Relationship between esophageal muscle thickness and intraluminal pressure: an ultrasonographic study

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1Division of Gastroenterology, University of California, San Diego and San Diego Veterans Affairs Medical Center, San Diego 92161; and 2Department of Bioengineering, University of California, San Diego, La Jolla, California 92039-0412

Received 27 June 2000; accepted in final form 15 January 2001

Pehlivanov, Nonko, Jianmin Liu, Ghassan S. Kassab, James L. Puckett, and Ravinder K. Mittal. Relationship between esophageal muscle thickness and intraluminal pressure: an ultrasonographic study. Am J Physiol Gastrointest Liver Physiol 280: G1093–G1098, 2001.—A number of studies show a close temporal relationship between the rate of change in muscle thickness as detected by high-frequency intraluminal ultrasonography (HFIUS) and intraluminal pressure measured by manometry. There is a marked variability in esophageal contraction amplitude from one swallow to another at a given level in the esophagus and along the length of the esophagus. Furthermore, peristaltic pressures are higher in the distal compared with the proximal esophagus. The goal of this study was to evaluate the relationship between the baseline and peak muscle thickness and the contraction amplitude during swallow-induced contractions along the length of the esophagus. Fifteen normal subjects were studied using simultaneous esophageal pressures and HFIUS or HFIUS alone. Recordings were made during baseline and standardized swallows in the lower esophageal sphincter (LES) and at 2, 4, 6, 8, and 10 cm above the LES. HFIUS images were digitized, and esophageal muscle thickness and peak contraction amplitudes were measured. In the resting state, muscle thickness is higher in the LES compared with the rest of the esophagus. Baseline muscle thickness is also significantly higher at 2 cm vs. 10 cm above the LES. In a given subject and among different subjects, there is a good relationship between peak muscle thickness and peak peristaltic pressures (r = 0.55) at all sites along the length of the esophagus. The positive correlation between pressure and muscle thickness implies that the mean circumferential wall stress is fairly uniform from one swallow to another, irrespective of the contraction amplitude.

MATERIAL AND METHODS

Experimental set up. These studies were performed in 15 healthy normal subjects. The study protocol was approved by The Human Investigation Committee of the University of California San Diego. Each subject signed an informed consent before participation in the study protocol. Subjects were asked to fast overnight, and investigations were performed in the right recumbent position. In 10 subjects, the esophageal pressures and ultrasonographic images were recorded simultaneously using a catheter assembly that consisted of a water-perfused pressure catheter system and an ultrasound probe with a 20-MHz transducer (UM-3R Olympus, Tokyo, Japan). The two catheters were attached to each other so that the transducer of the HFIUS probe and one of the side holes were a close temporal relationship between the rate of change of muscle thickness and the changes in esophageal pressure during a swallow-induced peristaltic contraction (1, 15, 19). Contraction and relaxation induced by distension of the esophagus can also be recorded using HFIUS.

Laplace's equation (2, 5, 8) states that the intraluminal pressure is directly proportional to the mean circumferential wall stress and the wall thickness-to-radius ratio. We hypothesize that the wall thickness-to-radius ratio changes in proportion to the pressure such that the circumferential stress in the wall of the esophagus remains constant. In a given individual, there is a marked variability in esophageal pressures from one swallow-induced contraction to another. We further hypothesize that the variability in pressure correlates with the muscle thickness during contraction. Therefore, the goals of our study are to determine the relationship between esophageal pressure, esophageal baseline muscle thickness, and esophageal muscle thickness at the peak of swallow-induced contraction. We studied the relationship between muscle thickness and esophageal pressure in the lower esophageal sphincter (LES) and at five different sites along the length of the esophagus.

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of the pressure catheter were located at the same level. In five normal subjects, only the ultrasound catheter was positioned into the esophagus to record ultrasound images during swallow-induced contractions.

**Study protocol.** The nasopharynx and oropharynx were anesthetized using 1% lidocain gel and 1% benzocain spray. The catheter assembly was positioned via the nose into the esophagus and stomach. A standard pull-through procedure was performed to estimate the length of the LES. The catheter assembly was then withdrawn every 2 cm until it reached 10 cm above the LES. Five wet swallows, each with 5 ml of tap water at room temperature, were performed with the HFIUS probe located at each of the following levels:

- middle of the LES and 2, 4, 6, and 10 cm above the upper edge of LES. Subjects were asked to refrain from swallowing 10 s before and 30 s after each wet swallow. The pressure tracings were recorded and saved onto a computer through a PC Polygraph using a commercially available program (Polygram–Esophageal Manometry Analysis Module, Version 2.0, Medtronic Synectics, Shoreview, MN). Ultrasound images were recorded in real time on videotape by using an ultrasound system (EU-M30, Olympus, Melville, NY) and a video cassette recorder. The pressure and ultrasound recordings were synchronized by using a time code device. In five subjects in whom the ultrasound catheter alone was used to record esophageal images, the transducer was positioned 5 cm above the LES. Four to five swallow-induced contractions were recorded in each of these five subjects.

**Data measurements.** Ultrasound images were digitized into a computer using an image capture board (Bravado 1000, Truvision) and Adobe Premiere 4.0 software (Adobe Systems, Mountain View, CA). Esophageal muscle layer thickness was measured on digitized images using an image analysis software called SigmaScan Pro (Jandel Scientific, San Rafael, CA) at two different phases of the esophageal activity: at baseline and at peak pressures. The pressure baseline images were selected at the time of end expiration, based on the manometric tracings, ~10 s before the corresponding wet swallow at each of the longitudinal levels in the esophagus. The peak pressure images were selected at the point corresponding to the peak intraesophageal pressure recorded during the wet swallows. The esophageal muscle thickness, originally measured in pixels, was then converted to millimeters. The images were magnified at $\times 12$ for the final measurements to increase the measurement accuracy. The muscle thickness was measured in five different sectors along the esophageal circumference, and an average value was computed. The baseline thickness represented the mean thickness obtained from the five images obtained before the five swallow-induced contractions. The thickness at the peak pressure was measured from the five swallow-induced contractions. The images were measured at each of the esophageal sites along the length of the esophagus. Additionally, the shape of the esophagus and the content of the esophageal lumen were noted at the esophageal baseline and at peak contractions. In subjects in whom esophageal ultrasound images without pressure were recorded, the images were analyzed for the muscle thickness and mucosa thickness at the peak of contraction.

**Biomechanical analysis.** Laplace’s equation for a cylinder of radius ($r$) and wall thickness ($h$), relates the lumen pressure ($P$) to the mean wall circumferential stress ($\tau$) by

$$\tau = P(r/h)$$  \hspace{1cm} (1)

During peak contraction, the esophagus may be approximated to a cylinder whose pressure-wall thickness relationship obeys $Eq. \ 1$. Because the lumen of the esophagus conforms to the shape of the probe, the radius of the esophagus corresponds to the radius of the probe, which is constant. Hence, linearity between the pressure and wall thickness implies the uniformity of circumferential wall stress. $Eq. \ 1$ can also be used to relate the variability between pressure and wall thickness. Assume that the variability in $\tau$, $P$, $h$, and $r$ is $\delta$, $\delta P$, $\delta h$, and $\delta r$, respectively, then the differential of $Eq. \ 1$ yields

$$\delta \tau = (r/h)\delta P + (P/h)\delta r - (Pr/h2)\delta h$$ \hspace{1cm} (2)

A relationship for the fractional variability can be obtained by dividing $Eq. \ 2$ by $Eq. \ 1$ to obtain

$$\frac{\delta \tau}{\tau} = \frac{\delta P}{P} + \frac{\delta r}{r} - \frac{\delta h}{h}$$ \hspace{1cm} (3)

Because the radius does not change and if we assume a uniform wall stress, then the fractional variability of pressure should be equal to the fractional variability of wall thickness.

**Statistical analysis.** Data are means ± SD unless otherwise stated. The Pearson correlation test was applied to estimate the relationship between pressure and esophageal wall thickness-to-radius ratio. The differences between muscle thickness values were estimated using $t$-test and Mann-Whitney Rank Sum test. All statistical tests were performed using a statistical program (SigmaStat, Jandel Scientific).

**RESULTS**

Ten healthy subjects (8 males, 2 females, mean age of 46.5 ± 13.8 yr) participated in the main study protocol. Two hundred and seventy-three wet swallows were recorded in these subjects. In two subjects, only three wet swallows were recorded at each level. There were eight swallows that resulted in failed peristaltic contractions, which were not analyzed. Thus a total of 265 wet swallows were analyzed for the main study protocol. In five study subjects, for whom only ultrasound images were recorded, a total of 24 swallows was analyzed for the determination of mucosa and muscle thickness.

**Muscle thickness in resting or baseline state.** The LES muscle is significantly thicker than that of the esophageal body, as shown in Table 1 and Fig. 1. The esophageal muscle is thicker in the distal (2 cm above LES) compared with the proximal (8 cm and 10 cm above LES) esophagus ($P < 0.05$; Fig. 1). In the resting

<table>
<thead>
<tr>
<th>Level</th>
<th>Baseline Thickness, mm</th>
<th>Peak Thickness, mm</th>
<th>Delta Thickness, mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>LES</td>
<td>1.92 ± 0.14 †</td>
<td>2.54 ± 0.13 †</td>
<td>0.62 ± 0.12 †</td>
</tr>
<tr>
<td>2 cm</td>
<td>1.28 ± 0.09</td>
<td>2.31 ± 0.17</td>
<td>1.04 ± 0.11</td>
</tr>
<tr>
<td>4 cm</td>
<td>1.14 ± 0.09</td>
<td>2.16 ± 0.16</td>
<td>1.00 ± 0.10</td>
</tr>
<tr>
<td>6 cm</td>
<td>1.09 ± 0.06</td>
<td>2.20 ± 0.15</td>
<td>1.13 ± 0.13</td>
</tr>
<tr>
<td>8 cm</td>
<td>1.07 ± 0.07 ‡</td>
<td>2.15 ± 0.15</td>
<td>1.08 ± 0.13</td>
</tr>
<tr>
<td>10 cm</td>
<td>1.06 ± 0.06‡</td>
<td>2.04 ± 0.14</td>
<td>0.98 ± 0.12</td>
</tr>
</tbody>
</table>

Values are means ± SE. Delta thickness is estimated as the average difference between baseline and peak thickness. LES, lower esophageal sphincter. * $P < 0.05$ vs. corresponding baseline values at same level. † $P < 0.05$ vs. all levels in the esophagus. ‡ $P < 0.05$ vs. 2 cm above LES.
state, the shape of the LES is somewhat round. The body of the esophagus, however, is usually “slit-like” in appearance except during contraction, when it becomes circular, as shown in Fig. 2. The mucosa of the esophagus is usually collapsed around the probe where there is no lumen between the esophageal wall and the probe.

Muscle thickness during swallow-induced contraction. The shape of the esophagus during contractions is circular where the mucosa conforms to the shape of the probe. The esophageal muscle thickness was measured at the point of peak pressure during wet swallows. The muscle thickness is larger at the 2-cm level compared with the rest of the esophagus, but the differences are not statistically significant (Table 1; Fig. 1).

Relationship between muscle thickness and esophageal contraction amplitude. In a given subject, there is significant variability of contraction amplitude from one swallow to another. The peak muscle thickness also differs from one swallow to another. There is significant correlation between the peak pressures and the peak muscle thickness in a given subject. The mean r values in eight subjects, with five swallows each, at 2, 4, 6, 8, and 10 cm upstream of the LES are 0.61, 0.83, 0.76, 0.84, and 0.78, respectively, as shown in Fig. 3. Figure 4 shows that, among 10 subjects and 268 swallows, there is a modest but significant correlation between the peak pressures and the peak muscle thickness (r = 0.55).

There is a poor correlation between the baseline muscle thickness and the peak pressures at different sites in the esophagus (r = -0.15). There is a moderate correlation, however, between the delta thickness (the difference between baseline and peak contraction) and

**Fig. 1.** Relationship between muscle thickness and pressure. Baseline muscle thickness is larger at 2 cm than at 8 and 10 cm above the lower esophageal sphincter (LES). There is a significant increase in esophageal muscle thickness at the peak of contraction (peak thickness) at all esophageal levels (data are means ± SE; *P < 0.05 vs. 2-cm level).

**Fig. 2.** Ultrasound images of the esophagus. Esophagus in the resting state (A) and during 2 swallow-induced contractions, with corresponding pressures of 132 (B) and 226 mmHg (C). Note that muscle thickness was greater in image C compared with B. T, ultrasound transducer; M, muscle layer.

**Fig. 3.** Correlation between esophageal muscle thickness and esophageal contraction pressure at 5 different sites in the esophagus. Data correspond to 8 subjects, each with 5 swallows. Mean r value at different levels in the esophagus ranged from 0.6 to 0.8.
Relationship between proximal and distal esophageal pressure and wall thickness. The esophageal contraction amplitudes during wet swallows also reveals lower pressures at 10 cm compared with the 2-cm site. These differences, however, are not statistically significant (Fig. 1). A similar trend is observed for the peak muscle thickness between the two sites. The delta muscle thickness, during contractions, is not different between the sites (Table 1), thus indicating that the difference between the two sites is related to the difference in the baseline thickness.

Variability in mucosa and muscle thickness. Twenty-four swallows were assessed for the variability in mucosa vs. muscle thickness in five subjects. The percent variability in the mucosa thickness from one swallow-induced contraction to another in five subjects ranges from 5.7 to 8.2% (6.6 ± 0.9%). However, the variability in muscle thickness is much larger, ranging from 10.4 to 44% (23.9 ± 16%). These differences are statistically significant (P < 0.05).

DISCUSSION

Our data show that the baseline LES muscle is thicker than the rest of the esophageal musculature. Furthermore, there is a gradient of muscle thickness in the body of the esophagus where it is somewhat thicker in the distal compared with the more proximal esophagus. Similar to the muscle thickness, the generated pressures are also higher in the distal compared with the proximal esophagus. The variability in the baseline muscle thickness is much larger, ranging from 10.4 to 44% (23.9 ± 16%). These differences are statistically significant (P < 0.05).
muscle thickness among healthy subjects is relatively small. A swallow that generates higher pressure during esophageal contraction is associated with a larger peak muscle thickness as well as a larger change of thickness. Swallow-to-swallow variability in the esophageal pressures during contractions is also associated with similar variability in the change in muscle thickness. On the other hand, there is minimal variability in the mucosa thickness from one swallow-induced contraction to another.

The validity of our hypothesis that changes in muscle thickness correlate with the changes in pressure depends on the premise that, besides contraction, no other factors alter the esophageal muscle thickness. Esophageal distension due to the presence of luminal contents and changes in mucosa thickness could influence the muscle thickness. The distension of the esophagus as a result of intraluminal contents or increase in mucosa thickness will result in stretching and hence a decrease in esophageal muscle thickness. The esophageal lumen was absent at the baseline as well as at the peak of contractions in normal subjects. The mucosa wraps around the ultrasound probe, thus leaving no space between the probe and the mucosa. Furthermore, the mucosa thickness does not vary significantly from one swallow to another. These observations suggest that distension and changes in mucosa thickness do not play a significant role in altering the muscle thickness.

A number of investigators have found a close temporal relationship between the changes in esophageal pressure and muscle thickness on ultrasonographic images during swallow-induced esophageal contraction (1, 15, 19, 22). Ours is the first study that shows a correlation between the variability in pressure and the variability in wall thickness in a given individual as well as among different subjects. This variability in pressure may be explained by the differences in the baseline thickness and by the change in thickness during peristaltic contraction. Recently, findings by Nicosia et al. (17), reported in an abstract form, also concur with our observations.

According to Laplace’s equation, the positive correlation between muscle thickness-to-radius ratio during esophageal contraction and intraluminal pressure serves to maintain a uniform circumferential stress in the wall of the esophagus as given by Eq. 1. Hence, a linear relationship between wall thickness-to-radius ratio and pressure may be a mechanism to keep the wall stress relatively constant during muscle contractions. Closure of the esophageal lumen during peristalsis is a must for an effective transport of the bolus during peristalsis. The reduction in stress at the time of contraction is important to prevent centrifugal bulging of the wall of the esophagus. If centrifugal bulging were to occur, transport of the bolus during peristalsis would be markedly impaired. Therefore, the increase in wall thickness is important in the genesis of intraluminal pressure as well as the reduction in wall stress during peristalsis, both of which are important for an efficient transport of the bolus. Laplace’s equation can also be used to explain the correlation between the variability in pressure and wall thickness. Equation 3 shows that the fractional variability in pressure is equal to the fractional variability in wall thickness if the radius and wall circumferential stress are constant.

Clouse and Staiano (4, 5), using a topographic technique, described several distinct segments in the body of the distal esophagus. These topographic plots were constructed on the basis of the esophageal contraction amplitudes. The reasons for the differences in the esophageal pressure in the distal compared with the proximal esophagus are thought to be due to the nature of the muscle, i.e., skeletal vs. smooth muscle, and due to differences in the neurotransmitters in the different parts of the esophagus. Our study indicates that part of the variability of the esophageal pressures could be explained by the baseline muscle thickness. The esophageal muscle is somewhat thicker in the most distal compared with the proximal esophagus, and the pressures are also somewhat higher in the distal compared with the proximal esophagus. Higher pressures in the distal compared with the proximal esophagus have been observed by several investigators (18, 20).

The mechanism of high-amplitude contractions in nutcracker esophagus and diffuse esophageal spasm is not known. Theoretically, a number of mechanisms may result in higher than normal contraction amplitude, a stronger neural stimulus, a larger neurotransmitter release at the neuromuscular junction, increased sensitivity of the receptors, and an increased sensitivity of the intracellular pathways that results in release of intracellular calcium from the storage sites. Another possible mechanism may be related to a greater muscle thickness that results in a larger increase in pressure for a given neural drive. Indeed, autopsy studies reveal that patients with diffuse esophageal spasms have marked hypertrophy of the esophageal muscles of the distal esophagus (3, 6, 7). Along those lines, using endoscopic ultrasonographic technique, Melzer et al. (14) described a patient with nutcracker esophagus whose esophageal wall was three to four times thicker than that of a normal subject. Kojima et al. (9) found a marked increase in muscle wall thickness in a patient with prolonged-duration esophageal contraction. Our own preliminary data, using HFIUS, show that patients with diffuse esophageal spasm and patients with nutcracker esophagus (high-amplitude esophageal contractions) indeed have marked hypertrophy of the esophageal wall (13, 16). According to Laplace’s equation, the increase in wall thickness that accompanies the increase in pressure implies that the tissue remodels in such a way as to maintain a constant value of circumferential stress in the wall of the esophagus.

This study was supported by a National Institute of Diabetes and Digestive and Kidney Diseases Grant R01-DK-51604-04A1.
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