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Tracheostomy in the Management of Pre-Operative Respiratory Failure in Liver Transplant Candidates

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1. Abstract

1.1. Background: Chronic respiratory failure in end-stage liver disease (ESLD) is associated with a high mortality and has been traditionally considered a contraindication for orthotopic liver transplantation (OLT) and the outcomes in patients undergoing pre-operative tracheostomy have not been well studied. In order to better understand clinical consequences of pre-operative tracheostomy in OLT recipients, we hypothesized that, in carefully selected candidates, tracheostomy should not be an absolute contraindication for OLT.

1.2. Methods: We analyzed preoperative characteristics and postoperative outcomes of pre-OLT tracheostomized patients at a single high-volume liver transplant center from 2015 to 2021 and compared them to OLT recipients requiring post-operative tracheostomy and to the overall cohort of adult OLT recipients without perioperative tracheostomy.

1.3. Results: Duration of tracheostomy prior to transplant was 50 days (IQR = 60), total duration of tracheostomy was 121 days (IQR = 35), and all patients were ultimately decannulated. Excluding one patient currently alive 15 months post-transplant, one-year and two-year survival for pre-OLT tracheostomized patients was 100% and 80%, respectively. In comparison to survival of pre-OLT tracheostomized patients, those requiring tracheostomy post-OLT had one-year and two-year unadjusted survival of 51.3% and 48.8% respectively, while the overall unadjusted one and two-year survival among all 710 patients was 83.0% and 81.9%.

1.4. Conclusions: Although chronic respiratory failure requiring tracheostomy is often considered a contraindication to OLT, our data suggests that, in a carefully selected population of OLT candidates, tracheostomy should not be considered a barrier to transplant and pre-OLT tracheostomized patients may actually demonstrate positive outcomes post-transplant.

2. Introduction

Orthotopic liver transplantation (OLT) is a lifesaving procedure for patients with end-stage liver disease (ESLD) and advanced hepatocellular carcinoma. Deceased donor livers are a scarce resource, and efforts to optimize distribution have increased the number of OLTs occurring among recipients with Model for End Stage Liver Disease (MELD) scores greater than 35 [1]. Recipients with higher MELD scores are more likely to develop pre-operative complications and have higher rates of ICU utilization and mechanical ventilation. Respiratory complications requiring mechanical ventilation are common among patients with ESLD, and recent studies suggest that preoperative respiratory failure is not a contraindication to OLT with proper patient selection [2-3].

The role of preoperative respiratory failure, mechanical ventilation, and tracheostomy in transplant outcomes has not been well studied.

Tracheostomy has been shown to be a safe and effective treatment for long-term airway management of respiratory failure after solid organ transplantation, including OLT [4-7]. Pre-operative tracheostomy (TrachPRE) is helpful in select patients, but the optimal timing for tracheostomy is not well known.[8-9] Previous studies have focused on OLT recipients requiring post-operative tracheostomies (TrachPOST), but no study to date has examined the risk factors and outcomes for recipients requiring pre-operative tracheostomy [10-13]. In order to better understand risks and outcomes in OLT recipients who underwent tracheostomy prior to the transplantation, we performed this retrospective case series analysis hypothesizing that, in carefully selected candidates, tracheostomy should not be an absolute contraindication for OLT.

3. Materials and Methods

3.1. Study Population

We reviewed the database of adult patients who received orthotopic liver transplant at the University of California, Los Angeles in the period 2015 to 2021. The study was approved by the UCLA Institutional Review Board (IRB:11-000489). Our search criteria selected only those who required tracheostomy in the perioperative transplant period, either prior to or following OLT during the index hospitalization. All included patients were older than 18 years and had end stage liver disease with a transplant MELD > 30. Patients who were candidates for double organ transplant or those with a history of previous OLT were excluded from our analysis. Preoperative characteristics and postoperative outcomes of pre-OLT tracheostomized patients werecompared to OLT recipients requiring post-operative tracheostomy, and to the overall cohort of adult OLT recipients without perioperative tracheostomy.

3.2. Statistical Analysis

The Shapiro-Wilk test was performed to determine normality of the data. The values were presented as means, with standard deviation representing variability for normally distributed parameters. Medians and interquartile ratios were presented for data that was not normally distributed. A value of p less than 0.05 was considered statistically significant. The analyses are descriptive and no a priori hypothesis was tested as the case series study design and sample size do not allow determination of association of risk factors with clinical outcomes.

4. Results

4.1. Patient Characteristics

Among the 710 patients who received OLT in the 6-year time period studied, 7.2% (N=50) required tracheostomy in the peri-operative OLT period for chronic respiratory failure. Of those patients, six (12%) required TrachPRE and this procedure was performed 6 to 130 days prior to the OLT (median 50, IQR 60). Five of six patients received percutaneous tracheostomies placed by the intensivist team at the bedside; one patient received an open tracheostomy by Head and Neck Surgery as they were noted to have a high-riding innominate artery and thrombocytopenia. None of the procedures reported clinically significant complications.

Notably, no patients with pre-LT tracheostomies had pre-existing chronic pulmonary conditions. Three patients were never smokers, and the remaining three were former smokers, with only one reporting >10 pack-year smoking history. Half of these patients required tracheostomy for a history of multifocal pneumonia with prolonged mechanical ventilation and failure to wean, although none had active concern for pneumonia present at time of transplant. The other three patients required tracheostomy for airway protection: two in the setting of prolonged altered mental status and one in the setting of hematemesis.

Pre-OLT characteristics of these patients are displayed in Table 1. TrachPRE individuals were on average 48 years old; half were men and half were women and they had an average BMI of 22.4. Average MELD in this cohort was 40.3. Four patients received OLT for alcoholic cirrhosis; two for non-alcoholic steatohepatitis (NASH). All were hemodialysis dependent at time of transplant. Four patients were on mechanical ventilational at the time of transplantation, with P/F ratio ranging between 243 – 576.

Based on Computed Tomography (CT) chest imaging in the month prior to transplantation, five of six patients displayed findings that were concerning for pneumonia versus aspiration pneumonitis, indicating most patients had some pre-existing acute lung disease. Descriptions of CT chest imaging may be found in Table 2.

Table 1: Demographic data and outcomes by patient for patients who required tracheostomy for respiratory failure prior to liver transplantation

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Average
Demographics							
Transplant Age	50	47	53	43	40	58	48.6 (SD = 6.0)
Gender	M	F	M	M	F	F	M: 50%, F: 50%
Race/Ethnicity	Asian-Asian Indian / Indian Sub-Continent	White-Not Specified / Unknown	White-Not Specified / Unknown	White-Not Specified / Unknown	White-Not Specified / Unknown	Asian-Filipino	--
BMI	22.4124	14.1714	23.1153	21.4656	25.2496	28.2581	22.4 (SD = 4.3)
Transplant Characteristics							
Diagnosis	Alcoholic cirrhosis	Alcoholic cirrhosis	NASH	Alcoholic cirrhosis	Alcoholic cirrhosis	NASH	--
Transplant MELD	40	33	40	42	45	42	40.3 (SD = 3.7)
HD at transplant	Yes	Yes	Yes	Yes	Yes	Yes	100%
Never Smoker	No	No	Yes	Yes	Yes	No	50%
Former Smoker	Yes	Yes	No	No	No	Yes	50%
Chronic pulmonary condition	None	None	None	None	None	None	0%
Mechanical Ventilation and tracheostomy characteristics							
Indication for tracheostomy	Hematemesis	Multifocal Pneumonia	Airway protection for AMS	Multifocal Pneumonia	Multifocal Pneumonia	Airway protection for AMS	--
Duration of tracheostomy prior to the OLT (days)	26	130	24	92	6	13	50 (IQR = 60)
Mechanical Ventilation on Day of Transplant?	Yes	No	Yes	No	Yes	Yes	67%
Ventilator Days Prior to Transplant	38	N/A	34	N/A	47	1	--
Ventilator Settings	VC 390 FiO2 40% PEEP 8	RA	PC 14 FiO2 40 PEEP 7	TC 10L FiO2 21%	PS 7 FiO2 25% PEEP 5	VC 400 FiO2 50% PEEP 5	--
P:F Ratio on Day of Transplant	243	576	287	476	304	450	390 (SD = 131)
RASS Score	-3 to -4	0 to -1	0 to -1	0	0 to -1	0 to -1	--
Sedation requirements	Fentanyl 150 mcg/ hr Propofol 50 mcg/ kg/min	None	None	None	None	Fentanyl 100 mcg / hr Propofol 50 mcg/kg/min	--
Outcomes							
Hospital days post-OLT	93	100	297	59	105	35	96.5 (IQR = 36)
Vent days post	34	7	56	2	81	3	20.5 (IQR = 47)
Immediate ICU stay post OLT duration	73	43	36	13	105	32	39.5 (IQR = 33)
Trach Duration	112	130	889	150	110	42	121 (IQR = 35)
Survival 1 year	Yes	Yes	Yes	Yes	Yes	Yes	100%
Survival 2 years	Yes	Yes	Yes	Yes	No, passed after 22 months from cervical cancer	unknown	80%

Table 2: Computed Tomography (CT) Chest imaging descriptions prior to transplant

Patient no.	Age	Sex	Computed Tomography (CT) Imaging Description
1	50	M	Diffuse, progressive ground glass opacities and bilateral consolidations
2	47	F	Right upper and right lower lobe ground glass opacities concerning for aspiration or infection. Left lower lobe atelectasis. Left pleural effusion.
3	53	M	Bilateral elevated hemidiaphragms with compressive atelectasis. Right upper lobe, right lower lobe, and lingular consolidations consistent with aspiration and / or pneumoniaingula.
4	43	M	Coarse calcifications in the lingula. Diffused textured and nontextured ground glass opacities consistent with acute lung injury. Post-inflammatory pleural parenchymal scarring with localized pulmonary fibrosis. Persistent airspace attenuation within both lower lobes consistent with multifocal pneumonia or aspiration.
5	40	F	Mild interval decrease in the bilateral dense consolidations and ground glass opacities concerning for multifocal pneumonia in the setting of aspiration. Left and right pleural effusions.
6	58	F	Mild pulmonary edema. Atelectasis of the right lower lobe and left lower lobe. Cannot exclude aspiration or pneumonia.

4.2. Outcomes and Complications

Following the OLT, the TrachPRE patients remained in the ICU for a median of 39.5 days (IQR = 33), and in the hospital for a median of 96.5 days (IQR = 36). They required mechanical ventilation for a median of 20.5 days (IQR = 47) post-transplant. In total, patients had their tracheostomy for an average of 121 days (IQR = 35). All patients were ultimately decannulated.

Excluding one patient currently alive at 15 months post-transplant, one-year and two-year survival for pre-OLT tracheostomized patients was 100% and 80%, respectively. One patient passed at 22 months due to cervical cancer.

In comparison to survival of pre-OLT tracheostomized patients, those requiring tracheostomy post-OLT had one-year and two-year unadjusted survival of 51.3% and 48.8% respectively, while the overall unadjusted one and two-year survival among all 710 patients was 83.0% and 81.9%.

5. Discussion

This case series is, to our knowledge, the first to report outcomes of high-MELD OLT recipients requiring tracheostomy prior to transplantation. Though chronic respiratory failure requiring tracheostomy is often considered a contraindication to OLT, our data suggest that, in a carefully selected population of OLT candidates, preperative tracheostomy may be a safe option to facilitate transplant and improve outcomes. Regardless of the indication for tracheostomy, outcomes for these patients were generally excellent with respect to their pulmonary status. Half of our patients underwent tracheostomy for complications of multifocal pneumonia, suggesting an ongoing fibrotic pulmonary process. Despite this, all patients were able to be weaned from tracheostomy and ultimately decannulated. None of the patients included in our study had any complications from tracheostomy, and our findings are consistent with other studies examining tracheostomy outcomes in both liver and other solid organ transplant recipients [4,6,7,14].

Positive outcomes reported in this case series should by no means lead to the onclusion that chronic respiratory failure requiring tracheostomy represents an acceptable risk for OLT. These patients likely had certain factors and characteristics that favored ongoing active listing for OLT despite their need for a tracheostomy. Previously published data suggest a high mortality in patients with cirrhosis admitted to the ICU requiring mechanical ventilation [15] Patients with cirrhosis admitted to the ICU with ARDS demonstrated higher mortality than those without cirrhosis (82.2% vs. 27.6%) [16] One important characteristic of our cohort is that, while all patients eventually received OLT in the state of multisystem organ failure which included chronic respiratory failure, none of these patients had chronic pulmonary conditions prior to their advanced end-stage liver disease. Half of the patients were originally intubated due to concern for airway protection, either from altered mental status or for hematemesis. The other half of patients underwent tracheostomy for complications of multifocal pneumonia. Of the patients who were tracheostomized for multifocal pneumonia, all were on minimal ventilator settings just prior to transplantation. They were also well-out from their pneumonia course, indicating that they no longer had an active infectious process but were otherwise experiencing ongoing pulmonary complications of their previous infection. The indications for tracheostomy in this cohort mirrored what could be considered a group of anticipated complications in critically ill high-MELD patients who are more susceptible to aspiration, pulmonary infections, or pulmonary edema. With this understanding, our data may suggest that pre-operative tracheostomy may be an acceptable intervention for a high-MELD OLT candidate struggling with airway protection or recovering from a recent pneumonia [17].

Our reported case series may mirror others in which tracheostomy is used as an intervention to recovery. Early tracheostomy in all critically ill patients requiring mechanical ventilation is not associated with improved outcomes, and chronically critically ill patients with poor prognosis do not show benefit from early tracheostomy.

However, in patients with acute neurologic pathologies, early tracheostomy after the event has been associated with better prognosis [18] Among patients with traumatic brain injuries, early tracheostomy (< 7 days after the event) has been associated with reduction in the duration of mechanical ventilation and the incidence of ventilator associated pneumonia [19]. As opposed to critically ill patients with chronic respiratory failure where tracheostomy is a last-resort measure to extend life, patients in our cohort required tracheostomy as an intervention to recovery.

This manuscript has several limitations. As a retrospective analysis of a small cohort from a single center, its results are not generalizable to a larger population of OLT recipients. Notably, apart from resolving multifocal pneumonia, patients with chronic pulmonary disease processes were not included in this study. Nevertheless, several strengths merit emphasis. This is the first study reporting the outcomes in tracheostomized patients receiving OLT. Our cohort included all patients fitting very strict selection criteria which excluded ESLD patients with MELD<30, non-adult patients and those who were either previously transplanted or candidates for double organ transplant such as liver and lung transplants. All patients were perioperatively co-managed by liver transplant surgery teams and pulmonary and critical care medicine teams and data presented are the result of a well-profiled cohort from a high-volume academic liver transplant center.

6. Conclusions

Based on this case series of patients who underwent tracheostomy prior to OLT, we conclude that, in a specific population of LT candidates, tracheostomy should not be considered a barrier to LT, and a carefully selected post-tracheostomy patient population may have positive outcomes post-OLT. Larger prospective studies will be necessary to better evaluate the role and clinical repercussions of pre-transplant tracheostomy in OLT candidates.

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