Discriminant Capacity of LES relaxation Parameters using High-resolution Manometry for the Diagnosis of Achalasia

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Aim

-The manometric evaluation of LES relaxation is arguably the most important measurement made during clinical esophageal manometry, as it differentiates achalasia from other non-specific esophageal motor disorders.
-The aim of this study was to determine normal values for LES relaxation parameters using high-resolution manometry (HRM) and to assess their accuracy in diagnosing achalasia.

METHODS

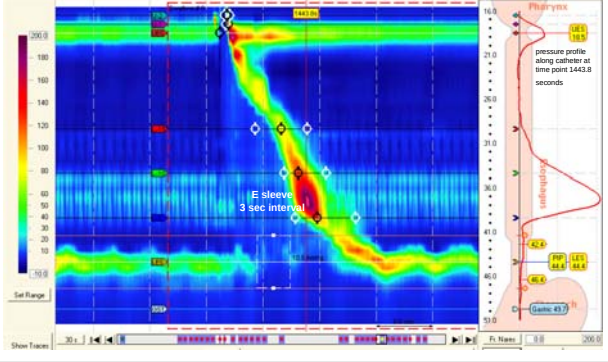
- 75 asymptomatic controls (38 male, age, 19 –48) were studied.

- A solid-state manometric assembly with 36 circumferential sensors uniformly spaced at 1 cm intervals was positioned to record from the hypopharynx to the stomach.

-Five minute baseline recording were obtained followed by ten 5 ml water swallows in both the upright and supine position.

- Each swallow was analyzed by two different investigators using Manoscan Data Analysis software.

Figure 1: Example of a normal water swallow. Isoncour plot and pressure profile along catheter at time point 1443.8 seconds

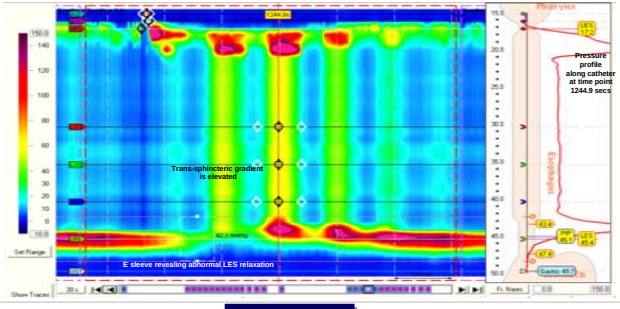


LES Relaxation Parameters

-Three methods of measuring LES relaxation were performed
1) absolute nadir pressure
2) an automated measurement of the lowest mean residual pressure over a 3 second interval within the post-deglutitive period (E-sleeve)
3) the trans-sphincteric gradient defined as the mean pressure 2 to 6 seconds after swallowing of the area 2 cm above and below the margins of the high pressure zone.

- Threshold values of two standard deviations above the mean values were then applied to a cohort of 20 achalasic patients (8 male, age, 19 –81) and 20 random non-achalasic patients referred for manometry (7 male, age, 21 –75) to assess sensitivity and specificity of these cut-off values.

Figure 2: Example of a patient with achalasia



RESULTS

Table 1. Normal values for LES relaxation Parameters

* P <0.05 vs Supine	Upright			Supine		
	Nadir LES Pressure (mmHg)	E-Sleeve (mmHg)	EGJ Gradient (mmHg)	Nadir LES Pressure (mmHg)	E-Sleeve (mmHg)	EGJ Gradient (mmHg)
Mean (SD)	0.4 (3.0)*	3.9 (3.7)*	-3.8 (2.9)*	4.6 (4.0)	7.8 (3.2)	1.0 (2.5)
Threshold Mean + 2 SD	6.5	11.5	2.0	12.6	15.0	6.0

-The mean values for nadir LES relaxation and the E-sleeve mean residual pressure values recorded by solid-state HRM in the supine position were slightly higher than values previously reported using water perfused HRM.
-In addition, the mean values for both the upright nadir LES relaxation pressure (0.3 mmHg, SD, 3.0) and the upright E-sleeve mean residual pressure (3.9 mmHg, SD, 3.7) were significantly lower than those measured in the supine period (P<0.05).
-The trans-sphincteric gradient was also significantly increased in the supine period compared to the upright period (Sup,1.1mmHg, SD 2.5; Up, -3.8 mmHg, SD 2.9, P<0.05).

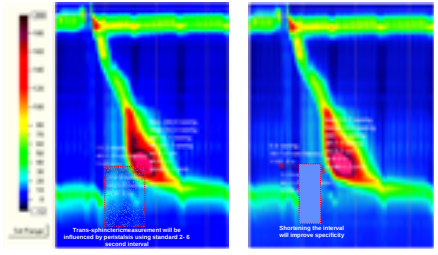
RESULTS

Table 2. Sensitivity and specificity for LES relaxation Parameters for the diagnosis of Achalasia

	Sensitivity / Specificity		
	Nadir LES Pressure	E-Sleeve	EGJ Gradient
Supine	60% / 85%	90% / 95%	90% 85%
Upright	95% / 75%	95% / 90%	100% / 75%

-Sensitivity and specificity was very good for both the upright and supine positions when the 3 second E-sleeve and trans EGJ gradient were used.
-The E-sleeve measurement of the lowest mean residual pressure over a 3 second interval during the post-deglutitive period was the most accurate single parameter.

Figure 3: Effect of peristalsis on trans- EGJ gradient measurement



In patients with intact peristalsis, the measurement of trans- EGJ gradient may be influenced by the leading edge of the peristaltic wavefront (see below). Adjusting for this factor improved the sensitivity and specificity of the EGJ gradient.

Improvement in Sensitivity and Specificity after EGJ gradient adjusted for peristaltic influence	
Upright	90% / 90%
Supine	100% / 90%

CONCLUSIONS

•In addition to providing a more physiologic setting for analysis of swallowing, upright HRM is more as accurate as supine HRM in discriminating achalasia from other esophageal motor disorders.

•The E-sleeve measurement is the single best parameter for distinguishing achalasia from other esophageal motor abnormalities

•The trans-sphincteric gradient is extremely sensitive for achalasia and specificity is improved if analysis is confined to a segment not involving distal peristaltic contractions

Characterization of Normal Peristalsis Using High-Resolution Manometry and Isobaric Contour Analysis: A New Paradigm of Peristaltic Performance

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*Department of Medicine, Northwestern University, Feinberg School of Medicine, Chicago, IL, #Department of Medicine, Washington University, St. Louis, MO, †Sierra Instruments, Los Angeles, CA

AIM

High-resolution manometry (HRM) has the potential to provide a more detailed description of peristalsis, however, there are currently no established normal values for HRM-specific parameters of peristaltic function. This study aimed to define normal characteristics of peristalsis capitalizing on the advantages of HRM: the isobaric contour tool.

METHODS

73 controls (36 male, ages 19-48) were studied.

A solid-state manometric assembly with 36 circumferential sensors spaced at 1 cm intervals was positioned to record from the hypopharynx to the stomach (Sierra Scientific Inc).

Ten 5 ml water swallows were performed in the sitting and supine position.

Peristaltic function was displayed in a topographic format and analyzed using software that allowed delineation of the anatomical/temporal boundaries of a pressure domain of designated magnitude (Manoscan™ isobaric contour and Matlab™ (Mathworks Inc)). The isobaric contour tool was used to define: 1) the integrity and velocity of a peristaltic contraction and 2) the location, amplitude and duration of the contractile segments in the proximal and distal esophagus.

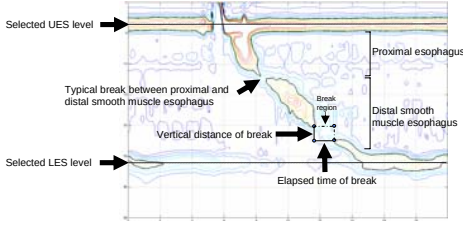


Figure 1: An isocontour plot of a peristaltic contraction wave during a swallow in an asymptomatic subject. Isobaric contour (solid black line) is set at 30 mmHg. Pressure values were referenced to atmospheric pressure.

Definition of Peristaltic Parameters

Intact peristalsis was defined as no breaks in the isobaric contour line of the smooth muscle esophagus. In other words, the isobaric contour line was continuous and encompassing the entire distal smooth muscle esophagus.

Dropped Peristalsis was defined as complete absence of peristaltic activity in the smooth muscle segment.

Velocity of peristalsis was defined as the distance (cm) from the upper esophageal sphincter to the lower esophageal sphincter divided by the time (sec) from upper esophageal sphincter opening to lower esophageal sphincter closing.

Median % with intact peristalsis was defined as the median % of subjects with no breaks in the isobaric contour line of the smooth muscle esophagus. Median values were used because of non-normal data distribution.

Median vertical distance of break was defined as the distance between two segments above and below a break defined by an isobaric contour level (see figure above).

Median elapsed time of break was defined as the amount of time that had elapsed between two segments above and below a break defined by an isobaric contour level (see figure below).

Median and minimum pressure in the break were defined as the median and minimum values of the pressure within the space-time break in the isobaric contour (see figure above)

RESULTS

•On average, the position of the peak contractile amplitude in the proximal esophagus and distal smooth muscle esophagus was similar in the sitting and supine positions (within 1-2 cm).
•A break in the 30 mmHg isocontour was common between the proximal esophagus and smooth muscle esophagus (sit 70/73, sup 40/73).
•Restricting the analysis to the smooth muscle esophagus revealed that the 30 mmHg isobaric contour was generally intact in either posture (Table 1).
•When present, the gap in the integrity of the 30 mmHg isobaric contour was located 13 cm proximal to the LES in both positions.
•Mean length of the gap was also similar in both positions
•sit, 3.8 cm (SD 3.0) sup, 3.0 cm (SD 3.2)

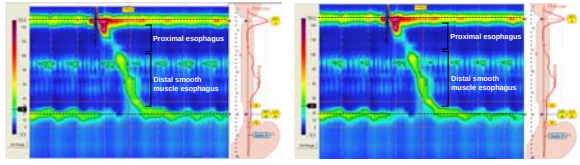
Table 1.	30 mmHg intact peristalsis of smooth muscle esophagus*	Velocity of intact contraction	Maximal contractile amplitude of smooth muscle esophagus	Maximal duration of contraction of smooth muscle esophagus
Sitting	80% (IQR 50%)	2.8 cm/s	100 mmHg (SD 32)	2 seconds (SD 1.0)
Supine	100% (IQR 10%)	2.6 cm/s	129 mmHg (SD 42)	3 seconds (SD 0.8)

*median % of 10 swallows with intact peristalsis in smooth muscle segment

Analysis of isobaric isocontour at pressure settings of 25,30,35 40 mmHg

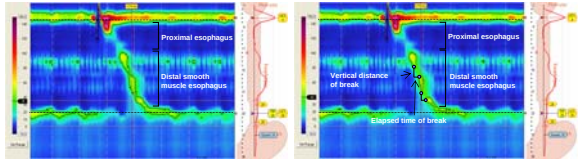
•The smooth muscle esophagus isobaric contour was generally intact at 25, 30, 35, and 40 mmHg (Table 2.).
•Only 19 of 730 swallows were associated with dropped peristalsis.
•Only 2 Subjects had more than 5/10 swallows with one or more breaks at an isobaric contour levels set at 30 mmHg.

Figure 2: One swallow in an asymptomatic patient shown at 25, 20, 35, and 40 mmHg isobaric contour levels (solid black line). There are no breaks in the smooth muscle esophagus at 25, 30, and 35 mmHg isobaric contour, however breaks emerge once the isobaric contour is set to 40 mmHg. Pressure values were referenced to atmospheric pressure.



25 mmHg isobaric contour

30 mmHg isobaric contour



35 mmHg isobaric contour

40 mmHg isobaric contour

Table 2.	Isobaric Contour Level (supine, smooth muscle segment)			
	25 mmHg	30 mmHg	35 mmHg	40 mmHg
# of swallows with intact peristalsis	708/730	698/730	692/730	674/730
Median % [IQR] with intact peristalsis	100 % [100 - 100]	100 % [100 - 100]	100 % [90 - 100]	100 % [90 - 100]
Median [IQR] vertical distance of break in cm	1.74 [1.07 – 2.35]	2.07 [0.97 – 2.88]	2.62 [1.47 – 3.78]	1.77 [1.16 – 3.44]
Median [IQR] elapsed time of break in sec	0.62 [0.39 – 0.79]	0.50 [0.35 – 0.79]	1.11 [0.52 – 1.52]	0.93 [0.60 – 1.30]
Median [IQR] pressure in the break in mmHg	19.27 [14.86 – 20.41]	21.39 [18.45 – 25.28]	21.49 [18.57 – 27.32]	29.34 [24.67 – 33.89]
Minimum pressure in the break in mmHg (mean ± SD)	11.86 ± 7.12	11.86 ± 7.12	11.95 ± 8.80	17.15 ± 10.64

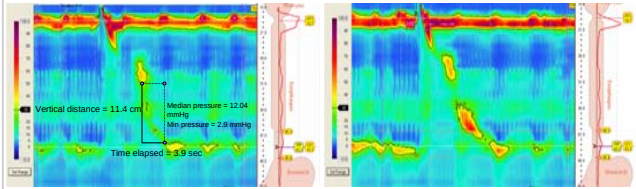


Figure 3: Two supine peristaltic contractions of a 35 y/o female who presented to Northwestern GI lab with dysphagia and chest pain. Manometric study showed peristaltic breaks (at isocontour of 30 mmHg) in 30% of water swallows in distal smooth muscle esophagus.

CONCLUSIONS

•Manoscan™ software in conjunction with HRM permits a fully automated analysis of esophageal peristalsis.
•Upright HRM yields similar findings to supine HRM and has the advantage of being more physiological.
•By concurrent visualization of the entire peristaltic appearance, HRM offers alternative measurement paradigms for peristaltic performance exemplified by the isobaric contour analysis.

Upper Sphincter Function During Transient Lower Esophageal Sphincter Relaxation (tLESR); It Is Mainly About Belching

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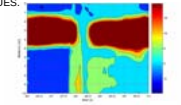
Northwestern University Feinberg School of Medicine, Chicago, IL; * Sierra Scientific Instruments, Los Angeles, CA

AIMS

- tLESRs are recognized both as a dominant mechanism of acid reflux and as an element of the belch reflex. The aim of this study was to analyze the interplay between acid reflux, common cavity generation, and upper esophageal sphincter relaxation (UESR) during meal-induced tLESRs.

METHODS

- 13 healthy subjects without hiatus hernia (3 males, ages 25 45) were studied.
- Esophageal motility was studied using a computerized 36 channel solid state microtransducer system with computerized topographic analysis. The sensors were uniformly spaced at 1 cm intervals, and were positioned to record from the hypopharynx to the stomach.
- Reflux was monitored simultaneously using an antimony pH probe positioned at 5 cm above the upper margin of the EGJ high pressure zone.
- Studies entailed baseline monitoring and 120 minutes postprandial recording in a sitting posture after a 1000 calorie high fat meal.
- Manometry data from ManoScan™ was converted to ASCII format and interpolated within Matlab (The Mathworks Inc., Natick, MA). Data were displayed as space time isocontours and the time interval of UES relaxation was delineated as the duration of pressure equalization with the pharyngeal cavity. The temporal variation of pressure was calculated by averaging the pressure from 3 manometric sites (spanning 2cm of the proximal esophagus) just distal to the lower margin of the UES.



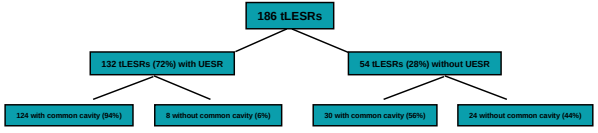
Measurement of esophageal pressure gradient

RESULTS

A total of 186 tLESRs occurred among the 13 subjects during the 2 hour postprandial period.

UES Function during tLESRs

- UESR occurred with 72% of the tLESRs (complete in 51%) and was almost always associated with a common cavity (94%, 124/132).
- The mean duration of complete UESR was 0.58 seconds (SD, 0.46).
- Subjects did not audibly belch but on questioning, some were aware of gas venting.

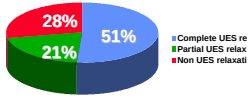


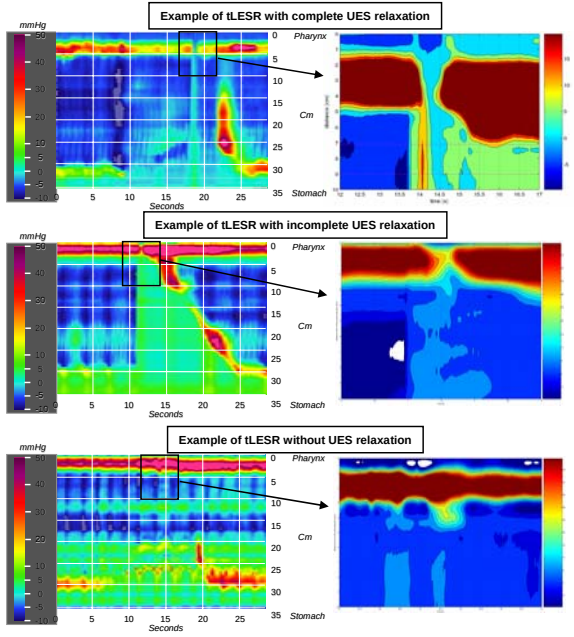
LES function during tLESRs

- Mean LES relaxation pressure during tLESRs was 0.6 mmHg (SD, 2.0) and the mean duration of relaxation was 15.7 seconds (SD, 5.9 sec).
- 82% (154/186) of tLESRs were associated with common cavities and 30% (55/186) were associated with acid reflux.

Esophageal pressure gradients and UES function during tLESRS

- Average proximal intraesophageal gradient during UES relaxations was 86.5 mmHg/second.
- tLESRs associated with UESR had higher proximal esophageal common cavity pressures compared to those without UESR (UESR 5.4 mmHg; no UESR 3.0 mmHg, P <0.05).
- During the 24 tLESRs without a common cavity or UESR, the UES exhibited either no change in pressure (18) or isolated UES contractions (6).
- The frequency of UESR was similar during tLESRs with (64%) or without (74%) acid reflux (p>0.05).





CONCLUSIONS

- The majority of post-prandial tLESRs are associated with brief periods of complete UESR, likely permissive of gas venting.
- Whether or not UES relaxation occurred during a tLESR was dependent on the magnitude of associated esophageal common cavity pressure but independent of whether or not acid reflux had occurred.
- These findings strongly support the notion that tLESRs are fundamentally an element of the belch reflex and that the associated UES response is a function of the degree of associated esophageal distention.

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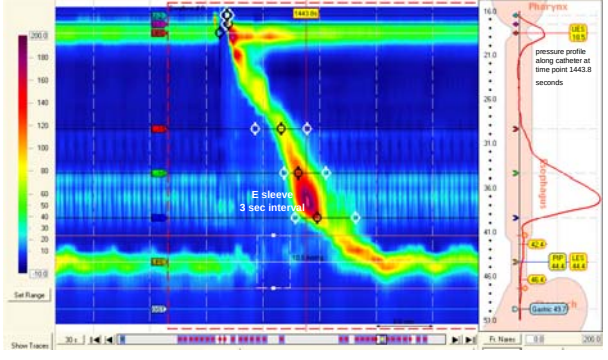

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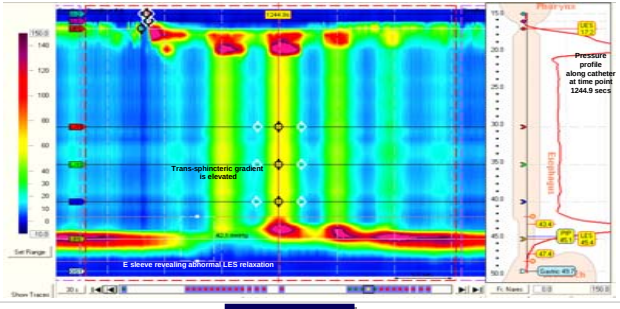
3) the trans-sphincteric gradient defined as the mean pressure 2 to 6 seconds after swallowing of the area 2 cm above and below the margins of the high pressure zone.

- Threshold values of two standard deviations above the mean values were then applied to a cohort of 20 achalasic patients (8 male, age, 19 –81) and 20 random non-achalasic patients referred for manometry (7 male, age, 21 –75) to assess sensitivity and specificity of these cut-off values.

Figure 2: Example of a patient with achalasia



RESULTS

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	Nadir LES Pressure (mmHg)	E-Sleeve (mmHg)	EGJ Gradient (mmHg)	Nadir LES Pressure (mmHg)	E-Sleeve (mmHg)	EGJ Gradient (mmHg)
Mean (SD)	0.4 (3.0)*	3.9 (3.7)*	-3.8 (2.9)*	4.6 (4.0)	7.8 (3.2)	1.0 (2.5)
Threshold Mean + 2 SD	6.5	11.5	2.0	12.6	15.0	6.0

-The mean values for nadir LES relaxation and the E-sleeve mean residual pressure values recorded by solid-state HRM in the supine position were slightly higher than values previously reported using water perfused HRM.
-In addition, the mean values for both the upright nadir LES relaxation pressure (0.3 mmHg, SD, 3.0) and the upright E-sleeve mean residual pressure (3.9 mmHg, SD, 3.7) were significantly lower than those measured in the supine period (P<0.05).
-The trans-sphincteric gradient was also significantly increased in the supine period compared to the upright period (Sup,1.1mmHg, SD 2.5; Up, -3.8 mmHg, SD 2.9, P<0.05).

RESULTS

Table 2. Sensitivity and specificity for LES relaxation parameters for the diagnosis of Achalasia

	Sensitivity / Specificity		
	Nadir LES Pressure	E-Sleeve	EGJ Gradient
Supine	60% / 85%	90% / 95%	90% / 85%
Upright	95% / 75%	95% / 90%	100% / 75%

-The E-sleeve measurement of the lowest mean residual pressure over a 3 second interval during the post-deglutitive period was the most accurate single parameter. Using ROC analysis it appeared that an E-Sleeve measurement of 13 mmHg had 100% sensitivity and 85% specificity.

Figure 3: ROC Analysis of E-Sleeve measurement for diagnosing Achalasia (Supine).

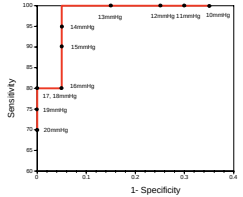
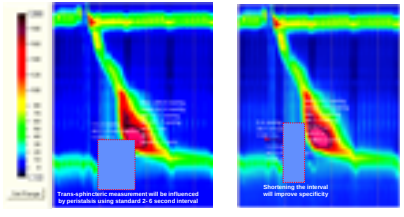


Figure 4: Effect of peristalsis on trans- EGJ gradient measurement



In patients with intact peristalsis, the measurement of trans- EGJ gradient may be influenced by the leading edge of the peristaltic wavefront. Adjusting for this factor improved the sensitivity and specificity of the EGJ gradient.

Improvement in Specificity after EGJ gradient adjusted for peristaltic influence	
Supine	90% / 90%
Upright	100% / 90%

CONCLUSIONS

•In addition to providing a more physiologic setting for analysis of swallowing, upright HRM is as accurate as supine HRM in discriminating achalasia from other esophageal motor disorders.

•The E-sleeve measurement is the single best parameter for distinguishing achalasia from other esophageal motor abnormalities. A value of 13 mmHg provides 100% sensitivity and 85% specificity.

•The trans-sphincteric gradient is extremely sensitive for achalasia and specificity is improved if analysis is confined to a segment not involving distal peristaltic contractions