Tracheostomy Post Liver Transplant: Predictors, Complications, and Outcomes

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Background: Liver transplant (LT) patients have an increased risk of postoperative respiratory failure requiring tracheostomy. This study sought to characterize objective clinical predictors of tracheostomy.

Material/Methods: The records for 2017 LT patients at a single institution were reviewed. Patients requiring tracheostomy were first compared with all other patients. A case-control subgroup analysis was conducted in which 98 tracheostomy patients were matched with 98 non-tracheostomy LT patients. For the case-control study, muscle mass was assessed using preoperative computed tomography scans.

Results: Among 2017 LT patients, 98 required tracheostomy (5%), with a 19% complication rate. Tracheostomy patients were older and had a higher model for end-stage liver disease score, a lower body mass index (BMI), and a greater smoking history. Tracheostomy patients had a longer hospital stay (45 *vs.* 10 days, *P*<0.001) and worse 1-year survival (65% *vs.* 91%, *P*<0.001). Ten-year Cox regression patient survival for tracheostomy patients was significantly worse (32% *vs.* 68%, *P*<0.001). In the case-control analysis, respiratory failure patients were older (*P*<0.01) and had a lower BMI (*P*=0.05). They also had a muscle mass deficit of −39% compared with matched LT controls (*P*<0.001). No significant differences were seen with pre-LT total protein or albumin or with forced expiratory volume in 1 s divided by forced vital capacity (FEV1/FVC) values.

Conclusions: Predictors for respiratory failure requiring post-LT tracheostomy include higher model for end-stage liver disease score, older age, lower BMI, greater smoking history, and worse sarcopenia. Patients requiring tracheostomy have dramatically longer hospital stays and worse survival.

MeSH Keywords: Frail Elderly • Liver Transplantation • Malnutrition • Postoperative Complications • Respiration, Artificial • Tracheostomy

Abbreviations: BMI – body mass index; CT – computed tomography; FEV1 – forced expiratory volume in 1 s; FVC – forced vital capacity; LT – liver transplant; MRI – magnetic resonance imaging; PACS – picture archiving and communication software; PDT – percutaneous dilational tracheostomy; PFT – pulmonary function testing; SPSS – Statistical Package for the Social Sciences; RRS – respiratory risk score

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Background

Prolonged mechanical ventilation after liver transplant (LT) has been shown to be associated with increased mortality [1]. Previous studies have identified the incidence of posttransplant respiratory complications to be approximately 59–87% [2,3]. Many clinical factors have been found to have an impact on post-LT respiratory failure requiring tracheostomy including older age, subjective nutritional deficiency, intraoperative bleeding, pre-LT mechanical ventilation, diagnosis of acute liver failure, and re-transplantation [2,4]. Further analysis is required to identify additional clinical factors useful in identifying these high-risk patients prior to transplant.

Screening of transplant candidates prior to LT is critical to optimizing the utility of scarce organs. Of note, a scoring system to calculate the risk of respiratory failure after liver transplantation was recently proposed. This scoring system defines respiratory failure as patients requiring >7.5 days on a respirator, and it takes into account many of the previously identified clinical factors to calculate risk [5]. However, preoperative pulmonary function testing (PFT) and objective measures of wasting and frailty were not included in the scoring system.

The purpose of this study was to further identify objective clinical predictors for posttransplant respiratory failure requiring tracheostomy. As LT patients are often deconditioned, chronically ill, and suffer from coagulopathy, this study also sought to better understand the impact of objective measures of pre-LT nutritional deficiency in patients with post-LT respiratory failure. Additionally, a thorough review of all tracheostomy procedures in these high-risk patients is reported to assess the incidence and types of tracheostomy-related complications.

Material and Methods

The electronic medical records of all LT recipients at a single center over a 16-year period were reviewed. Patients with post-LT respiratory failure were selected based on their requirement for posttransplant tracheostomy. Further chart review was then performed for these patients to determine demographics, pre-LT PFT results, smoking history, nutritional status, and clinical outcomes (hospital stay and patient survival). A case-control subgroup analysis was then conducted in which 98 tracheostomy patients were matched with 98 non-tracheostomy LT patients based on year of transplant, model for end-stage liver disease score (MELD), and sex. Data collection was complete except for 2 patients in the respiratory failure group who did not have computed tomography (CT) or magnetic resonance imaging (MRI) scans available for review. Additionally, pre-transplant PFT results were unavailable for 8 patients in the control group and 15 patients in the respiratory failure group.
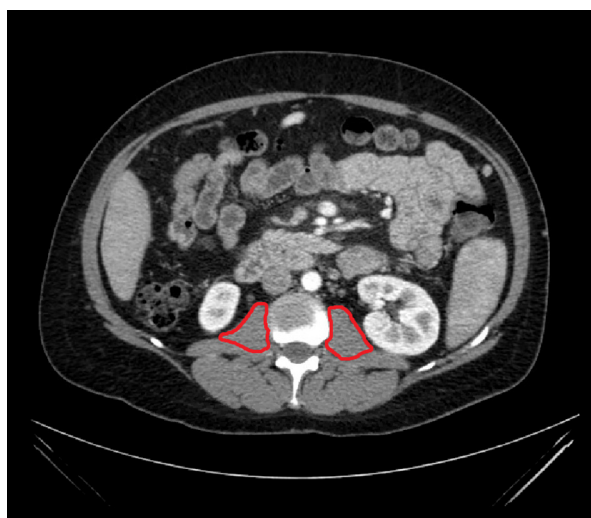
Figure 1. Cross section of patient CT scan at L2/L3 with bilateral psoas muscle areas highlighted.

Preoperative nutritional status was assessed using preoperative CT scans (or MRI if CT was not available) and biochemical measures of serum albumin and total protein. CT measurements were taken at the level of the L2/L3 intervertebral disc space, which has been determined to be an accurate approximation of total body composition [6]. Total psoas muscle area was obtained by outlining both the right and left psoas muscles and summing these measurements (Figure 1). In order to account for variations in patient size, all measurements were scaled for height, as has been done previously [7]. The sarcopenic index was obtained by dividing the total psoas area (cm^2) by the height in meters squared. Measurements were taken using Synapse picture archiving and communication software (PACS). The scaled measurements of the transplant patients were compared with the scaled measurements of MELD, transplant year, and sex-matched controls. The difference was calculated by subtracting the control measure from the transplant patient measure and a percent difference was calculated.

The original operative reports for all tracheostomy procedures were reviewed in detail. Extracted data included ventilator days until tracheostomy, operating surgeon, technique, complications, days to decanulation, and risk of death with tracheostomy. Any complications were described and required interventions were noted.

For this patient cohort, the posttransplant immunosuppression protocol has been described previously and includes induction therapy with rabbit antithymocyte globulin and steroids, followed by Prograf (tacrolimus) monotherapy [8]. Donor livers were recovered using standard procurement techniques including aortic and portal vein flushing and cold storage as has been described previously [9]. Ninety-five percent of all transplants during the study period were performed using

Table 1. Demographic data for liver transplant patients who did or did not require tracheostomy for respiratory failure in the first 6-months post transplant.

Overall	No tracheostomy 1919 (95.2%)	Tracheostomy 98 (4.8%)	p-Value
Recipient characteristics			
MELD (median (SD))	18 (7)	22 (9)	<0.001
Gender male	67%	66%	0.88
Race			
White	89%	90%	0.38
Black	6%	3%	
Other	5%	7%	
Age in years (median (SD))	55 (10)	58 (11)	0.02
Body mass index (median (SD))	28.2 (5)	26.5 (5)	<0.01
Retransplant	4%	2%	0.71
Tobacco use			
Never smoker	53%	48%	0.41
Former smoker	47%	52%	
Current smoker at transplant	19%	17%	0.65
Pack-years smoking*			
Zero	53%	48%	0.01
1 to 20	13%	26%	
20 to 40	25%	21%	
>40	9%	5%	
Outcomes			
Hospital stay (days, median (SD))	10 (31)	45 (64)	<0.001
1-year survival	91%	65%	<0.001

* Pack-years is the number of years of smoking multiplied by the average number of packs of cigarettes per day.

the piggyback hepatectomy technique, which has been described previously and was technically equivalent for all participating surgeons [10]. Overall median anesthesia time was 4 h 40 min. A temporary portal-cava shunt was not created in any of the cases, and there was no use of veno-venous bypass. An antifibrinolytic agent (aprotinin, or aminocaproic acid or tranexamic acid) was administered routinely during the transplant procedure.

Standard statistical testing was utilized for continuous and categorical variables, as indicated. The Cox proportional hazards model was constructed using a direct entry method. Covariates were included in the final model for P-value <0.10. Statistical testing was performed using the Statistical Package for the Social Sciences software (IBM SPSS Statistics Version 25 [2018], IBM Corporation, Armonk, NY, USA). Retrospective analysis of data for LT patients at our center was reviewed and approved by the institutional review board of the Indiana University School of Medicine.

Results

Among 2017 liver transplants, 98 patients required tracheostomy (5%). Tracheostomy patients had a higher MELD, older age, and a lower body mass index (BMI). Tracheostomy patients had a greater exposure to smoking. They did not differ in race or sex. Compared with the entire cohort, patients requiring tracheostomy after LT had significantly longer hospital stay (45 *vs.* 10 days, P<0.001) and worse 1-year survival (65% *vs.* 91%, P<0.001) (Table 1).

In the case-control analysis, tracheostomy patients were older (P<0.01) and had a lower BMI (P=0.05). These patients also had a muscle mass deficit of -39% compared with matched controls (P<0.001). No significant difference was found between groups in a comparison of biochemical markers of nutrition (serum total protein and albumin levels). Forced vital capacity (FVC) was found to be lower in the respiratory failure group (81% *vs.* 88%, P=0.03), as was the forced expiratory volume

Table 2. Subgroup analysis of 98 liver transplant patients with respiratory failure who required tracheostomy in the first 6-months post liver transplant.

	Number
Overall	98 (100%)
Clinical outcomes	
Days to tracheostomy post transplant (median (SD))	19 (35)
Surgeon*	
Transplant surgeon	92 (94%)
Other	6 (6%)
Days from tracheostomy to decanulation (median (SD))	46 (430)
Died with tracheostomy	18 (18%)
Pulmonary function tests**	
Forced vital capacity (FVC, % of predicted)	81% (20)
Forced expiratory volume in 1 second	
(FEV1,% of predicted)	76% (18)
FEV1/FVC (% of predicted)	75% (8)

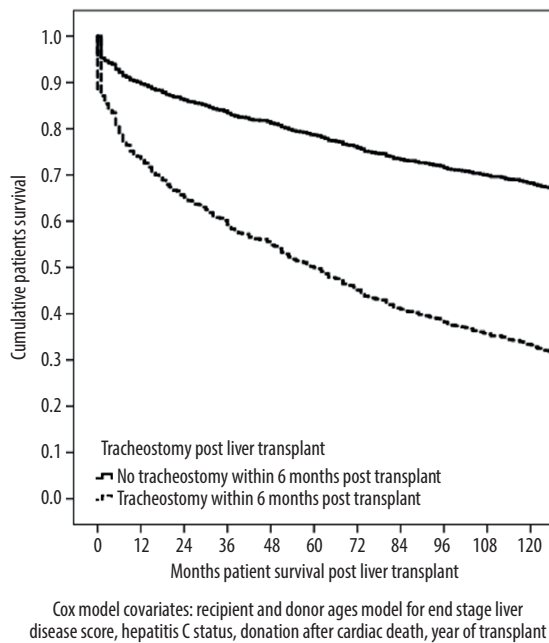|	Number
Complications	
Any complication related to tracheostomy	19 (19%)
Operative revision/post-operative hemorrhage	4
Tracheocutaneous fistula/non-closure	4
Bleeding requiring operative intervention	5
Subcutaneous emphysema	2
Pneumothorax/pneumomediastinum	3
Intraoperative unstable atrial fibrillation (cardioverted)	1

* 2 tracheostomies were performed percutaneously;
** 15 patients did not have PFT reports available.

Table 3. Case control analysis of muscle mass in patients with tracheostomy and matched controls without tracheostomy*.

	No tracheostomy (controls)	Tracheostomy (cases)	p-Value
Number	98	98	
Demographics			
Age (median (SD))	53 (12)	58 (11)	<0.01
Model for end-stage liver disease score (SD)	22 (9)	22 (9)	0.78
Body mass index (median (SD))	27.7 (6)	26.5 (5)	0.05
Pack-years smoking (mean, median SD)	13.0 (18)	12, 3 (20)	0.82
Skeletal muscle mass**			
Psoas index group median	4.6	3.2	<0.001
Psoas index matched difference		−39% (120)	
Biochemical markers of nutrition			
Serum albumin level (median SD)	3.0 (0.7)	2.9 (0.8)	0.97
Serum protein level (median SD)	6.5 (0.9)	6.4 (1.2)	0.97
Pulmonary function tests**			
Forced vital capacity (FVC, % of predicted (SD))	88% (19)	81% (20)	0.03
Forced expiratory volume in 1 second			
(FEV1,% of predicted (SD))	83% (18)	76% (18)	0.02
FEV1/FVC (% of predicted (SD))	76% (7)	75% (8)	0.45
Clinical outcomes			
Length of hospital stay (median (SD))	10 (41)	45 (64)	<0.001
1-year patient survival	94%	65%	<0.001

* Cases and controls matched for age, gender, MELD score and year of transplant; ** 2 patients in the tracheostomy group did not have CT or MRI available for review; *** 15 patients in the tracheostomy group and 8 patients in the control group did not have PFTs available.

Cox model covariates: recipient and donor ages model for end stage liver
disease score, hepatitis C status, donation after cardiac death, year of transplant

Figure 2. Cox proportional hazards patient survival post
transplant for 98 patients with respiratory failure who
required tracheostomy in the first 6-months post liver
transplant (n=2017 transplants).

in 1 s (FEV1) (76% *vs*. 83%, *P*=0.02). No significant difference
between the 2 groups was noted for FEV1/FVC. Similar to the
findings from Table 1, the case-control analysis showed an ex-
tended length of hospital stay (45 *vs*. 10 days, *P*<0.001) and
decreased 1-year patient survival (65% *vs*. 94%, *P*<0.001) for
the respiratory failure group (Table 2).

Subgroup analysis of the 98 tracheostomy patients was per-
formed. The median number of days between transplant and
tracheostomy was 19 days, with a median time of 46 days from
tracheostomy to decanulation (for survivors). Nearly all the pa-
tients failed multiple attempts at extubation prior to under-
going the tracheostomy procedure (Table 3). A transplant sur-
geon performed the tracheostomy procedure in 94% of cases.
All but 2 tracheostomies were placed using an open technique
in the operating room. Two tracheostomies were placed per-
cutaneously early in this series, but both required early revi-
sion due to the poor quality of the tissue. Therefore, the per-
cutaneous approach was abandoned at this center in post-LT
patients. Pulmonary function tests among tracheostomy pa-
tients included FVC of 81% of predicted, forced expiratory vol-
ume in 1 s (FEV1) of 76% predicted, and FEV1/FVC of 75% pre-
dicted. Of the 98 tracheostomy patients, 18 (18%) died with
their tracheostomy in place. A list of the most common com-
plications in these 98 patients is provided in Table 2. Four pa-
tients required early reoperation for dislodged tracheostomy

or hemorrhage. Five patients had late hemorrhage requiring
operative exploration to control bleeding. Four patients re-
quired operative closure of the tracheostomy site after devel-
oping a persistent tracheocutaneous fistula.

In a comparison of the tracheostomy group with the entire co-
hort, 10-year Cox patient survival was worse for the tracheos-
tomy patients (32% *vs*. 68%, *P*<0.001; Figure 2).

Discussion

Understanding clinical predictors of post-LT tracheostomy is es-
sential because of its association with increased costs, length-
ened hospital stay, and worse outcomes [1]. In support of pre-
vious studies, we report decreased 1- and 10-year survival
and markedly lengthened hospital stay for post-LT tracheos-
tomy patients [1,3]. To date, there have been many identified
risk factors for respiratory failure after LT including older age,
subjective nutritional deficiency, intraoperative bleeding, pre-
LT mechanical ventilation, diagnosis of acute liver failure, and
retransplantation [2,4]. However, to our knowledge, this study
represents the first time sarcopenic index has been identified
as a potential objective predictor of post-LT respiratory fail-
ure. The significant difference in sarcopenic index demonstrat-
ed between cohorts in the case-control portion of our analy-
sis suggests that this measurement may prove useful, without
adding cost, to the pre-LT screening process.

Recently, a study was done to validate the use of a scoring sys-
tem to predict the risk of respiratory failure after LT. The in-
vestigators were aiming to predict the risk of post-LT 3-month
mortality and prolonged ventilation. Their findings demonstrat-
ed that the respiratory risk score (RRS) could indeed be use-
ful to discriminate between patients with and without post-
LT respiratory failure. While the RRS includes many previously
identified variables associated with post-LT respiratory failure,
it does not appear to utilize any objective findings of nutrition-
al status [5]. Further, many of the included variables may not
be available unless the patient is already in the intensive care
unit. Calculation of the sarcopenic index requires little time
and utilizes imaging that the patient will have already under-
gone as part of their pretransplant workup.

Although hypoalbuminemia has previously been associated
with postoperative respiratory failure in patients receiving
noncardiac surgery, our case-control analysis demonstrates
that serum albumin and total protein may not be reliable clin-
ical predictors of post-LT respiratory failure [11]. This finding
could be explained by the chronically ill state of the majority
of LT patients. Regardless, this finding further illustrates the
importance of identifying unique and objective signs of poor
nutritional status, and the potential for sarcopenic index to fill

that need. Both cachectic patients and patients that experience sarcopenic obesity may be at risk for worse outcomes. An objective measure of nutrition, such as sarcopenic index, can be an important clinical indicator to aid physicians in identifying patients at risk for perioperative and postoperative complications such as respiratory failure. There are also clinical measures of frailty such as the 6-min walk test, the 5- and 10-m walk tests, and grip strength testing [12,13]. With further study, these noninvasive measures of overall physiologic reserve may become important predictors for successful recovery from LT.

Pulmonary function testing is a standard portion of pre-LT evaluation. Unfortunately, the utility of pre-LT PFT has not been well documented in the literature. One recent study showed that patterns of restrictive lung disease were indeed associated with prolonged ventilation time after LT. The actual clinical significance is uncertain, as time on the ventilator was increased by approximately 1 day [14]. To our knowledge, these are the first data to present screening PFT for LT recipients who subsequently developed respiratory failure requiring tracheostomy. However, it must be noted that several PFT reports were missing for patients in our cohort including 8 patients in the control group and 15 patients in the respiratory failure group. We found that patients who experience respiratory failure after LT had a lower group average FVC and FEV1, which suggests that worse pre-LT pulmonary function may be associated with post-LT respiratory failure. However, similar to the aforementioned study, we found FEV1/FVC was not significantly different for patients with post-LT respiratory failure [14]. This finding could be explained by the screening of patients with extremely poor pulmonary function prior to LT. Further work and a larger cohort are needed to better understand the predictive value of pre-LT PFT for posttransplant respiratory failure.

The tracheostomy procedure is generally low risk, and it is often performed at the bedside. In this series, a 19% complication rate was observed, with 4 transplant surgeons performing 94% of the procedures. Although none of these complications were associated with death, many patients had to be returned to the operating room for bleeding or tracheostomy revision. The 6 other tracheostomies were placed by otolaryngology in patients with a known complex history of previous tracheostomy or neck surgery. In this series, 2 percutaneous dilational tracheostomies (PDTs) were placed in post-LT patients. Both had significant complications requiring operative revision. In both cases, the patients had significant disruption (tearing) of the tracheal tissue, which appeared to be related to overall poor tissue quality. PDT requires a relatively rigid and healthy trachea that can withstand the force of passing dilators of increasing size through the tracheal wall. Although a small body of literature supports the overall safety of PDT placement in patients with liver disease, our experience is that standard tracheostomy appears to be safer for the post-LT patient [15,16].

As with any retrospective study, this analysis has intrinsic limitations including potential documentation error and selection bias. Although data from large registries have the advantage of increased statistical power, the findings from this single-center study offer a more granular picture. This level of detail is needed to appreciate and identify clinical predictors such as sarcopenic index, which must be computed individually for each subject. For the case-control analysis, matching criteria include year of transplant, sex, and MELD. Cases and controls were not matched by age and BMI, which both differed significantly between respiratory failure LT cases and LT controls and could be potential confounders. Unfortunately, in the matching process for this analysis, matching beyond 3 variables became very difficult. However, the employed matching criteria did provide the opportunity to identify the clinically relevant data that older patients with cachexia (i.e., elderly patients with lower BMI and sarcopenia) are at increased risk for post-LT tracheostomy.

Conclusions

The need to identify pretransplant clinical predictors of post-LT respiratory failure is clearly highlighted by the poor clinical outcomes, including very poor survival, observed in patients who fail to wean from the ventilator. These findings suggest that although serum protein and albumin levels are not as useful in predicting post-LT clinical outcomes, sarcopenic index and other markers of frailty may serve as important objective measurements of nutritional status in patients on the LT waiting list. Accurately identifying patients at high risk for poor outcome will facilitate patient selection and improve organ utility.

Conflicts of interest

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