



Editorial

Predicting the Price of the Pump: Examining the Incidence and Predictive Factors of Acute Kidney Injury Following Off-Pump Lung Transplantation



FAMED ECONOMIST THOMAS SOWELL once noted that “there are no solutions, only trade-offs,” and this adage rings true in the current debate regarding the best approach for intraoperative utilization of extracorporeal life support (ECLS) in lung transplantation.¹ Current literature reports a nearly even distribution of utilization of some form of ECLS intraoperatively versus no support at all,² and a recent survey reports significant variability in the usage of ECLS types including cardiopulmonary bypass or extracorporeal membrane oxygenation (ECMO).³ Although some data point toward the benefit of venoarterial (VA) ECMO as the preferred form of intraoperative support,⁴ the lack of rigorous multicenter trials or international consensus statements has led to the dominance of single-center studies in shaping current opinion regarding intraoperative lung transplantation support.

Beyond outcome comparisons of ECLS to no ECLS utilization, one aspect of tailoring an intraoperative approach may be related to balancing resultant perioperative morbidities and recipient characteristics such as etiology of end-stage lung disease (ESLD). For instance, a recent systematic review noted the negative influence of intraoperative ECLS on development of acute kidney injury (AKI),⁵ and perioperative bleeding has been shown to increase in the setting of perioperative ECMO use.⁶ On the other hand, use of VA ECMO intraoperatively has been reported to be associated with low rates of primary graft dysfunction.⁷ Finally, some data have shown the influence of etiology of recipient ESLD on intraoperative support requirements.⁸ Given the lack of definitive data to provide a universal solution to the question of an ECLS versus off-pump approach, the more data that become available to shape risk stratification of the respective “trade-offs” in the various techniques will build toward clarity among transplanting centers worldwide. It is within this clinical and research context that Chaudhry et al.⁹ present their research findings regarding predictive factors of AKI in off-pump lung transplantation.

The current study was designed as a single-center, retro-

spective cohort study at Vanderbilt University Medical Center. Inclusion criteria included all adult patients who underwent lung transplantation without ECLS between 2006 and 2016, and exclusion criteria were limited to patients who had perioperative ECLS.⁹ A total of 148 patients met inclusion criteria, and the primary outcome examined was the occurrence of AKI in the first 7 days postoperatively.⁹ In addition to examining this outcome, the authors sought to elucidate perioperative factors that were predictive for the development of AKI in off-pump lung transplantation. Acute kidney injury was evaluated as per the Kidney Disease: Improving Global Outcomes classification, and the authors defined AKI as an absolute increase of serum creatinine by 0.3 mg/dL or more within 48 hours or increasing serum creatinine of $\geq 150\%$ baseline within the primary outcome evaluation window of 7 days. Characteristics evaluated for potential predictive value of AKI included a plethora of recipient, surgical, and anesthetic factors. One of these factors included venous congestion, which was assessed by calculating the area under the curve (AUC) of the central venous pressure (CVP) greater than 12 mmHg. The authors chose a cutoff of 12 mmHg based on literature examining abdominal hypertension, which has been shown to be an influence on the development of AKI.⁹ Of note, CVP values of <0 or >50 mmHg were excluded from the AUC analysis secondary to the authors’ assessment that these values were not likely to be accurate measurements of ongoing right atrial physiology. In other characteristics, the medians for age and body mass index were 56 years and 25 ± 4.3 kg/m², respectively, 71% of patients underwent bilateral lung transplantation (BLT), and the most common etiologies of ESLD were idiopathic pulmonary fibrosis (IPF) (37.8%) and chronic obstructive pulmonary disease (COPD) (35.8%). Characteristics then were examined with exploratory univariate analysis to determine association with AKI, and subsequent multivariable logistic regression of select characteristics was performed to test independent association with AKI.

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The primary outcome of AKI was found in 63 of 148 patients (42.6%), with the predominance of AKI patients (68.2%) developing stage 1 AKI.⁹ Development of AKI resulted in a longer hospital stay (12 days *v* 10 days, $p < 0.001$), and exploratory univariate analysis revealed several recipient and surgical characteristics that were predictive of AKI. These included the following: younger age, lower preoperative hemoglobin level, amount of intraoperative packed red blood cell transfusion, acidosis on postoperative day 1, higher intraoperative peak lactate levels, and cystic fibrosis or COPD as recipient etiology of ESLD.⁹ Subsequent multivariable logistic regression was performed on these variables, as well as several other recipient characteristics including body mass index, surgery type, surgery duration, and AUC for both CVP and mean arterial pressure to capture the impact of venous congestion or hemodynamic instability on the development of AKI. After analysis, risks of AKI were seen to be decreased with every increase in 1 year of age (odds ratio [OR] 0.92, 95% CI: 0.87–0.98, $p = 0.008$) and with BLT as the surgery type as opposed to single lung transplantation (OR 0.09, 95% CI: 0.01–0.63, $p = 0.015$).⁹ Risk of developing AKI was noted to be increased when COPD was the etiology of recipient ESLD compared to IPF (OR 4.72, 95% CI: 1.44–15.56, $p = 0.011$). As the authors note, some of these findings contrast with current known literature on the topic of AKI in lung transplantation. For instance, increased age and BLT as the surgery type have been noted to be risk factors for AKI,⁵ whereas this current study found the opposite after multivariable logistic regression analysis of their cohort.⁹ Additionally, other factors that have been described to promote the development of AKI in lung transplantation, such as intraoperative hypotension, cystic fibrosis or IPF as etiology of ESLD, and PRBC transfusion, were not found to be predictive factors of AKI after multivariable analysis.^{5,9}

Whether or not to use ECLS for intraoperative lung transplantation is one of the major academic questions within lung transplantation management, and examining this study in the current research and clinical context of lung transplantation practice worldwide is key to understanding its application toward this question. Reports have described the impact of recipient, surgical, and anesthetic factors on perioperative outcomes in lung transplantation,^{10,11} yet current practice is often driven by single-center studies that are predominately retrospective in design. In addition to providing outcomes data from their cohorts, these studies provide us perspective to design future multicenter and prospective investigations to examine the influence of these diverse factors on overall outcomes. Examination of AKI in the off-pump population is an important topic, not only to provide us more data regarding incidence of this negative outcome, but also to analyze predictive factors that can be studied further. The authors' examination of etiology of ESLD as a potential contributing characteristic is an important one, not only because of their findings regarding the impact of COPD on AKI, but also because its inclusion to their study design represents a further progression of recent literature that has reported on the importance of examining ESLD in tailoring approaches to

intraoperative management.^{8,12} Applied to the broader question of whether or not to perform lung transplantation using ECLS support, these data from the study provide us insight as to which patients may be at increased risk for developing AKI in an off-pump cohort. As more understanding is gained as to the incidence and predictive risk factors for AKI in the off-pump cohort, the potential for a more comprehensive predictive model for perioperative risk within off-pump lung transplantation is realized, with future studies designed to compare this risk model against a model for an intraoperative ECLS approach.

The limitations of this study include a single-center retrospective observational design, limited sample size, and 10-year duration of study, which may lend itself toward era bias. However, when examining the findings of this study within morbidity risk stratification of the off-pump lung transplant population as well as the broader question of whether or not to use ECLS intraoperatively, the authors find a valuable addition to the literature that provides further insight into the incidence of AKI as well as predictive factors leading to perioperative AKI in lung transplantation. Although these data do not point to a definitive solution to the question regarding optimal intraoperative strategy, they do provide a further understanding into predictive modeling of the potential tradeoffs teams must consider when selecting whether or not to use ECLS for intraoperative support in lung transplantation.

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References

- Boettke P, Powell B. The political economy of the COVID-19 pandemic. *South Econ J* 2021;87:1090–106.
- Moreno Garijo J, Cypel M, McRae K, et al. The evolving role of extracorporeal membrane oxygenation in lung transplantation: Implications for anesthetic management. *J Cardiothorac Vasc Anesth* 2019;33:1995–2006.
- Subramaniam K, Rio JMD, Wilkey BJ, et al. Anesthetic management of lung transplantation: Results from a multicenter, cross-sectional survey by the society for advancement of transplant anesthesia. *Clin Transplant* 2020;34:e13996.
- Hoetzenecker K, Schwarz S, Muckenhuber M, et al. Intraoperative extracorporeal membrane oxygenation and the possibility of postoperative prolongation improve survival in bilateral lung transplantation. *J Thorac Cardiovasc Surg* 2018;155:2193–206;e2193.
- Lertjitbanjong P, Thongprayoon C, Cheungpasitporn W, et al. Acute kidney injury after lung transplantation: A systematic review and meta-analysis. *J Clin Med* 2019;8:1713.
- Adelmann D, Koch S, Menger J, et al. Risk factors for early bleeding complications after lung transplantation – a retrospective cohort study. *Transpl Int* 2019;32:1313–21.
- Hoetzenecker K, Benazzo A, Stork T, et al. Bilateral lung transplantation on intraoperative extracorporeal membrane oxygenator: An observational study. *J Thorac Cardiovasc Surg* 2020;160:320–7;e321.
- Fessler J, Davignon M, Sage E, et al. Intraoperative implications of the recipients' disease for double-lung transplantation. *J Cardiothorac Vasc Anesth* 2021;35:530–8.

- 9 Chaudhry R, Wanderer JP, Mubashir T, et al. Incidence and predictive factors of acute kidney injury after off-pump lung transplantation. *J Cardiothorac Vasc Anesth* 2022;36:93–9.
- 10 Martin AK, Yalamuri SM, Wilkey BJ, et al. The impact of anesthetic management on perioperative outcomes in lung transplantation. *J Cardiothorac Vasc Anesth* 2020;34:1669–80.
- 11 Martin AK, Renew JR, Jayaraman AL, et al. Analysis of outcomes in lung transplantation. *J Cardiothorac Vasc Anesth* 2019;33:1455–66.
- 12 Martin AK, Fritz AV, Wilkey BJ. Anesthetic management of lung transplantation: Impact of presenting disease. *Curr Opin Anaesthesiol* 2020;33:43–9.