there was a trend towards an increased risk of need for dialysis in those who received dexmedetomidine.[9] Although Ishikawa demonstrated fluid restriction was not an independent risk factor for AKI after lung cancer surgery, one of the speculated mechanisms of AKI after noncardiac surgery is ischemia-reperfusion followed by inflammation.[4,10,11] In animals, dexmedetomidine has shown protective effects in several models of ischemia-reperfusion, which is thought to be the principal mechanism of AKI in the context of surgery.[12–15] Sugita et al investigated the effects of dexmedetomidine infusion on renal ischemia-reperfusion injury in rats. They showed that a continuous infusion of dexmedetomidine improved renal ischemia-reperfusion injury.[16] Moreover, dexmedetomidine has shown to directly inhibit the release of renin in the kidney, leading to vasodilation.[17]

Based on these premises, the authors hypothesized that the use of intraoperative dexmedetomidine associated with decreased incidence of AKI after thoracic surgery. Specifically, they retrospectively analyzed data from patients who had lung cancer surgery in their institution.

MATERIALS AND METHODS

Patients

Data from a total of 1,207 patients who underwent resection of stages 1, 2, or 3a non-small-cell lung cancer (NSCLC) were taken from the authors' Institutional Review Board-approved database. Patients who were 18 years or older and had surgery for NSCLC between January, 2004 and December, 2012 were included in the analysis. All patients had general balanced anesthesia that typically consisted of a mixture of a volatile anesthetic in oxygen and muscle relaxation with a non-depolarizing muscle relaxant. The use of dexmedetomidine was at the discretion of the attending anesthesiologist who typically administered it at range from 0.2- to 0.7-µg/kg/h.

Patient data included age, sex, ASA (American Society of Anesthesiologists) physical status, body mass index (BMI), stage of disease, comorbidities including smoking and arterial hypertension, preoperative transfusion, angiotensin-converting enzyme (ACE) inhibitors, type of surgery (thoracotomy versus thoracoscopy), and dose of dexmedetomidine. The authors' database contained serum creatinine concentrations measured

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before surgery, on postoperative days 1, 2, and 3, and before hospital discharge. The highest postoperative creatinine concentration was used to define AKI according to Acute Kidney Injury Network (AKIN) criteria (Table 1).[3]

Statistical Methods

The primary outcome of this study was the incidence of AKI in patients who were treated intraoperatively with dexmedetomidine after lung cancer surgery compared with that of those who did not receive the drug. As a secondary outcome, the authors calculated 30-day and 1-year postoperative mortality. Summary statistics including mean, standard deviation, median, and interquartile were used for continuous variables and frequency counts and percentages for categoric variables. To detect a 2% significant drop in AKI rate, the authors needed 2,075 patients for the treatment group and 7,887 patients for the nontreatment group. Wilcoxon rank sum tests and Chi-square tests were used to compare continuous variables and categoric variables between 2 groups, respectively. A logistic regression model was fitted to determine factors independently associated with AKI. All potential covariates were added into the model, and the backward selection method was adopted at significance level of 0.15. Those variables that were not significant and therefore dropped out of the logistic model included age, creatinine value, hemoglobin value, dexmedetomidine, alcohol use, diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease, stroke, preoperative transfusion, and ACE inhibitor. A p value < 0.05 was considered statistically significant. All analyses were performed using SAS software (version 9.3, SAS Institute, Cary, NC).

RESULTS

Patient Characteristics

A total of 1,207 patients were included in the analysis (Table 1). The age of the patients ranged from 19 to 91 years old, with a median of 66. The median (interquartile) postoperative creatinine concentrations on postoperative days 1 (0.9, [0.8-1.1]), 2 (0.9, [0.8-1.1]), 3 (0.9, [0.7-1.1]), and before discharge (0.9, [0.7-1.1]) were similar to preoperative concentrations (0.9, [0.8-1.1]).

Overall, 98 patients (8.1%) developed AKI during their hospital stay. The incidence of stages 1 and 2 AKI on postoperative day 1 was 5.9% (n = 71) and 0.6% (n = 7), respectively (Fig 1). On postoperative day 2, there were

Table 1. Patients' Characteristics and Incidence of AKI (Any Stage) by Dexmedetomidine Use

		All patients	Dexmedetomidine		
Variable	Level	n = 1,207	No (n = 949)	Yes (n = 258)	p Value
Age, years (median [range])		66 (59-73)	66 (28-91)	65 (19-88)	0.09
Sex	Male	629 (52.1%)	480 (50.6%)	149 (57.8%)	0.04
	Female	578 (47.9%)	469 (49.4%)	109 (42.2%)	
BMI, median (range)		26.24 (23.54-29.78)	26.11 (9.76-190.66)	27.07 (16.1-57.32)	0.09
Preoperative Hb g/dL median (range)		13.2 (12-14.2)	13.2 (10.74-18.6)	13.3 (8.6-17.6)	0.39
Preoperative sCr mg/dL median (range)		0.9 (0.8-1.1)	0.9 (0.5-12.9)	0.9 (0.5, 2.4)	0.29
ASA physical status	1-2	152 (12.6%)	122 (12.9%)	30 (11.6%)	0.60
	3-4	578 (47.9%)	827 (87.1%)	228 (88.4%)	
Smoker	No	873 (72.3%)	670 (70.6%)	203 (78.7%)	0.01
	Yes	334 (27.7%)	279 (29.4%)	55 (21.3%)	
History of alcohol abuse	No	1032 (85.5%)	811 (85.5%)	221 (85.7%)	0.94
	Yes	175 (14.5%)	138 (14.5%)	37 (14.3%)	
Diabetes mellitus	No	1079 (89.4%)	851 (89.7%)	228 (88.4%)	0.55
	Yes	128 (10.6%)	98 (10.3%)	30 (11.6%)	
Arterial hypertension	No	650 (53.9%)	509 (53.6%)	141 (54.7%)	0.77
	Yes	557 (47.1%)	440 (46.4%)	117 (45.3%)	
Coronary artery disease	No	1030 (85.3%)	814 (85.8%)	216 (83.7%)	0.41
	Yes	177 (14.7%)	135 (14.2%)	42 (16.3%)	
Chronic obstructive pulmonary disease	No	1009 (83.6%)	788 (83.0%)	221 (85.7%)	0.31
	Yes	198 (16.4%)	161 (17.0%)	37 (14.3%)	
Stroke	No	1182 (97.9%)	930 (98.0%)	252 (97.7%)	0.75
	Yes	25 (2.1%)	19 (2.0%)	6 (2.3%)	
Perioperative transfusion	No	1183 (98%)	931 (98.1%)	252 (97.7%)	0.66
	Yes	24 (2%)	18 (1.9%)	6 (2.3%)	
ACE inhibitor	No	1034 (85.7%)	817 (86.1%)	217 (84.1%)	0.42
	Yes	173 (14.3%)	132 (13.9%)	41 (15.9%)	
Thoracotomy	No	314 (26%)	251 (26.4%)	63 (24.4%)	0.51
	Yes	893 (74%)	698 (73.6%)	195 (75.6%)	
Acute kidney injury (any)	No	1109 (91.9%)	869 (91.6%)	240 (93.0%)	0.45
	Yes	98 (8.1%)	80 (8.4%)	18 (7.0%)	

NOTE. Continuous variables were compared using Wilcoxon rank sum test. Categoric variables were compared using Chi-square test. A p value < 0.05 was considered statistically significant.

Abbreviations: ACE, angiotensin-converting enzyme; ASA, American Society of Anesthesiologists physical status; BMI, body mass index; Hb, hemoglobin; sCr, serum creatinine.