



Published in final edited form as:

Dysphagia. 2018 December ; 33(6): 768–777. doi:10.1007/s00455-018-9901-z.

Coordination of pharyngeal and laryngeal swallowing events during single liquid swallows after oral endotracheal intubation for patients with acute respiratory distress syndrome

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Abstract

Purpose—To evaluate timing and duration differences in airway protection and esophageal opening after oral intubation and mechanical ventilation for acute respiratory distress syndrome (ARDS) survivors versus age-matched healthy volunteers.

Methods—Orally intubated adult (> 18 years old) patients receiving mechanical ventilation for ARDS were evaluated for swallowing impairments via a videofluoroscopic swallow study (VFSS) during usual care. Exclusion criteria were tracheostomy, neurological impairment, and head and neck cancer. Previously recruited healthy volunteers (n=56) served as age-matched controls. All subjects were evaluated using 5-ml thin liquid barium boluses. VFSS recordings were reviewed frame-by-frame for the onsets of 9 pharyngeal and laryngeal events during swallowing.

Results—Eleven patients met inclusion criteria, with a median (interquartile range [IQR]) intubation duration of 14 (9, 16) days, and VFSSs completed a median of 5 (4, 13) days post-extubation. After arrival of the bolus in the pharynx, ARDS patients achieved maximum laryngeal closure a median (IQR) of 184 (158, 351) ms later than age-matched, healthy volunteers (p<0.001) and longer to achieve laryngeal closure with a median (IQR) difference of 151 (103, 217) ms (p<0.001), although there was no significant difference in duration of laryngeal closure.

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Compliance with Ethical Standards

Conflict of Interest

All authors declare that there is no conflict of interest.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Pharyngoesophageal segment opening was a median (IQR) of -116 ($-183, 1$) ms ($p=0.004$) shorter than in age-matched, healthy controls.

Conclusions—Evaluation of swallowing physiology after oral endotracheal intubation in ARDS patients demonstrates slowed pharyngeal and laryngeal swallowing timing, suggesting swallow-related muscle weakness. These findings may highlight specific areas for further evaluation and potential therapeutic intervention to reduce post-extubation aspiration.

Keywords

deglutition; deglutition disorders; dysphagia; intubation; mechanical ventilation; acute respiratory distress syndrome; fluoroscopy

Critical illness requiring orotracheal intubation with mechanical ventilation occurs in approximately 13–20 million patients globally¹ and continues to grow annually.^{2–6} During mechanical ventilation, muscle wasting and weakness occurs commonly and early after the onset of critical illness.^{7–9} With oropharyngeal swallowing requiring a synergistic activation of more than 30 muscles,^{10–12} there is great opportunity for dysfunction and poor patient outcomes as a result of critical illness with intubation and mechanical ventilation.^{13–16} Weakness during swallowing, leading to dysfunction and altered timings of the coordination of these nerves and muscles, may result in dysphagia with or without aspiration and worse patient outcomes.^{15–18} Aspiration, one consequence of dysphagia, can lead to pulmonary infection (e.g., aspiration pneumonia) that results in increased morbidity, longer hospital stay, increased hospital charges, and death.^{19–22} Surgical patients with aspiration pneumonia, for example, have a 4-fold increased odds of admission to the ICU and a 7-fold increased odds of inpatient mortality during their hospital stay.²¹

After critical illness, dysphagia is also an important issue. For instance, within 48 hours of oral endotracheal tube extubation from mechanical ventilation for acute respiratory failure, up to 56% of patients have dysphagia.^{13,23–27} However, referral to speech-language pathologists for a swallowing evaluation is relatively infrequent,²⁸ often delayed, and highly variable in clinical practice.²⁹ We previously reported a 33% referral rate for post-extubation swallowing assessment across 13 ICUs at 4 hospitals in a prospective study of acute respiratory distress syndrome (ARDS) patients.²⁸ In patients surviving ARDS, an archetypical example of critical illness,³⁰ resolution of dysphagia symptoms often takes 3–6 months, and in some cases up to 5 years.³¹

Despite its importance, there is limited understanding of changes in swallowing physiology after extubation and mechanical ventilation in critically ill patients. A systematic review of the literature demonstrated that existing research had heterogeneous and/or small patient samples, unclear/undefined outcomes, and inconsistent assessment methods.¹³ Moreover, existing studies largely address a single outcome of dysphagia—aspiration. Although early identification of aspiration is important, identifying the impaired swallowing physiology that leads to aspiration is valuable for considering targeted treatment plans, helping inform prognosis, and enhancing the ability of patients to work toward their recovery goals.^{32–34} Hence, the objective of this study was to evaluate the timing and duration of key swallowing events in ARDS patients after oral intubation and mechanical ventilation compared to age-

matched, healthy volunteers. The swallowing events of primary interest were those associated with airway protection and pharyngoesophageal segment (PES) opening, with a secondary objective of comparing temporal patterns of 8 distinct pharyngeal and laryngeal swallowing events with respect to initiation of the pharyngeal swallow.

Methods

Participants

Data were available from two groups for comparison: 1) patients ≥ 21 years old with ARDS³⁵ who were orally intubated with mechanical ventilation in an ICU, and 2) healthy volunteers. Eligible ARDS patients were part of a prospective cohort study, consecutively screened from 4 ICUs in 1 teaching hospital between 2004 and 2007, who had a videofluoroscopic swallow study (VFSS) completed as a part of routine clinical care, with 1 administration of 5-ml liquid barium. As part of pre-existing eligibility criteria for the prospective cohort study, ARDS patients were excluded from enrollment if they met any of the following criteria: 1) >5 days of mechanical ventilation before ARDS onset; 2) communication/language barrier or pre-existing cognitive impairment; 3) pre-existing ARDS of >24 hours duration before being transferred into the study site hospital; 4) physician order for limitations in life support (e.g., no use of vasopressors permitted) at study eligibility; 5) life expectancy of <6 months due to pre-existing illness (e.g., terminal cancer); and 6) tracheotomy during their ICU stay. This study was approved by the Johns Hopkins Medicine Institutional Review Board. Written informed consent was obtained from each patient or his/her proxy if the patient was incapable of consent.

Healthy volunteers were participants in a previous prospective cohort study.^{36,37} Inclusion criteria were: 1) consumption of liquids and solid foods as part of a regular diet, and 2) no swallowing complaints. Exclusion criteria were: 1) presence of a known swallowing disorder, 2) gastroesophageal symptoms and/or disease associated with dysphagia, 3) upper aerodigestive tract surgical procedures, 4) pulmonary, head and neck, and/or neurologic disease, 5) current medications with known effects on swallowing or breathing, and 6) use of any tobacco products within the past 10 years.

Instrumentation and Procedures

Swallowing physiology data was acquired using VFSS in a similar manner for both ARDS patients and healthy volunteers as described herein. All VFSS imaging used thin liquid barium (liquid Barospense[®] barium sulfate suspension). VFSSs for ARDS patients were originally recorded on 1/2-inch videocassettes using an S-VHS videocassette recorder that were later converted to digital recordings at 29.97 frames per second. Healthy volunteers were recorded directly to digital media at 30 frames per second and analyzed using the Digital Swallowing Workstation, model 7200 manufactured by Kay PENTAX Corp., Lincoln Park, NJ (currently PENTAX Medical), with details previously published.^{36,37}

All participants (i.e., ARDS patients and healthy volunteers) were positioned in lateral projection with ARDS patients seated and healthy volunteers standing. The field of view was often intentionally limited in the ARDS patients as a standard procedure in our facility to

reduce radiation exposure to the eyes, yielding a field of view that often included the oral cavity posterior to the incisors, whereas healthy volunteers had an anterior limit of patients' lips for the field of view. Aside from this difference in anterior limits of the field of view, both groups had similar views that included the posterior pharyngeal wall posteriorly, nasal cavity superiorly, and upper esophagus inferiorly.^{38–40}

The number of administrations of 5-ml liquid barium was variable, depending on whether the patient safely swallowed the first 5-ml or whether subsequent administrations were required to determine effectiveness of implemented swallowing strategies.^{38–40} The first 5-ml bolus of liquid barium was analyzed in ARDS patients to be comparable with the healthy volunteers. In the healthy volunteers, 5-ml liquid barium was self-administered via a 30-ml medicine cup (1 cup per trial) in 2 trials, with no statistically significant variability between trials;^{36,37} hence, for this analysis, only the first trial was evaluated. Both ARDS patients and healthy volunteers were evaluated in the lateral viewing plane and asked to hold the 5-ml bolus in their mouths before being asked to swallow. After loading the bolus, the fluoroscope was turned on and the subject was asked to swallow. The movement of the barium was visually followed from the oral cavity, through the pharynx, and through the PES as the bolus entered the esophagus. The fluoroscope was turned off at the completion of the swallow.

Data Analysis

All pharyngeal swallowing events analyzed for the current study were referenced from the swallowing events previously published.^{36,37} Throughout this study, the first video frame corresponding to each identified event was established as the event's onset. All onsets were identified using the slow motion, freeze-frame, and frame advance functions of the digital video players. Five blinded reviewers completed all kinematic assessments, with 3 reviewers for each swallowing event. Intraclass correlation coefficient was 0.99 across all events.

Nine swallowing events were evaluated in every subject (Table 1). For our primary objective, 6 of these 9 swallowing events (Table 2) were evaluated to analyze 3 pharyngeal duration measures associated with aspiration risk:^{41–45} 1) time to achieve maximum laryngeal closure (lc - mlc), 2) duration of laryngeal closure (mlc - lr), and 3) duration of PES opening (peso - lpeso). Analyses for the secondary objective examined the temporal pattern of the pharyngeal swallow considering all 9 swallowing events (Table 1), with initiation of the pharyngeal swallow, identified as onset of hyoid excursion (he), as the reference point. Onsets for all 9 events for ARDS patients were identified from the videos and recorded as a video frame number using VirtualDub (version 1.10.4, Avery Lee, virtualdub.org). The difference in number of video frames from he to each of the 8 remaining events, multiplied by 0.3336 per video frame for each of the ARDS patients and 0.03333 ms per video frame for each of the healthy controls, determined the time-to-onset for each swallowing event from initiation of the pharyngeal swallow.

Statistical Analyses

ARDS patients were age-matched to all available healthy volunteers using the original age categories of the healthy volunteers: 1) 21 – 40 years, 2) 41 – 60 years, and 3) 61 – 80 years.

³⁶ No difference in swallowing kinematics has been demonstrated between the sexes; thus, no sex matching was performed.⁴⁶ The median and interquartile ranges of differences between ARDS patients and healthy volunteers were calculated and compared using Wilcoxon rank sum tests. Given the 3 statistical comparisons planned for the primary objective, statistical significance was defined as $p < 0.017$, based on a Bonferroni correction (i.e., $\alpha = 0.05$ divided by 3 comparisons). Statistical analyses were completed using Stata/IC version 15.1 (Stata Corporation, College Station, TX).

Results

Demographics

Of a total of 191 ARDS patients, 26 (14%) completed a VFSS via a physician order, based on a speech-language pathologist recommendation. Of these 26 patients, 11 (42%) met all eligibility criteria and were included in the final analysis (Figure 1). These 11 patients, 8 (73%) female, had a median (interquartile range [IQR]) age of 53 (44, 67) years (Table 3). The median (IQR) duration of oral endotracheal intubation was 14 (9, 16) days, with a time to VFSS of 5 (4, 13) days after extubation.

Pharyngeal Duration Measurements

Swallowing duration measurements for ARDS patients versus healthy volunteers are presented in Table 4. ARDS patients took longer to achieve laryngeal closure, with a median (IQR) of 151 (103, 217) ms longer ($p < 0.001$) than healthy controls. Compared with healthy controls, pharyngoesophageal segment opening during the swallow was maintained a median (IQR) of -116 (-183, 1) ms shorter for ARDS patients. There was no significant difference ($p = 0.987$) between groups for duration of laryngeal closure. One ARDS patient (9%) demonstrated aspiration during the VFSS.

Swallowing Events

Mean onsets of 8 distinct swallowing events and differences between ARDS patients and healthy volunteers are presented in Table 5. There were large differences between the groups in 4 swallowing events from the time of initiation of the pharyngeal swallow: 1) time to achieve maximum laryngeal closure (mlc), 2) maximum hyoid excursion, 3) laryngeal reopening after completion of the pharyngeal swallow (lr), and 4) hyoid return to rest (hrr), i.e., total duration of the pharyngeal swallow. After initiation of the pharyngeal swallow, the time to achieve laryngeal closure (mlc), the time to achieve maximum hyoid excursion (mhe), and the time to reopen the larynx after the pharyngeal swallow (lr) were a median (IQR) of 118 (17, 218) ms ($p = 0.002$), 83 (0, 216) ms ($p = 0.006$) and 101 (68, 202) ms ($p < 0.001$) longer in ARDS patients, respectively. These 3 events contributed greatly to lengthening the pharyngeal swallow. Total duration of the pharyngeal swallow for ARDS patients was a median (IQR) of 635 (303, 968) ms longer ($p < 0.001$) compared to healthy volunteers (Figure 2).

Discussion

This study evaluated a prospective cohort of ARDS patients who were orally intubated and mechanically ventilated compared to an existing dataset of age-matched, healthy volunteers on 3 temporal measurements associated with aspiration risk during 5-ml thin liquid barium swallows using VFSS. To our knowledge, this is the first study to characterize the temporal relationships of swallowing events in a post-extubated ARDS patient population. We observed that ARDS patients had slow closure of the larynx during the swallow, lasting a median of 151 ms. This duration was nearly double that of healthy volunteers, placing patients at increased risk for entrance of liquids and solid food into the airway before the swallow begins and as the swallow continues through full closure of the larynx. Notably, only 1 (9%) of the 11 ARDS patients aspirated the 5-ml thin liquid bolus, suggesting that factors other than timing of swallowing are associated with aspiration in ARDS patients after extubation (e.g., sensation,⁴⁷ respiratory-swallow coordination^{48,49}). Although there was no difference in the duration of laryngeal closure, ARDS patients were delayed in re-opening their airway after the swallow. This potential protection, however, may be offset by their reduced duration of PES opening leading to greater retention of portions of the bolus after the swallow. Our sample size of ARDS patients was small and only 1 (9%) patient aspirated during the VFSS. As such, no conclusions may be made regarding the altered timings found in this study; however, our study raises the hypothesis that altered timing of swallowing events may not increase risk of aspiration in post-extubated ARDS patients.

Delayed initiation of the pharyngeal swallow has been attributed to altered and/or reduced sensation.^{12,50,51} For orally intubated ARDS patients, this change in sensation may arise from the extended duration of an endotracheal tube and/or minimal stimulation in the oral cavity and/or pharynx throughout the duration of intubation.^{15,16,52–54} Another possible cause may be depressed swallowing responses from sedation medications and sedation status.^{55–57} Given that an endotracheal tube and mechanical ventilation are often needed for survival of ARDS patients, altered sensation may be a consequence of intubation that becomes a target for rehabilitation. In isolation, entry of the bolus into the pharynx prior to the initiation of the pharyngeal swallow (i.e., hyoid excursion) is a normal variant.⁵⁸ Although there was no apparent delay in the initiation of the pharyngeal swallow, the lengthy period required to close the larynx requires some attention.

Oropharyngeal swallowing is performed by skeletal muscles and is, therefore, vulnerable to atrophy during critical illness.⁷ In patients who are critically ill and require intubation with mechanical ventilation, dysphagia may be manifested as slowed execution of swallowing movements.⁵³ Swallowing during intubation is initially eliminated when the neuromuscular block is administered during placement of the endotracheal tube. After the neuromuscular block wears off, typically in 30 minutes, swallowing may resume, depending on sedation, but frequency of swallowing during intubation is currently unknown. Healthy adolescents and young adults swallow an average of 300 times per hour during meals, 30 – 40 times per hour during a restful activity such as reading, and 8 times per hour while sleeping.⁵⁹ Comparatively, non-intubated patient populations swallow less frequently, but are highly variable.⁶⁰ The median duration of intubation was 14 days in these ARDS patients. Absent of mealtime stimuli to swallow, and given the severity of critical illness, we expected to see

substantive changes in the temporal coordination of swallowing, specifically in movements associated with hyolaryngeal excursion, airway closure, and PES opening due to the presence of an endotracheal tube and its influence of restricting movement of these structures.

The association of dysphagia with duration of endotracheal intubation with mechanical ventilation in critically ill patients is controversial.¹³ Patients who are critically ill, especially those who are intubated with mechanical ventilation, frequently experience muscle weakness, at least partially related to bedrest and disuse of skeletal muscles.^{61–63} Moreover, some data suggest that ICU length of stay is associated with dysphagia.^{64,65} If this were true, it would follow that dysphagia is less common in patients who are critically ill but do not require intubation with mechanical ventilation, a hypothesis that requires further research.

We cannot overlook the possibility that the extended time required for ARDS patients to close their larynx during swallowing may be the result of the reduced or altered sensation during intubation ultimately affecting sensorimotor muscle response, muscle weakness, or both. It has been suggested that residual sedation may be responsible for post-extubation dysphagia.⁵⁴ Patients in this study were evaluated by VFSS a median of 5 (IQR: 4, 13) days after extubation, sufficiently long enough for residual sedation to resolve. Moreover, 9 of the 11 patients had been discharged from the ICU at the time of the VFSS, and all patients were appropriately alert for completion of the VFSS as documented in the medical record and determined by the speech-language pathologist who completed the VFSS. The 2 patients still admitted to the ICU at the time of the VFSS were 4 and 5 days post-extubation, respectively. In the end, with an endotracheal tube removed, sedatives eliminated, and an alert patient, muscle weakness appears to be a plausible explanation.

Our secondary objective was to describe the temporal pattern of 8 distinct pharyngeal and laryngeal swallowing events in ARDS patients vs. healthy volunteers. The ARDS patients demonstrated 4 swallowing events that were substantially different: 1) longer time to achieve laryngeal closure, 2) longer time to achieve hyoid excursion, 3) longer time before the larynx reopens after the pharyngeal swallow, and 4) a longer duration of the pharyngeal swallow. The onsets of all other swallowing events demonstrated little difference between groups. These findings are aligned with previous muscle physiology studies in animals post-anesthesia, demonstrating little disturbance in the patterning but with overall lengthening of the swallow.^{12,66}

Of note, the temporal pattern changed for two events, with closure of the PES preceding laryngeal reopening in patients. This small adjustment in sequencing, however, may be explained by the larger variability for these time points observed in our patients. However, if this temporal shift in events remains robust in future studies, the previously stated conclusion that this shift in time allows for delayed reopening and protects the airway is tenuous. In fact, the risk of aspiration occurring after the swallow increases with the presence of residue remaining in the pharynx.

Limitations

Several limitations exist with this study. First, the sample size of ARDS patients was small, leading to reduced precision of the results and being underpowered to detect potentially clinically important associations and differences between groups of participants. Second, the recording media and equipment for recording were different between the ARDS patients and healthy volunteers. Although there is a minor frame rate loss when comparing the ARDS patients using a frame rate of 29.97 frames per second vs. the 30 frames per second in the healthy controls, the loss is nominal. Third, only ARDS patients who were intubated with oral endotracheal tubes were studied. These results may not be generalizable to other groups of ARDS patients who may not have been sufficiently concerning to clinicians and were not referred for a VFSS. These results also may not be generalizable to other types of critical illnesses requiring oral endotracheal intubation in the ICU. Despite these potential limitations, this study offers new insights into the physiology of impaired swallowing and potential targets for assessment of post-extubation dysphagia in critically ill patients recovering from ARDS.

Conclusions

This observational study found that this group of patients with ARDS who were orally intubated with mechanical ventilation and clinically referred for VFSS has significant changes in the timing of pharyngeal swallowing events. These preliminary findings may indicate specific areas for potential therapeutic intervention to aid in the recovery of dysphagia from critical illness.

Acknowledgments

The authors thank Lisa Aronson Friedman, Sc.M. for her statistical assistance and Therese Cole, M.A., CCC-SLP, BCS-S and Nicole Langton-Frost M.A. CCC-SLP, BCS-S for their contributions in analyzing video event timings. The authors also thank Bonnie Martin-Harris, Ph.D., CCC-SLP, BCS-S for the healthy volunteers data set.

Funding

This study was funded by the National Institutes of Health.

Research was supported by the National Institutes of Health (Grants: P050HL73994, R01HL088045, and 5K23DC013569).

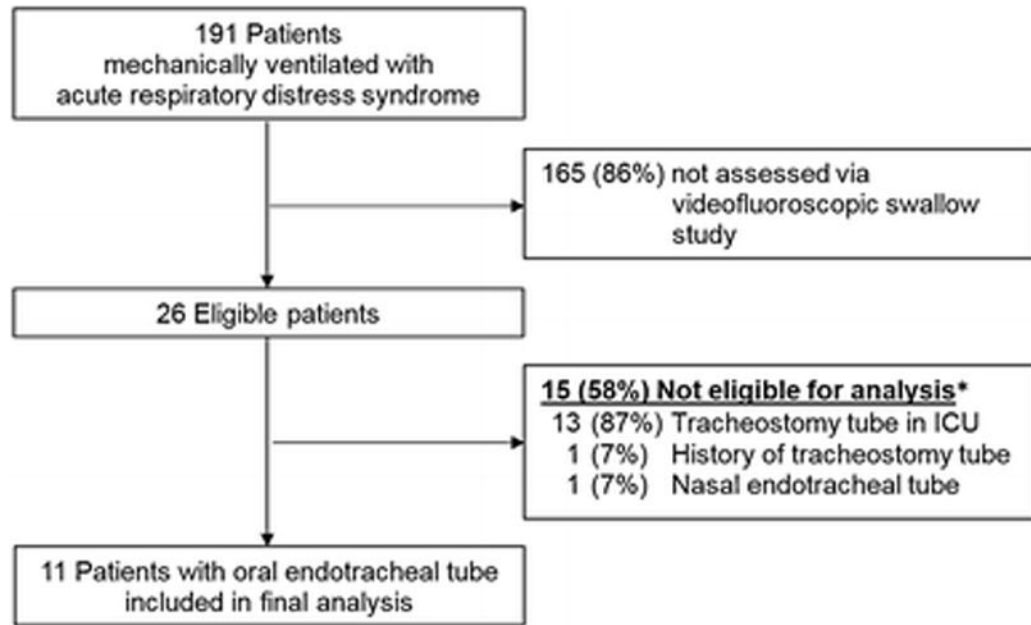
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* Percentages do not add to 100% due to rounding.

Figure 1.

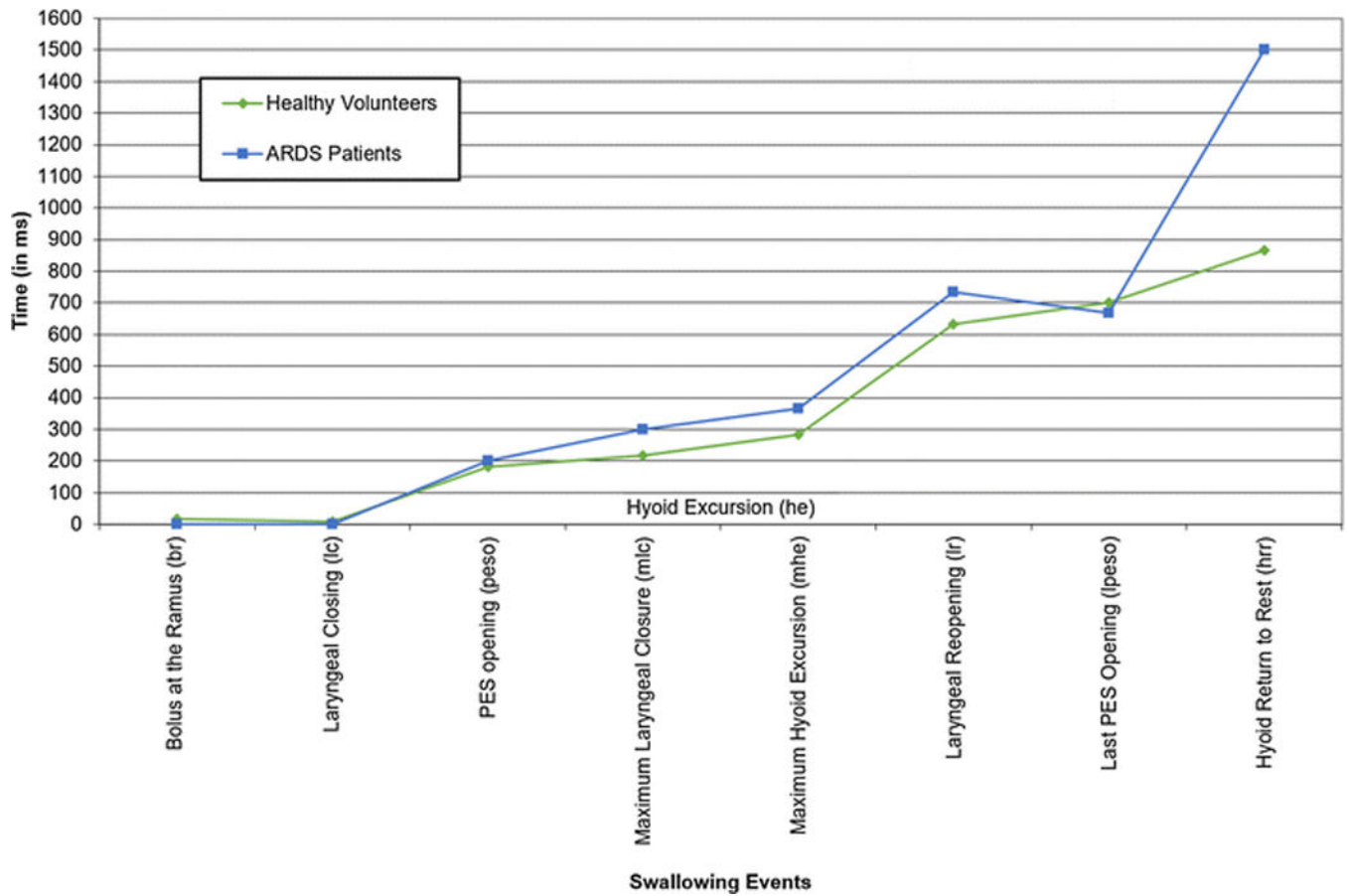


Figure 2. Swallowing event onsets, relative to initiation of the pharyngeal swallow (i.e., hyoid excursion), in patients with acute respiratory distress syndrome vs. healthy volunteers. Note: Variability is indicated in Table 5.

Table 1Operational definitions for swallowing event onsets^a

Event onsets	Definition	Event type ^b
Hyoid excursion (he)	Onset of superior and anterior movement of hyoid bone	Physiologic
Bolus at the ramus of the mandible (br)	Bolus head arrival at radiographic posterior angle of the ramus of mandible	Bolus flow
Laryngeal closing (lc)	Onset of forward displacement of arytenoid cartilages toward base of the epiglottis	Physiologic
PES opening (peso)	Onset of anterior-to-posterior widening of the area containing the cricopharyngeus located between C ₄ and C ₆	Physiologic
Maximum laryngeal closure (mlc)	Full apposition of arytenoid cartilages to base of the epiglottis	Physiologic
Maximum hyoid excursion (mhe)	Most antero-superior position of the hyoid bone	Physiologic
Laryngeal reopening (lr)	Separation of arytenoid cartilages from base of the epiglottis	Physiologic
Last PES opening (lpeso)	Last frame when PES is open before closing post-swallow	Physiologic
Hyoid return to rest (hrr)	Frame in which hyoid has returned (from its most superior and anterior position) to a stable, relaxed position	Physiologic

PES, pharyngoesophageal segment; t₀, reference time point

^aOperational definitions are based on previous work.^{23,24}

^bEvent type distinguishes between anatomical movements producing a physiological response in the swallow (physiologic) and flow of the bolus relative to an anatomical landmark (bolus flow).

Table 2

Operational definitions for selected duration measures.

Duration Measure	Definition
Time to achieve laryngeal closure	Laryngeal closing to maximum laryngeal closure (lc - mlc)
Duration of laryngeal closure	Maximum laryngeal closure to laryngeal reopening (mlc - lr)
Duration of PES opening	PES opening to last PES opening (peso - lpeso)

lc, laryngeal closure; lpeso, last PES opening; lr, laryngeal reopening; mlc, maximum laryngeal closure; PES, pharyngoesophageal segment; peso, PES opening (see Table 1 for definitions)

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Table 3

Participant characteristics.

	ARDS Patients (n = 11)
Demographics	
Female, no. (%)	8 (73)
Age, median (IQR) years	53 (44, 67)
Caucasian, No. (%)	6 (55)
Baseline Health Status Before Admission	
Charlson Comorbidity Index, Median (IQR) score	5 (2, 6)
Neurological disease, No. (%)	3 (27)
Upper gastrointestinal disease, No. (%)	5 (45)
ICU Admission Diagnosis Category, No. (%)	
Respiratory, including pneumonia	7 (64)
Non-pulmonary sepsis	1 (9)
Other	3 (27)
ICU Factors	
APACHE II severity of illness score, median (IQR)	29 (22, 42)
SOFA organ failure score, median (IQR)	8 (4, 11)
Intubation duration, median (IQR) days	14 (9, 16)
Reintubated, No. (%)	2 (18)
ICU length of stay, median (IQR) days	19 (12, 23)
VFSS after extubation, median (IQR) days	5 (4, 13)
Hospital length of stay, median (IQR) days	45 (23, 52)

APACHE II, Acute Physiology and Chronic Health Evaluation II; ARDS, acute respiratory distress syndrome; ICU, intensive care unit; IQR, interquartile range; SOFA, Sequential Organ Failure Assessment; VFSS, videofluoroscopic swallow study

Table 4Selected pharyngeal swallowing durations^a

	Time to achieve laryngeal closure (lc - mlc)	Duration of laryngeal closure (mlc - lr)	Duration of PES opening (peso - lpeso)
ARDS Patients, median (IQR) msec	334 (267, 467)	401 (333, 467)	401 (367, 534)
Healthy Volunteers, median (IQR) msec	184 (133, 267)	416 (350, 500)	542 (484, 646)
Age-matched Difference, median (IQR) msec	151 (103, 217) (p<0.001) ^b	13 (-83, 42) (p=0.987)	-116 (-183, 1) (p=0.004) ^b

IQR, interquartile range; lc, laryngeal closure; lpeso, last PES opening; lr, laryngeal reopening; mlc, maximum laryngeal closure; PES, pharyngoesophageal segment; peso, PES opening; (see Table 1 for definitions).

^a All times are calculated relative to the time of hyoid excursion (he), with a negative time representing events occurring before hyoid excursion.

^b Statistically significant at p<0.017 after Bonferroni correction for multiple comparisons

Table 5

Timing of onset of 9 swallowing events^a

	br	lc	peso	mlc	mhe	lr	lpeso	hrr
ARDS Patients, median	-0 (67, 100)	0 (0, 100)	200 (133, 300)	300 (267, 467)	367 (300, 500)	734 (734, 868)	667 (601, 801)	1502 (1168, 1902)
Healthy Volunteers median	17 (-33, 176)	8 (0, 49)	182 (124, 217)	217 (166, 283)	284 (233, 358)	633 (576, 700)	700 (658, 815)	865 (750, 958)
Age-matched Difference, median	-1 (-234, 66) (p=0.338)	-17 (-17, 83) (p=0.706)	50 (-50, 109) (p=0.145)	118 (17, 218) (p=0.002)	83 (0, 216) (p=0.006)	101 (68, 202) (p<0.001)	-50 (-116, 67) (p=0.145)	651 (303, 968) (p<0.001)

br, bolus at the ramus; IQR, interquartile range; lc, laryngeal closing; mlc, maximum laryngeal closure; peso, pharyngoesophageal segment (PES) opening; mhe, maximum hyoid excursion; lr, laryngeal reopening; lpeso; last PES opening; hrr, hyoid return to rest (see Table 1 for definitions)

^a All times are calculated relative to the time of hyoid excursion (he), with a negative time representing events occurring before hyoid excursion.