Synchrony between circular and longitudinal muscle contractions during peristalsis in normal subjects

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Submitted 24 May 2005; accepted in final form 12 September 2005

Mittal, Ravinder K., Bikram Padda, Vikas Bhalla, Valmik Bhargava, and Jianmin Liu. Synchrony between circular and longitudinal muscle contractions during peristalsis in normal subjects. *Am J Physiol Gastrointest Liver Physiol* 290: G431–G438, 2006. First published October 6, 2005; doi:10.1152/ajpgi.00237.2005.—The current understanding is that longitudinal muscle contraction begins before and outlasts circular muscle contraction during esophageal peristalsis in normal subjects. The goal of our study was to reassess the relationship between the contractility of two muscle layers using novel ways to look at the muscle contraction. We studied normal subjects using synchronized high-frequency ultrasound imaging and manometry. Swallow-induced peristalsis was recorded at 5 and 10 cm above the lower esophageal sphincter (LES). Ultrasound (US) images were analyzed for muscle cross-sectional area (CSA) and circularity index of the esophagus during various phases of esophageal contraction. A plot of the M mode US image, muscle CSA, and esophageal circularity index was developed to assess the temporal correlation between various parameters. The muscle CSA wave began before and lasted longer than the contraction pressure wave at both 5 and 10 cm above the LES. M mode US images revealed that the onset of muscle CSA wave was temporally aligned with the onset of lumen collapse. The peak muscle CSA occurred in close proximity with the peak pressure wave. The esophagus started to become more circular (decrease in circularity index) with the onset of the muscle CSA wave. The circularity index and muscle CSA returned to the baseline at approximately the same time. In conclusion, the onset of lumen collapse and return of circularity index of the esophagus are likely to be the true markers of the onset and end of circular muscle contraction. Circular and longitudinal muscle layers of the esophagus contract in a precise synchronous fashion during peristalsis in normal subjects.

**MUSCULARIS PROPIA** of the esophagus is organized into two distinct layers: the inner circular and outer longitudinal. The muscle fibers of the inner and outer layers are oriented in a circular and longitudinal direction, respectively. The two muscle layers contract in a coordinated fashion during peristalsis. Several studies have shown that at any given location in the esophagus, longitudinal muscle contraction begins before and outlasts circular muscle contraction. The majority of these studies were conducted using either radioopaque markers or strain-gauge techniques (3, 5, 20, 28). One of the limitations of these techniques is that they measure longitudinal muscle contraction over a segment rather than at a point location in the esophagus. High-frequency intraluminal ultrasound (HFIUS) imaging is novel and the only available technique that measures longitudinal muscle shortening or contraction at a point location in the esophagus (15). Similar to the HFIUS imaging technique and measuring longitudinal muscle contraction at a point location, the side-hole manometry technique also measures circular muscle contraction at a point location in the esophagus. Therefore, when used simultaneously, side-hole manometry and HFIUS imaging provide a unique opportunity to study the relationship between contractions of the two muscle layers at a point location, in vivo, in the human esophagus.

Nicosia et al. (15) recorded longitudinal and circular muscle contraction using simultaneous HFIUS imaging and manometry and demonstrated that longitudinal muscle contraction begins before and outlasts circular muscle contraction. We (2) recently reported on the use of M mode images to display US images of the esophagus over time (2). M mode display of the US images allows much better temporal resolution of the various events during a swallow sequence compared with traditional B mode US images. Visual inspection of the simultaneously recorded B mode HFIUS images along with the derived M mode US images and manometry not only confirmed the findings of Nicosia et al. (15) but also provided additional interesting findings. Our findings suggest that manometry does not record circular muscle contraction at its very onset and toward the end of contraction, which we believe is the reason that longitudinal muscle contraction appears to be longer in duration than circular muscle contraction. In fact, our data show that the two layers of the esophagus contract in a perfect synchronous fashion. We also describe novel markers of circular muscle contraction and relaxation on HFIUS images. The goal of our study was to reassess the precise correlation between contractions of two muscle layers using these novel markers.

**MATERIALS AND METHODS**

**Subjects.** Six healthy volunteers (3 men and 3 women, mean age 34 ± 10 yr) were studied. Subjects did not have any symptoms suggestive of esophageal motor disorder and were not taking any medications known to affect neuromuscular function of the gastrointestinal tract. The Human Investigation Committee of the University of California (San Diego, CA) approved the study protocol, and informed consent was obtained from each subject before the study.

**Study protocol.** After an overnight fast, recordings were obtained with subjects in the right recumbent position. An eight-lumen manometry catheter (Dent sleeve; Wayville, Australia) with four circumferentially placed side holes, located 2 mm from the distal end, in conjunction with an intravascular US catheter (IVUC) was used to record pressure and US images simultaneously (Fig. 1). The catheter...
assembly consisted of a 30-MHz, 3.2-Fr, MicroRail IVUC (Cardiovascular Imaging Systems; Sunnyvale, CA), which was placed through the core lumen of the manometry catheter in such a fashion that the US transducer was positioned just distal to the tip of the catheter (Fig. 1). The catheter arrangement allows one to record pressure and US images from approximately the same location (2–3 mm apart). Furthermore, the advantage with this system is that it captures a 360° image of the esophagus. The US transducer was encased in a water-filled polyethylene bag of the same diameter as the manometry catheter. The catheter assembly was introduced through the nose into the stomach after topical anesthesia of the nasal cavity and oropharynx using 1% lidocaine gel and 1% benzocaine spray. A station pull-through technique was used to determine the location of the lower esophageal sphincter (LES). Recordings were performed at two levels in the esophagus: 5 and 10 cm above the LES. Five to six swallows of 2 and 5 ml water at room temperature were recorded at each of the two levels. Swallows were performed 30 s apart, and subjects refrained from swallowing in between the swallows. Pressures were recorded on a computer through Polygraph ID and Polygram 98 (Medtronic Synectics; Shoreview, MN). US images were recorded on a VHS tape recorder using a HP Sonos 100 machine (Hewlett-Packard; Watertown, MA). Pressure and US recordings were synchronized using a time code device (Thalaner Electronics; Ann Arbor, MI) that encoded the analog time clock on the video images and a marker on the polygraph at a resolution of one hundredth of a second. Therefore, a time intervals of 10 ms can be resolved in this method of recording.

**Measurements and data analysis.** US images were digitized using a video editing device (Pinnacle Express, Pinnacle) on a personal computer (PC) program (Adobe Premiere 6.0, Adobe Systems; Mountain View, CA) and analyzed using a commercially available image analysis-software package (Sigma Scan Pro, Jandel Scientific; San Rafael, CA). US images were digitized and analyzed every 250 ms starting at 10 s before, during the entire period of manometric...
contraction, and 10 s after the pressure wave for each swallow (based on the pressure tracings). For each swallow, a total 30–50-s period was analyzed. Therefore, 120–200 total US images were analyzed for each swallow sequence. The inner and outer borders of the muscularis propria, which includes both the circular and longitudinal muscle layers and intermuscular septum, were identified and marked on the images using a PC and the image-analysis software package. The inner border represented the boundary between the outer margin of the mucosa and the inner margin of the circular muscle layer, and the outer border was the interface between the outer margin of the longitudinal muscle layer and the adventitia of the esophagus. The software program calculated the muscle cross-sectional area (CSA). The CSA of the inner ring was used to determine the luminal radius. The long and short axis of the esophageal circumference was determined from each B mode US image. The long axis was the longest line that could be drawn from one outer edge of the esophageal circumference to the opposite outer edge. A perpendicular line crossing the midpoint of the long axis from one outer edge to the opposite represented the short axis (Fig. 1). Baseline muscle CSA was measured from the four images during the 1-s period prior to each swallow sequence (4 frames before swallow). Baseline pressure was defined as the end-expiratory pressure before the onset of contraction. The onset of manometric contraction was defined at the point of the rapid upstroke on the pressure wave (rate of pressure rise > 40 mmHg/s). This point usually follows the bolus pressure wave, which is the initial slow and small increase in pressure, usually <10 mmHg above the baseline esophageal pressure. The end of pressure wave was defined as the point at which it returned to the baseline esophageal pressure value (Fig. 2).

We determined the precise temporal relationship among US images, muscle CSA, and contraction pressure wave using a plot that included M mode images of the esophagus, muscle CSA, and pressure wave aligned in a perfectly synchronized fashion. M mode images were constructed from the two-dimensional (2-D) US images using specially designed software developed in our laboratory. In brief, HFIUS images from the videotape (B mode images) were digitized off-line, frame by frame, for the entire duration of the swallow sequence, at a rate of 30 frames/s. By sectioning 2-D stacked HFIUS images along a line passing through the center of the catheter, identified on the 2-D image, an M mode image was created. Muscle CSA measured from the B mode US images and pressure waves obtained digitally from the physiological recordings were temporally aligned and superimposed on the M mode US images (Fig. 2).

The onset of muscle CSA wave was defined as the point when it increases from its minimal value (Fig. 2). The end of the muscle CSA wave was defined as the point when it returns to the baseline value. We also determined the onset of lumen collapse from the M mode US images, defined as the point at which the fully distended esophagus during swallow sequence starts to collapse, i.e., reduction of lumen dimension. Complete lumen collapse was defined as the point where the esophageal lumen all around the circumference of the mucosa completely collapsed on the US probe (Fig. 2 and 3). In addition, we determined the circularity index of the esophagus from the B mode US images during the period of analysis. For each B mode esophageal image, the smallest and largest diameters were determined, as shown in Fig. 1. The circularity index represented the ratio between these two (large/small) diameters. The circularity index ratio is equal to 1 when the esophagus is a perfect circle. The relationship among the onset of lumen collapse, onset and duration of muscle CSA wave, onset and duration of contraction pressure wave, and circularity index were determined during all swallows.

Statistical analysis. Data are shown as means ± SE. Student’s t-test was used for parametric data comparison, and the Mann-Whitney rank sum test was used for nonparametric data comparison. P < 0.05 was considered statistical significant.

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RESULTS

Duration of pressure wave, muscle CSA wave, and circularity index wave. The contraction durations (pressure wave) at 5 and 10 cm above the LES with a bolus volume of 2 ml were 3.43 ± 1.05 and 3.10 ± 0.38 s, respectively. The durations of the muscle CSA waves at the corresponding sites were 6.14 ± 0.85 and 7.13 ± 0.83 s, respectively, which were significantly longer than the contraction pressure durations (P < 0.05). The esophagus was not circular in shape at the baseline (before swallow) at both the 5- and 10-cm sites. During swallow, there was an increase in the size of lumen initially (esophageal distension), followed by the onset and then a complete collapse of the lumen on the manometric probe. The onset of lumen collapse and the increase in muscle CSA occurred at approximately the same time. With the onset of lumen collapse, the esophagus started to assume a relatively more circular shape.
and stayed that way during the entire period of contraction pressure wave. After the end of the pressure wave, the shape of the esophagus started to gradually return to the baseline value. The durations of the circularity index wave for a 2-ml bolus were 6.95 ± 1.86 and 7.21 ± 0.8 s at 5 and 10 cm, respectively, which were larger than the pressure wave duration but not different from the duration of the muscle CSA wave. The sequence of events described above was similar at the 5- and 10-cm sites.

An increase in the bolus volume increased the durations of the muscle CSA and the duration of the circularity index waves at 5-cm level but not at the 10-cm level above the LES. Bolus volume had no effect on the duration of contraction pressure at either of the two levels.

**Temporal relationship among the onset of manometric contraction, onset of muscle CSA, and onset of lumen collapse.** The plot of M mode ultrasound images of the esophagus, esophageal muscle CSA, and pressure wave revealed the precise temporal correlation among these events (Fig. 2). It shows that, at 5 cm above the LES, the increase in muscle CSA occurred earlier than the onset of manometric contraction by a period of 1.25 ± 0.12 and 1.5 ± 0.12 s for a 2- and 5-ml bolus, respectively. On the other hand, the onset of increase in muscle CSA occurred approximately at the same time as the onset of the esophageal lumen collapse for both bolus volumes. The rapid upstroke of the pressure wave coincided with the onset of complete collapse of the lumen on the manometric probe (Fig. 2). The increase in esophageal pressure before the contraction pressure is referred as the bolus pressure. Close inspection of the bolus pressure wave revealed that it had two components. The first component occurred as the bolus was first visualized on the US image and the second component started at the onset of the muscle CSA wave (Fig. 2).

**Effect of bolus volume on the relationship among the onset of lumen collapse, onset of muscle CSA, and onset of manometric contraction.** An increase in bolus volume from 2 to 5 ml caused an increase in the time interval between the onset of lumen collapse and manometric pressure, 1.23 ± 0.12 and 2.23 ± 0.20 s for 2- and 5-ml swallows, respectively, at 5 cm above the LES (Fig. 3; *P* < 0.05). Bolus volume did not affect the above parameters at the 10-cm level. There was no effect of bolus volume on the time interval between the onset of lumen collapse and the onset of increase in muscle CSA at either of the two recorded sites. Similarly, bolus volume had no effect on the time interval between complete lumen collapse and the pressure wave.

**Relationship between peak manometric contraction and peak muscle CSA wave.** The peak of muscle CSA occurred either at the same time as the peak pressure or a little bit earlier at both esophageal recording sites (Fig. 4). The time interval between the two peaks was ~0.01 ± 0.13 and 0.15 ± 0.10 s for the 2-ml bolus at the 5- and 10-cm sites, respectively. Changing the bolus volume had no effect on the time interval between peak muscle CSA and peak pressure.

**Relationship among the end of manometric contraction, end of muscle CSA wave, and end of circularity index wave.** The return of muscle CSA and circularity index to the baseline was 0.20 ± 0.26 and 0.48 ± 0.37 s (muscle CSA returning to baseline earlier) for a 2-ml bolus volume at 5 and 10 cm above the LES. These time intervals were within the margin of error for our measurement technique (0.5 s). The time delays between the end of manometric contraction and the end of muscle CSA wave were 1.63 ± 0.21 and 2.26 ± 0.33 s for 2- and 5-ml bolus volumes at 5 cm above the LES (Fig. 7). The temporal correlations among the end of the pressure wave, muscle CSA wave, and circularity index wave were not different between 5- and 10-cm sites above the LES.

**DISCUSSION**

Our data show the following: 1) the onset of the lumen collapse in the esophagus coincides with the onset of increase in muscle CSA, 2) complete collapse of the lumen of the esophagus is associated with the onset of manometric contrac-

![Fig. 4. Measurements before the onset of MC. Shown is a temporal correlation of the measurements of lumen area, MCSA, and manometric pressure recording. The three important points are the onset of LC, the onset of MCSA, and the onset of the pressure wave. Images were analyzed for various measurements at a frequency of 4 frames/s.](http://ajpgi.physiology.org/)
tion or the pressure wave, 3) peak muscle CSA and peak pressure occur approximately at the same time, 4) the pressure wave returns to the baseline earlier than the muscle CSA wave, and 5) the circularity index and muscle CSA return to the baseline values at approximately the same time.

The novel observations from our study are that 1) there is a close temporal correlation between the onset of esophageal lumen collapse and the increase in the muscle CSA and 2) the circularity index and muscle CSA return to the baseline values at the same time. On the basis of the law of mass conservation and the incompressibility principle, Nicostia et al. (15) proved that the increase in muscle CSA in HFIUS images is a marker of local longitudinal muscle shortening or, in other words, longitudinal muscle contraction. Our findings are consistent with the observations of Nicostia et al. in that the increase in muscle CSA began earlier than the increase in contraction pressure as recorded by manometry and that the contraction pressure returned to baseline earlier than the return of muscle CSA to baseline. If one considers the onset and end of manometric contraction as markers of the onset and end of circular muscle contraction, respectively, then indeed longitudinal muscle contraction begins earlier and ends later than circular muscle contraction. However, there may be alternative explanations, and it is possible that the above conclusions are not completely correct. During a swallow, the esophagus first distended by an aborally moving bolus, followed by a collapse of the lumen on the probe. We believe that the onset of lumen collapse rather than the onset of manometric contraction is a true marker of the onset of circular muscle contraction. One could argue that the onset of the lumen collapse is a passive phenomenon rather than due to active circular muscle contraction. Dodds et al. (5) and Kahrilas et al. (20), who used radiopaque markers to measure longitudinal muscle contraction and a barium bolus along with manometry to study circular muscle contraction, also considered the possibility that the onset of lumen collapse could be a marker of active circular muscle contraction. We found that there were two components of the bolus pressure wave. The first component corresponded with the arrival of the bolus (as can be seen in the US images), and the second component coincided temporally with the onset of the lumen collapse. The increase in pressure with the onset of lumen collapse may support active circular muscle contrac-

![Fig. 5. Relationship between CI and MC. Image 1 is from a time when MC is returning to baseline (down slope of contraction); note that it is fairly circular with a CI value close to 1.0. Images 6–18 are from the time period between the return of MC to baseline and return of MCSA to baseline. Note the change in the circularity of the esophagus in these B mode US images. Muscle CSA and CI return to baseline values at approximately the same time (see Fig. 6).](image)

![Fig. 6. Measurement parameters from the tail end of contraction. Shown are three measurement parameters: MCSA, the manometric pressure wave, and CI. The three points of interest are those that indicate the return of the manometric recording, MCSA, and CI back to their baseline values.](image)
two muscle layers occurs at approximately the same time during peristalsis. The increase in bolus volume increased the time interval between the onset of lumen collapse and the onset of contraction pressure as recorded by manometry. The reason is that a larger bolus causes larger distension of the esophagus, especially at the 5-cm level. The latter results in an increase in the time interval between the onset and completion of the lumen collapse. Our data show that the increase in muscle CSA remains temporally aligned with the onset of lumen collapse, suggesting the existence of a tight coupling between the onset of circular and longitudinal muscle contraction of the esophagus during peristalsis.

Changes in the shape of esophagus in HFIUS images during active muscle contraction have been reported during previous studies (12, 15). However, ours is the first study to report the dynamic relationship between changes in the circularity index of the esophagus during the entire swallow sequence in a systematic fashion. In the relaxed state, before swallow-induced changes, the esophagus is oblong or relatively noncircular in shape. During the entire period of manometric contraction, the shape of esophagus is relatively circular, with the circularity index approaching 1. We observed that the circularity index continued to increase during the period between the return of manometric pressure wave to the baseline value and the return of the muscle CSA wave to the baseline value. We also observed that there was a close temporal correlation between the return of the circularity index and the return of the muscle CSA wave to baseline values. Because circular muscle tension is likely to change the circularity of the esophagus (15), we believe that the manometry does not record circular muscle activity during the period when the circular muscle is still in the process of relaxing and not completely relaxed back to the baseline state. If one accepts changes in the circularity index as a marker of circular muscle contraction, then indeed circular and longitudinal muscle contractions return to baseline values at approximately the same time.

Animal studies show that, depending on the intensity of the electrical stimulus applied to the vagus nerve, one can elicit either longitudinal muscle contraction alone or a combination of circular and longitudinal muscle contractions of the esophagus (6, 7, 29). In human studies (1, 17), we observed sustained esophageal contraction of the esophagus, which is a marker of longitudinal muscle contraction, in the absence of manometric contraction (a marker of circular muscle contraction). Furthermore, several investigators, including us, have indicated a strong contraction of the longitudinal muscle of the esophagus in the absence of significant contraction pressure during transient LES relaxations (Refs. 22 and 23 and N. A. Tipnis, J. Liu, J. L. Puckett, and R. K. Mittal, unpublished observations). We (8) have also recently reported a dissociation between the peaks of contraction of the two muscle layers in patients with nutcracker esophagus. All of the above observations indicate that the two layers of the esophagus can indeed contract independent of each other under various physiological and pathophysiologic conditions. However, our present study shows that in normal subject and during peristalsis, there is a tight coupling and synchrony of contraction between the two muscle layers of the esophagus. A series of studies by Spencer and Smith (24–27) also showed a precise coordination between circular and longitudinal muscle in the guinea pig small
intestine and colon during peristaltic reflex elicited by luminal distension and mucosal stroking. It is very likely, therefore, that different motor patterns elicit different response in the two muscle layers of the esophagus.

We must recognize several possible limitations of our study. First, we analyzed B mode US images every 250 ms for muscle CSA and the circularity index. Therefore, the resolution of some of our parameters and accuracy of our temporal correlations are only 0.5 s. M mode US images, on the other hand, have much higher resolution, which allowed us to see the onset and completeness of lumen collapse and changes in muscle thickness more precisely. Second, the side hole of the manometry catheter that records manometric pressure is located 2–3 mm above the US transducer. The latter may result in small differences in temporal resolution due to different location of these transducers. However, we do not believe that such is the case because the speed of peristalsis in the distal esophagus is 20–50 mm/s and a 2- to 3-mm distance between the US transducer and side holes is unlikely to affect our measurement significantly. Finally, even though it appears reasonable to assume that the onset of lumen collapse and circularity index are possible markers of circular muscle and longitudinal muscle contractions, respectively, we can’t provide absolute proof for such. Furthermore, even though the measurement of longitudinal muscle contraction from US images, based on the law of mass conservation and incompressibility principle, appears to be based on the sound principles, it may be of significant interest to perform radiopaque clip markers and US imaging simultaneously. The strength of our study is that our observations have been made in humans in vivo and under physiological peristaltic conditions using novel and state-of-the-art techniques.

What is the clinical significance of synchrony between the contractions of two muscle layers? Circular muscle contraction increases esophageal pressure, and longitudinal muscle contraction increases esophageal wall thickness. Synchrony of contraction of the two muscle layers, under physiological conditions, assures a coordinated and concurrent increase in esophageal pressure and wall thickness. In accordance with Laplace’s law (stress = pressure × radius/thickness), an increase in muscle thickness during contraction reduces wall stress (13, 16, 18, 19, 21). Temporal synchrony between the contractions of two muscle layers assures a relative homeostasis of esophageal wall stress during the contraction period. The maximal thickness occurs at the time of maximum pressure and guarantees a relatively low wall stress at the peak of pressure (stress homeostasis). Stress homeostasis of the blood vessel wall and myocardium has been extensively studied and is crucial for the maintenance of normal function (9, 10, 11, 30). It is very likely that a low level of wall stress is also crucial for normal bolus transport during peristalsis. Asynchrony of contractions between the two muscle layers of the esophagus results in a situation where the maximal increase in muscle thickness and peak pressure occur at two different times, resulting in a disturbance of stress homeostasis. We speculate that esophageal diverticulum, analogous to aneurysm of blood vessels, is the result of alteration of stress homeostasis of esophageal wall. It is interesting that both asynchrony of contraction of two muscle layers (8) and esophageal diverticula occur in patients with high-amplitude contraction (4, 14). Another type of coordination between the two muscle layers relates to the amplitude of contraction. We and others have found that there is a direct relationship between the amplitude of contraction between circular and longitudinal muscle during peristalsis in normal subjects (14, 16). In a given subject as well as among normal subjects, there is a direct relationship between the contraction amplitude (marker of circular muscle activity) and change in the thickness or CSA of the muscularis propria (a marker of longitudinal muscle activity) during swallow-induced peristalsis. Patients with spastic disorders, on the other hand, do not show such a tight relationship. The effect of asynchrony of contraction of two muscle layers on wall stress and bolus transport during peristalsis needs further investigation.

GRANTS

This study was supported by National Institute of Diabetes and Digestive and Kidney Diseases Grant RO1-DK-60733.

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