OPEN

Association of Perioperative Variables and the Acute Respiratory Distress Syndrome in Liver Transplant Recipients

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Background. The assessment of perioperative risk factors for the development of acute respiratory distress syndrome (ARDS) has been described in various surgical populations. However, there are only limited data among patients undergoing liver transplantation (LT), particularly regarding the influence of intraoperative ventilation parameters. We sought to identify the perioperative risk factors associated with the development of ARDS in LT recipients. **Methods.** This is a single-center, retrospective cohort study of adult patients who underwent LT at a tertiary academic medical center between January 1, 2006, and January 31, 2016. Postoperative ARDS was identified using the Berlin definition. Multivariable logistic regression analysis was used to identify perioperative risk factors for ARDS. **Results.** Of 817 eligible patients who underwent an LT during the study period, 20 (2.45%) developed postoperative ARDS. In the preoperative model, ongoing dialysis (odds ratio, 6.41; $P < 0.01$) was identified as an independent risk factor of ARDS post-LT. A higher mean peak inspiratory pressure per increase of 1 cm H_2O (odds ratio, 1.31; $P < 0.01$) was the only independent risk factor in the intraoperative model. Patients who developed ARDS postoperatively had significantly greater intensive care unit and hospital stay compared to non-ARDS patients ($P < 0.001$). There were no significant differences in the 30-day ($P = 0.16$) and 1-year ($P = 0.51$) mortality between the groups. **Conclusions.** Dialysis at the time of transplant and elevated intraoperative mean peak inspiratory pressure were associated with the development of ARDS. ARDS post LT was associated with increased intensive care unit and hospital length of stay, but not increased mortality.

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Liver transplantation (LT) represents the only definitive treatment of end-stage liver disease. In the United States, nearly 6800 liver transplants are performed each year.[1] Since its first description in 1963 by Starzl et al,[2] the perioperative outcomes have markedly improved.[3] The proportion of patients discharged alive has increased (78.2%–91.8%), while the postdischarge mortality at 1-, 3- and 5-year remains variable, ranging between 6.7% and 8.0%, 15.2% and 17.2%, and 22.5% and 24.5%, respectively.[3] Despite continual advancements in surgical techniques and patient care, LT still confers a significant risk of perioperative morbidity and postdischarge mortality.[3]

Postoperative pulmonary complications are frequent following LT.[4-8] The surgical procedure encompasses an extensive upper abdominal dissection, which can itself lead to respiratory morbidities.[9] The intraoperative hemodynamic instability and the potential for massive blood loss leading to large volume shifts and transfusion of numerous blood products

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further contribute to the higher incidence of pulmonary complications among LT patients.[10-13]

Acute respiratory distress syndrome (ARDS) is a life-threatening clinical condition characterized by noncardiac hypoxemia following an identified insult that ultimately leads to respiratory failure.[14] It is considered one of the most devastating complications during the postoperative period of general surgical procedures with an overall in-hospital-associated mortality exceeding 30%.[15] Among LT patients, the incidence of ARDS has been reported as 0.9%–17.5%.[4-6,8] A recent study using the 2012 Berlin definition of ARDS,[14] reported an incidence of 4.1%.[7]

Aside from the use of lung-protective ventilation strategies[16] and fluid restriction,[17] the management of ARDS remains largely supportive. Despite a substantial investment in clinical and basic science ARDS research over the past few decades, the current treatment strategies are directed toward the identification and further prevention of risk factors.[18] Although the assessment of perioperative risk factors in ARDS has been documented in various surgical populations,[18,19] there are only limited data among LT recipients,[7] particularly regarding the potential influence of intraoperative ventilation parameters. In the present study, we sought to determine the incidence and the preoperative and intraoperative variables associated with the development of ARDS following LT in a large tertiary referral center.

MATERIALS AND METHODS

Study Design and Patient Selection

This is a single-center, retrospective cohort study of adult patients who underwent orthotropic LT at a tertiary-level academic medical center. The study population included persons aged 18 years or older who underwent LT at Mayo Clinic (Rochester, MN) between January 1, 2006, and January 31, 2016. Patients who developed postoperative ARDS were identified using an electronic search algorithm and verified by manual chart review applying the Berlin definition of ARDS.[14] Patients were initially identified by a Pao_2/FiO_2 ratio less than 300 mm Hg. A clinical review was subsequently completed to rule patients in or out for ARDS. If the patient was diagnosed with ARDS by the bedside clinician, the patient was ruled in. If a diagnosis of acute hypoxemic respiratory failure secondary to hypervolemia, cardiogenic shock, or if congestive heart failure was thought to contribute to hypoxia, ARDS was ruled out. In patients where the diagnosis was less clear, imaging studies, clinical documentation, and echocardiography were reviewed to establish a final diagnosis. Severity class of ARDS was assigned based on oxygenation (Po_2 and fraction of inspired oxygen ratio, Pao_2/FiO_2) following the same definition: mild (200 mm Hg < Pao_2/FiO_2 ≤ 300 mm Hg), moderate (100 mm Hg < Pao_2/FiO_2 ≤ 200 mm Hg), and severe (Pao_2/FiO_2 ≤ 100 mm Hg). The etiology of ARDS was collected by manual chart review. The type of ARDS was classified as primary (pulmonary cause) or secondary (nonpulmonary cause) based on the most likely etiology. Postoperative infections were also noted in a post hoc review of the ARDS cases (**Supplementary Table 1, SDC,** http://links.lww.com/TXD/A233). Patients who developed ARDS were treated in accordance with an established institutional protocol for ARDS management based on ARDS Network guidelines under the direction of the attending intensive care unit (ICU) physician. All transplanted patients underwent pretransplant evaluation including cardiopulmonary assessments per our institutional protocol. Transplantation was performed using partial inferior vena cava occlusion, and venovenous bypass was not utilized. Anesthesia was supervised by members of a dedicated transplant anesthesia team. A volatile-based anesthetic was used; intraoperative hemodynamic management including fluid administration was guided by invasive intraoperative monitoring, including pulmonary artery catheterization and/or transesophageal echocardiography at the discretion of the attending anesthesiologist. Ventilation management included the use of lung protective ventilation strategies. Exclusion criteria included individuals <18 years old, retransplanted patients, combined organ transplants (heart/liver, lung/liver, heart/lung/liver, or liver/kidney), and patients meeting the diagnostic criteria of ARDS preoperatively. This study was approved by the institutional review board at Mayo Clinic, Rochester, MN (Institutional Review Board protocol #15-009624). The requirement for written informed consent was waived.

Data Collection

Data were obtained from institutionally maintained databases and the electronic medical record. Electronic searches were supplemented by manual review as needed. Perioperative data were obtained from an institutionally maintained archive of perioperative data.

Etiology of liver disease was defined as the presumptive primary cause of liver failure when multiple etiologies were documented in the medical record. Perioperative variables obtained included perioperative renal replacement therapy, Charlson comorbidity index, hypertension, diabetes mellitus, chronic obstructive pulmonary disease, asthma, Model for End-Stage Liver Disease (MELD), operative duration, blood product requirements, vasoactive medications, and mechanical ventilation data. Preoperative, intraoperative, postoperative, and donor variables were compared between patients with and without postoperative ARDS.

Outcomes

The primary outcome was the incidence of post-LT ARDS using the Berlin definition. The secondary outcomes included 30-day and 1-year mortality, and hospital and ICU length of stay.

Statistical Analysis

Patient demographics, preoperative variables, and intraoperative factors were descriptively summarized by ARDS using frequencies and percentages for categorical variables and medians and interquartile ranges for continuous variables. Univariate comparisons of data distributions across ARDS status were analyzed using Chi-square/Fisher exact tests (where appropriate) for categorical variables, and Wilcoxon rank-sum tests for continuous variables.

Multivariable associations between preoperative variables, intraoperative factors, and ARDS status were analyzed using multivariable logistic regression models. Variables missing in fewer than 33% of the cohort (body mass index [BMI] 6%, peak inspiratory pressure [PIP] 10%, urine 12.9%, tidal volume [TV] 13.7%, cell saver volume 18.7%, red blood cell [RBC]) volume were substituted using imputation methods.[20,21] Data were assumed to be missing at random. We imputed 10 independent datasets and analyzed associations between variables and the outcomes in each imputation dataset. The final chosen variables were then combined across imputation sets to arrive at one final set of parameter estimates.[20,21]

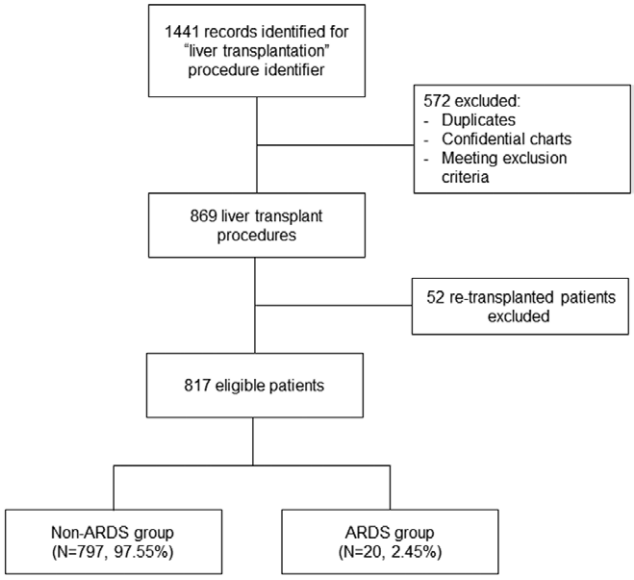

FIGURE 1. Selection of study population. ARDS, acute respiratory distress syndrome

Our final model variables were selected using a least absolute shrinkage and selection operator-based logistic regression. A total of 21 (age, sex, American Society of Anesthesiology physical status classification system, BMI, dialysis, etiology, hypertension, diabetes mellitus, chronic obstructive pulmonary disease, asthma, MELD, creatinine, bilirubin, international normalized ratio, operation time, RBC, cell saver volume [salvaged blood], urine, TV, PIP, and Pao_2) variables were considered. The chosen variables were then fit and summarized in a multivariable logistic regression model.

Univariate associations between ARDS and the outcomes of discharge alive from the hospital and ICU were analyzed using cumulative incidence curves, with death in the ICU/hospital treated as a competing event.[22] Associations between ARDS and death within 30 and 365 days were analyzed using cumulative incidence curves. All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC). A 2-sided $P < 0.05$ was considered significant.

RESULTS

Overview of the Study Cohort

Of 817 eligible patients who underwent an LT during the study period, 20 (2.45%) were complicated by the development of postoperative ARDS (Figure 1). Based on the Berlin definition of ARDS criteria,[14] half of these patients were classified as moderate ARDS (N = 10, 50%), with mild (N = 7, 35%) and severe (N = 3, 15%) less common. The majority (n = 16, 80%) of ARDS cases were diagnosed between postoperative days 0 and 2, and the rest occurred between postoperative days 3 and 7 (n = 4, 20%). In 19/20 cases, an associated infective process was identified postoperatively, but unlikely to be the inciting cause of ARDS (**Supplementary Table 1, SDC,** http://links.lww.com/TXD/A233).

Univariate Analysis of the Study Cohort

The baseline and preoperative characteristics among ARDS and non-ARDS study groups are displayed in Table 1. In the univariate analysis, there were no significant differences recorded in age, sex, Charlson comorbidity index, etiology of liver disease, and major comorbidities between both study groups. However, patients with ARDS had significantly higher BMI, requirement of dialysis, and American Society of Anesthesiology physical status classification compared with the non-ARDS group. Additionally, ARDS patients had significantly higher preoperative MELD scores, with serum creatinine levels and total serum bilirubin being higher.

In the univariate analysis of intraoperative data, the transfusion requirements of blood products including cell saver, fresh frozen plasma (FFP), and packed RBCs were significantly higher among patients with ARDS compared to those without the disease (Table 2). With the exception of vasopressin,

TABLE 1.
Preoperative factors by ARDS

Characteristic	NoN = 797	YesN = 20	*P*
Patient demographics			
Age			0.466[a]
Median (Q1, Q3)	56 (49, 61)	59.5 (51.0, 62.0)	
Range	18, 72	32, 66	
Sex			0.096[b]
Female	289 (36.3%)	11 (55.0%)	
Male	508 (63.7%)	9 (45.0%)	
ASA type			0.010[a]
Median (Q1, Q3)	4 (3, 4)	4 (4, 4)	
Range	2, 5	3, 5	
BMI			0.040[a]
Missing	55	1	
Median (Q1, Q3)	27.1 (23.4, 31.7)	31.8 (25.0, 38.0)	
Range	14.8, 90.9	20.3, 43.6	
Dialysis	21 (2.6%)	8 (40.0%)	<0.001[b]
Charlson Comorbidity Index			0.090[a]
Median (Q1, Q3)	6 (4, 8)	7.0 (6.0, 8.5)	
Range	0, 15	0, 12	
Etiology			0.102 [b]
Alcoholic cirrhosis	108 (13.6%)	5 (25.0%)	
PBC/PSC/autoimmune	226 (28.4%)	8 (40.0%)	
Others	463 (58.1%)	7 (35.0%)	
Comorbidities			
Hypertension	248 (31.1%)	9 (45.0%)	0.199 [b]
DM	220 (27.6%)	5 (25.0%)	0.805 [b]
COPD	33 (4.1%)	0 (0.0%)	1.000[c]
Asthma	55 (6.9%)	1 (5.0%)	1.000 [c]
Preoperative Laboratory values			
MELD			<0.001[a]
Median (Q1, Q3)	27.1 (20.8, 33.8)	36.2 (32.9, 39.5)	
Range	7.1, 59.2	23.5, 44.2	
Max creatinine (within 30 days)			<0.001[a]
Median (Q1, Q3)	1.6 (1.1, 2.5)	3.5 (2.3, 4.0)	
Range	0.6, 12.3	0.6, 5.5	
Max bilirubin (within 30 days)			0.005[a]
Median (Q1, Q3)	5.0 (3.2, 8.8)	8.8 (5.8, 18.1)	
Range	0.7, 58.0	2.3, 30.7	
Max INR (within 30 days)			0.114[a]
Median (Q1, Q3)	2.3 (1.8, 3.0)	2.7 (2.4, 2.9)	
Range	1.1, 10.2	1.6, 3.6	

Numbers indicate N (%) unless otherwise noted.[a]Wilcoxon.
[b]Chi-square.
[c]Fisher exact.
ARDS, acute respiratory distress syndrome; ASA, American Society of Anesthesiology; BMI, body mass index; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; INR, international normalized ratio; MELD, Model for End-Stage Liver Disease PBC, primary biliary cirrhosis; PSC, primary sclerosing cholangitis.

TABLE 2.

Intraoperative factors by ARDS

Characteristic	NoN = 797	YesN = 20	*P*
OR time (min)			0.999[a]
Median (Q1, Q3)	350.5 (300.9, 408.9)	357.8 (291.3, 408.9)	
Range	149.0, 788.9	262.7, 549.1	
Transfusion volume			
RBC (mL)			0.010[a]
Median (Q1, Q3)	1330 (663, 2100)	1756.4 (1444.8, 2970.0)	
Range	85.0, 14190.0	815.6, 9450.0	
FFP (mL)			0.024[a]
Median (Q1, Q3)	1555.7 (960.0, 2401.0)	2137.4 (1590.7, 2875.0)	
Range	27, 12720	536.0, 9744.0	
Cryoprecipitate (mL)			0.723[a]
Median (Q1, Q3)	207.5 (182.0, 378.5)	200 (190, 398)	
Range	0, 1108	53.3, 817.0	
Platelets (mL)			0.040[a]
Median (Q1, Q3)	510.0 (283.5, 874.0)	769.0 (435.0, 1147.5)	
Range	0, 3721	127.0, 2778.9	
Cell saver (mL)			0.094[a]
Median (Q1, Q3)	1012.5 (500.0, 2000.0)	1437.7 (1046.0, 1800.0)	
Range	78.3, 21153.0	361.8, 10350.0	
Urine (mL)			0.187[a]
Median (Q1, Q3)	381.3 (200.0, 590.8)	300 (60, 500)	
Range	3, 3475	10, 800	
Vasoactive medications (cumulative dose)			
Norepinephrine (μg)			0.354[a]
Median (Q1, Q3)	3.6 (0.0, 44.8)	19.4 (0.0, 46.0)	
Range	0.0, 383.5	0.0, 308.4	
Vasopressin (units)			0.040[a]
Median (Q1, Q3)	0 (0, 0)	0.0 (0.0, 30.6)	
Range	0.0, 185.4	0.0, 68.0	
Epinephrine (μg)			0.148[a]
Median (Q1, Q3)	0 (0, 0)	0 (0, 0)	
Range	0.0, 183.5	0.0, 41.3	
Phenylephrine (μg)			0.217[a]
Median (Q1, Q3)	0.0 (0.0, 12.7)	0 (0, 0)	
Range	0.0, 9066.2	0.0, 23.1	
Mean TV (mL/kg)			0.402[a]
Median (Q1, Q3)	5.8 (4.9, 6.6)	5.4 (4.6, 6.4)	
Range	0.0, 10.1	3.7, 8.2	
Mean PIP (cm H_20)			<0.001[a]
Median (Q1, Q3)	17.9 (15.7, 20.7)	26.2 (21.4, 29.9)	
Range	10.9, 41.4	16.2, 36.1	
Mean Pao_2			<0.001[a]
Median (Q1, Q3)	215.6 (177.3, 259.2)	160.8 (127.8, 179.5)	
Range	64.2, 425.0	83.6, 260.8	

[a]Wilcoxon.

ARDS, acute respiratory distress syndrome; FFP, fresh frozen plasma; OR, odds ratio; PIP, peak inspiratory pressure; RBC, red blood cell; TV, tidal volume.

the cumulative dose of vasoactive medications was similar between both study groups. Although, the mean PIP was significantly higher among ARDS patients compared to those without ARDS, the mean Pao_2 was lower in the ARDS group versus the non-ARDS group.

Multivariable Analysis of the Study Cohort

Two variables were selected using the least absolute shrinkage and selection operator-based logistic regression (dialysis and PIP). Our final model then consisted of dialysis and PIP (Table 3). Dialysis (odds ratio = 6.41; $P \leq 0.01$) and 1 cm H_2O increase in PIP (odds ratio = 1.31; $P < 0.01$) were significantly associated with increased odds of developing ARDS.

Postoperative Outcomes

ARDS patients were discharged alive from the ICU significantly slower than non-ARDS patients (Figure 2, $P < 0.001$), with a median discharge of 13.2 days (95% confidence interval [CI] 9.4, 20.0) days compared to 1.5 days (95% CI 1.4, 1.5) for non-ARDS patients. Similarly, ARDS patients had longer lengths of hospital stays relative to non-ARDS patients (Figure 3, $P < 0.01$) with a median discharged alive time of 39.9 days (95% CI = 27.8, 46.5) compared to non-ARDS

TABLE 3.

Patient characteristics associated with ARDS using multivariable logistic regression analysis

Characteristic	OR (95% CI)	*P*
Dialysis	6.41 (1.61, 25.50)	<0.01
PIP (per 1 cm H_2O increase)	1.31 (1.18, 1.46)	<0.01

The main effect terms were selected via LASSO regression analysis.
ARDS, acute respiratory distress syndrome; CI, confidence interval; LASSO, least absolute shrinkage and selection operator; OR, odds ratio; PIP, peak inspiratory pressure.

median days discharged alive of 9.9 days (95% CI = 9.6, 10.3; $P = 0.01$). There were no statistically significant differences in mortality within 30 days ($P = 0.16$) and 1 year of the procedure ($P = 0.51$) (**Supplementary Figures 1 and 2, SDC,** http://links.lww.com/TXD/A233).

DISCUSSION

This large single-center retrospective study of 817 patients revealed an incidence of ARDS post LT of 2.45%. One preoperative factor (ongoing dialysis) and 1 intraoperative factor (mean PIP) were associated with the development of ARDS post LT. Moreover, ARDS post LT was associated with increased ICU and hospital length of stay, but not increased mortality.

The reported incidence of ARDS post-LT has ranged between 1% and 30%.[4,8,12,23] The large variability is most likely owing to the changes in the diagnostic criteria/definition of ARDS during the past several decades.[24] In our study, the incidence of ARDS post-LT was 2.45%, which is consistent with the current data among other high-risk surgical patient populations.[25,26] The only study available in the literature with

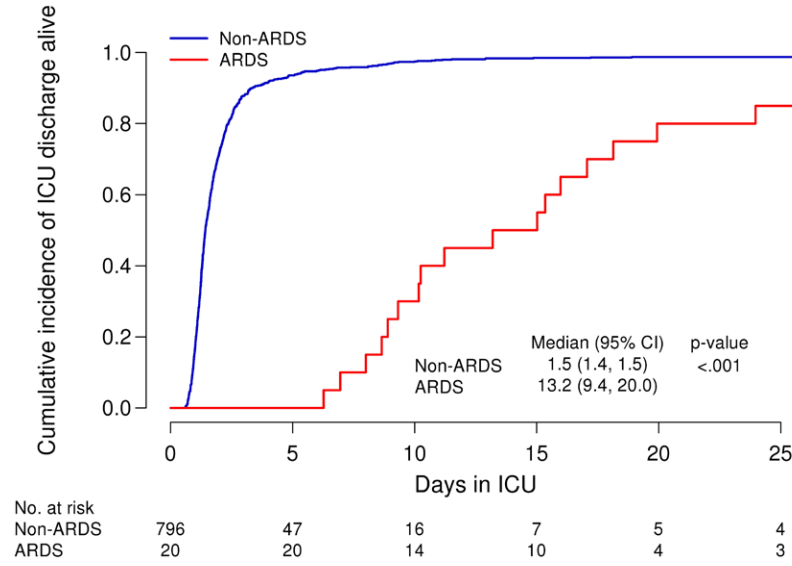

FIGURE 2. Cumulative incidence curves for ICU length of stay. Estimated cumulative incidence curves for ICU length of stay among ARDS and non-ARDS patients. ARDS, acute respiratory distress syndrome; ICU, intensive care unit.

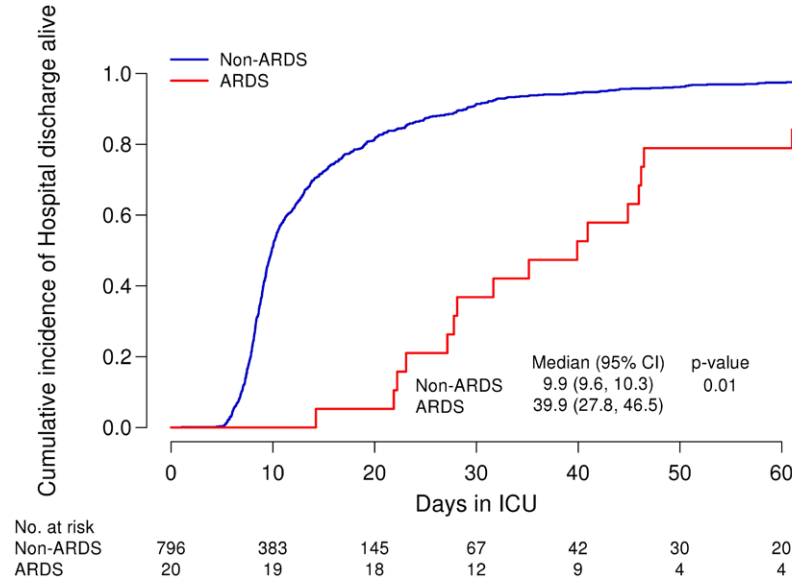

FIGURE 3. Cumulative incidence curves for hospital length of stay. Estimated cumulative incidence curves for hospital length of stay among ARDS and non-ARDS patients. ARDS, acute respiratory distress syndrome; CI, confidence interval; ICU, intensive care unit.

a comparable LT population after the introduction of the Berlin definition reported an incidence of ARDS of 4.1%.[7,14]

Although several recent clinical trials have focused on conditions associated with ARDS in general medical populations (ie, sepsis, pneumonia, massive blood transfusion, multiorgan dysfunction, and aspiration of gastric contents), there is a relative paucity of surgical population-specific data, especially among patients undergoing LT.[24] A previous large retrospective study conducted by Zhao et al analyzed the preoperative and intraoperative risk factors of ARDS post LT using the Berlin criteria.[7] Similar to our study, the authors found that although the MELD score was significantly higher among ARDS post-LT recipients in the univariate analysis, it was not an independent risk factor in the multivariable analysis.[7] However, they showed that an elevated preoperative total bilirubin level was associated with increased odds of ARDS.[7] We did not find any association between any of the components of the MELD score, including the bilirubin. We hypothesized that this could be related to a lack of power as we only had relatively few ARDS events in our cohort.

Furthermore, our study found an association between dialysis and the development of ARDS post LT. These results are consistent with a large retrospective analysis of a general surgical population that showed that renal failure is an independent risk factor of ARDS.[15] Although fluid overload is a well-described risk factor of ARDS, especially after blood product transfusion,[12,15] our data did not indicate a statistically significant association between intraoperative blood product administration (including RBCs, fresh frozen plasma, cryoprecipitate, and platelets) and ARDS in our multivariable analysis. However, the volume of blood product transfusion was significantly higher in the ARDS group compared to the non-ARDS group on our univariate analysis. The lack of association once we controlled for other variables could be explained by the low number of ARDS events in total and the covariates controlled during the matching process.

To our knowledge, this is the first study that assesses the impact of intraoperative ventilatory parameters in ARDS among patients post LT after the implementation of the Berlin definition criteria. Zhao et al[7] revealed that patients with preoperative requirement of intubation and ventilation had twice the odds of developing postoperative ARDS than patients without preoperative intubation. The authors did not have the ventilator settings data available at the time of their study, but highlighted the importance of additional studies to assess the impact of intraoperative ventilator settings in the outcomes of ARDS in LT recipients.[7] Here we found that higher mean PIP was associated with the development of ARDS.

Recent clinical practice guidelines endorsed by multiple societies recommended the use of mechanical ventilation using lower inspiratory pressures (plateau pressure < 30 cm H_2O) and lower TVs (4–8 mL/kg predicted body weight) in patients with ARDS.[27] Also, there is evidence that low-TV ventilation can benefit intermediate and high-risk patients undergoing major abdominal surgery.[28] In our study, patients were ventilated with either volume-controlled ventilation or pressure-controlled ventilation during the transplant procedure with both the mode and settings at the discretion of the attending anesthesiologist with the goal of providing lung protective ventilation. Any level of positive end-expiratory pressure was also set by the provider. We did not obtain plateau pressures, as this information was not available in the electronic intraoperative record. Intraoperatively, we found that higher mean PIP, but not necessarily higher TV, was associated with ARDS post LT. As low TV ventilation is our standard practice, perhaps we did not see an association between TV and the development of ARDS owing to a low number of patients in our study population receiving high TV. We suggest, however, that higher PIP identifies a group of patients with altered lung mechanics that are at risk for or are developing ARDS during LT.

Our study has several limitations. First, it is a retrospective study with the inherent limitations of this type of analysis. It precludes the ability to infer the causation of ARDS post LT and the clinical outcomes studied. Second, this is a single-center institutional cohort, which limits the external validity of the results. Third, we were unable to retrieve plateau pressure data from our database which limits an accurate estimation of the static compliance of the lungs. Nonetheless, we were able to collect the PIP data as a surrogate for airway resistance and lung compliance as PIP represents a close estimate of the plateau pressure in the absence of clinical conditions that affect the airway resistance. Fourth, the low number of actual cases and missing data for some variables might have limited our ability to detect differences between both study groups. Fifth, although there is a small chance of transfusion-related acute lung injury being misclassified as ARDS, we think this would only represent a very small number of our sample as our intensivists are well aware of transfusion-related acute lung injury given ongoing research and interest in the area at our institution. Finally, we were unable to capture donor organ variables that might have contributed to our outcome of interest such as the donor risk index. Further prospective studies should be conducted to assess the impact of the plateau pressure and the PIP in the intraoperative and postoperative outcomes of patients with ARDS post LT.

In summary, the incidence of ARDS post LT in our study population was 2.45% and the development of ARDS was associated with ongoing dialysis and an elevated mean PIP intraoperatively. Additionally, ARDS following LT is associated with an increased ICU and hospital length of stay. Clinicians should be cognizant of theses associations to identify patients at risk for postoperative lung injury following LT.

REFERENCES

1. Fayek SA, Quintini C, Chavin KD, et al. The current state of liver transplantation in the united states: perspective from American Society of Transplant Surgeons (ASTS) scientific studies committee and endorsed by ASTS council. *Am J Transplant.* 2016;16:3093–3104.
2. Starzl TE, Marchioro TL, Vonkaulla KN, et al. Homotransplantation of the liver in humans. *Surg Gynecol Obstet.* 1963;117:659–676.
3. Stepanova M, Wai H, Saab S, et al. The outcomes of adult liver transplants in the United States from 1987 to 2013. *Liver Int.* 2015;35:2036–2041.
4. Hong SK, Hwang S, Lee SG, et al. Pulmonary complications following adult liver transplantation. *Transplant Proc.* 2006;38:2979–2981.
5. Bozbas SS, Eyuboglu FO, Ozturk Ergur F, et al. Pulmonary complications and mortality after liver transplant. *Exp Clin Transplant.* 2008;6:264–270.
6. Golfieri R, Giampalma E, Morselli Labate AM, et al. Pulmonary complications of liver transplantation: radiological appearance and statistical evaluation of risk factors in 300 cases. *Eur Radiol.* 2000;10:1169–1183.
7. Zhao W, Ge X, Sun K, et al. Acute respiratory distress syndrome after orthotopic liver transplantation. *J Crit Care.* 2016;31:163–167.
8. Jensen WA, Rose RM, Hammer SM, et al. Pulmonary complications of orthotopic liver transplantation. *Transplantation.* 1986;42:484–490.

9. Ford GT, Rosenal TW, Clergue F, et al. Respiratory physiology in upper abdominal surgery. *Clin Chest Med.* 1993;14:237–252.
10. Khan H, Belsher J, Yilmaz M, et al. Fresh-frozen plasma and platelet transfusions are associated with development of acute lung injury in critically ill medical patients. *Chest.* 2007;131:1308–1314.
11. de Boer MT, Christensen MC, Asmussen M, et al. The impact of intraoperative transfusion of platelets and red blood cells on survival after liver transplantation. *Anesth Analg.* 2008;106:32–44, table of contents.
12. Pereboom IT, de Boer MT, Haagsma EB, et al. Platelet transfusion during liver transplantation is associated with increased postoperative mortality due to acute lung injury. *Anesth Analg.* 2009;108:1083–1091.
13. Benson AB, Burton JR Jr, Austin GL, et al. Differential effects of plasma and red blood cell transfusions on acute lung injury and infection risk following liver transplantation. *Liver Transpl.* 2011;17:149–158.
14. Ranieri VM, Rubenfeld GD, Thompson BT, et al.; ARDS Definition Task Force. Acute respiratory distress syndrome: the Berlin definition. *JAMA.* 2012;307:2526–2533.
15. Blum JM, Stentz MJ, Dechert R, et al. Preoperative and intraoperative predictors of postoperative acute respiratory distress syndrome in a general surgical population. *Anesthesiology.* 2013;118:19–29.
16. Acute Respiratory Distress Syndrome Network, Brower RG, Matthay MA, et al. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med*. 2000;342:1301–1308.
17. National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network, Wiedemann HP, Wheeler AP, et al. Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med*. 2006;354:2564–2575.
18. Kor DJ, Lingineni RK, Gajic O, et al. Predicting risk of postoperative lung injury in high-risk surgical patients: a multicenter cohort study. *Anesthesiology.* 2014;120:1168–1181.
19. Kor DJ, Warner DO, Alsara A, et al. Derivation and diagnostic accuracy of the surgical lung injury prediction model. *Anesthesiology.* 2011;115:117–128.
20. Schafer JL. Multiple imputation: a primer. *Stat Methods Med Res.* 1999;8:3–15.
21. Rubin DB. Multiple imputation after 18+ years. *J Am Stat Assoc*. 1996;91:473–489.
22. Gooley TA, Leisenring W, Crowley J, et al. Estimation of failure probabilities in the presence of competing risks: new representations of old estimators. *Stat Med.* 1999;18:695–706.
23. Li GS, Ye QF, Xia SS, et al. Acute respiratory distress syndrome after liver transplantation: etiology, prevention and management. *Hepatobiliary Pancreat Dis Int.* 2002;1:330–334.
24. Thompson BT, Chambers RC, Liu KD. Acute respiratory distress syndrome. *N Engl J Med.* 2017;377:562–572.
25. Licker M, de Perrot M, Spiliopoulos A, et al. Risk factors for acute lung injury after thoracic surgery for lung cancer. *Anesth Analg.* 2003;97:1558–1565.
26. Shari G, Kojicic M, Li G, et al. Timing of the onset of acute respiratory distress syndrome: a population-based study. *Respir Care.* 2011;56:576–582.
27. Fan E, Del Sorbo L, Goligher EC, et al; American Thoracic Society, European Society of Intensive Care Medicine, and Society of Critical Care Medicine. An official American Thoracic Society/European Society of intensive care medicine/society of critical care medicine clinical practice guideline: mechanical ventilation in adult patients with acute respiratory distress syndrome. *Am J Respir Crit Care Med.* 2017;195:1253–1263.
28. Futier E, Constantin JM, Paugam-Burtz C, et al; IMPROVE Study Group. A trial of intraoperative low-tidal-volume ventilation in abdominal surgery. *N Engl J Med.* 2013;369:428–437.