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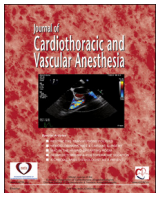

Original Article

Severity of Acute Kidney Injury in the Post-Lung Transplant Patient Is Associated With Higher Healthcare Resources and Cost

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Objective: Perioperative risk factors and the clinical impact of acute kidney injury (AKI) and failure after lung transplantation are not well described. The incidences of AKI and acute renal failure (ARF), potential perioperative contributors to their development, and postdischarge healthcare needs were evaluated.

Design: Retrospective.

Setting: University hospital.

Participants: Patients undergoing lung transplantation between January 1, 2011 and December 31, 2015.

Measured Data: The incidences of AKI and ARF, as defined using the Risk, Injury, Failure, Loss, End-Stage Renal Disease criteria, were measured. Perioperative events were analyzed to identify risk factors for renal compromise. A comparison of ventilator days, intensive care unit (ICU) and hospital lengths of stay (LOS), 1-year readmissions, and emergency department visits was performed among AKI, ARF, and uninjured patients.

Measurements and Main Results: Ninety-seven patients underwent lung transplantation; 22 patients developed AKI and 35 patients developed ARF. Patients with ARF had significantly longer ICU LOS (12 days *v* 4 days, $p < 0.001$); ventilator days (4.5 days *v* 1 day, $p < 0.001$); and hospital LOS (22.5 days *v* 14 days, $p < 0.001$) compared with uninjured patients. Patients with AKI also had significantly longer ICU and hospital LOS. Patients with ARF had significantly more emergency department visits and hospital readmissions (2 *v* 1 readmissions, $p = 0.002$) compared with uninjured patients. A univariable analysis suggested that prolonged surgical time, intraoperative vasopressor use, and cardiopulmonary bypass use were associated with the highest increased risk for AKI. Intraoperative vasopressor use and cardiopulmonary bypass mean arterial pressure < 60 mmHg were identified as independent risk factors by multivariable analysis for AKI.

Conclusion: The severity of AKI was associated with an increase in the use of healthcare resources after surgery and discharge. Certain risk factors appeared modifiable and may reduce the incidence of AKI and ARF.

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Key Words: RIFLE criteria; lung transplantation; cardiopulmonary bypass; cost analysis; readmission rate

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SINCE THE INCEPTION of lung transplantations, more than 51,000 procedures have been performed worldwide. Between 1988 and 1992, the median survival time was 4 years; and between 2004 and 2008, survival time improved to 5.7 years.[1] Long-term complications of lung transplantation such as diabetes mellitus, hypertension, acute rejection, and bronchiolitis obliterans syndrome have been well described. Renal dysfunction after lung transplantation also has been reported in the literature[2]; however, its incidence and severity vary widely. The purpose of this study included the following: (1) evaluate for differences in in-hospital outcomes in patients who developed acute kidney injury (AKI) and acute kidney failure (ARF) compared with patients who did not develop AKI or ARF; (2) compare the incidence of emergency room visits and readmissions between the groups; (3) characterize preoperative, intraoperative, and postoperative factors associated with the development of renal failure, and (4) perform a cost analysis for these measured outcomes.

Methods

In this single-center, retrospective study, data were collected from the electronic medical record system and paper charts from January 1, 2011 to December 31, 2015 at the University of California, San Diego. The study was approved by the university's Institutional Review Board (140101x), and the need for informed consent was waived. All patients undergoing either a single-lung transplantation (SLTx) or double-lung transplantation (DLTx) over the 4-year period were included in the study and were identified through the University of California, San Diego, cardiothoracic surgery database, which is a dataset maintained by the Division of Cardiothoracic Surgery and holds information regarding all its surgical patients. Patients were excluded from the study if they had undergone renal replacement therapy before their transplantation or if they had undergone either a heart-lung, lung-liver, or lung-kidney transplantation.

The primary outcome of interest was the development of AKI and ARF in patients undergoing lung transplantation. The Risk, Injury, Failure, Loss, End-Stage Renal Disease (RIFLE) criteria were used to classify the severity of AKI and to assess its occurrence after lung transplantation. Secondary outcomes of interest included ventilator days, intensive care unit (ICU) length of stay (LOS), hospital LOS, in-hospital mortality, need for renal replacement therapy, post-discharge 1-year mortality, frequency of emergency room visits, and hospital readmission rates in 1 year. The following data were collected from medical records: age, sex, type of lung transplantation (single *v* double), indication for surgery, baseline serum creatinine (sCr), and whether the patient had any of the following preoperative comorbidities: coronary artery disease, hypertension, pancreatic insufficiency, diabetes mellitus, chronic kidney disease, and hyperlipidemia. The following intraoperative data were collected: surgical time, cardiopulmonary bypass time (CPB), mean arterial pressure while on CPB, and duration of intraoperative vasopressors. In addition, the following data on medications were recorded: postoperative duration on vasopressors, diuretic use, antibiotics, and immunosuppressive agents. Serum creatinine data were tracked beginning on postoperative day (POD) 0 up to POD 7 in the absence of AKI. For patients who developed AKI or ARF, the sCr was followed until the value returned to baseline.

Baseline sCr was determined by the creatinine level before surgery. Using RIFLE creatinine criteria, an sCr twice the baseline within 7 days after surgery was defined as AKI and an sCR 3 times the baseline or anuria >12 hours was considered ARF.[3] Patients requiring renal replacement therapy postoperatively were classified as experiencing ARF because they had anuria for >12 hours. Chronic kidney disease (CKD) was defined using the National Kidney Foundation Kidney Disease Outcomes Quality Initiative CKD classification as a glomerular filtration rate (GFR) of <60 mL/min/1.73 m^2 for more than 3 months.[4] A GFR between 30-to-59 mL/min/1.7 m^2 is considered to be stage 3 CKD, between 15-to-29 mL/min/1.7 m^2 is classified as stage 4, and <15 mL/kg/m^2 is considered to be stage 5.

Patients received tacrolimus, 5 mg by mouth, on arrival to the hospital for lung transplantation in the preoperative setting. Intraoperatively, all patients received methylprednisolone, 500 mg intravenously, immediately before removal of the cross-clamp from the donor lung. Immediately after surgery, all patients were started on a continuous tacrolimus infusion. Mycophenolate mofetil and prednisone comprised the remainder of the immunosuppressant regimen. No patients in this study received cyclosporine as an immunosuppressant.

Statistics

R, a software environment for statistical computing (R version 3.3.0, R Core Team, Vienna, Austria), was used to perform all statistical analyses. Data were imported into R from a comma-separated values file. Patients were grouped into the following categories: (1) patients with AKI, (2) patients with ARF and (3) patients without AKI or failure. In each group, the continuous variables age, body mass index, and creatinine were expressed as mean $\pm$ standard deviation. Healthcare costs for each cohort were presented as the sample mean and its associated 95% confidence interval (CI), which was calculated using the standard error. For continuous variables, differences in the mean and median among groups were assessed using Student *t*-test and Wilcoxon rank sum test, respectively. Differences in categorical variables were assessed with Fisher exact test. In each case, either the patients with AKI or patients with ARF were compared with patients without injury/failure. A p value <0.05 was considered to be statistically significant. To assess the association of each of the clinical characteristics with the development of AKI, univariable logistic regression analysis was performed. The dependent variable in the model was defined as any AKI (either AKI or ARF as defined using RIFLE). The analysis was performed on the following: (1) all patients and (2) only patients who underwent CPB intraoperatively. The odds ratio (OR) with associated 95% CI were reported for each covariate. Any OR with a 95% CI that did not include 1.00 was considered to be statistically significant. A multivariable logistic regression analysis was performed next.

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