Proximal and distal esophageal contractions have similar manometric features

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Peghini, Paolo L., Kishore G. Pursnani, Matthew R. Gideon, June A. Castell, Jennifer Nieman, and Donald O. Castell. Proximal and distal esophageal contractions have similar manometric features. Am. J. Physiol. 274 (Gastrointest. Liver Physiol. 37): G325–G330, 1998.—The human esophagus is composed of striated muscle proximally and of smooth muscle distally with a transition zone between the two. Striated muscle contracts much faster than smooth muscle. The change in pressure over time (dP/dt) of the contraction amplitude should therefore be higher in proximal than in distal esophagus, reflecting the presence of striated muscle proximally. There were 34 normal esophageal manometries of patients analyzed for swallow amplitude and dP/dt in the pharynx and esophagus. An additional 11 healthy controls were similarly studied. Amplitudes in pharynx and proximal and distal esophagus were not different. The mid-esophagus had a pressure trough (P < 0.001). The dP/dt in the pharynx was much higher than that in the esophagus (P < 0.001). The dP/dt of proximal and distal esophagus were of the same order of magnitude. The manometric behavior of the striated muscle portion of the proximal esophagus differs from that seen in the pharynx and shows similar characteristics to distal esophageal smooth muscle.

Esophageal manometry; change in pressure over time; smooth muscle; striated muscle

According to the classical teaching, the proximal one-third of the esophagus is primarily composed of striated muscle and the distal two-thirds are composed of smooth muscle with a zone of gradual transition from one muscle type to the other between the two (20). This concept has been challenged, however, by anatomic studies in human cadavers, which showed that the striated muscle segment is often much more limited in extent (18, 26). The classical concept is supported by the common occurrence of a pressure trough in the middle esophagus, which is usually attributed to a transition zone from striated to smooth muscle (2, 11, 18, 19, 24). Striated muscle contracts faster than smooth muscle (10). Therefore, one would expect a steeper upstroke of the esophageal peristaltic contraction, i.e., a higher change in pressure over time (dP/dt), in the proximal compared with the distal esophagus.

Normal motility recordings were reviewed to test the hypotheses that the dP/dt in the proximal esophagus is higher than that in the distal esophagus due to the differences of velocity of contraction between the two muscle types.

Methods

Subjects. Esophageal manometry studies of 34 patients (20 females and 14 males) referred to our laboratory between 1992 and 1995 for complaints of chest pain or heartburn were reviewed. The mean age was 47 yr (range 28–82 yr). These studies were selected for analysis because their initial interpretation was that of normal esophageal motility. All patients were studied using an identical manometric protocol as described in Manometry and Measurements.

An additional group of 11 healthy controls with no history of esophageal symptoms were subsequently studied with an identical protocol. These included 7 females and 4 males with a median age of 41 yr (range 21–61 yr). This control group was added to verify that observations in the patients with normal manometric studies truly described normal physiological findings.

Manometry. Esophageal and pharyngeal manometry was performed with a catheter containing four solid-state transducers (Konigsberg Instruments, Pasadena, CA). Three of these transducers, one circumferential (distal) and two unidirectional, spaced 5 cm apart, were used in both the distal and proximal esophagus. The pharynx was measured with a second circumferential transducer, to compensate for the radial asymmetry of the pressure in this region (23). The manometry catheter was connected to a computer, and the data were stored on disk. All studies were performed after at least a 4-h fast. The catheter was passed through the nose and advanced into the stomach. The lower esophageal sphincter (LES) was studied using the slow pull-through technique. Then the catheter was placed with the distal sensor 3 cm above the proximal border of the LES, thereby placing two of the remaining transducers at 8 and 13 cm above the LES. Ten wet swallows, 5 ml of water each, were recorded. The catheter was then repositioned with the most proximal transducer being located 1 cm below the distal border of the upper esophageal sphincter (UES), thus placing the two distal transducers at 6 and 11 cm below the UES. Ten water swallows were repeated.

Esophageal manometry was done with the subject being studied in the supine position. For the study of the pharynx, patients and controls were changed into a sitting position, and the catheter was withdrawn to place one circumferential transducer at the proximal border of the UES and one in the pharynx 3 cm above that. Five swallows, also 5 ml of water each, were given for this part of the study. Catheter design and placements described above are illustrated in Fig. 1.

Measurements. For analysis, the studies were loaded onto a computer and the tracing was displayed on the screen. After adjustment of the esophageal baseline, the swallows were analyzed individually for all three catheter positions: distal and proximal esophageal as well as pharyngeal. Two parameters of muscle activity were assessed: amplitude and dP/dt. Amplitudes were measured as the difference between peak and baseline pressure. For calculation of the dP/dt an approximately linear segment on the ascending limb of the contraction wave was chosen. The change of pressure over this segment was divided by the corresponding change of time (Fig. 2). Ten swallows were analyzed at each transducer position for each individual, and the means of these values were used for further assessment. Amplitudes and dP/dt were compared between the different positions: pharynx at 3 cm...
above the UES, proximal esophagus at 1 cm below the UES, midesophagus at 6 cm below the UES, and distal esophagus as the average of 3 and 8 cm above the LES. The correlation between amplitude and dP/dt was calculated for the pharynx and the proximal and distal esophagus. The presence or absence of a distinct pressure trough in the middle esophagus was also identified. This was defined as contraction amplitude at either 13 cm above the LES and/or 6 cm below the UES of less than one-third of the mean distal esophageal amplitude (average between 3 and 8 cm above LES).

Statistics. Amplitudes and dP/dt between recording sites were analyzed using analysis of variance (ANOVA) with Newman-Keuls method for multiple comparisons. Comparisons of mean contraction values at specific recording sites between patient normals and healthy controls were made using unpaired t-test. Correlation between dP/dt and amplitude was calculated with two-variable linear regression. Two-tailed P values ≤0.05 were considered significant. Data are expressed as means ± SE. The statistical software used was True Epistat (4th Ed.; Epistat Services, Richardson, TX).

RESULTS

Mean contraction amplitudes in the pharynx (131 ± 8.2 mmHg) and the proximal (105 ± 6.6 mmHg) and distal esophagus (116 ± 6.2 mmHg) for the 34 patients with normal manometry studies were not different from each other (P > 0.05). A lower mean contraction amplitude was found in the middle esophagus (56 ± 4.6 mmHg) than in the proximal or distal esophagus or in the pharynx (P < 0.001, Fig. 3). Only 9 of the 34 patients (26%) had a distinct pressure trough in the midesophagus. Similar results were found in the 11 controls. Mean contraction amplitudes in the pharynx (115 ± 27 mmHg) and the proximal (83 ± 9 mmHg) or distal (95 ± 10 mmHg) esophagus were not different from each other (P > 0.05), and mean amplitude in the middle esophagus (43 ± 4 mmHg) was significantly lower than that occurring at the other three sites (P < 0.02). Mean values were not significantly different from those at corresponding sites in the patients (P > 0.05). Only 2 of the 11 controls (18%) had a distinct pressure trough in the midesophagus.

For the 34 patients mean dP/dt in the pharynx of 1,134 ± 37.6 mmHg/s was higher than the mean dP/dt of either the proximal or distal esophagus (P < 0.001, Fig. 4). Although the dP/dt was numerically considerably higher in the proximal (127 ± 5.8 mmHg/s) compared with the distal esophagus (89 ± 4.5 mmHg/s), this difference was not significant when analyzed together with the pharyngeal dP/dt using ANOVA. Again, the findings in the healthy controls were similar. Mean dP/dt in the pharynx (1,236 ± 10 mmHg/s) was higher than the mean dP/dt at either proximal (127 ± 23 mmHg/s) or distal (95 ± 10 mmHg/s) esophagus (P < 0.001).
proximal esophagus and pharynx is 9 times higher than in the proximal and 13 times higher than in the distal esophagus (*P < 0.001).

For the 34 patients, there was positive correlation between dP/dt and the amplitude of swallows. This correlation was stronger in the esophagus (r = +0.81 proximal and +0.91 distal) than in the pharynx (r = +0.68, P < 0.001 for all three). The corresponding regression equations are y = 26 + 0.98x for the proximal esophagus and y = 7.3 + 0.71x for the distal esophagus. The slopes of these two regression lines are not different (P > 0.05). The combined regression equation for proximal and distal esophagus is y = 15.1 + 0.86x. The slope of the combined regression line is eight times less steep than that of the pharynx (y = 138 + 6.9x, P < 0.001). These relationships are shown in Fig 5. Strong positive correlations between dP/dt and amplitude of swallows was also found for the 11 healthy controls (pharynx r = + 0.99; proximal esophagus r = +0.86; distal esophagus r = +0.92, P < 0.05 for all). Again, regression equations indicate that the slope in the pharynx (y = 114 + 11.7x) is approximately 10 times steeper than that in the proximal (y = 59 + 2.2x) or distal (y = 8 + 0.9x) esophagus.

**DISCUSSION**

According to the classical teaching, the upper one-third of the esophagus is primarily composed of striated muscle and the distal two-thirds are composed of smooth muscle. Between these two zones is a transitional zone where the two muscle types gradually change (20). This concept appears to be derived from a publication of Goetsch (8), who studied the esophagi of only two men and found that the proximal 25–30% consisted of striated muscle, whereas the distal 60% was smooth muscle, with the remainder being mixed. Two reports in which this question was studied more systematically gave somewhat different results. Treacy et al. (26) dissected the proximal esophagi of 10 routine autopsy cases at 2-cm intervals, and Meyer et al. (18) dissected postmortem esophagi of 11 patients without known esophageal disease at 1-cm intervals. The segment of exclusively striated muscle was confined to the most proximal esophagus. In the first study smooth muscle first appeared on the average 3.9 cm (range 2–6 cm) from the top of the intrinsic esophageal musculature. In the second study only the upper 0.9 ± 0.3 (SE) cm of the circular and the upper 1.4 ± 0.5 cm of the longitudinal muscle layer were purely striated. The point where striated and smooth musculature were present in equal amounts (50% each) was at 5.8 cm (range 4–8 cm) and at 4.7 ± 0.6 cm, respectively. The distal 62% (14.3 ± 0.8 cm) of the inner circular and 54% (12.4 ± 0.9 cm) of the outer longitudinal muscle layer of the esophagi studied by Meyer et al. (18) were exclusively composed of smooth musculature. The zone in between, accounting for 34% and 41%, respectively, was composed of a mixture of smooth and striated musculature. The histological composition of the esophageal musculature translates into functional parameters. Mayrand and Diamant (17) gave normal volunteers amyl nitrite, a smooth muscle relaxant, and mapped the esophagus manometrically. When manometry was compared after amyl nitrite with baseline, the proximal 5–6 cm of the esophagus were found to be unaffected, whereas amyl nitrite abolished all swallow-induced contractile activity in the distal 11–14 cm. Between these, there was a transition zone with reduced peristaltic amplitude. Radionuclide transit studies of patients with scleroderma and achalasia, both diseases affecting the smooth musculature, show intact function of the most proximal esophagus with impaired bolus clearance in the middle and distal esophagus (21). In the present study the proximal esophageal pressure transducer was placed 1 cm below the UES, which, according to all of the previously described data, is an area of purely striated muscle. Even if one accounts for the swallow-associated upward movement of the larynx, which results in an orad movement of the UES of 2.0–2.5 cm, the transducer is still in an area with exclusively or at least predominantly striated musculature, particularly because the transducer also moves upward, although to a lesser distance (13).

In vitro studies indicate that striated muscle contracts 10–50 times faster than smooth muscle, the latter reaching full contraction after 500 ms and the former after only 10–50 ms (10, 25). Therefore the dP/dt of striated muscle might be expected to be 10–50 times higher than that of smooth muscle, provided the

Fig. 4. Mean dP/dt ± SE in pharynx and esophagus. The dP/dt in the pharynx is 9 times higher than in the proximal and 13 times higher than in the distal esophagus (*P < 0.001).

Fig. 5. Correlation between dP/dt and amplitude in pharynx and proximal and distal esophagus. Slope of regression line for pharynx is significantly greater (P < 0.001) than that of proximal and distal esophagus, which are not different (P > 0.05).

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forces generated are within the same order of magnitude. This should be true, because the maximum strength of contraction per unit cross-sectional area developed by smooth muscle is equal to that of striated muscle (10, 25). Based on these facts, we hypothesized that the proximal, i.e., striated muscular esophagus, would have a higher dP/dt than the distal, smooth muscle esophagus. Although this was the case in our study, the difference between the two regions was small. The proximal esophageal dP/dt was only 1.4 times higher than the distal in the patients having normal motility studies and 1.5 times higher in the controls, both being much less than the expected factor of 10–50. There are two other reports in the literature that compared the proximal and distal esophageal dP/dt. Unlike our study, where amplitudes of distal and proximal esophagus were assessed relative to LES and UES, respectively, transducers in these studies were placed relative to the LES only, resulting in no defined position of the proximal transducer relative to the UES. Humphries and Castell (11), who assessed the esophagus in intervals of 2.5 cm, found no difference between proximal and distal esophageal dP/dt. Stef et al. (24), on the other hand, did find a higher dP/dt in the proximal esophagus. Assessed with water perfusion manometry, the dP/dt was 241 ± 19 (SE) mmHg/s in the proximal esophagus compared with 74 ± 3 and 85 ± 5 mmHg/s in the distal esophagus (24). However, the positioning of the catheter relative to the LES only might be a problem in this study, in which the most proximal recording site was placed at 21 cm above LES. Considering an average manometric length of the esophagus of 23 cm, with a range from 17 to 30 cm, it is possible that in some of the five subjects, this transducer was placed in the UES or pharynx, causing a falsely high dP/dt in the proximal esophagus (15).

One possible explanation for the absence of the expected difference of the dP/dt between proximal and distal esophagus is that the in vitro characteristics of muscle strips do not translate readily into the in vivo peristaltic contraction of the intact esophagus. A peristaltic contraction has two components, circular contraction, i.e., closure of the lumen, and propagation of the contraction wave. How much each of them contribute to the pressure profile is not known. In addition, any effect of longitudinal muscle contraction is also difficult to analyze. We assumed that circular contraction, i.e., shortening of the circular musculature, plays a much larger role than the propagation of the contraction wave. We also assumed that the biomechanical characteristics of muscle contraction translate into the pressure profile in the esophagus. This assumption is supported by studies in another hollow organ, the heart, which have shown the dP/dt in the ventricle to be a function of the velocity of myocardial contraction. Interventions increasing myocardial inotropy, such as exercise or the administration of norepinephrine, increase the dP/dt, and patients with myocardial disease have a low dP/dt (7, 16).

Our study is unique from others previously reported in that we also measured pressures in the pharynx, a purely striated muscle structure, in addition to those of the esophagus. The dP/dt of the pharynx was 9–10 times higher than that of the proximal and 13 times higher than that of the distal esophagus in the two study groups. This is within the order of magnitude by which striated and smooth muscle strips differ in their contraction velocities and therefore supports our assumption that muscle contraction properties translate into manometric parameters.

Because of the high interindividual variation of amplitudes and dP/dt, we calculated the correlation and regression characteristics between these two parameters to obtain a third parameter of muscle performance. There was good positive correlation between amplitude and dP/dt in the proximal and distal esophagus and in the pharynx in both study groups. The slopes of the proximal and distal esophagus were not significantly different. However, the slope of the pharynx was about 7 times steeper than that of the proximal and 10 times steeper than that of the distal esophagus.

According to our data, the proximal striated muscle of the esophagus behaves manometrically more like the distal smooth muscle of the esophagus than like the striated muscle of the pharynx. This relationship was found both in a small group of healthy controls and a larger group of patients having normal esophageal motility studies. Three reasons could account for this. First, the biomechanical properties of striated muscle of the proximal esophagus could be markedly different from striated musculature in the remainder of the body. Second, differences of the innervation of this type of muscle in the esophagus could result in slower contraction. Third, resistance to contraction and the geometry of lumen closure could differ between the three sites studied.

There are data indicating that striated muscle of esophageal origin contracts slower than striated muscle from extremities. Muscle strips of the former reach peak amplitude of contraction after about 75 ms compared with only 10–50 ms for skeletal striated muscle (5, 10). In the cat maximum shortening velocity of esophageal striated muscle is 50% less than that of soleus muscle. Similar results have been found in the rat and sheep (1, 6). Although these studies demonstrate that striated muscle of the esophagus contracts slower than ordinary striated muscle, the extent of this difference does not explain the 9- to 10-fold higher dP/dt of the pharynx compared with the proximal esophagus found in the present study.

The innervation of striated musculature of the esophagus has some characteristics that are unique. It is one of the few striated muscles that is not under voluntary control. It has, analogous to the smooth muscle of the gastrointestinal tract, a myenteric plexus situated between the longitudinal and circular muscle layer, the function of which is not clear. Like the striated musculature of the rest of the body, the muscle fibers of esophageal striated muscle have motor end plates innervated by lower motor neurons (9, 12). However, there are some morphological peculiarities pertaining to the innervation of this tissue. Unlike ordinary stri-
ated muscle, which is innervated by myelinated fibers, studies in the mouse and rat have found only unmyelinated nerve fibers innervating motor end plates of striated muscle of esophageal origin (9, 22). Because unmyelinated fibers have a slower conduction velocity than myelinated fibers, this may cause a delay of muscle contraction. However, because the intramural plexus is very short, this is not considered to be important (9). Esophageal striated muscle of guinea pigs has fewer motor end plates, with shallower and less branched clefts than those of striated muscle from extremities (27). A similar situation is found in the rat, where motor end plates of esophageal striated musculature are smaller compared with ordinary striated muscle. They also have morphological features, such as closeness of the terminal axones, which are reminiscent of not fully differentiated motor end plates found at the time of birth (9). The simpler structure of motor end plates of esophageal striated muscle may limit the speed of neuromuscular transmission. However, it is believed that the rate-limiting step in the velocity of contraction is confined to the rate of formation of cross bridges between actin and myosin and not to neuromuscular transmission (10, 27). A slower contraction velocity of striated muscle of esophageal origin may also result from a delay of electromechanical coupling. Latency periods after direct electrical stimulation of this type of muscle are about twice as long as those of the extensor digitorum longus muscle in the rat (1).

When the esophagus is studied in vivo, as opposed to isolated muscle preparations, factors other than only the contraction properties of the muscle in question determined our results. These include resistance to lumen closure by tissue and bolus as well as differences in the geometry of lumen closure. All of these could explain the lower proximal esophageal dP/dt compared with the pharynx, because there are marked anatomic differences between the two. However, they should not explain the similar dP/dt of proximal and distal esophagus, unless one would postulate that these factors only impede contraction in the proximal esophagus. The esophagus is a tubular organ composed of three layers (mucosa, submucosa, and muscularis propria) and is of similar structure throughout its whole length (20). The esophagus relaxes at the front of the bolus and contracts at its tail, thereby propelling the bolus (12). As it contracts against the tail of the bolus, it encounters some resistance. High bolus resistance would again have to occur only in the proximal esophagus to explain the dP/dt values found in our study. However, peristalsis is relatively homogeneous along the esophagus, and no data suggest that there is more resistance in the proximal esophagus (12). The same applies to differences of the geometry of lumen closure.

Our data confirm the presence of the well-established pressure trough in the middle esophagus (11, 19, 24), although noted in less than one-third of the subjects in both groups using the station manometric protocol in our study. Because it occurs at the region of the transition from striated to smooth muscle, it has been explained by the mixture of two muscle types. This assumption has been verified in the opossum, where it was shown that the trough in esophageal peristaltic activity is located within the histologically determined transition zone (14). Clouse and co-workers (2–4) recorded esophageal pressures at 1-cm intervals during swallows and generated surface plots (the 3 axes being time, position within esophagus, amplitude) and isobaric contour plots, which allow detailed analysis of the intraesophageal pressure profile. The presence of a pressure trough in the midesophagus was confirmed. The plots had different shape and peristaltic velocity between proximal and distal esophagus, suggesting differences in the neuromuscular properties of these regions. These findings underscore the duality of the esophageal muscular function, a duality that corresponds with the histology of the esophageal musculature. The neuromuscular organization of the esophagus might be even more complex.

In summary, our study indicates that striated muscle of the proximal esophagus contracts slower than expected. Although this is in agreement with data showing lower contraction velocity of muscle strips from the striated part of the esophagus and with morphological features likely to result in a less efficient neuromuscular transmission of this tissue, none of these factors is capable of explaining the extent of delay in contraction. We studied both a small group of healthy volunteers and a larger group of patients with normal esophageal motility studies. We measured the performance of the esophagus in vivo and therefore assessed the whole contraction apparatus, including biomechanical, neuromuscular, and tissue resistance factors. The results indicate that a decrease of contraction velocity distinguishes esophageal striated muscle from typical striated muscle and supports the previously expressed opinion that this type of tissue should be classified as a subtype of striated muscle, i.e., visceral striated muscle (27).

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