

Physiology of the oesophageal transition zone in the presence of chronic bolus retention: studies using concurrent high resolution manometry and digital fluoroscopy

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Abstract Distinct contraction waves (CWs) exist above and below the transition zone (TZ) between the striated and smooth muscle oesophagus. We hypothesize that bolus transport is impaired in patients with abnormal spatio-temporal coordination and/or contractile pressure in the TZ. Concurrent high resolution manometry and digital fluoroscopy were performed in healthy subjects and patients with reflux oesophagitis; a condition associated with ineffective oesophageal contractility and clearance. A detailed analysis of space–time variations in bolus movement, intra-bolus and intra-luminal pressure was performed on 17 normal studies and nine studies in oesophagitis patients with impaired bolus transit using an interactive computer based system. Compared with normal controls, oesophagitis patients had greater spatial separation between the upper and lower CW tails [median 5.2 cm (range 4.4–5.6) vs 3.1 cm (2.2–3.7)], the average relative pressure within the TZ region (TZ strength) was lower [30.8 mmHg (28.3–36.5) vs 45.8 mmHg (36.1–55.7), $P < 0.001$], and the risk of bolus retention was higher (90% vs 12%; $P < 0.01$). The presence of bolus retention was associated with a wider spatial separation of the upper and lower CWs (>3 cm, the upper limit of normal; $P < 0.002$), independent of the presence of oesophagitis. We conclude that bolus retention in the TZ is associ-

ated with excessively wide spatial separation between the upper and lower CWs and lower TZ muscle squeeze. These findings provide a physio-mechanical basis for the occurrence of bolus retention at the level of the aortic arch, and may underlie impaired clearance with reflux oesophagitis.

Keywords high resolution manometry, motility, oesophageal transport, oesophagus, transition zone.

INTRODUCTION

The primary function of the oesophagus, the transfer of liquids and solids to the stomach, results from mechanical responses to physiologically induced changes in tone within the muscularis propria, what we call ‘physio-mechanics’.¹ Previous studies have shown that transport through the mid oesophagus is achieved by the action of distinct contraction waves (CWs) in the upper and lower oesophagus separated by a ‘transition zone’ (TZ) at the aortic arch level.^{2,3} Concurrent manometry and fluoroscopy studies by Kahrilas *et al.*^{4,5} showed that bolus retention in the TZ was accompanied by a weakened peristaltic CW at this level. Based on these studies, Li *et al.*² developed a computer model to study the biomechanical basis of normal vs abnormal oesophageal transport and demonstrated that effective bolus transport across the TZ requires the existence of coordinated upper and lower CWs, and that impaired bolus transit results from a mismatch between these waves. The TZ manometrically manifests as a pressure trough at approximately 25% of the length of the oesophagus from the upper oesophageal sphincter^{3,6,7}, corresponding to a transition in the neuromuscular physiology of the oesophagus from striated to smooth muscle.⁸

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The hypothesis of separate upper and lower CWs as normal TZ physiology² was confirmed in a recent study by Ghosh *et al.*³ using concurrent high resolution manometry (HRM) and fluoroscopy. The tonic contraction that maintains luminal occlusion and drives the bolus aborad was relatively weak within the TZ compared with the proximal or distal oesophagus, making this region susceptible to bolus retention. Although liquid bolus retention is minimal in normal subjects, solid boluses often fail to clear the oesophagus with a single swallow; solid bolus retention is most frequent at the aortic arch level^{9,10}. Recent case reports have linked focal aperistalsis in the TZ region to symptomatic bolus retention at this level.¹¹

This paper tests the hypothesis that bolus retention in the TZ is a result of impaired coordination between upper (striated muscle) and lower (smooth muscle) CWs. We performed a detailed analysis of concurrent HRM with digital fluoroscopy data from a cohort of normal subjects and patients with impaired bolus transit in the aortic arch region. Patients with gastro-oesophageal reflux disease and oesophagitis were selected for study because ineffective oesophageal motility is prevalent and clinically relevant in this condition.^{4,12} Moreover, initial observations with HRM documented abnormal pressure activity in the TZ region in this patient group.¹³

A key limitation of previous studies is that conventional manometry with widely spaced pressure sensors (>2 cm separation) does not provide sufficient resolution to assess accurately the potential for success or failure of oesophageal bolus transport.^{11,14} In contrast, HRM with many closely spaced pressure sensors can quantify the segmental character of oesophageal motor activity⁶ and detect focal abnormalities of motor function that may produce impaired bolus transport.^{3,11,15,16} Moreover, HRM accurately measures intra-bolus pressure gradients along the lumen^{3,17-19}; and reflect the propulsive force that drives bolus transport.^{20,21} In the current study, we apply concurrent HRM and digital fluoroscopy to correlate intra-oesophageal space-time pressure variations with bolus transport in the TZ region of patients with chronic bolus retention.

MATERIALS AND METHODS

Concurrent HRM and digital fluoroscopy data were collected with the patient in the supine position to minimize hydrostatic pressure variations that would have further complicated the analysis. All swallows were with 10 ml boluses of high-viscosity barium (Micropaque, Guerbet; Roissy, France; viscosity

50 000 cP). Only swallows with complete fluoroscopy recording were used for analysis. A total of 17 studies in healthy subjects and nine studies in oesophagitis patients were subjected to detailed space-time analysis. Patients had reflux symptoms for at least 6 months with a positive oesophageal pH measurement and LA Grade A/B oesophagitis on endoscopy. None of the patients had a hiatus hernia on endoscopy. Antisecretory and prokinetic drugs were stopped 1 week prior to the study. Informed consent was obtained from all subjects and the study protocol was approved by the local Ethics Committee and radiation protection board.

Data collection

As described previously in detail³, HRM was performed concurrent with fluoroscopy. Pressure data were recorded with a water-perfused 21-channel assembly (Dentsleeve, Wayville, Australia) that included 19 oesophageal recording sites spaced 1.0–1.5 cm, a 6-cm sleeve, and a gastric recording site 1.0 cm distal to the sleeve. Pressure sensors were identified on fluoroscopy by tantalum markers. Manometric data were recorded at 25 Hz using a custom software system (TRACE! version 5.2.1; Geoffrey Hebbard, Royal Melbourne Hospital, Victoria, Australia). The catheter was inserted through an anaesthetized nostril, and the sleeve was placed across the high-pressure zone of the lower oesophageal sphincter. Fluoroscopic images were digitized at 4 Hz. Manometry and fluoroscopy data were temporally synchronized using a short (<0.25 s) electrical impulse generated by the fluoroscope.

Data analysis

Separate and concurrent assessment of the manometry and fluoroscopy data were performed to quantitatively relate the space-time pressure activity with bolus transport through the TZ.

HIGH RESOLUTION MANOMETRY

Because the bolus is driven by muscle tension, which is proportional to the transmural pressure difference¹, all intra-luminal pressures were referenced to average intra-thoracic pressure. High resolution manometry data were interpolated in space-time to 10 virtual ports cm⁻¹ at 50 Hz, and displayed with color isobaric contours (Fig. 5).³ Consistent with previous observations, a well-defined trough in temporal pressure amplitude (P_{amp}) was observed in the mid-oesophagus in every swallow.^{3,6,22} The spatio-temporal position of nadir pressure (P_{TZ}) was defined as the 'center' of the

TZ and the upper and lower margins of the TZ were defined by the locations of the maximum spatial gradients in pressure above and below the nadir pressure. The TZ length (ΔX_{TZ}) was defined as the distance between the upper and lower margins of the TZ and the temporal separation of the TZ (ΔT_{TZ}) was the time difference between the earlier and later temporal margins of the TZ. The TZ 'strength', defined as the average temporal pressure amplitude within the segment, reflects the average muscle force (per unit area) available to close the oesophageal lumen.¹

DIGITAL FLUOROSCOPY

Radiographic images of the bolus were visualized at 4 Hz. The bolus tail, defined as the position of luminal occlusion, correlates with the pressure upstroke.^{3,14,20} The same pattern of bolus transport was observed in every swallow for all patients and controls without exception (Fig. 1). As the bolus tail approached the aortic arch region, it slowed while its pressure weakened before suddenly 'jumping' a finite spatial distance to the initiation of a new CW below. Following the jump, the new bolus tail associated with the new CW moved into the distal oesophagus.

The trajectory of the upper contraction wave (UCW) was defined as the tail trajectory from the proximal striated oesophagus to when luminal closure was no longer clear (t_6 in Fig. 1). The tail trajectory of the lower contraction wave (LCW) was defined backwards in time starting below the TZ where the tail was clearly defined ($t > t_7$ in Fig. 1) to the end of the UCW (UCW_e) when the UCW tail 'jumped' to the LCW tail (see Fig. 1). As observed in Fig. 1, the muscle squeeze that initiated the LCW began as a localized 'indenta-

tion wave' (IW) at t_2 that increasingly occluded the lumen until, at full occlusion (time t_6) the LCW was initiated.

Upper and lower contraction wave trajectories were quantified using an interactive computer-based image analysis program developed within MATLABTM (The MathWorks Inc., Natick, MA, USA). The volume of any retained bolus was estimated by assuming an axisymmetric geometry and by approximating the bolus shape as an ellipsoid or cylinder, not including the volume of the catheter and any bolus retained from previous swallows.³ We estimated volumes above 0.5 ml as measurable bolus retention, as opposed to barium coating the catheter (t_7 in Fig. 1).

CONCURRENT ANALYSIS OF MANOMETRY AND IMAGE DATA

Manometrically measured pressures were spatially interpolated and displayed along the oesophageal lumen adjacent to the corresponding fluoroscopic image at fixed instants in time (Fig. 2) within a special purpose software system. The display of fluoroscopic image with concurrent spatial variation of pressure could be advanced or reversed to any time step in the data series. In this way, it was possible to identify the maximum pressure amplitude spatially along the lumen (P_A) and the pressure at the bolus tail (P_T) at each time instant. Thus, the trajectory of the bolus tail (X_T), pressure amplitude (X_A) and the indentation wave (X_I), and the pressure at the bolus tail (P_T), the pressure amplitude (P_A) and the indentation (P_I) were determined as functions of time.

Statistical analyses were carried out using the R statistics software (v 1.7.0, The Free Software Foundation,

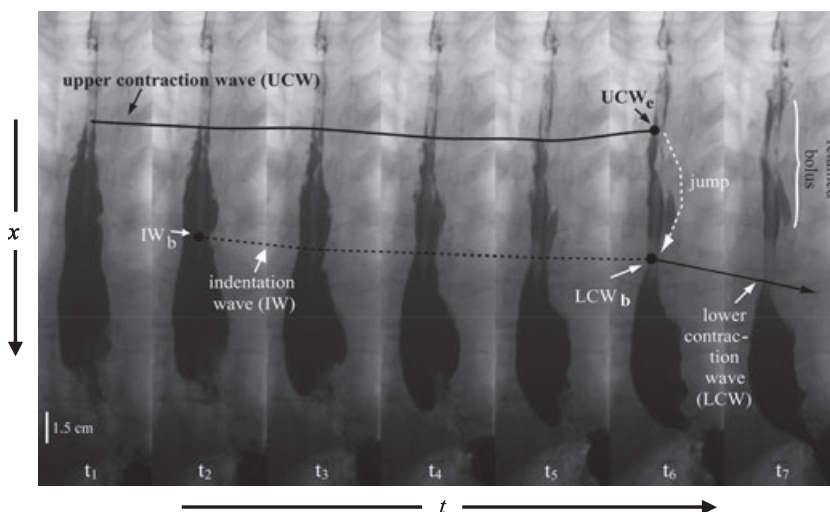


Figure 1 Example swallow showing bolus retention in the transition zone. The images are 0.25 s apart. The solid black lines mark the tails of the upper contraction wave (UCW) and lower contraction wave (LCW). UCW_e marks the end of the UCW and LCW_b the beginning of the LCW. An abnormally large spatial jump at t_6 between UCW_e and LCW_b leads to retention of bolus in between. An indentation wave (IW, dashed) develops into the LCW at LCW_b that continues into the lower esophagus.

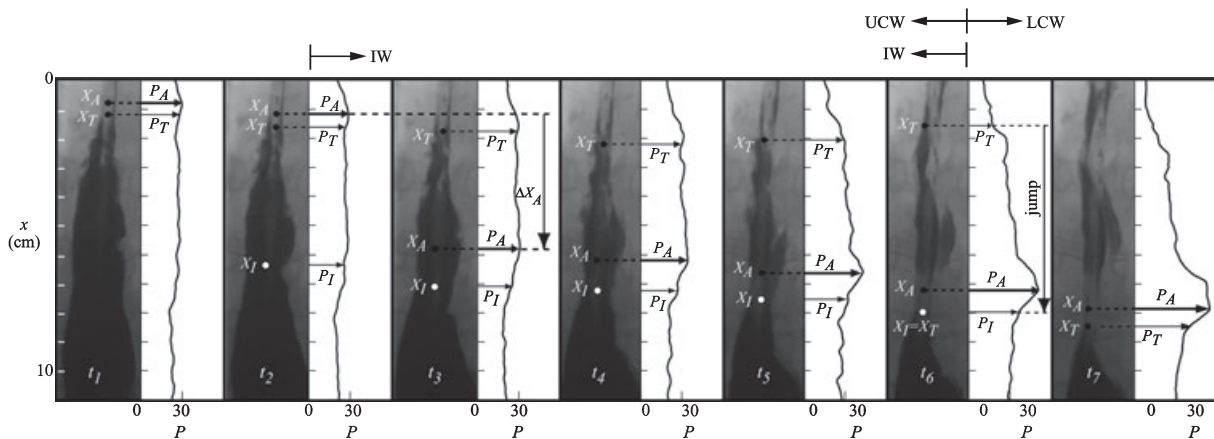


Figure 2 The spatial relationship between spatial pressure amplitude (P_A) and tail pressure (P_T) for the swallow shown in Fig. 1. Along the UCW P_A follows the tail and exceeds P_T to maintain luminal closure. Between t_4 and t_5 , P_A moves distal to P_T as pressure transitions to non-peristaltic behaviour in the transition zone (TZ). The trajectory of P_A is given by X_A vs time t . Between t_2 and t_3 , X_A jumps by an amount ΔX_A from the UCW into the transition zone. At time t_6 , P_A begins its association with the LCW.

Inc., Boston, MA, USA). Data are presented as the median (inter-quartile range) or mean \pm standard deviation (SD), as appropriate. P -values and 95% confidence intervals (CI_{95}) were calculated using a linear mixed effects model for swallows from the patient group. Comparison between subject groups (normal vs chronic bolus retention) was performed using ANOVA. To assess the determinants of successful bolus transport across the TZ region univariate regression was performed with bolus retention volume as the dependent variable and with HRM and videofluoroscopy data as fixed variables. Swallows from patients and normal controls were pooled to identify the physiological processes that determine bolus retention independent of the presence of disease. Significant variables were

entered into a multivariate model. In addition, the association of bolus retention and abnormal pressure activity in the TZ region was examined by chi-square contingency analysis (there were insufficient observations for ROC analysis). $\alpha < 0.05$ after correction for multiple comparisons was considered significant.

RESULTS

A total of 17 concurrent HRM and imaging studies in healthy subjects and nine studies in oesophagitis patients were analysed. Measurements of pressure activity and bolus transport across the TZ region are summarized in Table 1. The length of the manometrically defined TZ (ΔX_{TZ}) in oesophagitis patients

Table 1 Statistics of the transition zone

	Oesophagitis patients		Normal control	P -value
	Mean \pm SD	Median (IQR)	Median (IQR)	
L_E (cm)	23.5 \pm 1.7	24.0 (23.3–24.3)	25.5 (25.0–27.5)	$P < 0.001$
Upper margin TZ (cm)	4.4 \pm 0.5	4.3 (4.1–4.8)	5.2 (4.5–5.5)	$P = ns$
Center TZ (cm)	7.8 \pm 1.8	7.6 (6.9–8.8)	7.7 (6.6–8.8)	$P = ns$
Lower margin TZ (cm)	11.9 \pm 1.2	12.2 (11.0–12.3)	10.2 (8.4–10.9)	$P < 0.004$
ΔX_{TZ} (cm)	7.5 \pm 1.2	7.4 (6.7–7.7)	4.9 (3.9–6.1)	$P < 0.001$
$\Delta X_{TZ}/L_E$	0.33 \pm 0.06	0.32 (0.29–0.35)	0.19 (0.15–0.22)	$P < 0.002$
ΔT_{TZ} (s)	2.7 \pm 0.7	2.6 (2.3–2.8)	2.1 (1.9–2.4)	$P = 0.14$
P_{TZ} (mmHg) [†]	16.6 \pm 7.1	17.1 (11.7–17.5)	26.7 (23.0–43.2)	$P < 0.001$
TZ strength (mmHg) [‡]	30.9 \pm 6.8	30.8 (28.3–36.5)	45.8 (36.1–55.7)	$P < 0.001$
ΔX_{jump} (cm)	6.0 \pm 2.6	5.2 (4.4–5.6)	3.1 (2.2–3.7)	$P < 0.008$
ΔX_A (cm)	4.7 \pm 2.1	4.1 (3.9–4.6)	1.3 (1.0–2.9)	$P < 0.007$
Retained bolus (ml)	2.18 \pm 3.53	0.89 (0.57–1.38)	0.15 (0.0–0.29)	$P = 0.13$
Retained bolus (>0.5 ml)		9/10	2/16	$P < 0.01$

IQR, inter-quartile range. [†]Pressures are relative to thoracic pressure; [‡]TZ strength was defined as the average temporal pressure amplitude within the segment.

was approximately 2.5 cm wider compared to controls [7.4 cm (6.7–7.7) vs 4.9 cm (3.9–6.1), $P < 0.001$] and occupied a greater proportion of oesophageal length [33% (29–35) vs 19% (15–22), $P < 0.002$]. In contrast, the temporal separation of the TZ (ΔT_{TZ}) was statistically similar in both groups [2.6 s (2.3–2.8) vs 2.1 s (1.9–2.4), $P = 0.14$]. Statistically, the positions of the upper margins and centers of the TZ (defined by the nadir pressure) were not significantly different in patients and controls; however, the lower margin of the TZ was significantly more distal in the oesophagitis group [12.2 cm (11.0–12.3) vs 10.2 cm (8.4–10.9), $P < 0.004$] relative to the upper oesophageal sphincter. The TZ pressure (P_{TZ}) was significantly lower in oesophagitis patients than in controls [17.1 mmHg (11.7–17.5) vs 26.7 mmHg (23.0–43.2) mmHg, $P < 0.001$]. The strength of the TZ was also significantly lower [30.8 mmHg (28.3–36.5) vs 45.8 mmHg (36.1–55.7), $P < 0.001$]. The volume of retained bolus in the TZ region was greater for oesophagitis patients than for controls [0.9 ml (0.5–11.3) vs 0.2 ml (0.0–0.7)], and was highly variable in the oesophagitis group. All but one swallow in oesophagitis patients was accompanied by bolus retention (>0.5 ml) in the TZ region, whereas only two swallows in healthy controls had this level of bolus retention ($P < 0.01$). Complete bolus retention was observed in one oesophagitis patient in whom the TZ region was exceptionally wide (approximately 10 cm).

Physiology at the bolus tail

Two distinct CWs above and below the TZ were observed in every swallow in both healthy controls and in patients with reflux oesophagitis. The average spatial jump in the bolus tail from the UCWs to LCWs (ΔX_{jump}) was significantly longer in patients than controls [5.2 cm (4.4–5.6) vs 3.1 cm (2.2–3.7), $P = 0.008$].

The average trajectories of the bolus tails defining the UCW and LCW are compared between patients and normal controls in Fig. 3. In both groups, the bolus tail slowed as the UCW entered the TZ and ended well below the upper margin of the TZ. As this occurred, the IW initiated close to the distal margin of the TZ region in the patient group, but well within the TZ in normals. The progression of the IW is characterized by increasing occlusion of the bolus until a distinct tail is formed, indicating the start of the LCW. The formation of the LCW also marks the physical and hydrodynamic separation between the propagating and the retained bolus.

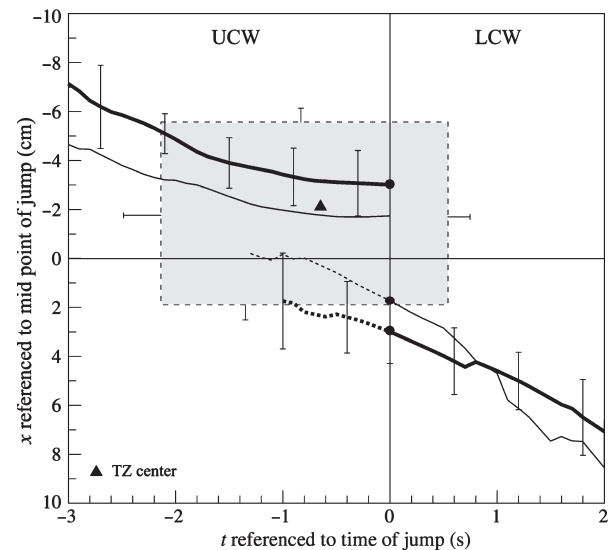


Figure 3 The bold lines show the average trajectories of the UCW, the LCW and the IW in patients; bars indicate standard deviation. The thin lines show the corresponding trajectories in healthy volunteers. The shaded box shows the average boundary of the manometrically defined transition zone in patients; the filled triangle marks the TZ center. Although the spatial separation of the UCWs and LCWs is greater in patients, the temporal separation is similar in both groups. Note that increased separation of the lower wave is related to an IW that initiates more distally within the TZ.

The average pressure at the bolus tail is shown in Fig. 4. In the patient group, pressure at the bolus tail of the UCW fell rapidly as the UCW entered the TZ region. At the same time, pressure associated with the IW increased, culminating with the formation of the LCW. In the oesophagitis patients, the IW pressure initiated at a magnitude much closer to the intra-thoracic pressure than normal, roughly the same as the UCW tail pressure during the same time period. During this formation period, the amplitude pressure P_A was associated in time and space with the tail of the LCW (Fig. 2).

Bolus transport through the transition zone

The time evolution of the spatial relationships between bolus tail pressure and location (P_T and X_T) and the maximum contractile amplitude pressure and location (P_A and X_A) for a representative swallow are shown in Fig. 2. The pressure amplitude ($P_A \geq P_T$) proximal to the bolus tail ($X_A \leq X_T$) maintains luminal closure, forcing bolus fluid at the tail into the TZ region. Between the time instants t_2 and t_3 , a jump in the pressure amplitude ΔX_A to a more distal location is observed. This new pressure amplitude follows an IW

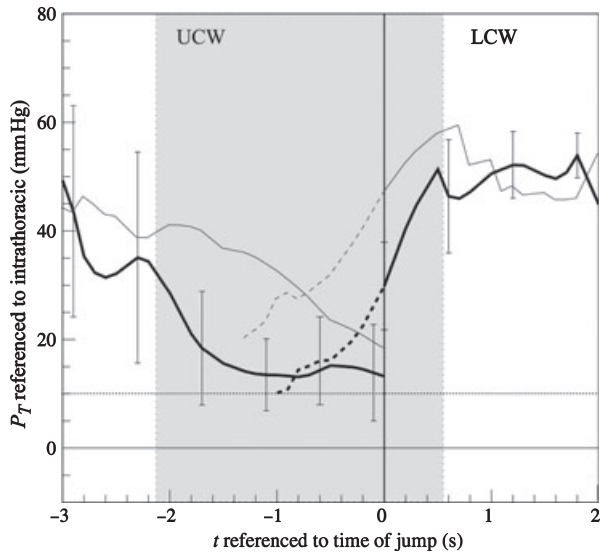


Figure 4 Bold lines show the ensemble averaged bolus tail pressure (P_T) along the upper, lower and indentation waves in patients; bars indicate standard deviation. The thin lines show the corresponding pressure in healthy volunteers. The shaded region shows the transition zone in patients. Pressure at the tail of the UCW falls more rapidly as it enters the TZ and reaches a lower nadir pressure in patients than in normal controls. On average, therefore, the ‘squeeze pressure’ (i.e. tone) available to clear the TZ region is less in the patient group than in controls.

of increasing occlusion (X_I), and culminates in the formation of a LCW at t_6 with corresponding peristaltic muscle contraction. The isocontour representation of intra-luminal pressure during this process is shown in Fig. 5 in comparison with a normal subject. The proximal pressure amplitude trajectory is associated with the propagating bolus tail of the UCW, while distal X_A vs t is associated with an IW generating a LCW. In both subject groups, the proximal pressure amplitude trajectory (X_A vs t) intersects the propagating bolus tail following the UCW within the TZ region inconsistent with a propagating peristaltic contraction ($X_A \leq X_T$ implies non-peristaltic motility). As pressure at the tail of the UCW falls and pressure at the IW tail rises, the pressure amplitude location X_A makes a distal ‘jump’. These jumps in ΔX_A are wider in oesophagitis patients than in controls [4.1 cm (3.9–4.6) vs 1.3 cm (1.0–2.9), $P = 0.007$].

The non-peristaltic nature of motility and bolus transport in the TZ is manifest not only by sudden changes in position of the pressure amplitude, but also by the jump in position of the bolus tail (ΔX_{jump}) from the upper to the LCWs (Fig. 3). To understand the patterning of circular muscle contraction in the TZ that creates the jump between CWs, we averaged the

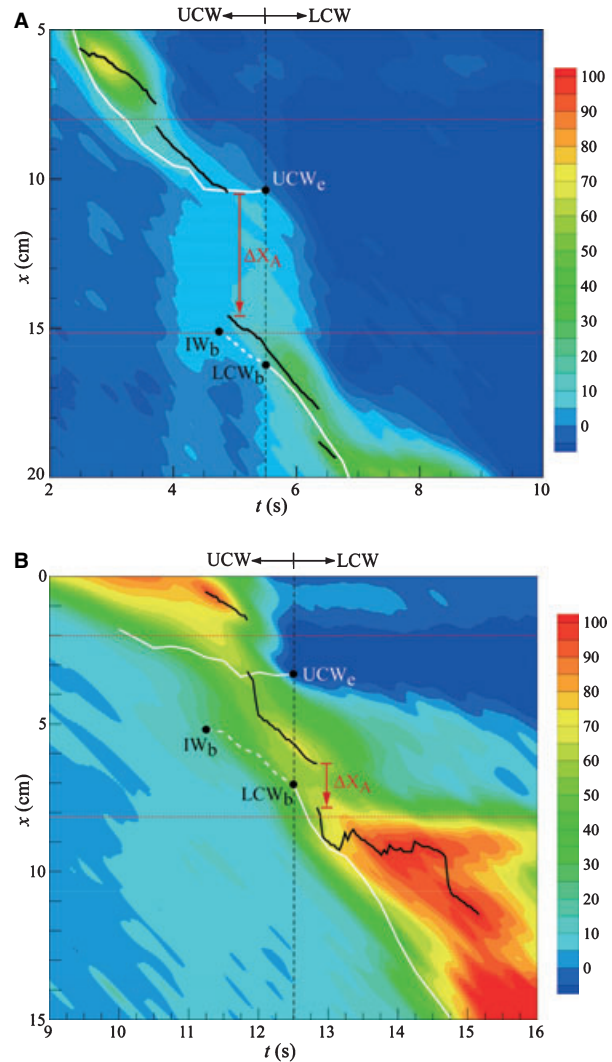


Figure 5 Spatio-temporal isocontours of intra-luminal pressure surrounding the transition zone during bolus transport in an esophagitis patient (A) and a normal control (B). Pressure magnitude relative to intra-thoracic pressure is given on the color scales (right). The UCW, LCW and IW trajectories are shown by white lines. Trajectories of pressure amplitude (X_A) are shown by black lines. The spatial jumps in X_A within the transition zone are denoted by ΔX_A . The horizontal dotted lines show the upper and lower margins of the transition zone. The UCWs and LCWs have wider separation, larger jump ΔX_A , and lower TZ pressure, in the esophagitis patient (A) compared with the normal control (B).

intra-luminal pressure distribution in the region between the UCW and the IW in the patient and normal groups at 5 equally spaced time instants between the initiation of the IW and the initiation of the LCW (Fig. 6). During the transition from UCW to LCW, the pressure from muscle squeeze within the TZ is overall lower in the patient group, and the transition from the pressure amplitude associated with the UCW

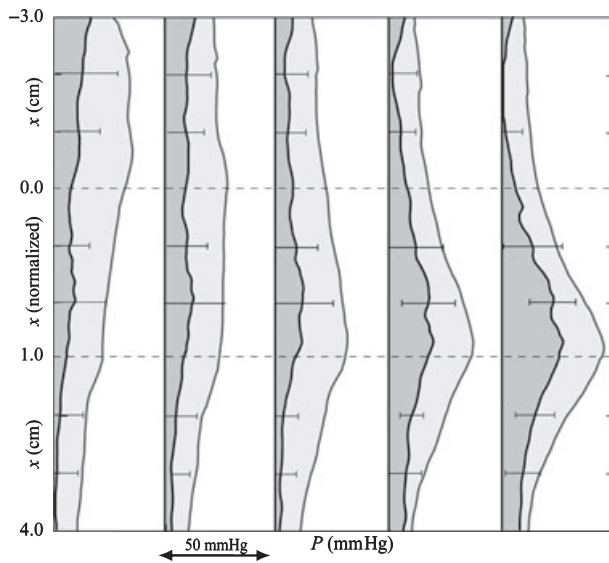


Figure 6 Comparison of average spatial variation in pressure within and surrounding the transition zone between patients (bold lines) and normal controls (light lines); bars indicate standard deviation. Time is normalized in five equal steps from the beginning of the IW (IW_b) to the time of the jump. The pressures are referenced spatially ($x = 0$) to the UCW, and the distance between the UCW and IW is normalized to 1; distances above the UCW and below the IW are not normalized. We observe that the pressure variations are non-peristaltic and that pressure magnitudes in the TZ (relative to thoracic) are much lower in magnitude and flatter in the patient group.

and the peak in pressure associated with the IW that forms the LCW is less distinct.

In Fig. 7 the average bolus tail pressure (P_T) and pressure amplitude (P_A) are plotted in the patient and normal groups during the transition from UCW to LCW in the TZ. The difference between P_A and P_T is an indicator of the occlusive force available to maintain luminal closure. Fig. 7 shows that not only the pressure amplitude and bolus tail pressures lower in the patient group, but also the difference between pressure amplitude and tail pressure ($P_A - P_T$) is lower and decreases more rapidly during the transition from UCW to LCW in the patient group. For swallows in oesophagitis patients, $P_A - P_T$ was typically 5–10 mmHg as the UCW transitioned to the LCW (e.g. $t_2 - t_4$ in Fig. 2), while in normal controls $P_A - P_T$ remained above 20–25 mmHg.

Determinants of bolus transport across the transition zone

Univariate regression revealed significant associations between the volume of bolus retention and these

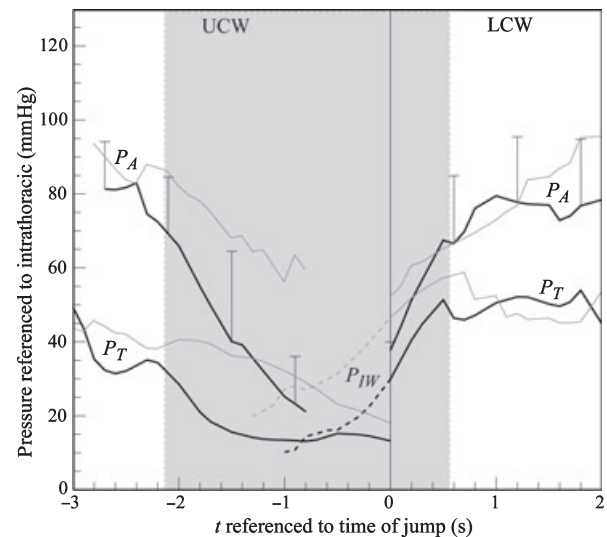


Figure 7 Comparisons of pressure amplitude P_A , tail pressure P_T and indentation wave pressure P_{IW} (dashed line) in the transition from upper to LCWs in the TZ. Bold lines are for the patient group and thin lines for normal controls. The shaded region denotes the transition zone for patients. In the patient group (bold lines), pressure amplitude P_A rapidly approaches the tail pressure P_T within the TZ, while in normal controls P_A and P_T remain separated. Thus, because luminal opening occurs when $P_A = P_T$, the probability that the lumen will fail to remain closed and that bolus will be retained in the TZ is higher in the patient group.

manometric variables: TZ strength ($P < 0.03$), temporal duration of TZ ($P < 0.02$) and spatial jump in pressure amplitude ($P < 0.002$). Higher TZ length was also associated with bolus retention ($P < 0.02$); however, this effect was weak and was covaried with ΔX_A . No correlation was found between bolus retention and the position of the TZ margins, the TZ center or the TZ nadir pressure. A multivariate regression model containing the variables ΔX_A , ΔT_{TZ} and TZ strength was significant and explained about half of the variance in bolus retention ($r^2 = 51\%$; $P < 0.001$). Removal of any one of these variables weakened the model; however, only the spatial jump in pressure amplitude (ΔX_A) was an independent significant contributor. From sensitivity analysis, a 1 cm increase in ΔX_A was accompanied by a 0.4 ml increase in bolus retention (95% CI: 0.02–0.8 ml; $P < 0.04$) while on contingency analysis the presence of bolus retention > 0.5 ml was associated with larger ΔX_A ($\Delta X_A > 3$ cm in 9/10 vs 3/16; $P < 0.002$). Bolus retention was associated with more distal positions of the distal TZ margin (> 11 cm from the upper oesophageal sphincter in 6/10 vs 1/16; $P < 0.01$). No other significant associations with manometric variables were obtained with the contingency model.

DISCUSSION

The functional anatomy and biomechanics of oesophageal bolus transport through the TZ is made complex by the transition from an upper UCW generated in the striated muscle oesophagus to a LCW associated with the distal smooth muscle oesophagus. This physio-mechanical study examined the hypothesis that bolus retention within the TZ is indicative of impaired coordination between the UCW and LCW.² Concurrent HRM and digital videofluoroscopy studies were performed in healthy controls and patients with reflux oesophagitis, a population known to have impaired bolus transport. Patients with oesophageal dysmotility on conventional manometric criteria and those with a hiatus hernia on endoscopy were excluded to avoid these potential confounding factors. Space-time changes in intra-luminal pressure with the passage of bolus fluid through the TZ were quantified. The results confirmed that impaired coordination between the upper and lower CWs is associated with bolus retention in the TZ.

Detailed analysis was performed to explain the physio-mechanics by which the observed differences in space-time pressure-flow properties result in bolus retention at the TZ. Figs 1, 2 and 5 describe the passage of a single bolus through the TZ. Figs 3–7 quantify the findings statistically and compare the oesophagitis patient group with normal control subjects. Pressures were always referenced to intra-thoracic pressure because the total stress in the circular muscle layer is proportional to this transmural pressure difference.¹ Events in space and time were referenced to manometric or radiographic landmarks relevant to local physio-mechanics of the TZ (we reference to the position of the jump from UCW to LCW in Figs 3, 4 and 7, to the nadir pressure (TZ center) in Fig. 5 and to the trajectory of the UCW in Fig. 6).

The characteristic pattern of contractile events and bolus transport was the same in oesophagitis patients and controls. Robust features observed in each swallow were; (i) a manometrically well-defined pressure trough; and (ii) a fluoroscopically well-defined transition ('jump') in the position of the bolus tail from an upper to a lower wave trajectory (Fig. 1). The precise spatiotemporal concordance between the TZ pressure trough from HRM and the location of the jump from imaging confirms the existence of distinct upper and lower CWs as a fundamental characteristic of oesophageal physiology.³ We find that the details by which muscle tone transitions from the UCW to the LCW is critical to the success of bolus transport across the TZ region. Above and below the TZ, maximum contractile

pressure in the UCWs and LCWs is larger than the pressure at the bolus tail ($P_A > P_T$), thus maintaining luminal occlusion. Moreover, the location of the pressure amplitude (X_A) is closely related to that of the bolus tail (X_T) in space and time during peristaltic contractions. In contrast, as the UCW approaches the TZ, it slows and P_A drops towards P_T . At the same time, the LCW originates a few centimeter below the tail of the UCW as an IW along the fluid-filled lumen. The contraction pressure at the IW (P_I) increases with the occlusion until the IW becomes fully occlusive (Fig. 2), at which time, the location of maximum pressure (X_A) jumps from the weakening UCW to the strengthening LCW (ΔX_A).

If insufficient pressure, or TZ strength (muscle tone), is maintained in the TZ during this process and/or a significantly wider spatial separation exists between the UCW and IW/LCW (ΔX_T), then bolus fluid is retained. This was consistently the case with oesophagitis patients, almost all of whom had chronic bolus retention, whereas controls did not. We find that increased separation between upper and lower CWs is associated with a reduction in TZ strength, a combination that resulted in the failure of bolus fluid to be cleared from the TZ before the initiation of the LCW. The LCW 'pinches off' fluid from the bolus driven by the UCW before it can be completely removed by muscle contraction in the TZ segment. The spatio-temporal plots of superposed pressure and bolus tail trajectories in Fig. 5 highlight the wider separation between the UCW and LCW and the lower TZ strength in oesophagitis patients compared with normal controls. The non-peristaltic nature of contraction in the TZ is evident by the crossing of the trajectory of the pressure amplitude (X_A) with the bolus tail trajectory (X_T) in the TZ (Fig. 5) and by the transition in P_A and P_T from the UCW to the LCW (Fig. 7). In oesophagitis patients this non-peristaltic contractile process is inefficient (Fig. 6) and leads to bolus retention.

Independent of the presence of oesophagitis, wide spatial separation between the two CWs above and below the TZ was the single most important factor that determined the risk of bolus retention in the TZ. On univariate regression analysis, three factors were independently associated with the volume of bolus retention: spatial separation, temporal separation and TZ strength. However, on multivariate analysis only spatial separation was statistically significant. These findings suggest that although both tone and spatio-temporal separation are relevant to bolus retention, close spatial coordination between the UCW and LCW is the more important determinant of bolus retention. Detailed analysis revealed that increased spatial

separation of the CWs with bolus retention was a consequence of a more distal initiation of the IW/LCW in the smooth muscle oesophagus rather than a slower temporal progression of the IW in forming the LCW.

This analysis provides a mechanistic basis for bolus retention at the level of the aortic arch. Radiographic studies often document solid bolus retention in the proximal oesophagus in healthy subjects.^{9,23} This is also a common site for symptomatic bolus impaction, oesophageal hypersensitivity and injuries induced by caustic medicinal pills.^{11,24,25} Imaging alone cannot determine the cause of bolus retention, and conventional manometry has insufficient spatial resolution to detect the segmental neurofunctional physiology of the oesophagus associated with the pressure gradients that drive bolus transport across the TZ.^{11,26,27} This study exemplifies the value of concurrent HRM fluoroscopy in the study of oesophageal physio-mechanics.

In summary, this study shows that close spatial coordination of the UCWs and LCWs with sufficient circular muscle squeeze in between are necessary to clear the bolus from the TZ, and subsequently transport a complete bolus to the stomach. Ongoing research with larger patient groups will establish whether this pathophysiologic mechanism explains impaired oesophageal clearance or symptoms in patients with reflux oesophagitis, functional dysphagia and other motility disorders.

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