Distension-related responses in circular and longitudinal muscle of the human esophagus: an ultrasonographic study

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Yamamoto, Yoshihiro, Jianmin Liu, Terrence K. Smith, and Ravinder K. Mittal. Distension-related responses in circular and longitudinal muscle of the human esophagus: an ultrasonographic study. Am. J. Physiol. 275 (Gastrointest. Liver Physiol. 38): G805–G811, 1998.—Both circular muscles (CM) and longitudinal muscles (LM) of the esophagus participate in peristalsis. Various measurement techniques have yielded conflicting information as to the temporal correlation between contraction in the two muscle layers. High-frequency intraluminal ultrasound (HFIUS) is a novel technique to detect contraction of LM and CM of the esophagus. We investigated the temporal correlation between the CM and LM contraction during ascending excitatory and descending inhibitory reflexes using HFIUS. A manometric catheter equipped with two balloons and a 12.5-MHz ultrasound transducer catheter was used to study 10 normal healthy subjects. The changes in muscle thickness and pressure, proximal and distal to esophageal distension, were recorded at 5 and 10 cm above the lower esophageal sphincter (LES). The esophageal distension induced an increase in pressure and an increase in muscle thickness of both CM and LM layers proximal to the distension site. The onset of increase in muscle thickness and peak muscle thickness in two layers occurred at the same time. There was a close temporal correlation between the changes in pressure and changes in muscle thickness. Atropine inhibited the distension-related pressure and muscle thickness increase in both layers. Distal to the esophageal distension, there was no change in pressure but a decrease in the thickness of the two muscle layers. The decrease in muscle thickness of the two layers occurred at the same time. The responses of the two muscle layers to distension were similar at 5- and 10-cm sites above the LES. HFIUS is a relatively noninvasive technique to study the LM layer response during peristalsis in vivo. Our data indicate that the two muscle layers may contract and relax together during distension-related peristaltic reflexes in the esophagus.

esophageal distension; peristalsis

NEUROMUSCULAR APPARATUS of the esophagus and extrinsic nerves are responsible for the genesis of peristalsis (3). Both circular and longitudinal muscle layers of the esophagus participate in peristalsis. The circular muscle contraction during peristalsis is believed to be of fundamental importance in bolus propulsion, but the role of longitudinal muscle is not clear. A part of the reason for the latter is that the contraction of longitudinal muscle is relatively difficult to study in vivo.

In the small intestine, contraction and relaxation of the circular and longitudinal muscles during peristalsis are thought to be in the opposite phase; i.e., proximal to a bolus, there is contraction of the circular and relaxation of the longitudinal muscle layer, and distal to a bolus, the reverse is the case (24). However, in the esophagus, different patterns of longitudinal muscle contraction have been described by using different techniques. Experiments conducted in vitro (organ bath), in which esophageal shortening was used to study the longitudinal muscle contraction, described contractions during the entire period of distension (duration response) (2). A similar response was observed in the in vivo studies, in which peristalsis was induced by balloon distension and vagal stimulation (5). On the other hand, the radiopaque marker technique showed that an esophageal contraction is associated with two patterns of longitudinal muscle contraction, an initial shortening of the entire esophagus followed by a peristaltic contraction in the longitudinal muscle layer (6). However, none of the above techniques records localized contraction of the longitudinal muscle.

Sugarbaker et al. (18) used strain gauge and muscle flap techniques in the opossum esophagus to record localized contractions and found that peristalsis was present in both circular and longitudinal muscle layers. Furthermore, their data showed that the longitudinal muscle contraction begins before and outlasts the circular muscle contraction at any given site in the esophagus. However, their technique cannot be used to study the human esophagus in vivo.

High-frequency intraluminal ultrasonography (HFIUS) relies on changes in muscle thickness as a marker of muscle contraction (9–11, 20). HFIUS records a cross-sectional image of the esophagus in which the longitudinal and circular muscle layers are seen distinctly. The temporal correlation between the circular and longitudinal muscle contraction during a swallow-induced peristalsis has recently been reported (12). The goals of our study were 1) to describe the individual muscle layer response during ascending excitatory reflexes (AER) and descending inhibitory reflexes (DIR) in the human esophagus and 2) to determine whether there were differences in the two muscle layer responses at two different sites along the length of the esophagus.

METHODS

Subjects

These studies were performed on 10 healthy human subjects (5 males and 5 females, with a mean age of 32 yr, range 24–56 yr). None of these subjects had symptoms suggestive of esophageal disease, and they were not taking any medications known to affect the esophageal motor function. The protocol for the study was approved by the Human Investigations Committee of the University of Virginia, and all subjects signed a written informed consent before participation in the study.
Catheter Design

A specially designed manometric catheter was used for these experiments. The catheter had a Dent sleeve device for continuous recording of LES pressure and two silicon balloons (2 cm in length and 2 cm in diameter when inflated with 10 ml of air). The two balloons were located 5 and 15 cm above the upper end of sleeve device (Fig. 1). Two side holes located 5 cm proximal to each balloon recorded pressures at the respective sites. Each of the manometric ports and the sleeve device were continuously perfused at a rate of 0.5 ml/min by using a low-compliance pneumohydraulic infusion pump. Manometric recordings were obtained using a Synectics Polygraph and a computer software system (Synectics Medical, Stockholm, Sweden).

HIUUS Imaging

The ultrasound images of the esophagus were obtained using a catheter-based transducer system. This catheter was 6.2Fr diameter and 200 cm in length and housed a 12.5-MHz transducer (from Microvasive, Boston, MA). The catheter was filled with 1 ml of sterile water to promote acoustic coupling between the transducer and the esophagus. The ultrasound transducer rotated within the catheter to produce a real-time 360° cross-sectional image at a rate of 12 times/s with an axial resolution of 0.1 mm and a penetration depth of 2.0 cm. The images were videotaped in real time. The ultrasound catheter was taped to the manometric catheter, with the transducer positioned 5 cm proximal to the distal balloon and at the same level as one of the side hole.

A video timer (Thalasmer Electronics, Ann Arbor, MI) synchronized the pressure and video-image recordings. We have used the same system in our previous studies to synchronize video fluoroscopic images and pressure records (13).

Experimental Protocol

Studies were performed with the subjects in the supine position after they had fasted and refrained from smoking and alcohol for 12 h. The manometric and ultrasound catheter assembly was positioned through the nose. The following study protocols were used.

Protocol 1: pressure and ultrasound images at 10 cm above LES. In five subjects, the catheter was positioned in such a way that the ultrasound transducer and the side hole above the distal balloon were 10 cm above the upper end of the LES (Fig. 1B). For the studies of AER, the distal balloon was inflated by injecting a given volume of air in <2 s. The balloon volumes used were 4, 6, and 8 ml in sequence. Each distension lasted 10 s, and subjects refrained from swallowing for 30 s before and for the entire period of distension. Each balloon volume was tested two to three times in each subject. AER was also studied in these five subjects after administration of atropine in the dose of 15 μg/kg as an intravenous bolus.

For the studies of DIR, two separate experiments were conducted. In the first experiment, only the proximal balloon was inflated. The pressure and images were recorded 5 cm below the site of distension. The protocol for the balloon inflation was the same as outlined in the previous paragraph. In a second set of experiments, a sustained distal balloon inflation of 30 s was performed, and, 10 s into this inflation, the proximal balloon was inflated for 10 s. For these experiments, the distal balloon volume used was 8 ml, and the proximal balloon volumes varied between 4, 6, and 8 ml. Again, each sequence was repeated two to three times in each subject.

Protocol 2: pressure and ultrasound images at 5 cm above LES. Five different normal subjects were studied using this protocol. The goal of these experiments was to study esophageal muscle response at a distal esophageal site, 5 cm above the LES. Both AER and DIR were studied in a fashion identical to protocol 1 except that the locations of the ultrasound probe and the side hole were different (Fig. 1A). The duration and volumes of balloon inflation tested were similar to the ones used in protocol 1.

Data Analysis

The video images were captured in a computer using a video digitizer (Braquo, Truevision, Indianapolis, IN) at the rate of 1 frame/s from a time period starting 5 s before balloon inflation to 5 s after the deflation of the balloon. Images were displayed at a resolution of 640 × 480 pixels (20 pixels = 1 mm). Each image was analyzed for the thickness of circular and longitudinal muscle in a blinded fashion, i.e., without the knowledge of pressure record. Approximately 270° circumference of the esophagus was visualized in these images because the remainder was obscured by the manometric catheter. The wall thickness was measured at three sites spaced equally around the circumference of esophagus. From these measure-
ments, the mean wall thickness in millimeters and percent changes from baseline thickness were calculated. The pressure at each of the corresponding time intervals of the video images was measured. The data from pressure and muscle thickness were superimposed on each other to determine the temporal correlation between the two. The muscle thickness at the time of peak pressure was also determined and graphed separately. All data are expressed as means ± SE. The differences in muscle thickness and pressures were compared between the baseline and esophageal distension at various balloon volumes by ANOVA and the Student’s t-test. 

P < 0.05 was considered significantly different.

RESULTS

Baseline Measurements

The ultrasonographic images of the esophagus showed five distinct layers (Fig. 2). These layers were as follows: mucosa along with submucosa, circular muscle, intermuscular septum, longitudinal muscle, and adventitia. These five distinct layers were identified at both 5 and 10 cm above the LES. The thickness of circular and longitudinal muscle layers were not different at 10 cm (0.48 ± 0.02 and 0.26 ± 0.01 mm) compared with 5 cm above the LES (0.53 ± 0.03 and 0.31 ± 0.01 mm), respectively.

Ascending Excitatory Reflex

Distension of the distal balloon induced an increase in pressure above this balloon. The increase in pressure was associated with an increase in the thickness of both circular and longitudinal muscle layers. The onset of muscle thickness in the two layers was simultaneous and usually occurred at the same time as the increase in pressure (Fig. 3). The peak increase in the muscle thickness in the two layers occurred at the same time and coincided with the pressure peak. There was a close temporal association between the increase in pressure and the increase in muscle thickness. The decrease in thickness of two muscle layers occurred at the same time but lagged behind the pressure drop by 2–3 s. The AER-induced pressure and muscle thickness changes were observed at both the levels in the esophagus, i.e., 5 and 10 cm. The temporal correlation between the circular and longitudinal muscle contraction was similar at the two esophageal sites. The AER-induced increase in pressure was directly proportional to the balloon volume, being larger at bigger balloon volumes.
Similar to pressure, the increase in muscle thickness was also directly related to the balloon volume. The increase in muscle thickness with the increases in balloon volume was seen in both longitudinal and circular muscle layers.

The AER response to 8-ml distension was compared before and after atropine (Fig. 5). There was a decrease in the baseline circular and longitudinal muscle thickness after atropine of 35.7 and 28.9%, respectively. Atropine also reduced the increase in pressure during AER significantly (55 ± 3 vs. 7 ± 3 mmHg). The increase in longitudinal and circular muscle thickness during AER was also reduced significantly by atropine (0.94 ± 0.04 vs. 0.38 ± 0.02 mm for circular and 0.44 ± 0.01 vs. 0.24 ± 0.02 mm for longitudinal muscle).

**Descending Inhibitory Reflex**

Distension of the proximal balloon induced either a small decrease or no change in pressure distal to the balloon (Fig. 6). There was usually a transient increase in pressure after balloon deflation. During balloon distension, there was a decrease in the thickness of both circular and longitudinal muscle layers distal to the distension (Fig. 6). The onset of decrease in the thickness of two muscle layers occurred at the same time, and maximal decrease, which occurred a few seconds later, was also simultaneous. The balloon volume of 8 ml resulted in a muscle thickness that was significantly smaller compared with the baseline circum-

![Fig. 4. Effect of balloon volume on peak pressure and peak muscle thickness proximal to distension. Mean data from 15 observations at 5 cm (A) and 10 cm (B) above LES in 5 subjects are shown. Peak pressure and peak muscle thickness were directly related to balloon volume. Increase in thickness was greater in circular compared with longitudinal muscle layer.](image)

![Fig. 5. Effect of atropine on pressure and changes in muscle thickness proximal to distension. Mean data from 15 observations made in 5 subjects are shown. Atropine inhibited pressure and increase in wall thickness in response to esophageal distension. Inhibitory effects of atropine were seen in both longitudinal and circular muscles.](image)

![Fig. 6. Temporal correlation between pressure and muscle thickness distal to distension. Proximal balloon was inflated with 8 ml of air. Pressure and muscle thickness were recorded at 5 cm (B) and 10 cm (A) above LES. Each graph represents mean data from 5 observations in 5 subjects. Note that there was either a small or no change in pressure distal to distension but longitudinal (lm) and circular muscle (cm) thickness was significantly decreased. Decrease in distal muscle thickness in response to esophageal distension represents descending inhibition in longitudinal and circular muscle layers.](image)
lar (0.42 ± 0.01 vs. 0.3 ± 0.01 mm) and longitudinal muscle (0.24 ± 0.06 vs. 0.19 ± 0.08 mm) thickness (Fig. 7). The DIR response at the 10 cm site was similar to the response at the 5 cm site. The decrease in muscle thickness with 8-ml balloon volume was significant for both circular and longitudinal muscle layers.

Effect of Proximal Esophageal Distension in Presence of a Sustained Distal Esophageal Distension

The esophageal distension with 8 ml of balloon volume in the distal esophagus induced an increase in pressure and an increase in circular and longitudinal muscle thickness 5 cm above the balloon (AER). This increase in pressure was not sustained in the presence of a sustained balloon inflation. The pressure and muscle thickness gradually fell during the sustained inflation. Distension of the proximal esophagus in the presence of a sustained distal esophageal distension resulted in an abrupt cessation or inhibition of AER. The inhibition of AER was seen as a drop in pressure and a decrease in muscle thickness. This decrease in pressure and muscle thickness was abrupt and distinctly different from the slow decrease in pressure and muscle thickness that occurred in the absence of proximal esophageal distension. The decrease in muscle thickness was observed in both the longitudinal and circular muscle layers. The larger volume distensions in the proximal balloon tended to induce a larger inhibition of the AER (Fig. 8). The inhibition of AER by a proximal balloon distension was seen at both locations in the esophagus, with the 5-cm site showing more prominent inhibition than the 10-cm site.

DISCUSSION

In summary, our results show that the intraluminal pressure increase during AER is associated with an increase in the thickness of both longitudinal and circular muscle layers of the esophagus. On the other hand, there is no change in the intraluminal pressure but a decrease in the thickness of two muscle layers during DIR. Furthermore, we find that the responses in the two muscle layers of the esophagus during AER and DIR are similar at 5- and 10-cm sites above the LES.

The pressure response to esophageal distension in our study is similar to one described in the literature; i.e., proximal to the level of distension, there is an increase in the esophageal pressure, and distal to the distension, there is quiescence or inhibition (4, 14, 21, 22). The increase in pressure proximal to the distension site has also been termed as esophageal propulsive force (22). We termed these two reflexes as AER and DIR because similar terminology has been used in the

Fig. 7. Effect of balloon volume on pressure and muscle wall thickness distal to distension. Each bar represents mean data from 15 observations at 5 cm (A) and 10 cm (B) above LES in 5 subjects. Decrease in muscle thickness with esophageal distension was related to balloon volume. Circular muscle response to balloon distension was more sensitive compared with longitudinal muscle response.

Fig. 8. Effect of a proximal balloon inflation (8 ml) in presence of a sustained distal esophageal distension of different volumes. Muscle thickness was measured at peak of contraction and relaxation. Each bar represents mean data from 15 observations at 5 cm (A) and 10 cm (B) above LES in 5 individuals. Note an increase in pressure and wall thickness in response to distal distension. A proximal distension in presence of sustained distal distension resulted in a drop in pressure and decrease in circular and longitudinal muscle wall thickness.
other areas of the gastrointestinal tract. These two reflexes are fundamental to peristalsis in the entire gastrointestinal tract. Ours is the first study to describe in detail the patterns of contraction in the two muscle layers induced by esophageal distension by using ultrasonography.

Several investigators have studied the correlation between changes in muscle thickness, intraluminal pressure, and strain gauge recordings. They report a direct correlation between the increase in muscle thickness and contraction recorded by other modalities (9, 11, 12, 20). We reported the changes in muscle thickness and intraluminal pressure in an in vitro organ bath under both isotonic and isometric conditions of longitudinal esophageal shortening in an earlier study and found a close temporal correlation between the increase in pressure and muscle thickness (25). Our findings that atropine inhibits the increase in pressure and increase in muscle thickness of both circular and longitudinal muscle layers during AER further supports the argument that increase in muscle thickness indeed represents contraction of the muscle layers.

There is a general consensus that the circular muscle contracts in a peristaltic fashion, with contraction above and relaxation below the site of a bolus. However, there is less agreement with regard to the longitudinal muscle contraction during peristalsis. Radiopaque marker motion (6, 7) and strain gauges (16, 18) are two experimental techniques used in vivo to measure longitudinal muscle contraction. The radiopaque marker technique in animals and humans has provided consistent findings, in which, during primary and secondary peristalsis, there is an initial shortening of the entire esophagus followed by a sequential longitudinal muscle contraction along the length of the esophagus. Pouderoux et al. (16) recently measured radiopaque marker motion along with the esophageal propulsive force and concluded that during a swallow-induced peristalsis, both circular and longitudinal muscles contract for the same duration and in a sequential or peristaltic fashion. They also found that the longitudinal muscle contraction is slightly ahead of the circular muscle contraction (16). This conclusion was based on the observation that there was a segmental shortening distal to the esophageal propulsive force. Our findings are in agreement with their study in that both muscle layers contract together and contract for the same duration of time during the excitatory phase. However, unlike their study, we did not find contraction of the longitudinal muscle distal to the site of distension; instead, we found there was a decrease in the longitudinal muscle thickness or relaxation. We believe that this difference may be related to the differences in the methodology. A study by Miller et al. (12), who used HFIUS and manometry and studied swallow-induced peristalsis, also found the pattern of contraction in the two muscle layers to be similar to the ones we report in this study, and our unpublished observations with swallow-induced peristalsis confirm their findings. It is interesting that longitudinal muscle of the lower esophageal sphincter also contracts and relaxes with increases and decreases in its pressure, respectively (8).

A surgically implanted strain gauge is thought to measure localized longitudinal muscle contraction (1). Sugarbaker et al. (19) used surgically made muscle flaps to measure contraction in the longitudinal and circular muscle layers and found that there is sequential contraction in the longitudinal and circular muscle layers. The longitudinal muscle contracted slightly before and outlasted the circular muscle contraction at any given point along the length of the esophagus. Our observation that there is a tight correlation between the contraction of two muscle layers at two different sites in the esophagus would also indicate that, similar to circular muscle, peristalsis also occurs in the longitudinal muscle layer. Peristalsis in the esophagus is dependent on latency of contraction (2). What is the basis of latency in the esophageal longitudinal muscles? The latency in the circular muscle is due to the presence of nitric oxide-containing inhibitory nerves (15, 26). Blockade of nitric oxide results in reduction of the latency of circular muscle contraction. Two observations that we made during our experiments indicate that, similar to circular muscle, inhibitory innervation may also exist for the longitudinal muscle: 1) distal to distension, there was relaxation of the longitudinal muscle; and 2) in the presence of a sustained AER, either a swallow (unpublished observation) or proximal distension results in relaxation of the circular as well as longitudinal muscle. Animal experimentation, however, has not observed the electrophysiological correlates of inhibition in the longitudinal muscle layer of the esophagus. Robertson et al. (23), however, have recently reported inhibitory phenomenon in the longitudinal muscles of the colon. Furthermore, NADPH-containing immunoreactivity (a marker of nitric oxide, an inhibitory neurotransmitter) is present in the longitudinal muscle layer of the esophagus, although its concentration is smaller than that in the circular muscle layer (17).

In summary, our findings indicate that, in the esophagus, contraction and relaxation of the circular and longitudinal muscle layers during distension-related peristaltic reflexes occur together. We hypothesize that contraction of the longitudinal muscle brings together the rings of circular muscle to maximize the circular muscle force required for bolus propulsion. Furthermore, similar to the circular muscle, there appears to be a descending inhibition in the longitudinal muscle layer of the esophagus during peristalsis. We suggest that HFIUS is a relatively noninvasive technique to study the longitudinal muscle function in vivo in humans, and future studies using this technique may help determine the role of longitudinal muscle in bolus propulsion in health and disease states.

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