Earlier Is Better: Evaluating the Timing of Tracheostomy After Liver Transplantation

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BACKGROUND: Respiratory failure after orthotopic liver transplantation is associated with increased mortality and prolonged hospitalization. METHODS: A retrospective analysis was conducted through the query of the National In-patient Sample for subjects who underwent orthotopic liver transplantation and tracheostomy after transplantation from 2000 to 2011. Tracheostomies by post-transplantation day 14 were considered "early," whereas those after day 14 were "routine." A Cox proportional hazards model was used to evaluate the impact of early tracheostomy on post-tracheostomy length of stay. RESULTS: There were 2,149 weighted discharges. Of these, 783 (36.4%) had early tracheostomy after transplantation. The subjects who received an early tracheostomy after transplantation were more likely to have a Charlson Comorbidity index[22] score of ≥3 (early 71.1% vs late 60.0%; *P* = .038). Early tracheostomy after transplantation had lower in-hospital mortality (early 26.4% vs late 36.7%; *P* = .01). Unadjusted median post-tracheostomy length of stay was 31 d for early tracheostomy after transplantation versus 39 d for late tracheostomy after transplantation (*P* = .034). Early tracheostomy after transplantation was associated with 20% decreased odds of in-hospital mortality (hazard ratio 0.80; *P* = .01). Early tracheostomy had 41% higher daily rate of discharge alive (hazard ratio 1.41; *P* < .001). CONCLUSIONS: Early tracheostomy after transplantation was associated with lower in-hospital mortality, shorter post-tracheostomy length of stay, and quicker discharge alive. These results supported our hypothesis that, among subjects with respiratory failure after orthotopic liver transplantation, early tracheostomy after transplantation may be associated with more favorable outcomes than a delayed approach. *Key words: tracheostomy; liver transplantation; mortality; length of stay.* [Respir Care 2020;65(12):1883–1888. © 2020 Daedalus Enterprises]

Introduction

Long-term consequences of pulmonary complications can be devastating in patients who undergo orthotopic liver transplantation and are associated with increased mortality.[1-3] Mortality is high in these patients, who experience infectious[1,4] and noninfectious[3,5] pulmonary complications. Although these complications are usually multi-factorial in nature, they commonly result from pneumonia,[1,2,4,5] malnutrition,[6,7] hepatopulmonary syndrome,[7,8] transfusion reactions,[8,9] and volume shifts.[10] Tracheostomy has been shown to be a safe and effective treatment for long-term airway management of respiratory failure after solid organ transplantations, including orthotopic liver transplantation.[1,11,12]

Among patients who require prolonged intubation after orthotopic liver transplantation, there exists uncertainty as to the ideal time to perform post-transplantation

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tracheostomy. Previous literature presents conflicting evidence with regard to the optimal timing for tracheostomy in patients who are critically ill.[13] Decreased mortality has been seen in several patient populations at different follow-up intervals, whereas other studies have not observed this same result.[14-18] There also are discordant findings in relation to the length of time spent in the ICU[14,17] and ventilator-associated pneumonia,[16,19,20] with certain studies showing that early tracheostomy is beneficial, and others reporting that the timing of the tracheostomy does not affect outcomes.[14,16,17,19,20] The purpose of this study was to compare the clinical outcomes between the subjects who underwent early versus late tracheostomy after orthotopic liver transplantation. We hypothesized that patients who had orthotopic liver transplantation and with respiratory failure will benefit from early tracheostomy.

QUICK LOOK

Current knowledge

Respiratory failure after orthotopic liver transplantation is associated with increased mortality and prolonged hospitalization. Previous literature shows that, in certain patient populations, early transition from ventilation via endotracheal tube to tracheostomy may lead to improvement in both of these metrics. The benefit of early tracheostomy specifically in orthotopic liver transplantation has not been confirmed.

What this paper contributes to our knowledge

The subjects who received early tracheostomy after transplantation had lower in-hospital mortality, shorter post-transplantation length of stay, and quicker discharge alive. This was seen despite these subjects having a higher comorbidity burden.

Methods

A retrospective analysis was conducted by identifying all patients who underwent orthotopic liver transplantation followed by post-transplantation tracheostomy between 2000 and 2011 in the Healthcare Utilization Project Nationwide In-patient Sample. Developed by the Agency for Healthcare Research and Quality, the Nationwide Inpatient Sample is a 20% stratified cluster sample of hospital discharges in the United States. It represents the largest all-payer publicly available data set in the United States and contains ~10 million discharges annually across the United States.[21] All investigators with access to the data have completed online training and certified Data User Agreements with the Healthcare Utilization Project. The current study included completely de-identified data, and it was approved as exempt from review by the Yale Human Investigations Committee. Therefore, informed consent was not obtained from the subjects.

Patient Selection

The Nationwide In-patient Sample includes up to 25 International Classification of Disease, Ninth revision, Clinical Modification (ICD-9-CM) diagnosis and 15 ICD-9-CM procedural codes. Data were assessed for subjects who had a procedure code for orthotopic liver transplantation (ICD-9-CM 50.5) and then a subsequent code for tracheostomy (ICD-9-CM 31.1 and 31.29). These subjects were then stratified into 2 groups based on whether their tracheostomy was on or before post-transplantation day 14 (early) or after post-transplantation day 14 (routine). The cutoff of 14 d has previously been used by several groups when evaluating the timing of postoperative tracheostomy.[14,16,17]

Statistical Analysis

Differences in sex, age, and Charlson comorbidity index[22] were identified and adjusted for in the analyses. The Charlson Comorbidity index[22] score is a composite score, based on patient comorbidities, that has been proven to predict 10-year mortality. The chi-square test was used to compare mortality between the groups, and the Wilcoxon rank-sum test was used to compare continuous, non-normally distributed variables, for example, length of stay. The Cox proportional hazards model was used to identify the association of tracheostomy with post-tracheostomy length of stay. Post-tracheostomy length of stay was calculated as the time from transplantation until discharge or in-hospital death. To account for the competing risk of mortality, we used Fine-Gray proportional hazards models to generate cause-specific hazard.[23] Statistical significance was set at a P value of .05. All statistical analyses were performed using SAS v. 9.4 (SAS Institute, Cary, North Carolina).

Results

There were 2,149 weighted discharges of subjects who underwent orthotopic liver transplantation and tracheostomy after transplantation identified. Of these, 783 of these tracheostomies (36.4%) were "early" and the remaining 1,366 (63.6%) were "routine" based on the previously described cutoff of 14 d. Of the 783 subjects who underwent early tracheostomy, 227 (29.0%) were performed within the first 7 postoperative days. This group represented 10.6% of the entire cohort. Given the limited size of this data subset, many clinical subgroups, such as age, deaths,

Table 1. Demographic Data for the Subjects Who Underwent Orthotopic Liver Transplantation and Tracheostomy

Demographic	Early Tracheostomy (≤14 d)	Late Tracheostomy (>14 d)	*P*
Subjects, *n* (%)	783 (36.4)	1367 (63.6)	
Sex, *n* (%)			.12
Men	468 (59.8)	734 (53.7)	
Women	315 (40.2)	632 (46.3)	
Age group, *n* (%)			.45
18–45 y	145 (18.5)	226 (16.5)	
46–60 y	389 (49.8)	771 (56.4)	
≥61 y	248 (31.7)	369 (27.0)	
Age, mean ± SD y	54.3 ± 25.1	54.3 ± 20.1	
Race, *n* (%)			.27
Black	68 (8.7)	95 (6.9)	
Hispanic	88 (11.3)	228 (16.6)	
Missing	73 (9.3)	135 (9.9)	
Other	44 (5.7)	145 (10.6)	
White	509 (65.1)	765 (56.0)	
Charlson Comorbidity index score, *n* (%)*			.038
0	20 (2.5)	30 (2.2)	
1	131 (16.8)	391 (28.6)	
2	76 (9.7)	126 (9.2)	
≥3	556 (71.1)	820 (60.0)	

* From Reference 22.

and so forth, were non-reportable, in compliance with the Healthcare Utilization Project Nationwide In-patient Sample Data Use Agreement. Further adjusted analyses showed no significant effect for tracheostomy within 7 d on mortality (OR 95% CI 0.86 [0.42, 1.73]; $P = .66$) or pneumonia (OR 95% CI 1.02 [0.65, 1.61]; $P = .94$). There was no significant difference in the overall time to discharge between the 7 d and 14 d groups. Therefore, our analysis continued using the previously mentioned cutoff of 14 d.

The mean age of the subjects in the cohort was 54.3 y, and there was no significant difference between the groups ($P = .45$). In addition, there were no significant differences in distributions of sex ($P = .12$) or race ($P = .27$). Those who underwent early tracheostomy after transplantation were found to have higher Charlson Comorbidity index[22] scores, with a higher percentage of subjects having scores of ≥3 (71.1 vs 60.0%; $P = .038$) (Table 1). The subjects who received early tracheostomy after transplantation had lower in-patient mortality than those who received routine tracheostomy after transplantation (26.4 vs 36.7%; $P = .01$) (Table 2). In addition, the subjects with early tracheostomy after transplantation had a shorter median total stay (50 vs 71 d; $P = .03$) and shorter median length of stay after tracheostomy (31 vs 39 d; $P = .034$) (Table 2).

In the proportional hazards model, early tracheostomy after transplantation was associated with a 20% decreased odds of in-hospital mortality in comparison with routine tracheostomy after transplantation (hazard ratio 0.80; $P = .01$). Sex, age, Charlson Comorbidity index[22] score, location of the surgery, and year of surgery were not related to in-hospital mortality (Table 3). Furthermore, after accounting for competing risk of mortality, early tracheostomy had a 41% higher daily rate of discharge alive during the post-transplantation hospitalization (hazard ratio 1.41; $P < .001$) (Fig. 1).

Discussion

Herein, we present the largest analysis of the clinical outcomes of subjects undergoing tracheostomy after orthotopic liver transplantation. The current analysis demonstrates that, when compared with late tracheostomy (>14 d after transplantation), early tracheostomy is associated with both decreased in-patient mortality and decreased length of hospital stay. This decreased mortality has been shown in other patient populations. This finding was consistent with similar analyses of tracheostomy timing in other patients who

Table 2. Comparison of Outcome Measures Between Early and Routine Tracheostomy

Measures	Early Tracheostomy (≤7 d)	Late Tracheostomy (>14 d)	*P*
Subjects per group, *n* (%)	783 (36.4)	1367 (63.6)	
In-patient mortality, *n* (%)	207 (26.4)	501 (36.7)	.01
Pneumonia, *n* (%)	302 (38.6)	631 (46.2)	.12
Total length of stay, d			
Mean ± SD	64.6 ± 102.9	87.1 ±108.7	.08
Median (IQR)	50 (35–78)	71 (54-106)	.03
Post-tracheostomy length of stay, d			
Mean ± SD	42.6 ±90.3	49.7 ± 94.4	<.001
Median [IQR]	31 (20–48)	39 (23–61)	<.001

IQR = interquartile range

Table 3. Proportional Hazards Model of Variables Predicting In-Hospital Mortality

Parameter	Hazard Ratio	95% CI	*P*
Tracheostomy			
Routine	Ref	Ref	Ref
Early	0.80	0.67–0.95	.01
Sex			
Men	Ref	Ref	Ref
Women	0.89	0.75–1.05	.16
Charlson Comorbidity index score			
0	Ref	Ref	Ref
1	1.00	0.52–1.90	>.99
2	0.79	0.46–1.37	.40
3	0.85	0.50–1.44	.53
Age group			
18–45 y	Ref	Ref	Ref
46–60 y	1.02	0.83–1.25	.85
≥61 y	0.98	0.78–1.22	.83
Location			
Northeast	Ref	Ref	Ref
South	1.52	1.00–2.33	.05
Midwest	1.16	0.90–1.50	.24
West	0.98	0.75–1.28	.88
Years 2008–2011	0.96	0.81–1.13	.62

Ref = reference

were critically ill. Rumbak et al[14] showed that subjects in the ICU who received a tracheostomy within 2 d of mechanical ventilation had lower mortality at 30 d than those who received tracheostomy at > 14 d after mechanical ventilation.

Other studies[15-17] have not shown this same difference in mortality based on timing of tracheostomy. Young et al[15] did not see this reduced mortality in cardiac subjects in the ICU when comparing those with tracheostomy within 4 d with those with tracheostomy after 10 d. Similarly, Zheng et al[16] saw a similar mortality at 60 d in surgical subjects in the ICU who received tracheostomy within the first 4 d of mechanical ventilation compared with those on day 15 of mechanical ventilation. Trouillet et al[17] did not find a mortality difference at 90 d in subjects who required mechanical ventilation and who received tracheostomy immediately after cardiac surgery when compared with those who had tracheostomy performed on ventilation day 15.

Our analysis of the Nationwide In-patient Sample also demonstrates 2 other significant improvements in outcomes associated with early tracheostomy: decreased post-tracheostomy length of stay, and decreased total in-patient length of stay. These findings are supported by the existing literature. Both Zheng et al[16] and Rumbak et al[14] showed fewer days in the ICU and fewer days on mechanical ventilation.

The benefits of less time on mechanical ventilation in relation to mortality, in-patient length of stay, and rates of pneumonia for patients who are critically ill are well established. We have made progress in patients with orthotopic liver transplantation by decreasing the time to postoperative extubation in the more straightforward cases.[24,25] Our study offers insight into optimal management for patients with more complex issues. Previous literature has shown that the preoperative assessment of the presence of diabetes, renal

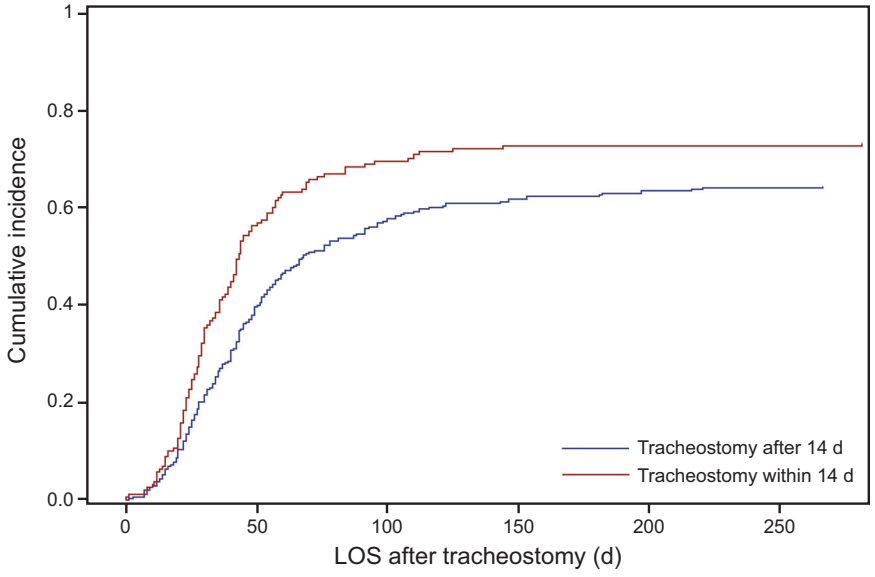

Fig. 1. Cumulative incidence of the subjects who were discharged alive after tracheostomy. LOS = length of stay.

dysfunction, and ventilation support; postoperative pulmonary edema and cerebral dysfunction; and the use of a deceased donor can be helpful in predicting the likelihood of postoperative mechanical ventilation requirement.[26,27] By providing evidence that early tracheostomy after orthotopic liver transplantation is associated with decreased mortality and length of hospital stay, we hope to encourage providers to evaluate the need for post-transplantation tracheostomy early and to consider the potential benefits that early tracheostomy can provide to their patients.

Our study has several limitations. The Healthcare Utilization Project Nationwide In-patient Sample database does not include readmission data and, as such, we were not able to assess mortality or other postoperative complications that took place after the initial discharge of a patient who had a transplantation. We propose that these in-patient hospital data provide substantive and valuable insight into the effects of early versus routine tracheostomy after transplantation, but readmission data would be helpful to further qualify the long-term implications of both scenarios. In addition, the Nationwide In-patient Sample does not provide information adequate enough for a detailed review of a patient's preoperative in-patient course or the hospital-specific care patterns. Thus, we were unable to include these nuances in the evaluation of predictors of mortality. Inaccuracies in ICD-9-CM coding as well as the absence of transplantation-specific variables, for example, Model for End-Stage Liver Disease,[28] make it difficult to evaluate the preoperative health status of the patients included in this study. Further, the lack of specific information about ventilation parameters, including duration and re-intubation as well as the initial indication for intubation makes our assessment of the success less complete. Nonetheless, the robust sample used for this analysis likely mitigates any effects of outliers on the outcome measures evaluated.

Conclusions

Despite significantly higher comorbidity scores, early tracheostomy after transplantation was associated with lower in-patient mortality and a shorter time to discharge. These results suggest that patients who have orthotopic liver transplantation and with respiratory failure and prolonged mechanical ventilation benefit significantly from early tracheostomy.

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