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Changes in Esophageal and Lower Esophageal Sphincter Motility with Healthy Aging

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ABSTRACT

Background & Aims: Swallowing difficulties become increasingly prevalent in older age. Differences exist in lower esophageal sphincter (LES) function between older and younger patients with dysphagia, but the contribution of aging per se to these is unclear.
Methods: Esophageal motor function was measured using high resolution manometry in older (aged 81±1.7 yrs) and younger (23±1.7 yrs) asymptomatic healthy adults. After baseline recording, motility was assessed by swallowing boluses of liquid (right lateral and upright postures) and solids. Basal LES pressure, integrated relaxation pressure, distal esophageal peristaltic amplitude, distal contractile integral and velocity were measured. Data are presented as mean ± SEM.
Results: Despite a trend for lower basal LES pressure (15.8±2.9 mmHg vs. 21.0±0.2 mmHg; P=0.08), completeness of LES relaxation was reduced in older subjects (liquid RL: P=0.003; UR: P=0.007; solid: P=0.03), with higher integrated relaxation pressure when upright (liquid: 6.9±1.1 vs. 3.1±0.4 mmHg; P=0.01; solids: 8.1±1.1 vs. 3.6±0.3 mmHg; P=0.001) and a longer time to recovery after liquid boluses (right lateral: P=0.01; upright: P=0.04). In young, but not older adults, esophageal peristaltic velocity was increased when upright (3.6±0.2 cm/sec; P=0.04) and reduced with solids (3.0±0.1 cm-s; P=0.03). Distal contraction amplitude was higher with solid cf. liquid in the younger individuals (51.8±7.9 mmHg vs. 41.4±6.2 mmHg; P=0.03). In elderly subjects, the distal contractile integral was higher with liquid swallows in the upright posture (P=0.006).
Conclusion: There are subtle changes in LES function even in asymptomatic older individuals. These age-related changes may contribute to the development of dysphagia.

Key words: aging – esophageal motility – lower esophageal sphincter – manometry.

INTRODUCTION

Changes in the outcomes of esophageal motor function are apparent with aging. Older patients have higher rates of disordered swallowing and other feeding problems [1-3]. In particular, older patients have a decreased peristaltic response to wet swallows when compared to their younger counterparts [4, 5]. Studies by Soergel et al described an increase in both simultaneous and failed esophageal contractions in nonagenarians [6], and more recently decreased contraction amplitude, polyphasic esophageal contractions, esophageal dilatation and decreased sphincter relaxations have been reported in older individuals [7-9]. However, the relationship of these findings to increasing age per se is unclear, with the suggestion that these changes reflect neurodegenerative conditions (such as those associated with diabetes mellitus) that are more prevalent in older individuals [10]. Conversely, although basal lower esophageal sphincter (LES) pressure is increased and swallow-induced relaxation incomplete in older patients with dysphagia [11], it is uncertain whether these differences are related to the underlying disease mechanisms or a function of normal aging.

The aim of the current study was to determine the effects of older age (≥80 years) on esophageal and LES motor function in asymptomatic healthy adults, using high resolution manometry (HRM). Specifically, the study aimed to identify motor dysfunctions not diagnosed by conventional manometry or radiology [12], using a series of closely spaced pressure sensors to simultaneously view the entire swallowing mechanism, with a specific focus on LES motility [13]. This approach permits a more detailed analysis of motor function than has previously been undertaken in these individuals [12, 14-16]. An additional aim was to evaluate whether changes in body position or bolus characteristics affect the motor parameters differently in older age compared to younger subjects.

MATERIAL AND METHODS

Subjects

Studies were performed in 10 older (7M; aged 81 ± 1.7 yrs; BMI 25.1 kg/m^2) and 10 younger (6M; 23 ± 1.7 yrs; BMI 21.9 kg/m^2) asymptomatic healthy adults. None had a history of gastrointestinal disease, including gastro-esophageal reflux disease, previous abdominal surgery, diabetes mellitus or was taking any medication known to affect gastrointestinal motility. Subjects provided written informed consent prior to entering the study, which was approved by the Research and Ethics Committee of the Repatriation General Hospital (Protocol no. 41/07).

Manometry

Esophageal pressures were measured using a HRM technique, with motility displayed as a continuum of pressure and time using a color display. Intraluminal pressures were measured using a 16 channel silicone-rubber manometric assembly (Dentsleeve International, Toronto, Canada). The 9 most proximal side-holes (channels 1-9) were spaced 3 cm apart and spanned the pharynx and esophageal body (24 cm). The remaining 7 side-holes (channels 10-16) were spaced at 1cm intervals for high resolution recordings across the LES, with the most distal channel positioned in the proximal stomach. All lumina were perfused with degassed distilled water at a rate of 0.15ml/min using a low compliance perfusion pump (Dentsleeve International, Ontario Canada). Data were recorded at 25Hz and analyzed using specialized software (Trace Version 1.2v, Hebbard, Melbourne, Australia). All pressures were referenced to intra-gastric pressure.

Study protocol

Studies were performed after a 4-hour fast. The manometric assembly was passed transnasally into the stomach, via an anaesthetized nostril. Subjects were initially studied in the right lateral (RL) posture and allowed 10 minutes to adapt to the assembly. A basal LES pressure (BLESP) was recorded for 30 seconds. Ten 5mL liquid (water) swallows were performed in the RL posture and repeated when the subjects sat upright (UR). Manometry was also recorded during 5 standardized solid boluses (2x2cm piece white bread with crust removed) in the UR position. Subjects chewed the bread and indicated when they were ready to swallow.

Data and statistical analysis

Manometry recordings were analyzed manually by two observers (LKB and CMB) who were blinded to subject age. Analysis of esophageal motility was performed as described previously [11] and the following measurements were derived: (i) BLESP at end-expiration (mmHg), (ii) resting LESP at 4 seconds prior to swallow (mmHg), (iii) number of complete LES relaxations (defined as a ≥75% drop in LESP), (iv) integrated relaxation pressure (IRP4, lowest LES pressure for four contiguous or non-contiguous seconds in a ten second period following swallow onset, mmHg), (v) total LES relaxation time (recovery of LES pressure to baseline after initiation of swallow, sec), (vi) amplitude of distal esophageal pressure (4cm above the LES, mmHg), (vii) mean distal contractile integral (DCI, mmHg-s-cm) and (viii) peristaltic velocity (calculated between peak amplitude of first and last esophageal channel, cm-s) (Fig. 1).

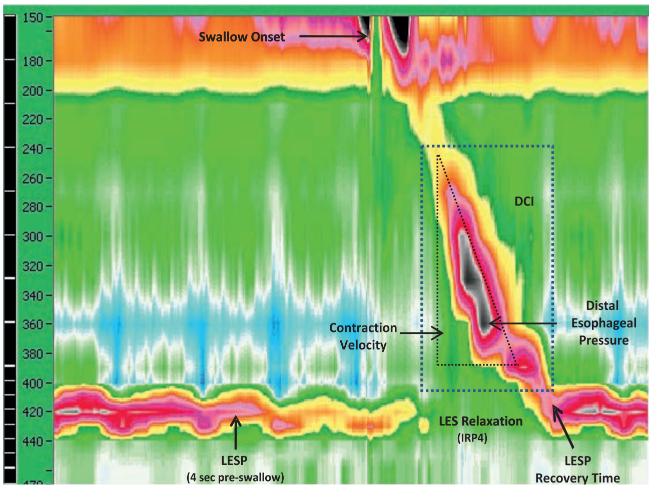

Fig. 1. Example of swallow pressure topography spanning from the pharynx (15-20cm) to stomach (44-47cm), in a younger subject with normal peristalsis and lower esophageal sphincter (LES) relaxation. Pressure data (amplitudes shown by colour gradient) are displayed with time on x-axis and location of sensors on y-axis. Points of measurement for motility parameters are indicated with arrows. Pressure sensors located in the region of the LES are spaced 1-cm apart, spanning a 6cm segment.

All data are presented as mean ± SEM. Values between and within groups were compared using Student's *t*-test (two-tailed). A P-value <0.05 was considered significant.

RESULTS

The study protocol was well tolerated by all subjects. No adverse effects were reported and none of the swallows were associated with dysphagia.

Effects of age

There was a trend for lower BLESP in the older group (15.8 ± 2.9 mmHg), when compared to younger subjects (21.0 ± 0.2 mmHg; P=0.08).

The percentage of swallows with complete LES relaxation (≥75% reduction) after deglutition was lower in older subjects with all boluses, compared to the younger group (water RL: 85 ± 4.0% vs. 99 ± 1.0%, P=0.003; water UR: 70 ± 9.5% vs. 99 ± 1.0%, P=0.007; and solids UR: 54 ± 10.3% vs. 84 ± 6.5%; P=0.03) (Fig. 2).

The mean IRP4 was significantly higher in older subjects in the UR posture with both liquid (6.9 ± 1.1 mmHg vs. 3.1 ± 0.4 mmHg; P=0.01) and solid (8.1 ± 1.1 mmHg vs. 3.6 ± 0.3 mmHg; P=0.001) boluses, compared to younger subjects (Fig. 3). There was no difference in IRP4 in the RL posture between age groups.

The time for recovery of LES tone to baseline after relaxation (swallow-induced) was longer in older subjects with

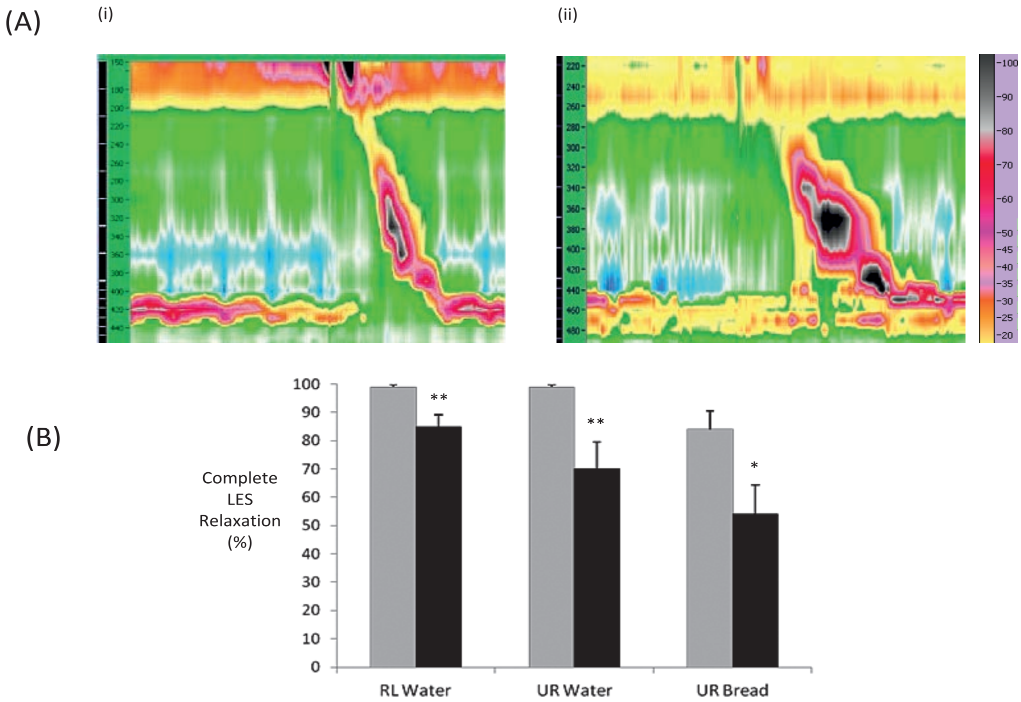

Fig. 2. A) Example of a manometric trace from a (i) young and (ii) older healthy subject in the upright posture, showing reduced LES relaxation with older age; B) Percentage of complete LES relaxations (defined as ≥75% drop in resting pressure) in young (light bars) and older (dark bars) subjects during liquid swallows in the right lateral (RL) and upright (UR) postures and with solids (bread). * P<0.05; ** P<0.01 vs. young.

liquid in both postures (RL: 10.6 ± 0.5 s vs. 9.0 ± 0.3 s, P=0.01; UR: 9.7 ± 0.5 s vs. 8.2 ± 0.2 s, P=0.04), but not solids (9.9 ± 1.4 s vs. 9.6 ± 0.3 s, P=0.82; cf. young).

There were no differences between age groups in resting (pre-swallow) LES pressure, distal esophageal contraction amplitude, distal contractile integral or peristaltic velocity.

Effects of posture and bolus consistency (Table I)

In older adults, the percentage of swallows with complete LES relaxation was lower with solids (54 ± 10.3%) when compared to UR liquid boluses (70 ± 9.5%; P=0.02). There was a trend for more complete relaxation with liquids in the RL when compared to the UR posture (RL: 85 ± 4.0% vs. UR: 70 ± 9.5%; P=0.08). In the younger group, nearly all liquid swallows achieved complete LES relaxation (99% in both postures), and was only slightly reduced with solids (84 ± 6.5%, P=0.06).

The IRP4 in younger subjects was not affected by changes in posture or bolus consistency. In older adults, the mean relaxation pressure with liquids was higher in the UR posture

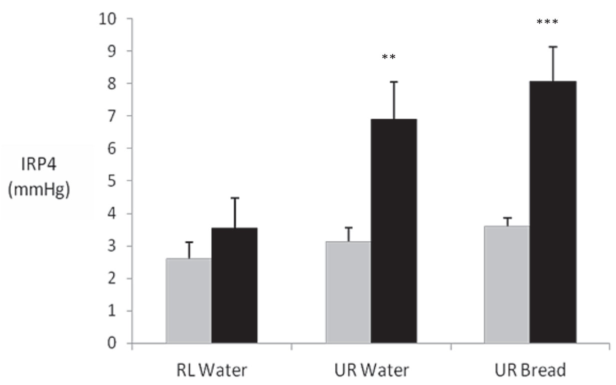

Fig. 3. Integrated relaxation pressure (IRP4) in young (light bars) and older (dark bars) subjects in right lateral (RL) and upright (UR) postures and with solids (bread). There is an increase in IRP4 in the sitting posture in older subjects when compared to young. ** P<0.01; *** P<0.001, vs. young.

Table I. Effects of posture and bolus consistency on measured variables in young and older healthy subjects

Variable (Mean ± SEM)	Liquid		Solid
	RL	UR	
LES Relaxation (% complete)			
Young	99 ± 1.0	99 ± 1.0	84 ± 6.5
Elderly	85 ± 4.0	70 ± 9.5	54 ± 10.3*
Mean IRP4 (mmHg)			
Young	2.6 ± 0.5	3.1 ± 0.4	3.6 ± 0.3
Elderly	3.5 ± 0.9**	6.9 ± 1.1	8.1 ± 1.1
Duration LES Relaxation (s)			
Young	9.0 ± 0.3*	8.2 ± 0.2	9.6 ± 0.3**
Elderly	10.6 ± 0.5	9.7 ± 0.5	9.9 ± 1.4
Distal Contraction Amplitude (mmHg)			
Young	40.6 ± 7.5	41.4 ± 6.2	51.8 ± 7.9*
Elderly	37.6 ± 9.1**	49.5 ± 8.7	43.9 ± 10.3
Peristaltic Velocity (cm-s)			
Young	3.1 ± 0.1*	3.6 ± 0.2	3.0 ± 0.1*
Elderly	3.1 ± 0.3	3.0 ± 0.3	3.3 ± 0.3
Distal Contractile Integral (mmHg-s-cm)			
Young	946.7 ± 201	852.8 ± 190	1143.5 ± 215
Elderly	834.8 ± 260**	1223.5 ± 292	1440.9 ± 488

RL: right lateral; UR: upright; * P<0.05 and ** P<0.01 vs. UR

(6.9 ± 1.1 mmHg) when compared to RL (3.5 ± 0.9 mmHg; P=0.01). However, there was no difference in the relaxation pressure between liquid and solid boluses when UR. Neither posture nor bolus type had any effect on the resting LES pressure in either age group.

In younger subjects, the total LES relaxation time was shorter with liquid swallows in the UR posture when compared to RL (8.2 vs. 0.2 mmHg vs. 9.0 ± 0.3 mmHg; P=0.03). Relaxation time was longer with solids (9.6 ± 0.3 mmHg) than liquid swallows (P=0.002). There was no difference in LES relaxation time in the older age group between postures or with solids.

The distal esophageal contraction amplitude was higher with solid boluses when compared to liquids in younger subjects (51.8 ± 7.9 mmHg vs. 41.4 ± 6.2 mmHg, P=0.03). This was not seen in older individuals. However, distal contractions were affected by change in posture in older adults, with a higher peristaltic amplitude (49.5 ± 8.7 mmHg vs. 37.6 ± 9.1 mmHg, P=0.007) and DCI (1223.4 ± 292 mmHg-s-cm vs. 834.8 ± 260 mmHg-s-cm, P=0.006) recorded in the UR position with liquids, when compared to RL.

In the younger group, the UR posture increased the esophageal peristaltic velocity (3.6 ± 0.2 cm-s) compared to RL (3.1 ± 0.1 cm-s; P=0.04). Velocity was decreased with the introduction of bread boluses (3.0 ± 0.1 cm-s; P=0.03). There were no differences in peristaltic velocity between postures or bolus consistency in older adults (Fig. 4).

DISCUSSION

Disordered swallowing is particularly prevalent in older individuals, although the underlying mechanisms are poorly understood. Using detailed analysis of manometric data, this study demonstrates that although overall esophageal function is well preserved, functional disturbances exist in healthy older adults that are likely to predispose to dysphagia. The major findings were a reduction in the percentage of swallows with complete LES relaxation and a higher integrated relaxation pressure, when compared to younger subjects. These abnormalities were especially evident when sitting and with increased bolus consistency. There was also a lack of response of motility parameters to changes in bolus stimuli or posture in older age.

The most significant differences between the older and younger subjects were observed at the esophago-gastric junction (EGJ). Analysis of this region in older subjects showed a lower percentage of complete LES relaxations (drop >75% from resting pressure) in both the RL and UR postures. For example, only half of the solid swallows were associated with complete LES opening. This was consistent with a higher integrated LES relaxation pressure with both liquid and solid swallows when sitting, in the otherwise asymptomatic elderly adults. We have previously reported impaired relaxation in elderly patients with dysphagia [11], but basal LES pressure was increased in patients, rather than reduced as seen in the current study. Together, these findings suggest that a high incidence of impaired LES relaxations per se is insufficient to result in dysphagia.

Interestingly, the healthy older subjects demonstrated an increase in both the integrated relaxation pressure and DCI with a change in body position from RL to sitting. Previous studies describing the effects of posture on relaxation pressure have produced conflicting results [17, 18]. These have been attributed to methodological differences in the angle of posture studied. The higher IRP observed in healthy older adults when seated suggests impaired swallow-induced relaxation and/or loss of LES compliance. The reasons for this are unclear, but may reflect local anatomical features (crural diaphragm, compression from adjacent organs) or changes within the LES muscle or its innervation.

The changes in LES function in older adults were most obvious with a higher bolus consistency, i.e. the highest rate of incomplete LES relaxation was found with bread. Several healthy studies have shown an incremental esophageal response to increased bolus viscosity [19, 20]. In the current study, a stronger distal contractile amplitude and longer LES relaxation period were recorded in the younger cohort with solid compared to liquid boluses. These alterations in motility parameters were not observed in the older subjects and this lack of response to varying the bolus stimuli (together with

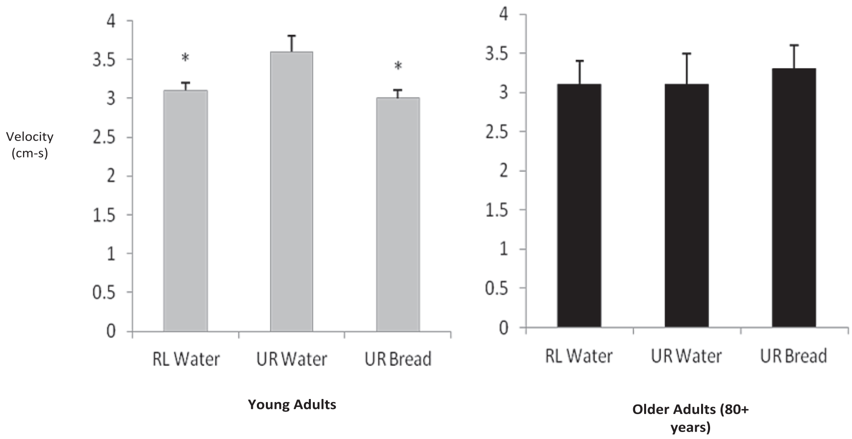

Fig. 4. Esophageal peristaltic velocity in young (light bars) and older (dark bars) subjects during liquid swallows in the right lateral (RL) and upright (UR) postures and with solids (bread). Velocity was not affected by changes in posture or bolus consistency in older subjects. * P<0.05 vs. UR Water, Young

abnormal LES relaxation) could potentially compromise clearance. Elderly subjects did show an increase in the DCI in response to sitting, which is in keeping with the higher distal peristaltic amplitude in the UR posture. The reasons for this postural effect on the distal esophagus in the elderly are unclear.

Alterations in the velocity of esophageal peristalsis were also observed in young adults in response to changes in body position and bolus characteristics, being faster with liquids in the UR posture when compared to RL position, and then reduced with the introduction of solids. This finding is consistent with previous studies [21, 22] that have demonstrated a similar postural effect on distal propagation velocity in healthy humans. In the study by Tutuian et al (2003) using intraluminal impedance, the transit of viscous material was slower than with liquids, and both mediums propagated faster in a higher postural inclination [22]. Interestingly, in the current study older age had no effect on peristaltic velocity, and was again unaffected by changes to either posture or bolus consistency.

There is a lack of knowledge about the outcomes of the motor changes on esophageal flow. It is therefore not possible to draw conclusions regarding movement of material; however, these data are consistent with the higher incidence of transit abnormalities and incomplete esophageal emptying reported in older adults [23]. Future studies including flow measurement, either by fluoroscopy or impedance, may provide further insights. The inclusion of only 10 subjects in each group is also a potential limitation of the study. However, whilst this may not fully describe the variation in older individuals, it is unlikely that any additional major differences between the groups have been missed. Further studies with larger numbers may be required to provide a better picture of variability in healthy older humans. However, recruiting older individuals, especially into more invasive studies presents challenges.

CONCLUSION

High resolution manometry demonstrates that esophageal function is well preserved in healthy older humans, although the LES response to deglutition is less effective. The previously reported reduction in LES relaxation in elderly dysphagic patients is also observed in asymptomatic individuals. However, basal LES pressure is reduced in healthy older adults, in contrast to patients with dysphagia. The underlying cause of these abnormalities at the EGJ and potential effects on swallow function may merit further investigation. These data, however, suggest that the functional reserve is reduced in older healthy individuals and only minor changes may be required to precipitate symptoms.

Conflicts of interest: All authors declare that they have no competing interests.

Authors' contributions: LKB contributed to performing the study, data analysis and interpretation and writing the manuscript; CMB to data acquisition and analysis, manuscript revision; CC to writing and revision of the manuscript; AF to data analysis and manuscript revision; RH and RJLF to study concept and design, data interpretation and critical revision of the manuscript.

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