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ORIGINAL ARTICLE

Variation in Temporal Measures of Swallowing: Sex and Volume Effects

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Abstract Temporal measures of healthy swallowing appear to be variably sensitive to bolus and participant factors based on a recent meta-analysis of studies in the deglutition literature. In this carefully controlled study of healthy young volunteers, balanced for sex and height, we sought to understand the influence of bolus volume and participant sex on the three durations and three intervals most frequently reported in the deglutition literature. Three boluses per target volume (5, 10, and 20 ml) were repeated for each participant ($n = 20$, 10 male) using a spontaneous swallow paradigm in lateral view videofluoroscopy. None of the temporal durations or intervals was found to be correlated with participant height above an a priori cutoff point of $r \geq 0.3$. Further, none of the temporal durations or intervals varied significantly by participant sex. Bolus volume significantly impacted upper esophageal sphincter (UES) opening duration, laryngeal closure duration, the laryngeal closure-to-UES opening interval, and the pharyngeal transit time interval, but not hyoid movement duration or the stage transition duration interval. When participants are sampled in such a manner as to represent the range of height reported to be typical for both sexes in the population, sex does not significantly influence temporal measures of swallowing.

Keywords Deglutition · Deglutition disorders · Dysphagia · Swallowing · Temporal · Duration · Interval · Sex · Volume · Height

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Introduction

The gold standard tool for the assessment and management of dysphagia (swallowing disorders) is the videofluoroscopic (VF) swallowing study, which involves administering food and liquid mixed with a radiopaque contrast agent under fluoroscopy. The VF offers real-time dynamic viewing of swallowing physiology. The pharyngeal phase of swallowing involves a complex sequence of temporal events in a relatively short span of time, which can be broadly grouped into durations (the length of time for a distinct physiological swallow event to occur) and intervals (the length of time between two gestures in the swallow sequence). Aberrant swallow timing in patient populations has been linked to laryngeal penetration and aspiration [1–3].

A recently published study examined the most frequently reported duration and interval measures in the healthy swallowing literature (36 publications) and demonstrated different degrees of variability across temporal measures and variable effects of bolus volume, sex, and age on these measures [4]. Six parameters were chosen for meta-analysis in that study: three durational measures [upper esophageal sphincter (UES) opening duration (UESD), laryngeal closure duration (LCD), and hyoid movement duration (HMD)] and three interval measures [laryngeal closure-to-UES opening (LC-to-UES), pharyngeal transit time (PTT), and stage transition duration

(STD)]. Modified forest plots of means with 95 % confidence interval error bars were used to compare variability across studies. Trends attributable to factors such as bolus volume and age were noted whenever information was available from the original studies. The authors concluded that a variety of factors play a potential role in contributing to the observed variability in temporal measures of swallowing, including differences across studies in operational definitions, statistical analyses, stimulus factors, participant factors, and procedural factors.

The contribution of bolus volume has been studied extensively in the healthy deglutition literature. Some temporal variables have clear and consistent trends, e.g., UESD which regularly displays longer durations for greater volumes (see, e.g., [5–12]). Other temporal variables such as STD have mixed findings; some studies have reported longer STD values at larger volumes (see, e.g., [3, 5, 13]), while others have reported shorter durations at larger volumes (see, e.g., [8, 14]) and others still describe mixed findings [15]. A full review of trends by bolus volume for the six temporal measures of interest can be found in the Molfenter and Steele review [4].

The impact of sex on temporal measures of swallowing is unclear in the literature. Some research has demonstrated that sex has no effect (e.g., [15, 16]), while others report that women display longer durations (e.g., [10, 17, 18]). Dantas et al. [18] suggest that longer durations in women are required for safe swallowing because women are smaller than men, arguing that the relative size of the bolus to the individual is larger, therefore requiring longer swallow durations for transit and clearance.

In this study we sought to clarify the true impact of bolus volume and participant sex on timing measures in healthy swallowing using the same six timing parameters reviewed in Molfenter and Steele [4] (Table 1). Our approach was to tightly control other factors recognized as possible contributors to variability in swallow timing, including participant age, sex, and height, the volume and number of boluses administered, and the use of a spontaneous, self-fed (noncommand) paradigm. Our hypothesis was that under these conditions, duration measures (measures of a swallowing event, such as the opening of the UES) would vary significantly with changes in bolus volume because the event would require more time to be completed with larger boluses. Conversely, however, we hypothesized that interval measures of swallow timing (the time lapse between two component events) would not be influenced by bolus volume. Finally, using a sample in which participant height was systematically distributed across ranges typical for both sexes in the broader population, we hypothesized that sex would not significantly impact any temporal measures of swallowing (durations or intervals).

Table 1 Description, abbreviations, and formulas for the durations and intervals included in this study

Timing variable	Abbreviation	Formula
Durations		
UES opening duration	UESD	UES closure–UES opening
Laryngeal closure duration	LCD	Laryngeal closure–Laryngeal opening
Hyoid movement duration	HMD	Hyoid rest–Hyoid onset
Intervals		
Laryngeal closure-to-UES opening	LC-to-UES	Laryngeal closure–UES opening
Pharyngeal transit time	PTT	UES closure–bolus past mandible
Stage transition duration	STD	Hyoid onset–bolus past mandible

Materials and Methods

Participants

Twenty healthy young volunteers (10 male, 10 female) consented to undergo a standardized VF protocol. Exclusion criteria included a history of swallowing difficulty, neurological deficits, head/neck surgery (other than routine dental surgery, tonsillectomy, or adenoidectomy), or possible pregnancy. All participants were under 45 years old, with a mean age of 31.5 years (standard deviation = 5.7 years). Participants were strategically recruited to ensure a distribution of height that spanned both the lower and upper quartiles for nationally reported height by sex [19]. Participant height was measured in centimeters (cm) with the participant's shoes removed and head in a neutral position using a free-standing stadiometer. Figure 1

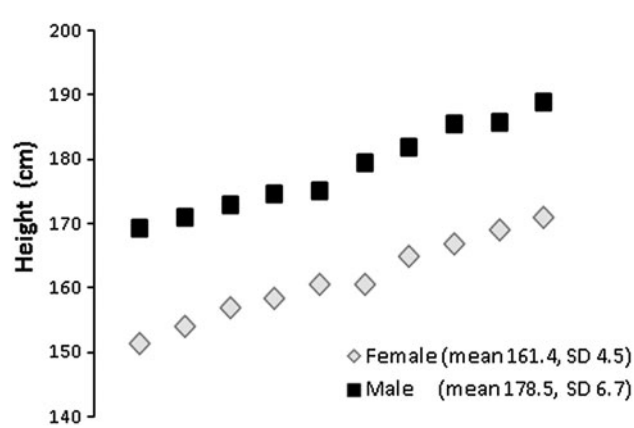

Fig. 1 Distribution of participants by height and sex

demonstrates the distribution of participant height by sex in our sample. The local institutional research ethics board approved this study and written consent was obtained from each participant prior to study participation.

VF Stimuli

Each participant performed a total of 16 swallowing tasks. Nine of these swallows per participant are included in the present analysis: three swallows each of 5, 10, and 20 ml of ultrathin liquid barium, a 22 % weight/volume (w/v) suspension [20]. Three repetitions per bolus condition were included in order to sample intrasubject variability adequately while minimizing VF exposure time [16].

Each bolus was presented to the participant in a 30-ml medicine cup. Non-VF pilot testing demonstrated that residual material remained in the cup after each sip. Given that we were particularly interested in bolus volume contributions to temporal measures of swallowing, we devised a system to tightly control bolus volume. First, in order to compensate for expected residue in the cup, we carefully pipetted 1 ml more than the target sip volume into the cup. Second, each cup was weighed before and after each stimulus was swallowed so that the exact volume consumed could be determined. Finally, whenever piecemeal deglutition was observed for a particular stimulus, the corresponding data were excluded from the analysis, given that we could not accurately measure the volume of the portions of the bolus ingested in each subswallow. Across the entire data set of 180 ultrathin liquid swallows, there were seven instances of piecemeal deglutition: one occurrence at 5 ml and six occurrences at 20 ml. However, despite these procedures, the post-swallow cup weights showed that participants swallowed bolus volumes that were smaller than the target volume. For the 5-ml target condition (6 ml in the cup), the average volume consumed was 3.54 ml (95 % CI = 3.42–3.67). For the 10-ml target condition (11 ml in the cup), the average volume consumed was 8.03 ml (95 % CI = 7.78–8.28). Similarly, for the 20-ml target condition (21 ml in the cup), the average volume consumed was 17.34 ml (95 % CI = 16.84–17.85).

VF Procedure

All VFs were completed using a Toshiba Ultimax fluoroscope (Toshiba America Medical Systems, Inc., Tustin, CA) with the participant seated in lateral view. VFs were conducted at full resolution (30 pulses per second) and captured and recorded on a Digital Swallowing Workstation (KayPentax, Lincoln Park, NJ) at 30 frames per second. The cups containing the stimuli were arranged on a table within easy reach of the participant. Cups were presented in sets of three (of the same condition). The order of bolus volume was randomized by set for the three ultrathin liquid conditions. The fluoroscope was turned on and the participant was instructed to self-feed each three-bolus array of stimuli at a spontaneous, comfortable pace. This method of self-feeding and spontaneous swallows was chosen to promote natural drinking behavior and to avoid differences in swallow timing known to be associated with cued swallowing [21]. The indication for turning off the fluoroscope after the final bolus of each three-swallow sequence was visualization of the hyoid returning to rest. The mean (±SD) radiation exposure time across participants was 1.75 ± 0.31 min.

VF Post-processing and Analysis

Each three-swallow sequence was spliced out of the larger VF recording starting 30 frames before the bolus passed the shadow of the mandible on the initial swallow and finishing 30 frames after the hyoid returned to rest on the third swallow (or when the fluoroscope was turned off, in the event this occurred first). These videoclips were randomized and individually opened in ImageJ (National Institutes of Health, Bethesda, MD) and advanced frame-by-frame to identify the following seven events:

- *Hyoid onset* the first marked upward/forward movement of the hyoid associated with an immediately occurring subsequent swallow.
- *Bolus past mandible* the head of the bolus touching or passing the ramus of the mandible. In the event that the participant was not seated completely upright or perpendicular to the fluoroscopy beam, resulting in a view in which both mandibular rami were visible, the more superior ramus was used as the landmark for defining this event.
- *Laryngeal vestibule closure* the first frame depicting a seal between the posterior surface of the epiglottis and the arytenoids.
- *Laryngeal vestibule opening* the first frame depicting a release of the seal between the posterior surface of the epiglottis and the arytenoids.
- *UES opening* the first frame showing the head of the bolus passing through the UES, represented by the opening of the narrowest region between C4 and C6 [8] (and confirmed by a visible column of barium in the proximal esophagus on the same or the immediately occurring subsequent frame).
- *UES closure* the first frame depicting the UES closing behind the tail of the bolus in the region between C4 and C6.
- *Hyoid rest* the frame depicting the lowest position of the hyoid bone post swallow, with concurrent epiglottic return and pharyngeal relaxation.

These seven frames were used to derive each of the six temporal variables of interest (Table 1). For statistical analyses, all temporal durations and intervals were converted from frames to milliseconds (ms) by dividing the frame measures by 29.97 and multiplying by 1,000. Inter- and intrarater reliabilities were tested for each temporal parameter on a random selection of 10 % of the swallows by using two-way mixed intraclass coefficients (ICC) for consistency. Results appear in Table 2. Intrarater reliability scores ranged from 0.86 to 0.99 and interrater reliability scores ranged from 0.73 to 0.98. We acknowledge that one score, UESD, demonstrated interrater reliability within only the “fair to good” range of 0.40–0.75 [22]. Closer examination revealed an average three-frame discrepancy in defining the UES closure frame between raters. We feel this discrepancy may be related to difficulty visualizing the location of the UES at the height of the swallow in healthy individuals who completely obliterate the pharynx during pharyngeal pressure generation.

Penetration-Aspiration Scale scores [23] were also rated to ensure functional healthy swallowing in this sample. All 180 swallows were rated as scores of 1 (no penetration, 167/180) or 2 (high transient penetration, 13/180), which is consistent with previous reports of healthy populations [24, 25].

Statistical Analysis

All statistical analyses were conducted using IBM SPSS Statistics ver. 20. Two-tailed p-values < 0.05 were considered statistically significant. Pearson’s correlation coefficients (r) were first used to examine the relationship between each of the six temporal variables (ms) and participant height (cm). A priori, it was decided that for variables with $r \geq 0.3$, height would be tested as a covariate in subsequent statistical models. Mixed-model repeated-measures analysis of variance (ANOVA) with a between-participant factor of sex and within-participant

Table 2 Descriptive statistics for each of the six temporal variables by bolus volume and inter- and intrarater reliability ratings

Volume (ml)	Mean (ms)	Standard error	Lower 95 % CI	Upper 95 % CI	Interrater reliability [ICC (95 % CI)]	Intrarater reliability [ICC (95 % CI)]
Durations						
UES opening duration						
5	282	14	254	310	0.73 (0.29–0.90)	0.94 (0.83–0.98)
10	320	14	292	348		
20	357	14	328	385		
Laryngeal closure duration						
5	452	27	396	508	0.98 (0.95–0.99)	0.99 (0.97–1.00)
10	490	27	434	546		
20	528	27	471	584		
Hyoid movement duration						
5	954	41	870	1,039	0.95 (0.88–0.98)	0.87 (0.65–0.95)
10	1,008	41	924	1,092		
20	999	42	913	1,085		
Intervals						
LC-to-UES opening interval						
5	19	13	−8	46	0.82 (0.52–0.93)	0.86 (0.64–0.95)
10	20	13	−7	50		
20	−5	13	−33	22		
Pharyngeal transit time						
5	471	27	415	527	0.85 (0.60–0.94)	0.95 (0.86–0.98)
10	512	27	456	568		
20	528	28	471	585		
Stage transition duration						
5	32	23	−16	79	0.91 (0.76–0.97)	0.98 (0.94–0.99)
10	56	23	9	103		
20	73	24	25	121		

CI confidence interval, *ICC* intraclass coefficient repeated factor of trial within bolus volume (with or without the height covariate, as explained above) were run in order to test the influence of bolus volume and participant sex on each of the six dependent variables. When main effects were significant, post hoc pairwise comparisons were conducted with Sidak adjustment for multiple comparisons.

Results

Descriptive statistics for all six temporal variables (three durations and three intervals), separated by bolus volume and sex, appear in Table 2. Given that participant size has been proposed as a factor to explain sex differences in temporal measures of swallowing, the relationship between each temporal measure and participant height was tested. None of the variables demonstrated a correlation above $r \geq 0.3$ (Table 3). Therefore, height was discounted as a potential influence on swallow timing and height covariates were not included in any of the statistical models for the variables.

Analysis of the contributions of bolus volume and participant sex to UESD revealed a significant main effect for volume [$F(2, 149.42) = 41.306$, $p = 0.000$], while sex and the interaction term were nonsignificant. Post hoc pairwise comparisons are summarized in Fig. 2. Results revealed that UESD increased significantly with larger bolus volumes for all pairwise volume comparisons: 3.54-ml condition (mean = 282.2 ms, SE = 13.6), 8.03-ml condition (mean = 319.8 ms, SE = 13.6), and 17.34-ml condition (mean = 356.8 ms, SE = 13.8).

The investigation of the contributions of bolus volume and participant sex to LCD yielded similar results, with a significant main effect for volume [$F(2, 149.23) = 17.980$, $p = 0.000$] but no significant main effect for sex. The interaction term was nonsignificant. Post hoc pairwise comparisons are summarized in Fig. 3 and demonstrated significant differences in LCD for all pairwise volume comparisons, with increasing bolus volume resulting in longer LCD. The mean LCD was 451.7 ms (SE = 26.9) for the 3.54-ml condition, 489.9 ms (SE = 26.9) for the 8.03-ml condition, and 527.7 ms (SE = 27.1) for the 17.34-ml condition.

When the contributions of bolus volume and participant sex to HMD were analyzed, no significant main effects or interactions were found.

Analysis of the contributions of bolus volume and participant sex to the LC-to-UES interval revealed a significant main effect for volume [$F(2, 149.607) = 5.027$, $p = .008$], while sex and the interaction term were non-significant. Post-hoc pairwise comparisons are summarized in Fig 4. Results revealed a significantly shorter LC-to-UES interval in the 17.34-ml condition (mean = −5.48 ms, SE = 13.27) compared with both the lower volumes

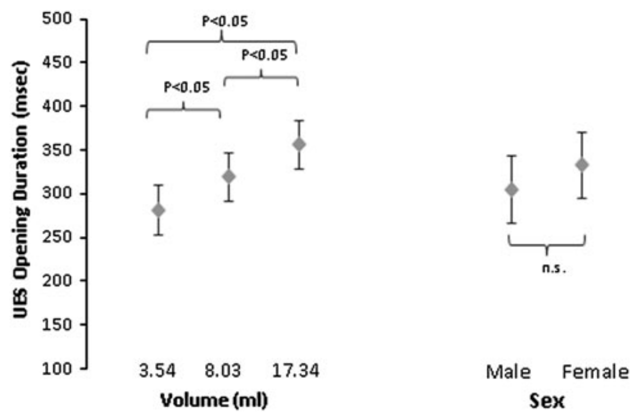

Fig. 2 Post-hoc pairwise comparisons of UES Opening Duration (ms) and 95 % CI by bolus volume (ml) and by participant sex. *n.s.* not significant

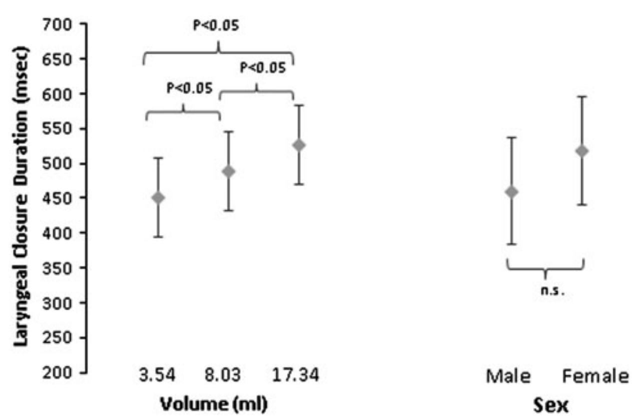

Fig. 3 Post-hoc pairwise comparisons of Laryngeal Closure Duration (ms) and 95 % CI by bolus volume (ml) and by participant sex. *n.s.* not significant

Table 3 Pearson's *r* correlations between temporal variables and participant height (cm)

Timing variable	Correlation (*r*) with height	Significance (2-tailed)
Durations		
UES opening duration	−0.09	0.22
Laryngeal closure duration	−0.17	0.03
Hyoid movement duration	0.20	0.01
Intervals		
Laryngeal closure-to-UES opening	0.11	0.16
Pharyngeal transit time	0.12	0.12
Stage transition duration	0.07	0.36

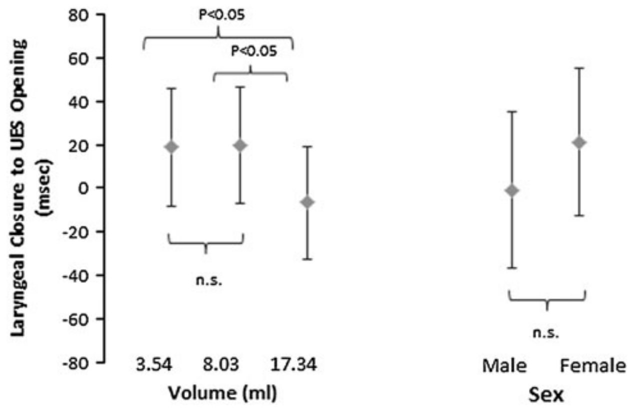

Fig. 4 Post-hoc pairwise comparisons of Laryngeal Closure-to-UES Opening Duration (ms) and 95 % CI by bolus volume (ml) and by participant sex. *n.s.* not significant

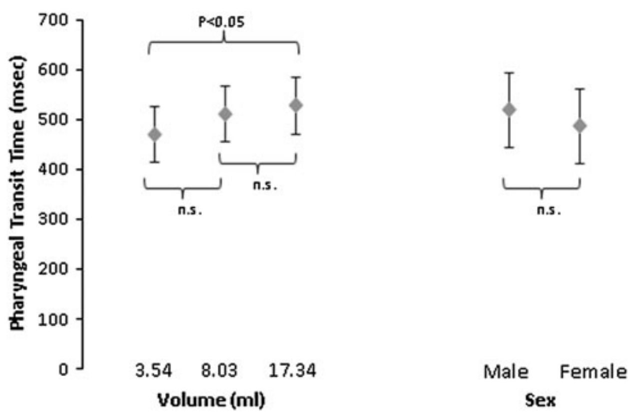

Fig. 5 Post-hoc pairwise comparisons of Pharyngeal Transit Time (ms) and 95 % CI by bolus volume (ml) and by participant sex. *n.s.* not significant

(3.54-ml, mean = 18.81 ms, SE = 13.08 and 8.03-ml, mean = 20.02, SE = 13.05). No significant difference between the 3.54-ml and 8.03-ml condition was found.

Analysis of the contributions of bolus volume and participant sex to the PTT interval revealed a significant main effect for volume [$F(2, 149.596) = 4.690$, $p = 0.011$], while sex and the interaction term were nonsignificant. Post hoc pairwise comparisons are summarized in Fig. 5. Results revealed a significantly longer PTT interval in the 17.34-ml condition (mean = 527.71 ms, SE = 27.68) than in the 3.54-ml condition (mean = 470.95 ms, SE = 27.26). No significant differences were revealed between the intermediate volumes.

When the contributions of bolus volume and participant sex to the STD interval were analyzed, no significant main effects or interactions were found.

In summary, none of the six parameters of interest demonstrated a sex effect, while four of six variables (UESD, LCD, LC-to-UES, and PTT) demonstrated significant sensitivity to bolus volume.

Discussion

In the current study, we sought to understand the contributions of bolus volume and participant sex to the most frequently reported duration and interval measures of swallow timing in the healthy deglutition literature. Our sample of young, healthy participants was recruited to systematically span a population-representative range of heights in both men and women. Importantly, height for the tallest women in this sample overlaps with height for the shortest men, thus creating a sample where height does not automatically distinguish the sex groups (Fig. 1). We have demonstrated for the first time that the durational and interval measures analyzed in this study do not vary according to participant height (as measured by correlations that failed to reach a conservative criterion of $r \geq 0.3$). Further, we have demonstrated that when height is distributed across population-appropriate ranges for both sexes, sex does not appear to influence temporal measures of swallowing (durations or intervals).

We hypothesized that bolus volume would significantly impact all three duration measures of swallowing. In fact, we observed that volume significantly impacted only two of the three duration measures explored in our study: UESD and LCD. For these durations, larger bolus volumes resulted in a longer opening of the UES and longer closure of the laryngeal vestibule. We were surprised to learn that HMD did not differ by bolus volume given that previous literature has demonstrated that hyoid excursion does vary by bolus volume [11, 26–28]. One possible explanation for this is that duration of movement (in ms) does not adequately capture the complex dimensions of a swallow. For example, it may be that differences in hyoid bone movement velocity (distance over time) will explain differences peak position across bolus volumes while durations do not.

We hypothesized that bolus volume would not impact interval measures of swallow timing, but we learned that two of our three intervals (LC-to-UES and PTT) were significantly influenced by main effects of volume. Larger bolus volumes caused shorter temporal intervals between the closing of the laryngeal vestibule and the opening of the UES and longer temporal intervals between the bolus passing the ramus of the mandible and the closing of the UES (though these trends were not consistently significant between each level of volume comparison). This finding is consistent with trends reported in the literature for these two variables [4]. We were especially surprised by this finding for the LC-to-UES interval given the close temporal proximity of the two swallow gestures comprising the

LC-to-UES interval and its tight confidence intervals in a previously published meta-analysis [4]. PTT, on the other hand, is an interval for which the influence of bolus volume is less surprising, given that the UES opening duration (inherently tied to this interval by its offset) has repeatedly been shown to be sensitive to bolus volume. STD is thought to represent the trigger of the pharyngeal swallow in response to arrival of the head of the bolus in the upper pharynx. It is therefore logical that this triggering does not depend on the size of the bolus.

We would like to point out that the investigations in this study were limited to temporal measures for ultrathin liquid swallowing in healthy young individuals. Importantly, this work needs to be expanded to older age groups, given the known impact of advancing age on temporal measures of swallowing [11, 17]. Logemann [11] has suggested that women have a protective “flexibility” in the oropharyngeal swallow mechanism that allows them to better compensate for aging than men. An important component of future work in healthy older adults will be to determine the sensitivity of temporal durations and intervals to aging and to ensure appropriate representation of typical population heights (as we have done here) so that participant height can be teased apart from sex as an influence on timing measures. Further, future work should focus on the relationship between various temporal durations and intervals and penetration/aspiration. Once these relationships have been tested across a variety of age spans, normative references can be established for the purpose of comparison for patient populations and to serve as treatment targets and for outcome measurement.

Conclusion

In this height-distributed sample of healthy young adults who swallowed three repeated boluses each of three target volumes of ultrathin liquid barium (22 % w/v), participant sex did not impact swallowing durations or intervals. Bolus volume significantly impacted UES opening duration, laryngeal closure duration, the laryngeal closure-to-UES opening interval, and the pharyngeal transit time interval. Neither hyoid movement duration nor the stage transition duration interval was influenced by bolus volume. Future work in height-representative samples of older adults is warranted.

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Conflicts of interest The authors have no conflicts of interest to disclose.

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