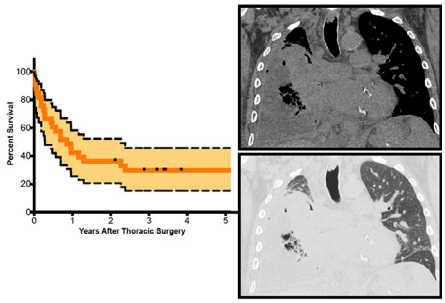
Predictors of Outcomes After Thoracic Surgery in Orthotopic Liver Transplant Recipients With Pleural Disease

Aditya S. Shirali, MD,[*] Jonathan Grotts, MA,[†] David Elashoff, PhD,[†] Igor Barjaktarevic, MD, PhD,[‡] Kathryn H. Melamed, MD,[‡] Julie Van Hassel, MS,[*] Robert B. Cameron, MD,[*] Jay M. Lee, MD,[*] and Jane Yanagawa, MD[*]

Orthotopic liver transplant (OLT) recipients are at high risk for postoperative pulmonary complications. We aim to determine factors associated with morbidity and mortality in OLT recipients that required thoracic surgery for pleural space complications. A retrospective review was performed of 42 patients who underwent thoracic surgery after OLT between 2005 and 2015. Preoperative data and postoperative outcomes were reviewed. Time to mortality was summarized using Kaplan-Meier curves. Outcomes associated with 30-day morbidity and mortality as well as long-term mortality were analyzed with univariate analysis. Between 2005 and 2015, 1735 OLTs were performed at our institution. We identified 42 patients who required thoracic surgery. Of these 42 OLT recipients, 33 patients required thoracic surgery for pleural space complications. The median interval between OLT and thoracic surgery for pleural space complications was 5.7 months (interquartile range 2.2–14.1). The most common surgical indications were chronic pleural effusion ($n = 12$, 36.4%) and empyema ($n = 10$, 30.3%). The most common thoracic operations were decortication and empyema evacuation. The 30-day morbidity was 69.7%. Bilirubin and empyema were significantly associated with 30-day morbidity (odds ratio [OR] = 2.3, $P = 0.023$; OR = 16.3, $P = 0.015$). The 30-day, 1-year, and 5-year mortality rates were 15.2%, 57.6%, and 70.2%, respectively. Vasopressor requirement was significantly associated with 30-day mortality (OR = 10.2, $P = 0.031$). The development of pleural space complications requiring surgery in OLT recipients suggests a poor prognosis. Hyperbilirubinemia and pleural space infections were associated with high postoperative morbidity in OLT recipients requiring thoracic surgery for pleural space complications.

Semin Thoracic Surg 31:604–611 © 2019 Elsevier Inc. All rights reserved.

Keywords: Pleural effusion, Thoracic surgery, Liver transplant



Pleural space complications portend poor prognosis in liver transplant recipients.

Central Message

Thoracic surgery for pleural space complications in liver transplant recipients is associated with significant risk. Patients with pleural space infections have high postoperative morbidity.

Perspective Statement

Liver transplant recipients are vulnerable to thoracic pathologies. A subset of these patients ultimately require thoracic surgery for pleural space complications, yet no evidence exists to guide thoracic surgeons in the management of this challenging patient population. We find that hyperbilirubinemia and pleural space infections are associated with high rates of postoperative morbidity.

Abbreviations: OLT, orthotopic liver transplantation; PPC, postoperative pulmonary complication; MELD, Model for End-Stage Liver Disease; OR, odds ratio; CI, confidence interval; VATS, video-assisted thoracoscopic surgery; IQR, interquartile range; HR, hazards ratio; ICU, intensive care unit

*Division of Thoracic Surgery, Department of Surgery, David Geffen School of Medicine at UCLA, Los Angeles, California
†Department of Medicine Statistics Core, David Geffen School of Medicine at UCLA, Los Angeles, California
‡Division of Pulmonary and Critical Care Medicine, David Geffen School of Medicine at UCLA, Los Angeles, California

Funding: None declared (A.S.S., J.G., D.E., J.V.H., R.B.C., J.M.L., J.Y.).

Author Contributions: A.S.S. and J.Y. had full access to all the data in the study and are responsible for the integrity of the data and accuracy of data analysis. I.B., K.H.M, J.V.H., R.B.C, and J.M.L contributed substantially to the study design, data analysis and interpretation, and writing of the manuscript. J.G and D.E. provided statistical analysis.

Role of Sponsors: The sponsor had no role in the design of the study, the collection and analysis of the data, or the preparation of the manuscript.

Address reprint requests to Jane Yanagawa, MD, David Geffen School of Medicine at UCLA, Box 957313, Room 64-124 CHS, 10833 Le Conte Avenue, Los Angeles, CA 90095-7313. E-mail: jyanagawa@mednet.ucla.edu

1043-0679/$–see front matter
https://doi.org/10.1053/j.semtcvs.2019.02.003

INTRODUCTION

Orthotopic liver transplantation (OLT) recipients are susceptible to postoperative pulmonary complications (PPC) due to a multitude of factors, including long operative times, massive blood loss and blood transfusions, and poor preoperative clinical condition.[1] Studies assessing the frequency of PPCs in OLT recipients have found pleural effusions to be the most prevalent, occurring in 69% of patients.[2,3] Although most pleural effusions in this population are treated conservatively with thoracenteses or tube thoracostomies, a subset of patients fail these measures and require surgery for pleural space complications. While several studies have assessed outcomes following cardiac and abdominal surgical intervention in liver transplant recipients, no study has investigated the morbidity and mortality following thoracic surgery for pleural disease in this patient population.[4,5]

The purpose of this study is to summarize our institution's experience with the surgical management of pleural space pathology in liver transplant recipients and to determine the predictors of surgical morbidity and mortality in this unique patient population.

METHODS

We reviewed our institutional database for patients who underwent OLT and subsequently required thoracic surgery between January 1, 2005 and December 31, 2015. Our principal study cohort consisted of patients who specifically underwent thoracic surgery for pleural space complications. The institutional review board approved this retrospective research and waived the need for individual informed consent.

Medical records were retrospectively reviewed for patient preoperative demographic information, preoperative clinical characteristics, operative procedures, postoperative complications, and last follow-up visit or date of death. Patient preoperative demographic and clinical information were collected pertaining to OLT and immediately prior to thoracic surgery. Patients were defined as having chronic obstructive pulmonary disease based on a forced expiratory volume in 1 second divided by a forced vital capacity that was <0.7 in the presence of a smoking history, obtained prior to OLT. Patients were identified as having portopulmonary hypertension when they were found with pulmonary arterial hypertension, as defined by right heart catheterization with mean pulmonary artery pressure greater than 25 mm Hg at rest and pulmonary capillary wedge pressure less than 15 mm Hg, in the setting of coexisting portal hypertension. Model for End-Stage Liver Disease (MELD) score was calculated based on serum bilirubin, INR, creatinine, and need for dialysis immediately prior to OLT. Liver disease etiologies included hepatocellular carcinoma, hepatitis C, alcohol, primary sclerosing cholangitis, drug toxicity, cryptogenic cirrhosis, hepatitis B, primary biliary cirrhosis, genetic, and other, which included Budd-Chiari syndrome and nonalcoholic steatohepatitis cirrhosis. Patients were identified as having trapped lung if they exhibited persistent hydropneumothorax following tube thoracostomy preoperatively or intraoperative inability to expand the lung. The surgical indications included in this study were chronic pleural effusions, acute hemothorax requiring intervention within 24 hours due to hemodynamic compromise, subacute hemothorax, and empyema. Chronic pleural effusions included in this cohort included nonmalignant pleural effusions refractory to medical therapy and tube thoracostomy. Subacute hemothoraces were defined as hemothoraces managed conservatively with tube thoracostomy, but ultimately requiring surgery greater than 24 hours following the development of hemothorax due to respiratory compromise. The surgical procedures performed included decortication, hemorrhage control, retained hemothorax evacuation, empyema evacuation, talc pleurodesis, and pleurectomy. The postoperative complications analyzed included pneumonia, atelectasis, bacteremia, intrathoracic hemorrhage, reintubation, prolonged intubation (>72 hours), tracheostomy, multisystem organ failure, atrial fibrillation, pulmonary embolism, empyema, and myocardial infarction.

Statistical Analysis

Descriptive statistics for categorical variables are reported as frequency and percentage, and continuous variables are reported as median (interquartile range or IQR) as appropriate. For comparisons of continuous and categorical variables, the Wilcoxon Rank Sum Test or Fisher's exact test were used as appropriate. All statistical tests were two-sided with $P < 0.05$ defined as achieving significance. Results from univariate analyses are reported as odds ratios (OR) with a 95% confidence intervals as well as Wilcoxon P values, as this is a more conservative test with the available sample size. OR were calculated based on a Firth regression model. Kaplan-Meier curves were used to display survival. Multivariable logistic regression was not performed due to the small sample size. A univariate Cox proportional hazards model was used to evaluate the relationship between covariates and time to mortality due to the small sample size. Covariates with an insufficient sample size (eg, pleural effusions after OLT) were not reported. Results from the Cox proportional hazards model are reported as hazards ratios with a 95% confidence intervals. All statistical analyses were performed using SPSS (SPSS, Chicago, IL).

RESULTS

We identified 1735 patients who underwent OLT between January 1, 2005 and December 31, 2015, of whom 42 patients subsequently required thoracic surgery. Among these 42 patients, 33 underwent thoracic surgery for pleural space complications and served as the principal study cohort. The 9 patients excluded from the pleural space complication cohort included 6 patients who underwent lung resection for malignancy, 2 patients who required esophageal repair for iatrogenic perforation, and 1 patient who

Table 1. Patient Demographics Prior to Liver Transplantation ($N = 33$)

Characteristic	Value
Age (y)	58 (51–64)
Gender	
Male	20 (61%)
Female	13 (39%)
Smoker	21 (63.4%)
Past	20/21 (95.2%)
Current	1/21 (4.8%)
Pack-years	10 (8–30)
COPD	1 (3.0%)
Portopulmonary hypertension	6 (18.1%)
Chronic pleural effusions	15 (45.5%)
Pleural effusions requiring tube thoracostomy	15/15 (100%)
Liver disease etiology	
Hepatocellular carcinoma	12 (36.4%)
Hepatitis C	8 (24.2%)
Alcohol	3 (9.1%)
Primary sclerosing cholangitis	2 (6.1%)
Drug toxicity	2 (6.1%)
Cryptogenic	1 (3.0%)
Hepatitis B	1 (3.0%)
Primary biliary cirrhosis	1 (3.0%)
Genetic	1 (3.0%)
Other	2 (6.1%)
MELD prior to OLT	35 (28–40)

COPD, chronic obstructive pulmonary disease; MELD, Model of End-Stage Liver Disease; OLT, orthotopic liver transplantation.
Values are *n* (%) or median (IQR).

Table 2. Patient Clinical Characteristics Prior to Thoracic Surgery ($N = 33$)

Characteristic	Value
Surgical indication	
Chronic pleural effusion	12 (36.4%)
Empyema	10 (30.3%)
Hemothorax—acute	8 (24.2%)
Hemothorax—subacute	3 (9.1%)
Interval between OLT and thoracic surgery (mo)	
Chronic pleural effusion	6.6 (2.4–20.9)
Empyema	6.7 (3.5–28.4)
Hemothorax—acute	2.2 (1.6–7.3)
Hemothorax—subacute	3.4 (2.7–6.3)
Pleural effusions after OLT	32 (97.0%)
Pleural effusions requiring tube thoracostomy	20/32 (62.5%)
Trapped lung	22 (66.7%)
Ascites	10 (30.3%)
Vasopressor requirement	6 (18.2%)
Dialysis	15 (45.5%)
Creatinine (mg/dL) ($n = 18$)	1.4 (1.0–1.8)
INR	1.2 (1.1–1.3)
Bilirubin (mg/dL)	1.1 (0.5–3.4)
Emergent operation	8 (24.2%)
Previous thoracic surgery	0
ICU status	22 (66.7%)
ICU length of stay (d)	20 (11.5–66.75)

ICU, intensive care unit; MELD, Model of End-Stage Liver Disease; OLT, orthotopic liver transplantation.
Values are *n* (%) or median (IQR).

underwent thoracic duct ligation for chylothorax. Table 1 summarizes the demographics of the entire cohort of 33 patients. The median age of patients at thoracic surgery was 58 (IQR 51–64); 20 patients were male (61%). The most common indication for OLT was hepatocellular carcinoma (12 patients, 36.4%) and hepatitis C (8 patients, 38.1%). Median MELD score prior to liver transplantation was 35 (IQR 28–40). Fifteen (45.5%) of patients had chronic pleural effusions prior to OLT, all of whom required tube thoracostomy.

Patients' clinical characteristics prior to thoracic surgery, but after OLT, are summarized in Table 2. The most frequent indication for surgery among OLT patients was recurrent chronic pleural effusions, which was found in 12 patients (36.4%). This was followed by empyema in 10 patients (30.3%). Empyema was secondary to pneumonia in 7 patients with the remaining 3 patients developing empyema secondary to seeding from thoracentesis for management of refractory chronic pleural effusion. Eleven patients required surgery for hemothoraces—8 (24.2%) for hemorrhage control and 3 (9.1%) for hemothorax evacuation. These hemothoraces were iatrogenic, secondary to thoracentesis or tube thoracostomies causing hemorrhage. The median interval between OLT and thoracic surgery was 5.7 months (IQR 2.2–14.1); however, this varied by surgical indication. Those requiring surgery for chronic pleural effusion or empyema had a median interval of 6.6 months (IQR 2.4–20.9) and 6.7 months (IQR 3.5–28.4), respectively. Nearly all patients (32/33, 97.0%) developed pleural effusions following OLT, 20 of whom required tube thoracostomy. Trapped lung was found in 22 patients (66.7%). Six patients (18.2%) required vasopressor support prior to surgery due to hemodynamic instability, 4 of them being in hemorrhagic shock. Dialysis was required in 15 patients (45.4%). Among those not undergoing dialysis, the average creatinine was mildly elevated at 1.4 mg/dL (IQR 1.0–1.8). The median INR and bilirubin levels for the entire cohort were 1.2 (IQR 1.1–1.3) and 1.1 mg/dL (IQR 0.5–3.4), respectively.

Operative interventions for our cohort of OLT recipients with pleural space complications included decortication, hemorrhage control, retained hemothorax evacuation, empyema evacuation, pleurodesis, and pleurectomy. Among the 12 patients who had chronic pleural effusions, 9 (75%) underwent talc pleurodesis, 8 (66.6%) underwent decortication, and 3 (25%) underwent pleurectomy. Two patients (16.7%) with chronic pleural effusions underwent all 3 interventions. Five of the patients (42%) with chronic pleural effusions underwent both talc pleurodesis and

decortication alone, while 2 patients (16.7%) with chronic pleural effusions underwent talc pleurodesis and pleurectomy alone. Three patients (25%) did not undergo pleurodesis; instead, 1 underwent decortication and pleurectomy and 2 underwent decortication alone. Among the 10 patients who required surgery for empyema, 10 (100%) underwent empyema evacuation, 8 (80%) underwent decortication, and 4 (40%) patients underwent pleurectomy. Four patients (40%) underwent empyema evacuation, decortication, and parietal pleurectomy. Out of the remaining 6 patients, 4 (40%) underwent decortication and empyema evacuation, while the remaining 2 patients (6.1%) underwent empyema evacuation alone without decortication due to significant bleeding and coagulopathy. Among the 8 patients with acute hemothorax, all 8 (100%) underwent hemorrhage control and 3 (37.5%) underwent decortication during hemorrhage control. Decortication was performed in patients with trapped lung. Among the 3 patients with subacute hemothorax, all 3 (100%) underwent retained hemothorax evacuation and 1 (33.3%) also underwent decortication. Fifteen patients (45.5%) underwent video-assisted thoracic surgery (VATS). Eight out of the 15 patients (53.3%) eventually require conversion to thoracotomy. The remainder of the patients (18 patients, 55.5%) underwent thoracotomy.

Tables 3 and 4 summarize the postoperative complications and risk factors for 30-day morbidity, respectively. The 30-day postoperative morbidity rate was 69.7%. Three (9.1%) patients had 1 complication, 4 (12.1%) patients had 2 complications, and 16 (48.4%) patients had greater than or equal to 3 complications. Univariate analysis identified bilirubin (OR = 2.3, P = 0.023), and surgical indication of empyema and empyema evacuation (OR = 16.3, P = 0.015) as being statistically significantly associated with 30-day postoperative morbidity. Chronic pleural effusions were found to be less frequently associated with 30-day postoperative morbidity (OR = 0.1, P = 0.016).

Table 3. Postoperative Complications and Mortality (N = 33)

Characteristic	Value
30-day morbidity	23 (69.7%)
Prolonged intubation (>72 h)	12/33 (36.4%)
Pneumonia	11/33 (33.3%)
Reintubation	11/33 (33.3%)
Atelectasis	9/33 (27.3%)
Multisystem organ failure	7/33 (21.2%)
Bacteremia	6/33 (18.2%)
Tracheostomy	3/33 (9.1%)
Intrathoracic hemorrhage requiring reoperation	2/33 (6.1%)
Atrial fibrillation	1/33 (3.0%)
Pulmonary embolism	0/33 (0%)
Empyema	0/33 (0%)
Myocardial infarction	0/33 (0%)
30-day mortality	5 (15.2%)
1-year mortality	19 (57.6%)
5-year mortality	23 (70.2%)
Median survival time (mo)	10.4 (3.0–35.0)

Values are n (%) or median (IQR).

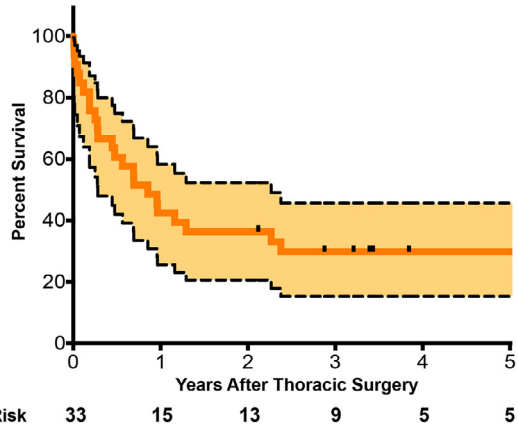


Figure 1. Kaplan-Meier survival curve for OLT recipients with pleural space complications after thoracic surgery. Survival curve (orange) represents overall survival of the patient cohort with pleural space complications (n = 33). Peripheral curves (hashed black) indicate the 95% confidence intervals. Number of patients at risk are reported below each time point. (Color version of figure is available online at http://www.semthorcardiovascsurg.com.)

Tables 3 and 5 summarize postoperative mortality rate and risk factors for 30-day mortality. The 30-day mortality was 15.2% (5/33). There were no intraoperative deaths. Of the 5 patients who died within 30 days of their operation, all 5 ultimately expired due to persistence of their presenting problem: hemorrhage or multisystem organ failure due to sepsis. Univariate analysis identified vasopressor requirement (OR = 10.2, P = 0.031) to be associated with 30-day mortality. Tables 3 and 6 summarize postoperative mortality rate and risk factors for long-term mortality, respectively. The mortality rate was 39.4% at 6 months, 57.6% at 1 year, and 70.2% at 5 years after thoracic surgery (Fig. 1). The median survival time was 10.4 months (IQR 3.0–35.0). Univariate analysis identified age (HR = 1.06, P = 0.011), male gender (HR = 2.88, P = 0.027), post-OLT ascites (HR = 2.86, P = 0.014), bilirubin (HR = 1.17, P = 0.007), empyema (HR = 2.38, P = 0.041), empyema evacuation (HR = 2.38, P = 0.041), and pleurectomy (HR = 2.61, P = 0.036) to be associated with long-term mortality.

DISCUSSION

Pulmonary complications are a serious and common problem for OLT recipients in the postoperative period. Among our cohort of OLT recipients who underwent thoracic surgery, the vast majority (33/42 or 79%) of patients with PPCs ultimately requiring operation were those with pleural space complications. The surgical management of pleural space complications is a clinically frustrating dilemma in patients both before and

Table 4. Univariate Analysis of Risk Factors for 30-Day Morbidity ($N = 33$)

Characteristic	No Morbidity ($n = 10$)	30-Day Morbidity ($n = 23$)	Odds Ratio (95% CI)	P Value
Prior to OLT				
Age	55.0 (22.1–72.3)	60.9 (42.1–69.8)	1.1 (1.0–1.1)	0.240
Male	4 (40%)	16 (69.6%)	3.2 (0.7–14.9)	0.139
Smoker	7 (70%)	14 (60.9%)	0.7 (0.1–3.1)	0.710
COPD	0 (0%)	1 (4.3%)	1.4 (0.1–211.4)	1
Portopulmonary hypertension	3 (30%)	3 (13%)	0.4 (0.1–2.1)	0.336
Chronic pleural effusions	3 (30%)	12 (52.2%)	2.3 (0.5–11.6)	0.283
MELD	31 (22–40)	38 (22–46)	1.1 (1.0–1.2)	0.195
Liver disease etiology				
Hepatocellular carcinoma	5 (50%)	7 (30.4%)	0.5 (0.1–2.0)	0.433
Hepatitis C	1 (10%)	7 (30.4%)	2.9 (0.5–30.4)	0.382
Alcohol	0 (0%)	3 (13%)	3.6 (0.3–499.4)	0.536
After OLT/prior to thoracic surgery				
Pleural effusions	10 (100%)	22 (95.7%)	0.7 (0–14.6)	1
Trapped lung	5 (50%)	17 (73.9%)	2.7 (0.6–12.4)	0.240
Ascites	1 (10%)	9 (39.1%)	4.1 (0.8–43.3)	0.123
Vasopressor requirement	2 (20%)	4 (17.4%)	0.8 (0.1–5.2)	1
Dialysis	4 (40%)	11 (47.8%)	1.3 (0.3–6.0)	0.722
INR	1.1 (1.1–1.6)	1.2 (0.9–2.3)	2.4 (0.2–114.2)	0.657
Bilirubin (mg/dL)	0.6 (0.3–1.5)	2.3 (0.2–15.1)	2.3 (1.1–9.1)	0.023
Emergent operation	2 (20%)	6 (26.1%)	1.3 (0.3–8.0)	1
ICU status	6 (60%)	16 (69.6%)	1.5 (0.3–6.8)	0.696
ICU length of stay	7.5 (0–88)	12 (0–289)	1.0 (1.0–1.0)	0.952
Operative data				
Indication				
Chronic pleural effusions	7 (70%)	5 (21.7%)	0.1 (0–0.6)	0.016
Empyema	0 (0%)	10 (43.5%)	16.3 (1.7–2190.3)	0.015
Hemothorax—acute	2 (20%)	6 (26.1%)	1.3 (0.3–8.0)	1
Hemothorax—subacute	1 (10%)	2 (8.7%)	0.7 (0.1–8.9)	1
Decortication	5 (50%)	15 (65.2%)	1.8 (0.4–0.8)	0.461
Hemorrhage control	2 (20%)	6 (26.1%)	1.3 (0.3–8.0)	0.687
Retained hemothorax evacuation	1 (10%)	2 (8.7%)	0.9 (0.1–19.8)	1
Empyema evacuation	0 (0%)	10 (43.5%)	16.3 (1.7–2190.3)	0.032
Pleurodesis	4 (40%)	5 (21.7%)	0.4 (0.1–2.0)	0.400
Pleurectomy	1 (10%)	6 (26.1%)	2.4 (0.4–25.0)	0.397

CI, confidence interval.
Values are *n* (%), median (IQR).

after OLT. Prior to transplantation, patients are high risk for surgery due to risk for bleeding and liver decompensation. For example, patients with Child-Pugh Class A and B cirrhosis have a 12.5% in-hospital mortality rate after thoracoscopy with decortication.[6–8] In addition, a meta-analysis of multiple types of pleurodesis—the most common being mechanical, talc, tetracycline—for the management of hepatic hydrothorax found the procedure to be associated with a morbidity rate of 82% that frequently requires reintervention due to reaccumulation of high volumes of pleural fluid.[9] After transplantation, patients are deconditioned and require immune-suppression, which also limits options for the management of these pleural space complications. As a result, most of these thoracic pathologies in this patient population are treated with conservative management; however, in some cases, surgery is unavoidable. In general, infection inadequately treated with medical management or chest tube therapy, acute hemothorax with hemodynamic instability, progressively symptomatic recurrent pleural effusions, and symptomatic subacute hemothorax were the indications for surgery. Unless pressed for surgery, nonsurgical recommendations were generally proposed for this population of high-risk patients.

In the present study, we show that thoracic surgery performed in OLT recipients with pleural space complications is associated with high 30-day morbidity of 69.7%. Univariate analysis of 30-day postoperative morbidity identified elevated bilirubin and empyema as variables associated with high early postoperative morbidity. Post-OLT hyperbilirubinemia can be due to a multitude of reasons, such as primary graft injury, immune-mediated graft dysfunction, biliary complications, and infections that are specific to different time points following liver transplantation.[10] Our patients exhibited mild

Table 5. Univariate Analysis of Risk Factors for 30-Day Mortality ($N = 33$)

Characteristic	No 30-Day Mortality ($n = 28$)	30-Day Mortality ($n = 5$)	Odds Ratio (95% CI)	P Value
Prior to OLT				
Age	56.6 (22.1–72.3)	63.4 (58.1–69.8)	1.1 (1.0–1.2)	0.132
Male	15 (53.6%)	5 (100%)	9.6 (0.9–1301.6)	0.131
Smoker	18 (64.3%)	3 (60%)	0.8 (0.1–5.4)	1
COPD	1 (3.6%)	0 (0%)	1.7 (0–35.9)	1
Portopulmonary hypertension	4 (14.3%)	2 (40%)	3.9 (0.5–27.3)	0.216
Chronic pleural effusions	11 (39.3%)	4 (80%)	4.6 (0.7–92.3)	0.152
MELD	34 (22–46)	38 (31–40)	1.1 (0.9–1.4)	0.613
Liver disease etiology				
Hepatocellcular carcinoma	12 (42.9%)	0 (0%)	0.1 (0–1.2)	0.133
Hepatitis C	6 (21.4%)	2 (40%)	2.5 (0.3–15.9)	0.639
Alcohol	3 (10.7%)	0 (0%)	0.7 (0–8.5)	1
After OLT/prior to thoracic surgery				
Pleural effusions	27 (96.4%)	5 (100%)	0.6 (0.4–1123.7)	1
Trapped lung	19 (67.9%)	3 (60%)	0.7 (0.1–4.7)	0.100
Ascites	8 (28.6%)	2 (40%)	1.7 (0.2–10.7)	0.627
Vasopressor requirement	3 (10.7%)	3 (60%)	10.2 (1.5–85.9)	0.031
Dialysis	11 (39.3%)	4 (80%)	4.6 (0.7–50.0)	0.152
INR	1.1 (0.9–1.8)	1.5(1.1–2.3)	21.9 (1.4–1305.7)	0.074
Bilirubin (mg/dL)	1.0 (0.2–13.7)	1.3 (0.9–15.2)	1.1 (0.9–1.4)	0.182
Emergent operation	6 (21.4%)	2 (40%)	2.5 (0.3–15.9)	0.574
ICU status	17 (60.7%)	5 (100%)	7.2 (0.7–983.3)	0.143
ICU length of stay	7.5 (0–289)	8 (2–72)	1.0 (1.0–1.0)	0.398
Operative data				
Indication				
Chronic pleural effusions	12 (42.9%)	0 (0%)	0.1 (0–1.2)	0.133
Empyema	7 (25%)	3 (60%)	4.0 (0.7–28.6)	0.149
Hemothorax—acute	6 (21.4%)	2 (40%)	2.5 (0.3–15.9)	0.574
Hemothorax—subacute	3 (10.7%)	0 (0%)	0.7 (0–8.5)	1
Decortication	18 (64.3%)	2 (40%)	0.4 (0.1–2.4)	0.360
Hemorrhage control	6 (21.4%)	2 (40%)	2.5 (0.3–15.9)	0.574
Retained hemothorax evacuation	3 (10.7%)	0 (0%)	0.7 (0–8.5)	1
Empyema evacuation	7 (25%)	3 (60%)	4.0 (0.7–28.6)	0.111
Pleurodesis	9 (32.1%)	0 (0%)	0.2 (0–1.9)	0.290
Pleurectomy	5 (17.9%)	2 (40%)	3.1 (0.4–20.3)	0.282

CI, confidence interval.
Values are *n* (%), median (IQR).

hyperbilirubinemia (median 1.1 mg/dL, IQR 0.5–3.4) at the time of thoracic surgery which took place at a median of 5.7 months after OLT. This is unlikely to reflect overt allograft dysfunction, a process characterized by marked hyperbilirubinemia greater than 10 mg/dL approximately 1 week post-OLT, but nevertheless suggests underlying liver dysfunction.[11] While the etiology of hyperbilirubinemia is unclear in our small dataset, we demonstrate a clear relationship between hyperbilirubinemia, a marker of overall liver injury, and early postoperative morbidity.

Our data also demonstrate that OLT recipients with empyema requiring thoracic surgery are at greater risk for development of 30-day postoperative complications as compared to the general population. For example, in a study of 420 patients of the general population undergoing VATS vs open empyema evacuation and decortication, rates of pneumonia were 4.5% vs 6.6%, ventilator dependence were 13% vs 25.8%, reintubation were 2.5% vs 11%, tracheostomy were 8.9% vs 17%, and sepsis were 1.2% vs 5.5%, respectively.[12] We similarly found that empyema evacuation was associated with high 30-day postoperative morbidity on univariate analysis. The immune suppression required in OLT recipients may contribute to poor outcomes in pleural space infections. Empyemas requiring surgery were found to occur approximately 6.7 months from OLT, a time at which post-OLT pneumonias are characterized by opportunistic pulmonary infections due to intensive immune suppression.[13,14] This relationship is also seen in the setting of renal transplantation, where 80% of complications

Table 6. Univariate Analysis of Risk Factors for Long-Term Mortality ($N = 33$)

Characteristic	Hazard Ratio (95% CI)	*P* Value
Prior to OLT		
Age	1.06 (1.0–1.1)	0.011
Male	2.88 (1.1–7.4)	0.027
Smoker	1.39 (0.6–3.4)	0.471
COPD	1.73 (0.2–13.2)	0.595
Portopulmonary hypertension	0.69 (0.2–2.3)	0.549
Chronic pleural effusions	2.27 (1.0–5.2)	0.052
MELD	0.98 (0.9–1.0)	0.345
Liver disease etiology		
Hepatocellular carcinoma	0.59 (0.2–1.5)	0.253
Hepatitis C	2.50 (1.0–6.3)	0.050
Alcohol	0.59 (0.1–2.5)	0.460
After OLT/prior to thoracic surgery		
Trapped lung	2.34 (0.7–6.4)	0.095
Ascites	2.86 (1.2–6.6)	0.014
Vasopressor requirement	1.36 (0.5–4.0)	0.573
Dialysis	2.02 (0.9–4.6)	0.096
INR	4.16 (0.9–18.8)	0.064
Bilirubin (mg/dL)	1.17 (1.0–1.3)	0.007
Emergent operation	1.00 (0.4–2.7)	0.995
ICU status	0.8 (0.3–1.9)	0.594
ICU length of stay	1.0 (1.0–1.0)	0.604
Operative data		
Indication		
Chronic pleural effusions	0.60 (0.3–1.5)	0.266
Empyema	2.38 (1.0–5.5)	0.041
Hemothorax—acute	1.00 (0.4–2.7)	0.995
Hemothorax—subacute	0.34 (0.1–2.6)	0.298
Decortication	1.57 (0.7–3.8)	0.318
Hemorrhage control	1.0 (0.4–2.7)	0.995
Retained hemothorax evacuation	0.34 (0.1–2.3)	0.298
Empyema evacuation	2.38 (1.0–5.5)	0.041
Pleurodesis	0.58 (0.2–1.6)	0.279
Pleurectomy	2.61 (1.1–6.4)	0.036

CI, confidence interval.

within the first year were due to pulmonary infections.[15] Given the high postoperative morbidity associated with the development of pleural space infections, it is imperative that pleural effusions are aggressively medically managed at the time of diagnosis to prevent the development of infections that have such devastating complications.

The retrospective nature and small study population are significant limitations of this study. Our patients represent a highly selected population of liver transplant recipients. The majority of patients with PPCs requiring intervention are treated with thoracenteses or tube thoracostomies, and undergo thoracic surgery only after failure of these conservative interventions or to manage subsequent complications of these procedures. Furthermore, those patients with significant graft dysfunction are infrequently candidates for surgery due to overwhelming coagulopathy and are treated nonoperatively. Although OLT recipients with pleural space complications treated nonoperatively are an important cohort of patients that also warrant investigation, we sought to focus on the outcomes of those patients who required thoracic surgery to better guide thoracic and transplant surgeons on the management of this complicated patient population. Despite the small sample size, this study identifies important preoperative variables that portend poor postoperative outcomes in OLT recipients with pleural space complications.

CONCLUSION

In brief, thoracic surgery in liver transplant recipients with pleural space complications is associated with significant 30-day mortality and morbidity. Surgical intervention in the context of empyema and post-OLT hyperbilirubinemia is associated with higher rates of early postoperative complications. The post-OLT patient population presents a unique clinical challenge to the transplant and thoracic surgeon that should call attention to the critical importance of preventing pleural space complications.

SUPPLEMENTARY MATERIAL

The following is the supplementary data to this article:

Video 1. Aditya S. Shirali describes the findings in this study, namely, that thoracic surgery in OLT recipients with pleural space complications is associated with high postoperative morbidity.

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