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Duration of oral endotracheal intubation is associated with dysphagia symptoms in acute lung injury patients

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Abstract

Purpose: The purpose of this study is to evaluate demographic and clinical factors associated with self-reported dysphagia after oral endotracheal intubation and mechanical ventilation in patients with acute lung injury (ALI).

Materials and methods: This is a prospective cohort study of 132 ALI patients who had received mechanical ventilation via oral endotracheal tube.

Results: The primary outcome was binary, whether clinically important symptoms of dysphagia at hospital discharge were reported by patients, using the Sydney Swallowing Questionnaire score 200 or more. Of 132 patients, 29% reported clinically important symptoms of dysphagia. Of 18 relevant demographic and clinical variables, only 2 were found to be independently associated with clinically important symptoms of dysphagia in a multivariable logistic regression model: upper gastrointestinal comorbidity (odds ratio, 2.82; 95% confidence interval, 1.09–7.26) and duration of oral endotracheal intubation (odds ratio, 1.79; [95% confidence interval, 1.15–2.79] per day for first 6 days, after which additional days of intubation were not associated with a further increase in the odds of dysphagia).

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Conclusions: In ALI survivors, patient-reported, postexubation dysphagia at hospital discharge was significantly associated with upper gastrointestinal comorbidity and a longer duration of oral endotracheal intubation during the first 6 days of intubation.

Keywords

Deglutition; Dysphagia; Intubation; Mechanical ventilation; Acute lung injury

1. Introduction

There are an estimated 5.7 million intensive care unit (ICU) admissions in the United States annually [1], with at least one-third requiring intubation with mechanical ventilation [2,3]. The number of adults requiring mechanical ventilation is growing, most rapidly for individuals more than 65 years old, with an expected 80% increase from 2000 to 2026 [4,5].

With the introduction of an oral endotracheal tube, laryngeal injury [6,7] and altered laryngeal sensation [8–11] frequently occur and may result in impaired swallowing [12]. Postextubation swallowing disorders (ie, dysphagia) have been reported in 14% to 83% of adult patients undergoing prolonged mechanical ventilation [13–17].

Dysphagia can have significant sequelae, including aspiration leading to lung injury and death [18–22]. Clinical studies of dysphagia after extubation have largely evaluated the presence of aspiration alone and are frequently limited by small sample sizes and heterogeneous patient groups [23,24]. Acute lung injury (ALI) is an archetype of critical illness [25], with patients having a high severity of illness, prolonged mechanical ventilation, and ICU-acquired muscle weakness, all of which may put patients at high risk for postextubation dysphagia. The aim of this study was to evaluate the association between the duration of oral endotracheal intubation and patient-reported dysphagia at hospital discharge in mechanically ventilated ICU patients with ALI.

2. Materials and methods

2.1. Study population

This evaluation was conducted as part of a prospective, multisite cohort study [26] evaluating consecutive mechanically ventilated patients with ALI, as defined by the American-European Consensus Conference criteria [27]. Eligible patients were recruited from 13 ICUs at 4 teaching hospitals in Baltimore, MD. Key patient exclusion criteria for this prospective cohort study were (1) more than 5 days of mechanical ventilation before ALI, (2) preexisting cognitive impairment or communication/language barrier, (3) transfer into a study site ICU with preexisting ALI of more than 24-hour duration, (4) limitations in advancing ICU care at the time of study eligibility (eg, no use of vasopressors), and (5) preexisting illness with a life expectancy of less than 6 months. To avoid including patients with primary neurologic disease or head trauma, neurologic specialty ICUs at participating hospitals were excluded from the study. In addition, because of this evaluation's focus on dysphagia symptoms after oral endotracheal intubation, for purposes of this analysis, we excluded study patients who (1) had a tracheostomy or nasal endotracheal tube during their

ICU stay, (2) had a history of prior tracheostomy, (3) were not consented, not eating by mouth or not capable of completing the Sydney Swallowing Questionnaire (SSQ) (eg, due to physical or cognitive impairment) at hospital discharge, or (4) discharged directly to another acute care hospital (ie, discharge from study site hospital did not represent the ultimate timing of acute care hospital discharge). All institutional review boards at participating sites approved this study, and written informed consent was obtained from each study participant or their substitute decision maker.

2.2. Primary outcome

The primary outcome measure for this evaluation was self-reported, clinically important dysphagia symptoms at hospital discharge. Dysphagia symptoms were assessed using the SSQ. The SSQ is a patient-reported, 17-item, validated symptom inventory used to assess severity of dysphagia symptoms [28]. The SSQ primarily uses a visual analog scale, with items scored 0 to 100 and the total SSQ score ranging from 0 to 1700. The SSQ was scored in the same manner as the original validation study [28], with higher scores representing increased patient-perceived difficulty with swallowing. Scores 200 or more are considered indicative of clinically important dysphagia [28], which was the primary binary outcome used in this evaluation.

2.3. Primary exposure

The primary exposure measure was duration of incident oral endotracheal intubation, measured in days. Patients extubated for less than 48 hours before being reintubated were considered to be continuously intubated from the initial placement of the oral endotracheal tube until extubation for 48 continuous hours or more [29].

2.4. Covariates

Patient and ICU variables evaluated for their potential association with dysphagia in this study were selected based on the existing literature and investigators' prior knowledge in this field. The following patient characteristics were considered: age, sex, race, and body mass index (BMI). Body mass index was categorized according to the standard criteria [30] to assist with clinical interpretation. Overall comorbidity burden (as measured by the Charlson Comorbidity Index [31]) was evaluated. We also evaluated preexisting neurologic comorbid disease (defined as stroke and any other neurologic disease [eg, transient ischemic attack, Parkinson disease, multiple sclerosis, and dementia]) and comorbid upper gastrointestinal disease (defined to include peptic ulcer, hiatal hernia, and gastroesophageal reflux disease). The following variables related to patients' critical illness were also included in this evaluation: ICU admitting diagnosis category, severity of illness at ICU admission (Acute Physiology and Chronic Health Evaluation [APACHE] II score [32]), organ dysfunction at ALI onset (Sequential Organ Failure Assessment [SOFA] [33]), reintubation, and ICU length of stay.

2.5. Statistical analysis

Descriptive statistics were reported using median and interquartile range (IQR) for continuous data and proportions for categorical data. A Wilcoxon rank sum test was used to

test for a significant difference in the time between extubation and completion of SSQ at hospital discharge for patients with vs without dysphagia. To confirm the appropriateness of modeling the odds of dysphagia as a linear function of each continuous variable, we examined a locally weighted smoother scatterplot [34–36] of the predicted odds vs the variable. Of all continuous variables, only the primary exposure variable demonstrated a potentially nonlinear relationship with the primary outcome, with a linear increase observed during the first 6 days of oral endotracheal intubation, followed by a plateau with minimal change thereafter (Fig. 1).

The associations of individual variables with the primary outcome (ie, binary indicator of dysphagia) were evaluated using logistic regression, with associations presented as odds ratios (OR). To prevent overfitting the multivariable logistic regression model, we limited the number of variables in this model to a ratio of 1 variable per 10 outcomes [37,38]. Individual covariates were included in the multivariable logistic model if they exhibited a bivariable association with the primary outcome with a $P < .10$. To address the nonlinear association of mechanical ventilation duration with the primary outcome in regression analyses, the duration of intubation was modeled using a linear spline with a “knot” at 6 days; thus, permitting different linear associations between the duration of intubation and the primary outcome before and after the designated “knot” [36,39].

As a secondary analysis, we evaluated the association of individual variables with the continuous SSQ score using linear regression, with associations presented as relative medians (RM). Because the distribution of SSQ scores was right skewed, we used the log-transformed SSQ score as the outcome variable for this model. As in the logistic regression model, duration of intubation was modeled using a linear spline with a “knot” at 6 days, and individual covariates were included in the final multivariable model if they exhibited bivariable associations with the outcome with a $P < .10$.

There were no missing data for all covariates considered in the final multivariable logistic and linear regression models. Variance inflation factors [40,41] were used to confirm the lack of multicollinearity in both multivariable models. A post hoc sensitivity analysis excluding patients with upper gastrointestinal comorbidities was conducted with no material change in the results. Model fit was confirmed using a Hosmer-Lemeshow test [42] for the logistic regression model. Cook’s distance and dfbeta statistics were used to determine influential points for the linear regression model. A 2-sided $P < .05$ was considered statistically significant. All statistical analyses were completed using Stata statistical software, version 12.1 (Stata Corporation, College Station, TX).

3. Results

The prospective cohort study enrolled a total of 520 ALI patients, with 51% (n = 144) of the 283 hospital survivors being eligible for this evaluation and 132 (92%) of these eligible patients having complete SSQ data for analysis (Fig. 2). For these 132 patients, median (IQR) age was 48 (40, 56) years, with 52% male and 58% white race (Table 1). A minority of patients had neurologic (14%) or upper gastrointestinal (18%) comorbidities. The median (IQR) APACHE II and SOFA scores were 23 (19, 28) and 8 (5, 10), respectively; and the

median (IQR) durations of oral endotracheal intubation, ICU stay, and hospital stay were 8 (5, 11), 12 (8, 16), and 21 (14, 30) days, respectively.

The median (IQR) SSQ score was 82 (25, 285) with 45 (34%) patients having clinically important symptoms of dysphagia (ie, SSQ score, ≥200). The median (IQR) time between extubation and hospital discharge was 11 (7, 19) days for all patients, with no significant difference comparing those with vs without dysphagia ($P = .849$).

For the logistic regression analysis, duration of oral endotracheal intubation and upper gastrointestinal comorbidity exhibited unadjusted associations with dysphagia of $P < .10$ and were included in the multivariable model (Table 2). Based on this multivariable model, duration of oral endotracheal intubation was significantly associated with dysphagia with an OR (95% CI) of 1.79 (1.15–2.79; $P = .010$) for each day of intubation up to 6 days. Odds of dysphagia did not change with increasing duration of intubation beyond day 6 (OR = 0.98, 95% CI = 0.90–1.07; $P = .724$). Upper gastrointestinal comorbidity was statistically significant with an OR (95% CI) of 2.82 (1.09–7.26; $P = 0.032$).

For the linear regression analysis, 4 variables exhibited unadjusted associations of $P < .10$ and were included in the multivariable model: duration of intubation, upper gastrointestinal comorbidity, Charlson Comorbidity Index, and SOFA score at hospital admission. These variables were included in a multivariable model. In this multivariable model, duration of oral endotracheal intubation was significantly associated with the log-transformed SSQ score with an RM (95% CI) of 1.31 (.04–1.63; $P = .020$) for each day of intubation up to 6 days and no significant association (RM = 0.98, 95% CI = 0.92–1.05; $P = .553$). Upper gastrointestinal comorbidity was also statistically significant (RM = 2.16, 95% CI = 1.05–4.46; $P = .037$), with neither Charlson Comorbidity Index nor SOFA significant in the multivariable model.

4. Discussion

In this multisite prospective cohort study of ALI patients with oral endotracheal intubation, we found that 34% of patients reported clinically important symptoms of dysphagia and that preexisting upper gastrointestinal comorbidity and the duration of oral endotracheal intubation during the first 6 days of intubation were independently associated with dysphagia. After endotracheal intubation for 24 hours or more, there is a range of dysphagia prevalence estimates, with most studies reporting more than 20% based on clinical and/or instrumental evaluations across multiple patient populations (eg, medical, surgical, cardiac, and trauma) [13–17]. A recent study found that, even with less than 48 hours of intubation, 84% of patients had at least mild dysphagia [43]. The 34% prevalence in our study may be conservative due to use of a patient-reported survey of dysphagia and the relatively later timing of evaluation (ie, hospital discharge vs shortly after extubation) [15,16,43,44].

The literature has conflicting results regarding the association of the duration of endotracheal intubation and dysphagia. This lack of agreement among prior studies is likely due to variable methods for evaluating dysphagia, heterogeneous patient samples, analyses not adjusting for confounding, and small sample sizes [23]. Only 3 studies used regression

analysis to adjust for confounding. One study prospectively evaluated patients who were intubated for more than 24 hours, using electromyography to measure initiation of the pharyngeal swallow and showed no association of intubation duration with swallow initiation [9]. A second study retrospectively reviewed patient medical records and found a positive association of duration of short-term (ie, intraoperative) oral endotracheal intubation with dysphagia in cardiac surgery patients undergoing intraoperative transesophageal echocardiography [45]. The third study prospectively recruited patients who were intubated for more than 10 days, using a fiberoptic endoscopy to evaluate swallowing function and demonstrated that reduced muscle strength, a penetration-aspiration scale [46] score more than 1, and duration of mechanical ventilation are associated with symptomatic aspiration [47]. It is difficult to directly compare our data with these studies because of differences in study design and patient populations. Greater investigation in this field is needed to have a larger foundation of epidemiological data.

Laryngeal injury begins within the first day of intubation, including edema, tissue damage, and voice dysfunction [6,7], each of which is a risk factor for postextubation dysphagia [17,48–50]. With endotracheal intubation for longer than 48 hours, laryngeal injury can lead to permanent vocal fold damage, vocal fold paralysis, and dysphagia resulting in aspiration [8,51–53]. Our finding of daily increased odds of dysphagia and severity of swallowing dysfunction during the first 6 days of oral endotracheal intubation suggests a critical period during which reduction in intubation duration (eg, through measures such as reduced sedation and daily spontaneous breathing trials [54–56]) may reduce dysphagia risk. Consistent with other studies, we did not find an association of age or sex with dysphagia [9,15–17,44,45].

We found that patients with upper gastrointestinal comorbidities have a 3-fold increased odds of having clinical important dysphagia symptoms. This finding is not surprising given the overlap of symptoms associated with globus pharyngeus and gastroesophageal reflux and dysphagia in the questions of the SSQ [28,57–60]. Of note, we did not find an association between patients with neurologic comorbidities and clinically important dysphagia symptoms. This finding is not consistent with prior research that showed 93% of patients with neurologic impairments had dysphagia after extubation and that longer durations of intubation were independently associated with moderate-severe dysphagia; however, that study focused exclusively on patients with primary diagnoses of neurologic disorders, an exclusion criterion for the present study [24].

4.1. Limitations

This study has several potential limitations. First, due to the nature of critical illness and the emergent need for mechanical ventilation, it is not possible to evaluate patients for dysphagia before intubation. Consequently, only the prevalence, rather than incidence, of dysphagia could be estimated in this study. Second, our study used the SSQ, a patient-reported measure, instead of a clinical or instrumental assessment of dysphagia. Hence, physiologic aspects of swallowing were not assessed. Third, we exclusively studied ALI patients recruited from 4 teaching hospitals in Baltimore, and a substantial proportion of ALI survivors were not eligible for this analysis (as per a priori eligibility criteria), which

may limit the generalizability of the study findings. However, our relatively large and homogenous sample (compared with prior studies in this field) is a strength of the present study. Given the relative ease of administration of the SSQ, we encourage further research in other ICU populations, including studies using instrumental assessment of swallow physiology, to consider evaluating dysphagia symptoms using the SSQ.

5. Conclusions

Our multisite, prospective cohort study suggests that approximately one-third of orally intubated ALI patients had clinically important symptoms of dysphagia at hospital discharge. Preexisting upper gastrointestinal comorbidity was independently associated with dysphagia along with the duration of oral endotracheal intubation through the first 6 days of intubation. Our results may help focus attention on the risk of dysphagia after oral endotracheal intubation and encourage further research aimed at reducing complications associated with the duration of endotracheal intubation and its effects on swallowing.

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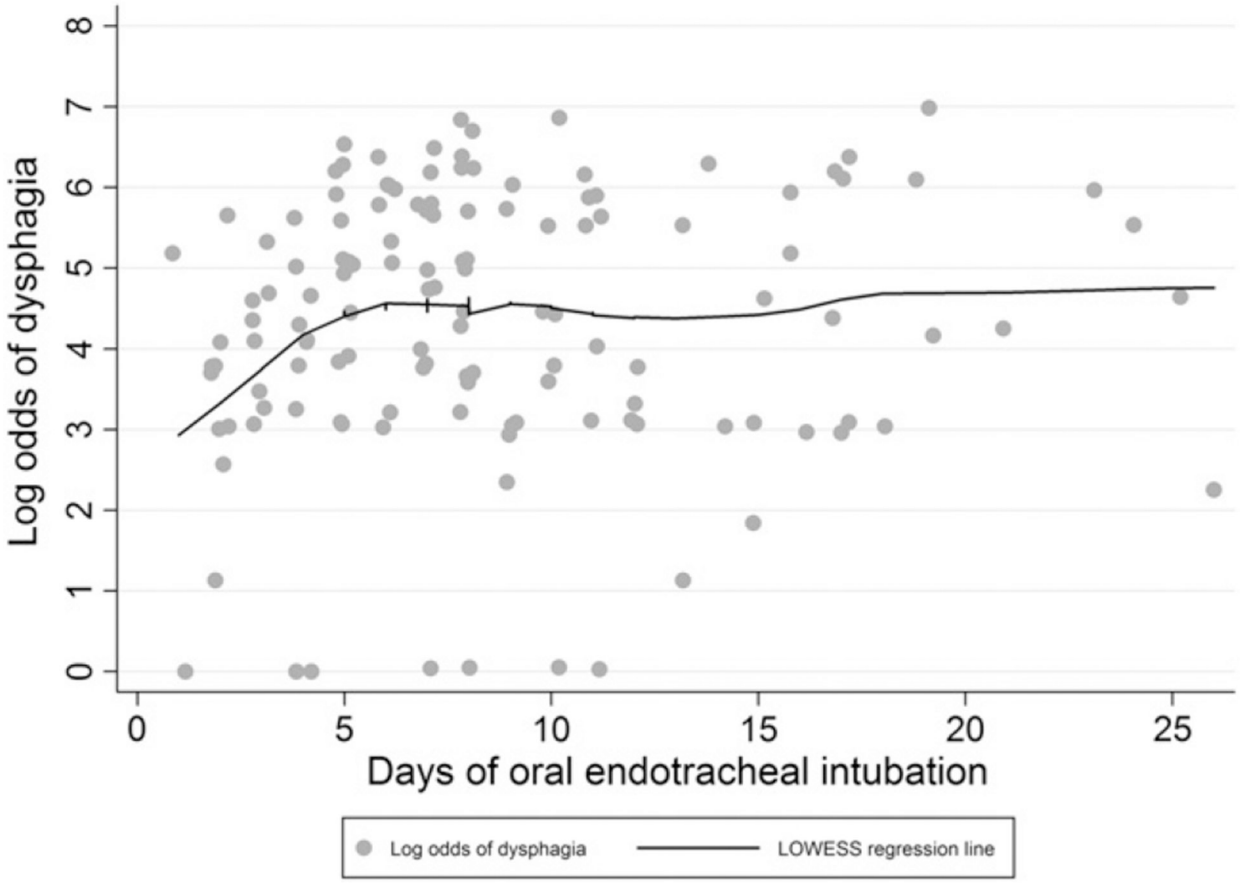

Fig. 1.

Log odds of dysphagia (ie, SSQ score, ≥200) vs duration of mechanical ventilation with an oral endotracheal tube.

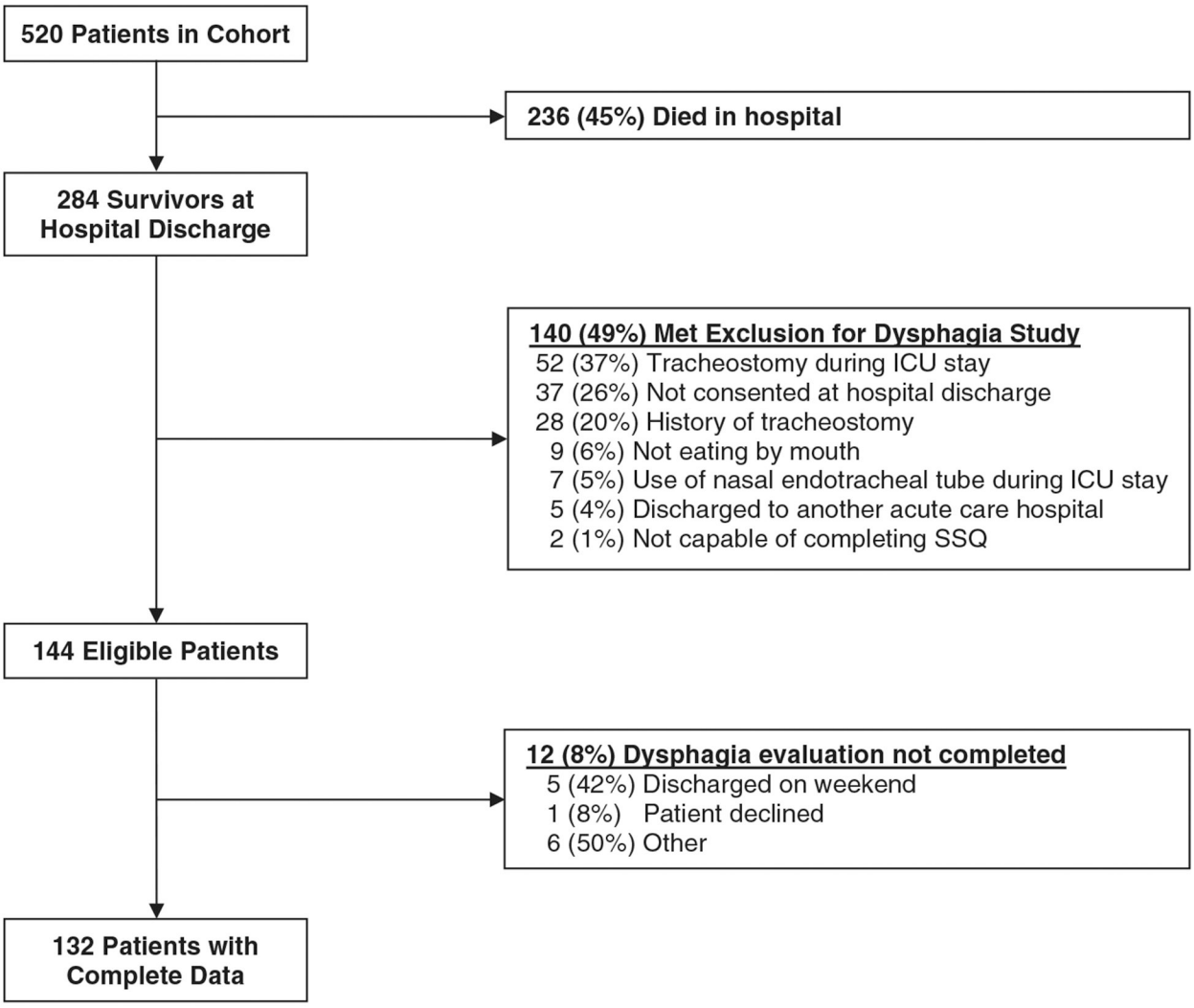

Fig. 2.
Study flow diagram.

Table 1

Acute lung injury patient characteristics, by dysphagia status

	Total (N = 132)	No dysphagia (n = 87)	Dysphagia[a] (n = 45)
Demographics			
Age, median (IQR) years	48 (40, 56)	48 (38, 57)	45 (40, 53)
Male, no. (%)	69 (52)	46 (53)	23 (51)
White, no. (%)	77 (58)	53 (61)	24 (53)
Baseline health status before admission			
Charlson Comorbidity Index, median (IQR) score	1 (0, 3)	1 (0, 3)	2 (0, 4)
Neurologic disease[b], no. (%)	19 (14)	10 (11)	9 (20)
Upper gastrointestinal disease[c], no. (%)	24 (18)	11 (13)	13 (29)
BMI[d]			
Underweight (<18.5 kg/m^2)	5 (4)	3 (4)	2 (5)
Normal (18.5–24.9 kg/m^2)	31 (26)	22 (28)	9 (23)
Overweight (25–29.9 kg/m^2)	42 (36)	30 (38)	12 (31)
Obese (≥30 kg/m^2)	40 (34)	24 (30)	16 (41)
ICU admission diagnosis[e], no. (%)			
Respiratory (including pneumonia)	77 (58)	51 (59)	26 (58)
Nonpulmonary sepsis and infectious disease	20 (15)	12 (14)	8 (18)
Upper gastrointestinal	11 (8)	7 (8)	4 (9)
Trauma	6 (5)	4 (5)	2 (4)
Cardiovascular	5 (4)	4 (5)	1 (2)
Other	13 (10)	9 (10)	4 (9)
ICU factors			
APACHE II score at ICU admission, median (IQR)	23 (19, 28)	24 (20, 28)	22 (17, 26)
SOFA score at ALI onset, median (IQR)	8 (5, 10)	7 (5, 10)	8 (6, 10)
Ever reintubated, no. (%)	23 (17)	16 (18)	7 (16)
Duration of orotracheal intubation, median (IQR) days	8 (5, 11)	7 (4, 11)	8 (5, 11)
ICU length of stay, median (IQR) days	12 (8, 16)	11 (7, 15)	13 (8, 18)

[a] Sydney Swallowing Questionnaire score ≥200 or more is considered indicative of clinically important dysphagia [28].

[b] Includes stroke and any other neurologic disease (eg, transient ischemic attack, Parkinson disease, multiple sclerosis, and dementia).

[c] Includes peptic ulcer, hiatal hernia, and gastroesophageal reflux disease.

[d] Body mass index was not available for 14 patients.

[e] Percentages may not add to 100% due to rounding.

Table 2

Factors associated with dysphagia in ALI patients with oral endotracheal intubation

	Bivariable association		Multivariable model	
	OR (95% CI)	P^a	OR (95% CI)	P^a
Primary exposure				
Orotracheal intubation ≤6 days, per day	1.81 (1.17, 2.80)	.008	1.79 (1.15, 2.79)	.010
Orotracheal intubation >6 days, per day	0.98 (0.90, 1.06)	.598	0.98 (0.90, 1.07)	.724
Demographics				
Age	1.00 (0.97, 1.02)	.827		
Male	0.93 (0.45, 1.91)	.848		
White	0.73 (0.35, 1.52)	.403		
Baseline health status before admission				
Charlson Comorbidity Index	1.08 (0.93, 1.24)	.304		
Neurologic disease[b]	1.93 (0.72, 5.15)	.192		
Upper gastrointestinal disease[c]	2.81 (1.14, 6.92)	.025	2.82 (1.09, 7.26)	.032
BMI				
Normal (18.5–24.9 kg/m^2)	(Reference)			
Underweight (<18.5 kg/m^2)	1.63 (0.23, 11.45)	.624		
Overweight (25–29.9kg/m^2)	0.98 (0.35, 2.72)	.966		
Obese (≥30 kg/m^2)	1.62 (0.60, 4.43)	.339		
ICU admission diagnosis				
Respiratory (including pneumonia)	(Reference)			
Nonpulmonary sepsis and infectious disease	1.31 (0.48, 3.60)	.603		
Upper gastrointestinal	1.12 (0.30, 4.18)	.865		
Trauma	0.98 (0.17, 5.71)	.983		
Cardiovascular	0.49 (0.05, 4.61)	.533		
Other	0.87 (0.25, 3.10)	.832		
ICU factors				
APACHE II score at ICU admission	0.98 (0.93, 1.03)	.439		
SOFA score at ALI onset	1.10 (0.98, 1.22)	.105		
Ever reintubated	0.82 (0.31, 2.16)	.684		
ICU length of stay	1.04 (0.99, 1.10)	.110		

[a] *P* calculated using simple and multiple logistic regression analysis for bivariable and multivariable results, respectively. Covariates were included in the multivariable logistic model based on a bivariable association at $P < .10$.

[b] Includes stroke and any other neurologic disease.

[c] Includes ulcer, hernia, and reflux.