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Impaired bolus clearance in asymptomatic older adults during high resolution impedance manometry

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Running Head: Presbyesophagus during HRIM

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ABBREVIATIONS:

HRIM	high-resolution impedance manometry
LES	lower esophageal sphincter
AIM	automated impedance manometry
EGJ	esophago-gastric junction
IRP4	4 sec integrated relaxation pressure
ICD	isocontour defect size (20mmHg)
CFV	contractile front velocity
DCI	distal contractile integral
DL	distal latency
EPT	esophageal pressure topography
PeakP	peak pressure
PNI	pressure at nadir impedance
IBP	intrabolus pressure
TNIPP	time of nadir impedance to peak pressure
PFI	pressure flow index
Imp at PP	impedance at peak pressure
IR	impedance ratio
Max Adm	maximum admittance

KEY MESSAGES

- This study uses HRIM and pressure flow analysis to demonstrate impaired esophageal motility and subsequent failed bolus transit in healthy older adults
- Our aim was to characterize bolus clearance in asymptomatic individuals, and identify if any subtle changes in esophageal propulsive physiology exist in extreme older age
- Esophageal HRIM was performed in the upright posture in 45 healthy volunteers using a 3.2mm solid-state catheter and Solar GI system. Liquid and viscous swallows were analysed using Chicago classification criteria and pressure-flow parameters (Esophageal Aimplot™)
- Impaired bolus clearance occurred commonly in subjects aged > 80 years, particularly with increased bolus consistency
- Older individuals also had a higher prevalence of failed or rapid peristaltic sequences, and evidence of impaired lower esophageal sphincter relaxation, compared to younger subjects
- Pressure flow analysis in older subjects revealed a higher impedance ratio, most marked in those with decreased bolus clearance

ABSTRACT

Background: Dysphagia becomes more common in old age. We performed high-resolution impedance manometry (HRIM) in asymptomatic healthy adults (including an older cohort > 80 years) to assess HRIM findings in relation to bolus clearance.

Methods: Esophageal HRIM was performed in a sitting posture in 45 healthy volunteers (n=30 young control, mean age 37±11 yrs and n=15 older subjects aged 85±4 yrs) using a 3.2mm solid-state catheter (Solar GI system, MMS) with 25 pressure (1cm spacing) and 12 impedance segments (2cm intervals). Five swallows each of 5 ml liquid (L) and viscous (V) bolus were performed and analysed using esophageal pressure topography metrics and Chicago classification criteria as well as pressure-flow parameters. Bolus transit was determined using standard impedance criteria. A P value <0.05 was considered significant.

Key Results: Impaired bolus clearance occurred more frequently in asymptomatic older subjects compared to young controls during liquid (40 vs. 18 %, X^2=4.935; P<0.05) and viscous swallowing (60 vs. 17 %; X^2=39.08; P<0.001). Both longer peristaltic breaks (P<0.05) and rapid peristalsis (P<0.01) occurred more commonly in the older cohort and were associated with failed clearance of liquid and viscous swallows (P<0.001). Decreased peristaltic vigor (DCI < 450 $mmHg.s^{-1}.cm^{-1}$) was also associated with reduced liquid clearance in both age groups (P<0.001), and of viscous swallows in the older group (P<0.001).

Conclusions and Inferences: Impaired liquid and viscous bolus clearance, EPT and pressure flow changes were seen in in asymptomatic older subjects.

Keywords: Aging, bolus clearance, deglutition, manometry, presbyesophagus, pressure flow analysis

INTRODUCTION

Dysphagia is common in older individuals (1), particularly in extreme older age (2-4). With a rapidly aging population in most developed countries, dysphagia will be an increasing clinical problem in the future. Although swallowing and eating disorders are particularly common in hospital and nursing homes (1, 5), community dwelling individuals are also affected (4). Aged dysphagia (presbyphagia) is multifactorial, with edentulousness, salivary changes, neuromuscular disease(s), diabetes mellitus, tumors and paraneoplastic phenomena, drugs, surgical interventions and structural or age-related physiological changes, all contributing factors (1). Many individuals are affected by oropharyngeal dysphagia, however several causes of esophageal dysphagia occur more commonly in the aged (6, 7). Soergel originally described presbyesophagus occurring in those aged over ninety years of age (2), associated with delayed oesophageal clearance on radiology, as defined as clearance duration in excess of 20 seconds (2). The consequences of dysphagia in older subjects include aspiration pneumonia, dehydration and social isolation. Furthermore, associated malnutrition and sarcopenia can lead to a poor prognosis during any intercurrent illness (8).

Although the data are conflicting, previous manometric studies have reported several changes in esophageal motility that are unique to older adults. A study in healthy volunteers aged from 23 to 86 years showed increased oesophageal stiffness and reduced peristaltic function (both primary and secondary) with advancing age (9). Further to this, a pilot study of esophageal clearance including volunteers over 65 years suggested a trend towards impaired liquid and viscous bolus clearance in older men (10). Previous work by our group demonstrated changes in LES function in the elderly (over 80 years), in particular incomplete relaxation and reduced basal pressure, although no changes in peristaltic function were observed (11). In contrast, a recent study by Kawami et al. found the adequacy of secondary peristalsis was reduced in older age (over 65 years), but the success of primary peristalsis, the distal contractile integral and LES pressure were similar between young and healthy older subjects (12). Interpretation of results is hampered by varying definitions used to describe the age limit for older cohorts.

Software based esophageal pressure-flow analysis (PFA) of HRIM recordings has recently been described in an attempt to understand the correlation between pressure-flow findings and patient symptoms and outcomes (13-18). Esophageal PFA adds to the traditional use of impedance to track bolus transit (via impedance drop and return to 50% of baseline) by determining maximum luminal cross sectional area at the nadir impedance (19-21). This enables the accurate determination of bolus related pressures and the relationship of these to both distending and contractile forces (21, 22). Recent data by Kim et al. have shown that the inverse of impedance (admittance) *linearly* correlates with esophageal cross sectional area measured with intraluminal ultrasound (20), confirming the correlation of nadir impedance with intraluminal bolus presence (19, 21). Furthermore, esophageal PFA has shown symptom correlation in patients with broad dysphagia, post-surgical (15) and non-obstructive (16, 17) dysphagia. This analysis may also be a useful adjunct in studying asymptomatic individuals, including the ability to detect subtle abnormalities not obvious using the Chicago classification system (23).

We hypothesized that failed bolus clearance would occur more commonly in asymptomatic older subjects during viscous swallows. The aim of this study was to use intraluminal impedance methods to characterize bolus clearance in the upright posture for both healthy aged and young cohorts. Further aims were to determine the manometric correlates of intraluminal impedance-detected failed clearance and to perform pressure flow analyses to detect subtle changes in esophageal propulsive physiology.

MATERIALS AND METHODS

Study Participants

Forty-five healthy volunteers (aged 20 - 93 years, 21M) were recruited through community advertisement. A screening history was performed in all subjects to exclude (i) past or present swallowing difficulties, (ii) symptoms suggestive of a motility disorder, (iii) upper gastrointestinal conditions including gastro-esophageal reflux disease, (iv) diabetes mellitus, (v) previous history of gastrointestinal surgery and (vi) prescription medications known to affect GI motility. To further exclude underlying dysphagia, all potential subjects performed a previously validated Dakkak questionnaire (24) to assess the esophageal phase of swallowing for different food consistencies. Only subjects with a normal score (Dakkak = 0) were included in the study. Body weight and height, and current or past smoking history were also recorded. Enrolled subjects were stratified into the following two groups: younger controls and older subjects (>80 years).

The study protocol was approved by the Southern Adelaide Clinical Human Research Ethics Committee. All participants gave written informed consent prior to enrolment, and studies were performed at the Repatriation General Hospital, Daw Park, South Australia. AIM pressure-flow analysis of the pharynx has previously been reported in this cohort of subjects (4). The esophageal data reported in the current study includes only individuals where technically satisfactory esophageal tracings were also obtained.

Measurement Technique

High Resolution Impedance Manometry (HRIM) was performed in a sitting posture using a 10 French (3.2 mm diameter) solid-state pressure-impedance assembly. This incorporated 25 pressure-sensors (1cm spacing) and 12 adjacent impedance segments (2cm in length) (Unisensor Inc, Attikon, Switzerland). Pressure and impedance data were acquired at 20Hz

(Solar GI acquisition system, MMS, Enschede, The Netherlands). In order to obtain esophageal tracings, this catheter was repositioned following pharyngeal recordings in the majority of subjects and the swallowing protocol repeated. This explains why it was not possible to additionally obtain swallows in the supine posture in these subjects. The PFA analysis to date, including esophageal swallows, are described in the upright or semi recumbent postures only.

Study Protocol

Following nasal administration of co-phenylcaine forte spray and 2% lignocaine gel, subjects were intubated with the sensors in a posterior orientation. The assembly was positioned with the recording segment spanning the esophageal transition zone to proximal stomach. Following a 10 minute accommodation period, subjects received five 5ml and 10ml boluses of liquid (0.9% normal saline) and standardized viscous bolus (EFT Viscous Swallow Challenge Medium, viscosity 13,000 cP; Sandhill Scientific, Denver, Co. USA) via a syringe and asked to swallow once on cue. Studies were performed in a sitting posture with head in a neutral position.

Data Analysis

Esophageal Pressure Topography (EPT)

Analysis of EPT was based on the *Chicago Classification Version 3.0* diagnostic algorithm and definitions for esophageal manometry (25) using Solar GI HRIM software (Medical Measurement Systems; Utrecht, The Netherlands). For Chicago analysis and bolus clearance, both 5 and 10ml bolus were analyzed, however only median results for the 5ml bolus volume are displayed (Tables 1&2). Only studies with more than eight complete liquid or viscous swallows were included in the analysis of the Chicago classification and for the assessment bolus clearance. The Chicago parameters of 4 second integrated relaxation pressure (IRP4), peristaltic break length / isocontour defect (ICD), contractile front velocity (CFV), distal contractile integral (DCI) and distal latency (DL) were measured.

The IRP4 (mmHg) was determined as the lowest maximum LES pressure measured with an electronic sleeve sensor for four contiguous or non-contiguous seconds in a ten second period following swallow onset. The ICD (cm) was determined as the axial length of defects in the 20mmHg isobaric contour (26). DCI (mmHg.s.cm) was determined for the distal esophageal segment as amplitude x duration x length of the contraction in excess of 20mmHg. The CFV (cm s^{-1}) was determined as the slope of the tangent approximating the 30mmHg isocontour between the proximal transition zone and contractile deceleration point (CDP). The DL (s) was determined as the time from swallow onset (either through upper esophageal sphincter (UES) relaxation or the onset of impedance drop at the most proximal channel) to the CDP.

Pressure Flow Analysis (PFA)

Data were exported as comma separated values (CSV) and esophageal PFA was performed using MATLAB based automated software (The MathWorks Inc, Natick, MA, USA; Esophageal AIM*plot* software; T Omari©). Five observer-determined regions of interest (ROI) were used to guide analyses (13, 18). Pressure and/or flow metrics were determined across the LES and esophageal body distal to the transition zone (10). These included: (i) pressure at nadir impedance (PNI, mmHg), (ii) peak pressure (PeakP, mmHg), (iii) intra-bolus pressure (IBP, mmHg), (iv) IBP slope (mmHg s^{-1}), (v) time interval from nadir impedance to peak pressure (TNIPP, sec), (vi) pressure flow index (PFI) and (vii) ratio of nadir impedance to impedance at the time of peak pressure (Impedance Ratio).

The TNIPP is indicative of the latency from bolus distension to esophageal contraction. The PFI (previously named dysphagia risk index (15)) was developed in the context of post-fundoplication dysphagia and amplifies differences in key metrics in relation to symptoms. This variable is calculated using the formula PFI = (IBP * IBP slope)/(TNIPP), and is higher in circumstances of greater bolus pressurization in relation to bolus flow (18). For example, PFI is increased in both post-fundoplication dysphagia (15) and non-obstructive dysphagia (16, 17). Impedance Ratio (IR), which is indicative of bolus clearance, was calculated as a marker of incomplete bolus transit. It defines the proportion of the bolus present at the time of peak esophageal contraction pressure relative to the bolus present at the time of maximal esophageal distension/flow (high ratio = incomplete transit)(17, 18, 21).

Conventional Impedance-Based Assessment of Esophageal Bolus Transport

Bolus presence time (BPT) was determined for all impedance segments as the time interval between bolus entry (50% drop from 3 sec pre-swallow basal impedance) and bolus exit (recovery to more than 50% of basal value for more than 5 sec) (27). Total bolus transit time (TBTT) was determined by measuring the entry time from the most proximal to the most distal paired impedance rings above the level of the LES. Due to the variable total length across which impedance was measured, all TBTT values were transformed to the standardized 15cm length as previously described (27, 28). An abnormal BPT at any level was reported as failed transit and a TBTT ≥ 15sec for liquids and ≥ 17sec for viscous boluses were likewise reported as abnormal (28). Per patient analysis of all liquid and viscous swallows was performed. Bolus clearance was considered normal with ≥80% clearance of liquid and ≥70% with viscous (27, 28).

Statistical Analysis

Data were analysed using Sigmaplot 13 (Systat Software Inc., San Jose, Ca) and Prism Plus 6.0 (Graphpad, San Diego, Ca). Data was assessed for a normal distribution using the D'Agostino & Pearson omnibus and Shapiro –Wilk normality tests. Initial comparisons were made through determination of one-way ANOVA with Dunn's multiple comparison analyses. Pairwise comparisons were done via independent sample t-test or Mann Whitney U-test when non-normally distributed. Data presented are mean ± SEM or median [IQR]. Correlation for per subject bolus clearance was determined with Spearman rank correlation using percent cleared bolus. A two-way ANOVA was used to compare per subject category (young controls and older subjects) and per clearance (cleared and non-cleared) with Holm-Sidak pairwise multiple comparison procedure for Chicago and pressure flow metrics. A P-value of <0.05 was considered statistically significant throughout.

RESULTS

All subjects tolerated the study procedure well and no adverse events were reported. Older subjects (n=15; aged 85±4years) were significantly older than the control group (n=30; aged 37±11 years) (P<0.001).

Analysis of Swallows by EPT Criteria

The results of Chicago classification analyses are summarized in Table 1.

Chicago Classification of EPT

Analysis of *liquid swallows* using Chicago Classification showed a slightly higher proportion of normal swallows (60%) in the younger control group, when compared to older subjects (53.3%). Failure to trigger peristalsis occurred in 26.7% in those aged above 80 years, and only 3.4% of younger controls. The remaining abnormal swallows were classified as ineffective esophageal motility and were more prevalent in the control group (controls: 36.6% vs. older subjects: 20%).

Analysis of *viscous swallows* showed the same proportion of normal swallows in younger controls (cf. liquid), but was lower within older subjects (42.8%). In controls, 26.7% of the remaining swallows met criteria for ineffective esophageal motility, and 13.3% were classified failed peristalsis. There was an equal distribution (28.6%) of failed and ineffective motility in the older subjects with viscous bolus.

Effects of Aging on EPT Parameters

There was a larger ICD in older subjects when compared to controls, for both liquid (P=0.05) and viscous (P=0.03) swallows. The CFV of the distal esophagus was significantly increased in older subjects with both bolus consistencies (Liquid: P=0.004 and Viscous: P=0.003). The

IRP4 was significantly higher in older subjects during viscous swallows (P=0.002), but not liquids. There were no differences in DCI or DL between young and older subjects.

Effects of Bolus Consistency on EPT Parameters

In healthy controls, the CFV was increased with liquids (3.5 ± 0.2 cm s^{-1}) when compared to viscous swallows (2.8 ± 0.1 cm s^{-1}; P<0.001). In the younger group, the DL was longer with viscous bolus (6.7 ± 0.2 s vs. 6.01 ± 0.2 s; P=0.03). In older subjects, a higher IRP4 was recorded during viscous (14.5 ± 2.1 mmHg) when compared to liquid swallows (8.9 ± 1.5 mmHg; P=0.02).

Analysis of Swallows using Pressure Flow Analysis (PFA)

The pressure-flow results for liquid and viscous swallows are summarized in Tables 2 and 3.

Effects of Aging on PFA Swallow Metrics

The impedance ratio (IR) was higher in the older subjects for both bolus consistencies (L: P=0.002 and V: P<0.001). With viscous bolus only, a higher IBP (P=0.05) and IBP slope (P=0.02) were recorded in the older cohort. There was a strong trend for a longer latency time of TNIPP with liquids in older subjects, when compared to younger controls (P=0.07).

Effects of Bolus Consistency on PFA Swallow Metrics

In both age groups, the IBP and IBP slope were higher with viscous bolus than liquid. The TNIPP was shorter during viscous swallows in controls (2.7 ± 0.1 sec vs. 4.0 ± 0.2 sec; P<0.001) and older subjects (2.9 ± 0.21 sec vs. 4.5 ± 0.2 sec; P<0.001). Viscous bolus increased the IR when compared to liquid (controls: P<0.001 and older subjects: P=0.02) in all subjects.

Effect of Peristaltic Break Size on PFA Metrics with Viscous Bolus

When comparing those subjects with an ICD <2cm, the IBP was higher in older subjects when compared to young (23.5 ± 8.7 mmHg vs. 11.4 ± 0.73 mmHg, P=0.03). IR was significantly increased (O: 0.50 ± 0.01 vs. YC: 0.30 ± 0.01; P=0.005) in older subjects.

In those subjects with a larger peristaltic break (ICD >2cm), a higher PeakP was obtained in younger controls (39.2 ± 2.8 mmHg vs. 27.2 ± 4.5 mmHg; P=0.03). The IBP slope (O: 6.8 ± 1.3 mmHg s^{-1} vs. YC: 4.0 ± 0.5 mmHg s^{-1}; P=0.03) and IR (0.60 ± 0.01 vs. 0.40 ± 0.01; P<0.001) were increased in the older subjects, and a significantly higher PFI was recorded (36.1 ± 6.8 vs. 15.8 ± 2.7; P=0.006).

Within both age groups, subjects with an ICD > 2cm had a lower PeakP when compared to those with a smaller peristaltic break (<2cm) (YC: 39.2 ± 2.8 mmHg vs. 77.2 ± 6.6 mmHg, P=0.02; and O: 27.2 ± 4.5 mmHg vs. 89.9 ± 21.0 mmHg; P=0.02).

In control subjects only, a larger ICD reduced both the IBP (>2cm: 7.2 ± 0.7 mmHg vs. <2cm: 11.4 ± 0.7 mmHg; P=0.01) and PFI (15.8 ± 2.7 vs. 90.0 ± 20.0; P=0.04), and increased the TNIPP (3.1 ± 0.1 sec vs. 2.5 ± 0.1 sec; P=0.03), when compared to smaller breaks.

Within the older group, the IR was found to be higher with a larger ICD (>2cm: 0.60 ± 0.01 vs. <2cm: 0.50 ± 0.01; P=0.05).

Bolus Clearance

Figures 3 & 4 show Chicago classification and pressure flow analysis metrics for controls (YC) and older subjects (O) with and without bolus clearance. The Spearman rank correlation of per subject bolus clearance are shown in Table 4.

Clearance of liquid bolus was significantly lower in asymptomatic older subjects (60%) when compared to younger controls (82%) during upright swallowing (Chi-square = 4.935; P <

0.05). There was a more marked reduction with viscous bolus, with successful clearance achieved in 83% of younger controls and only 40% of older subjects (Chi-square = 39.08; $P < 0.001$).

During two-way ANOVA, longer peristaltic breaks ($F(1,90)=17.21$; $P<0.001$) and rapid peristalsis ($F(1,89)=14.155$; $P<0.001$) were strongly associated with failed liquid clearance in the older group. Measures indicating decreased peristaltic vigor (DCI, mean peakP) occurred in both groups, while increased impedance ratio were present only in those older individuals with failed liquid clearance (data not shown).

For failed viscous clearance, longer peristaltic breaks ($F(1,88)=7.129$; $P=0.009$) and rapid peristalsis ($F(1,88)=4.502$; $P<0.05$) were again strongly associated. Decreased peristaltic vigor (DCI, mean peakP) and increased intra-bolus pressures were also associated in the older group, when compared to controls. Increased impedance ratio was found in both groups.

DISCUSSION

This is the first study to perform pressure flow analysis (PFA) in the esophagus to determine subtle changes in esophageal physiology that occur with healthy aging. Asymptomatic individuals at the extreme of age have evidence of impaired *oropharyngeal* swallowing when studied using pressure flow analysis (4). The current study extends this approach to the esophagus to study those at extreme older age (over eighty years). Our results show that, in addition to impaired oropharyngeal function, asymptomatic older subjects also have impaired esophageal function leading to failed bolus transit, which is most pronounced with increasing bolus consistency (29).

Older individuals have a greater proportion of ineffective and failed swallows when compared to young controls. Although there is significant debate in the literature, it is widely assumed that esophageal motor function deteriorates in older age. Studies in healthy volunteers (aged between 20 and 90 years) and some patient cohorts have shown decreased peristaltic activity, both primary and secondary, and reduced esophageal compliance with advancing age (7, 9, 30-34). There is conflicting data on whether peristaltic amplitude is reduced (33-34), increased (35) or remains unchanged (36) in older age. Using the newer measure of distal contractile integral (DCI), our study supports the latter with no difference in contractile vigor observed between the young and older group (when successful peristalsis was achieved). However, a reduced DCI remained a correlate of failed clearance in both groups in our study and the previous findings suggesting decreased peristaltic vigor, may simply reflect a greater proportion of asymptomatic older subjects with ineffective esophageal motility. Longer peristaltic breaks in excess of 2-5cm, a known correlate of failed bolus clearance (26, 37), were seen in many older individuals and the mean peristaltic break length was increased for both liquid and viscous swallows (Table 1).

We have previously shown abnormal LES function in individuals over 80 years, as evidenced by higher resting pressure and incomplete relaxation (11), which is consistent with an earlier study by Ren et al (30). Other studies, however, have been unable to demonstrate any age effects on the LES (12, 36). In the current study, a higher IRP4 was observed during viscous swallows in the healthy older group (Table 1). Furthermore, distal esophageal intra-bolus pressures were increased during both liquid and viscous swallows (Table 3), and the intra-bolus pressure slope (reflecting the rate at which pressure increases) was also higher with viscous bolus in this older cohort. These findings are in keeping with EGJ outflow resistance increasing with age. In concert with longer peristaltic breaks, the presence of EGJ outflow obstruction and consequent increased intrabolus pressures lead to a high likelihood of proximal bolus escape leading to failed bolus clearance as witnessed in our study. Although elevations in distal intrabolus pressures have previously been associated with increasing bolus perception (18), this was not the case in our older cohort and one could postulate a decline in activation of sensory afferent pathways in this group. The previously reported decreased distal esophageal distensibility (9) is supported by the increased intrabolus pressures observed in the older group. We postulate that decreased distensibility of the distal esophagus, associated with decreased bolus presence, leads to decreased peripheral activation of stretch receptors, involved in LES relaxation (Brookes 1996 - 38). It is however also possible that decreased LES opening in older subjects are additionally the result of mechanical factors or incoordination of central and peripheral LES relaxation. More work is needed to elucidate the causes of EGJ dysfunction in the aged.

Esophageal pressure flow analysis is a novel approach aimed at detecting additional abnormalities not evident with EPT. This approach has been used in studying patients with post-fundoplication dysphagia (15) and non-obstructive dysphagia (16, 17). Among several metrics produced by the analysis, the pressure flow index and impedance ratio have proved useful in classifying individuals within a pressure flow matrix (Figure 5), which assesses bolus pressurization and clearance . Figure 5 is a pressure flow matrix of the findings of our study for both younger controls and older subjects. Esophageal PFA performed in healthy older subjects demonstrates diminished clearance (higher IR) and/or augmented pressures relative to flow (higher PFI) resulting from decreased peristaltic integrity and/or reduced LES relaxation. Of interest, the impedance ratio was increased for older cohorts with and without impaired bolus clearance by standard criteria. This is in keeping with imaging studies, which have shown an increased frequency of intra-esophageal stasis (10) and incomplete esophageal emptying (29) with both liquid and viscous swallows in asymptomatic volunteers aged above 65 years. Standard impedance criteria used to date may not be entirely reliable in determining bolus clearance when compared to radiological findings, particularly in the case of failed contractions (39), as seen frequently in our older cohort. Impedance ratio may represent a superior measure of bolus clearance in this context (21).

Our study has several limitations. Upright manometry is not usually performed and may limit the applicability of our findings. In this posture, bolus transport is aided by gravity (40) and consequently less peristaltic contribution is needed to assist clearance. This is particularly true for liquid and forms the premise for performing esophageal manometry using liquid swallows in the supine posture. Despite this, liquid clearance was impaired in association with longer peristaltic breaks in our older subjects. Expanded protocols including increased consistencies and upright posture are becoming more commonplace as a correlate of physiological swallowing. The catheter specification (25cm length) used for this study required re-positioning in the majority of individuals in order to capture the complete distal esophagus from the transition zone to proximal stomach. Although this was achieved, it meant that a drop in impedance at the most proximal channel was used to define swallow onset, which may shorten the distal latency. Despite this limitation, the distal latencies described are consistent with those obtained using a longer catheter with the same recording system (35, 41).

In conclusion, our study of asymptomatic individuals over eighty years of age showed the modern equivalent of presbyesophagus, with ineffective and failed peristalsis, rapid contractions with a normal latency and decreased LES relaxation. Pressure flow analysis also revealed evidence of lower maximum admittance, suggestive of decreased esophageal distensibility, which manifests as increased intrabolus pressurization and impaired bolus clearance.

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Author Contributions

CC and TO developed study concept and design, data analysis and writing the manuscript; LB performed the research, data analysis and writing the manuscript; SK performed the research and data analysis; CB and AT performed the studies; RH and RJF in study design, data interpretation and critical revision of manuscript

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TO holds a patent on pressure flow analysis.

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TABLE 1: Chicago variables for liquid and viscous swallows in the upright posture in young controls(YC) and older (O) subjects. P-Value is for t-test??.....

		LIQUID (5ml)						VISCOUS (5ml)					
		MEAN	**SEM**	**MEDIAN**	**P5**	**P95**	**P value**	**MEAN**	**SEM**	**MEDIAN**	**P5**	**P95**	**P value**
IRP4 (mmHg)	YC	8.0	0.9	8.0	0.9	14.8	0.7	7.6	0.9	7.0	0.5	16.6	**0.002**
	O	8.9	1.5	9.0	-0.3	17.6		14.5	2.1	16.0	1.3	25.0	
ICD (cm)	YC	2.1	0.5	1.0	0.0	7.6	**0.05**	2.0	0.5	0.2	0.1	7.5	**0.03**
	O	4.4	1.2	1.2	0.1	12.0		4.8	1.5	1.5	0.1	13.3	
CFV (cm S^{-1})	YC	3.5	0.18	3.2	2.4	5.5	**0.004**	2.8	0.1	2.7	2.1	3.4	**0.003**
	O	6.2	1.2	3.6	2.2	14.7		5.2	1.1	3.7	2.1	12.6	
DCI (mmHg S^{-1} cm^{-1})	YC	766.9	123.1	668.5	85.0	1688.7	0.87	701.5	119.3	550.0	44.1	1827.8	0.31
	O	728.5	224.0	495.0	4.8	2363.0		1050.5	427.5	340.5	21.7	3737.4	
DL (s)	YC	6.01	0.2	6.2	4.2	8.3	0.6	6.7	0.2	6.8	4.2	8.7	0.2
	O	6.3	0.3	6.4	4.2	8.0		6.0	0.6	6.2	2.6	8.3	

TABLE 2: Impedance/pressure metrics derived from AIMplot analysis during liquid swallows in young controls(YC) and older (O) subjects. P-value is for t-test……

		MEAN	SEM	MEDIAN	P5	P95	P Value
PeakP (mmHg)	YC	65.64	5.80	63.60	28.06	108.54	0.33
	O	55.61	8.85	57.28	19.49	111.97	
PNadImp (mmHg)	YC	4.32	0.23	4.38	2.25	6.19	0.17
	O	8.66	8.85	3.83	0.74	27.48	
IBP (mmHg)	YC	5.66	0.46	5.28	2.44	10.54	0.13
	O	10.50	4.45	5.15	2.38	30.92	
IBP slope (mmHg s^{-1})	YC	4.60	0.97	2.34	0.11	17.15	0.49
	O	3.57	4.52	2.95	0.06	7.65	
TNIPP (sec)	YC	4.01	0.2	3.80	2.83	5.66	**0.076**
	O	4.50	0.2	4.54	3.28	5.52	
PFI	YC	64.42	21.04	10.14	0.32	337.08	0.3
	O	34.87	0.20	4.76	-0.52	105.28	
IR	YC	0.27	0.02	0.26	0.13	0.46	**0.002**
	O	0.42	0.05	0.31	0.24	0.76	

TABLE 3: Impedance/pressure metrics derived from AIMplot analysis during viscous swallows in young controls (YC) and older (O) subjects. P-value is for t-test??.....

		MEAN	SEM	MEDIAN	P5	P95	P Value
Peakp (mmHg)	YC	64.54	5.55	63.18	29.42	103.27	0.9
	O	63.03	14.58	41.62	20.43	172.09	
PNadImp (mmHg)	YC	7.01	0.50	6.79	3.09	11.73	**0.04**
	O	14.06	5.00	10.59	1.86	38.48	
IBP (mmHg)	YC	9.90	0.65	10.27	4.80	16.54	**0.05**
	O	17.30	5.29	12.52	5.54	43.21	
IBP slope (mmHg s-1)	YC	8.01	0.96	6.39	2.64	16.97	**0.02**
	O	17.3	5.2	8.09	3.79	19.00	
TNIPP (sec)	YC	2.72	0.09	2.67	1.98	3.69	0.3
	O	2.90	0.21	2.91	1.76	4.05	
PFI	YC	65.30	14.78	26.39	9.50	246.69	0.99
	O	65.19	27.34	38.80	2.32	219.06	
IR	YC	0.36	0.01	0.35	0.22	0.50	**<0.001**
	O	0.55	0.03	0.59	0.32	0.72	

TABLE 4: Correlation of Chicago Classification & Pressure Flow Metrics with percent Bolus Clearance per Subject. Data are Spearman rank correlation coefficients ($^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$)

	Liquids (r)		Viscous (r)	
	Young Controls	**Older**	**Young Controls**	**Older**
Chicago Classification Metrics				
IRP4 (sec)	0.147	-0.250	0.175	-0.050
PB (cm)	-0.432^{***}	-0.755^{***}	-0.277^{*}	-0.581^{***}
CFV (cm/s)	0.028	-0.536^{**}	-0.028	-0.114
DCI ($mmHg.s^{-1}.cm^{-1}$)	0.478^{***}	0.835^{***}	0.435^{***}	0.462^{**}
DL (sec)	-0.221	-0.160	-0.160	0.197
Pressure Flow Metrics				
PeakP (mmHg)	0.482^{***}	0.837^{***}	0.418^{***}	0.480^{**}
PNI (mmHg)	0.046	0.309	0.340^{**}	0.293
IBP (mmHg)	-0.124	0.214	0.375^{**}	0.283
IBPslope (mmHg/s)	-0.259	-0.001	0.404^{***}	0.285
TNIPP (sec)	-0.050	0.194	-0.219	0.001
PFI	-0.354^{**}	-0.013	0.366^{**}	0.041
IR	-0.476^{***}	-0.567^{***}	-0.307^{*}	-0.489^{***}

FIGURE LEGENDS