Pressure, Tension, and Force of Closure of the Human Lower Esophageal Sphincter and Esophagus

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ABSTRACT The mechanical characteristics of the circular muscle of the human lower esophageal sphincter and esophagus were studied in subjects with competent and incompetent sphincters. Pressure-diameter curves were constructed by producing various degrees of circumferential stretch with pressure-measuring probes of increasing diameter. The circumferential membrane tension (force of closure) and the circumferential stress (muscle tension) of the circular muscle layer were also calculated from these data.

The pressure-diameter curves of competent and incompetent sphincters were different in magnitude and shape. Incompetent sphincters had lower pressures at all diameters, with pressures gradually increasing with larger probe diameter. In contrast for competent sphincters the pressure was highest near closure, with an initial decline and then an increase in pressure with increasing probe diameter. Both shape and magnitude of pressure-diameter curves of competent and incompetent sphincters were interchangeable when manipulated by pharmacologic agents. Urecholine increased the pressures and changed the incompetent pressure-diameter curve to the levels of the competent sphincter; conversely, Pro-Banthine decreased pressures and changed the shape of the competent pressure-diameter curve to the levels of the incompetent sphincter.

Force of closure and circular muscle tension curves of competent and incompetent sphincters were similar in shape but were higher at all diameters for competent sphincters. Force of closure and circular muscle tension increased with larger probe diameter. However, the diameter of optimal tension development was larger than the largest probe used and certainly far from closure.

Fundoplication increased the magnitude and changed the shape of the incompetent pressure-diameter curve to one similar to a competent curve. This pressure change was associated with an increase in the force of closure, suggesting that fundoplication modified the length-force of closure characteristics of the incompetent sphincter.

INTRODUCTION

High resting pressure in the lower esophageal sphincter (LES)[1] is generated by tension developed in the circular smooth muscle. In man LES function has been studied by measuring sphincter pressure (1) and "sphincter strength" (2). No previous attempt has been made, however, to estimate the circumferential wall tension (force of closure) and the circumferential stress (muscle tension) in the circular muscle layer in the in vivo human esophagus and LES.

In the rat we have shown (3) that at closure high sphincter pressures in the LES are maintained by relatively low muscle tension. As the sphincter is stretched open by probes of increasing diameter, the pressure falls at first, despite higher tension developed in the muscle wall. Laplace's law explains these differences between pressure and tension characteristics; the pressure measured depends to a large extent on the diameter of the probe used and its ratio with LES wall thickness. In the present study we determined the influence of probe diameter on pressure and force of closure and estimated in vivo the tension developed by the human LES and esophageal circular muscle.

METHODS

14 normal volunteers and 22 patients with reflux esophagitis were studied. Informed written consent was obtained from all patients. Before inclusion in the study all subjects

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[1] *Abbreviations used in this paper:* LES, lower esophageal sphincter; P-D, pressure-diameter.

had a barium swallow, Bernstein test (4), esophagoscopy, esophageal biopsy (5), intraesophageal pH study (6), and a standard triple lumen esophageal manometry with a probe 0.5 cm in diameter (7, 8). The normal volunteers did not have any history or objective evidence of gastroesophageal reflux and had normal resting LES pressures of 19.0±5.9 mm Hg (competent sphincter). Patients with reflux esophagitis had heartburn and other symptoms of reflux for at least a 2-yr period and had objective evidence of esophagitis with abnormally low resting LES pressures of 8.5±2.0 mm Hg. Only patients with sphincter pressures less than 12 mm Hg (incompetent sphincter) were included.

Pressure-diameter (P-D) characteristics. The P-D characteristics of the LES were determined in 14 normal subjects and 19 patients with reflux esophagitis by introducing separately and randomly single motility catheters attached to a Plexiglas "olive" with a side opening (Fig. 1). Olives of 0.25, 0.5, 0.75, and 1.0 cm in diameter were used. The catheters were perfused with water at the rate of 1.25 ml/min (8). After recording stable gastric pressures, resting sphincter pressures were obtained with three complete pull-throughs, 0.5 cm at a time. Final resting sphincter pressures were means of maximal, stable, and reproducible (within a 3-mm Hg range) yield pressures of these three pull-throughs. The P-D characteristics were also determined in the esophagus in six normal volunteers and eight patients with reflux esophagitis. The amplitude of esophageal contractions was measured at 20–22, 30, and 38–40 cm from the incisors. Three swallows separated by 45-s intervals were recorded at each location.

In seven normal subjects the P-D characteristics of the LES were studied before and 10 min after intravenous administration of 15 mg of Pro-Banthine (G. D. Searle & Co., Chicago, Ill.), and pressure measurements were completed within 30 min. Preliminary studies had shown that the maximal effect of intravenous Pro-Banthine on sphincter pressure takes place within 10 min, and low sphincter pressures remain stable during the entire 30-min period of study. P-D characteristics were also studied in patients with sphincter incompetence: (*a*) In seven patients with sphincter incompetence before and after the subcutaneous administration of 5 mg of Urecholine (Merck & Co., Inc., Rahway, N. J.). Roling, Farrell, and Castell (9) have shown that maximal stimulated sphincter pressures are observed 20 min after the subcutaneous administration of Urecholine, and remain stable for a period of 30 min. Our pressure measurements were completed within this period of time. And (*b*) in five patients with sphincter incompetence before and 1 yr after a successful anterior fundoplication. A successful anterior fundoplication was determined by the complete symptomatic relief, adequate repair of the hiatus hernia, negative Bernstein test and esophagoscopy, and improvement of sphincter competence by manometry and pH probe (10).

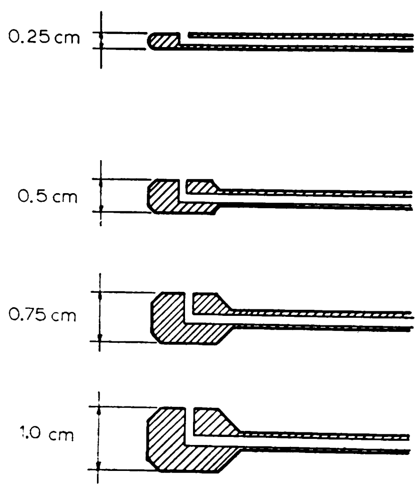

FIGURE 1 Motility catheters attached to a Plexiglas "olive" with a side opening used in the study of P-D curves of the circular muscle of the human LES and esophagus.

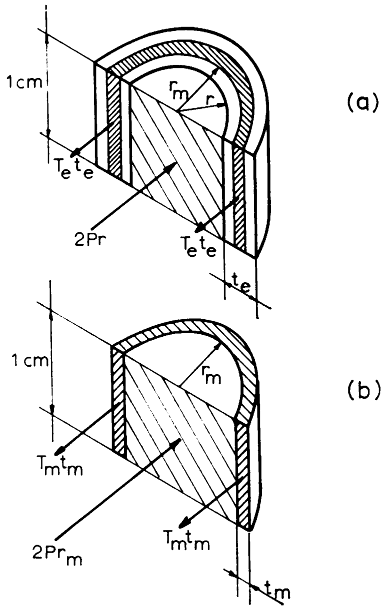

FIGURE 2 (*a*) Forces acting on an esophageal section of unit length. Force due to intraluminal pressure ($2Pr$) is equilibrated by the force of closure ($2T_e t_e$). (*b*) Forces acting on a section of circular muscle layer of unit length at equilibrium.

Force of closure. The force of closure is the membrane tension in the esophageal wall in the circumferential direction. This membrane tension, given in grams per centimeter, is equal to the force exerted by a circumferential strip of esophageal wall, 1 cm in width ($T_e t_e$ in Fig. 2*a*). The force of closure is measured directly by the product, Pr, of the measured intraluminal pressure, P, and the radius, r, of the pressure measuring probe (see Appendix *a*).

Circular muscle tension. The circular muscle tension, T_m, is the average circumferential stress in the circular muscle layer. This stress, given in grams per square centimeter, is the circumferential force per unit area of circular muscle (Fig. 2*b*). It is given by:

$$T_m = Pr_m/t_m, \qquad (1)$$

where P is the intraluminal pressure, r_m the inner radius of the circular muscle layer, and t_m its thickness (see Appendix *b*). Since the ratio r_m/t_m could not be measured in vivo, it was estimated from postmortem measurements of esophageal and LES dimensions.

Sphincter pressures are usually reported in millimeters Hg or centimeters H_2O and muscle tension in gram force per square centimeter. In this report, however, to express

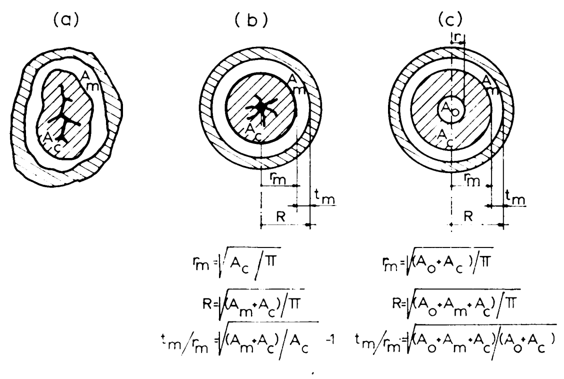

FIGURE 3 (*a*) Typical esophageal or LES cross section. (*b*) Thickness (t_m) and radius (r_m) of circular muscle are calculated from measurements of cross-sectional area by assuming the mucosa and muscle to be concentric circles. (*c*) The ratio t_m/r_m of muscle thickness and muscle inner radius in the presence of a probe can be determined by assuming that the cross-sectional areas of muscle and mucosa remain unchanged.

our results uniformly, we used grams per square centimeter for pressure and tension and grams per centimeter for force of closure. 1 $g/cm^2 = 1$ cm $H_2O = 0.74$ mm Hg.

Esophageal and LES dimensions. Six human esophageal sphincter specimens including 10 cm of esophagus and a stomach cuff were dissected at autopsy. The length of the esophageal portion was measured before resection. The specimens were mounted vertically on a stand with the esophagus stretched to its *in situ* length. The preparation was frozen by immersion in liquid nitrogen and subsequently several sections of the sphincter and esophagus were taken. The frozen sections were photographed and projected onto a screen ($10\times$ enlargement). The cross-sectional areas of mucosa and circular muscle were thus measured, and the radius and thickness of mucosa and circular muscle were calculated by assuming the cross sections to be concentric circles (Fig. 3; see Appendix *c*).

APPENDIX

The following nomenclature is used throughout: A_c, cross-sectional area of mucosa; A_m, cross-sectional area of circular muscle; A_o, cross-sectional area of olive; F, force of closure ($=T_e t_e$); P, intraluminal pressure; r, probe or lumen radius; r_m, inner radius of circular muscle; R, outer radius of circular muscle; t_e, thickness of esophageal wall; t_m, thickness of circular muscle; T_e, average esophageal wall tension; T_m, average circular muscle tension.

(*a*) *Force of closure.* The force of closure, F, defined as the circumferential force exerted by a unit length of esophagus can be obtained from the following equation:

$$F = T_e t_e = Pr. \tag{2}$$

Eq. 2 defines force of closure and can be derived as follows: consider a section of esophagus 1 cm long (Fig. 2a) and a longitudinal plane bisecting it. Let r be the inner radius and t_e the thickness of the esophageal strip so obtained. The force exerted by the intraluminal pressure acting on the inside surface equals the product of the pressure and the area of the axial plane dividing the esophagus ($P \times 2r \times 1$). This force is equilibrated by the circumferential tension in the esophageal wall. The resultant tension is the product of the average wall tension, T_e, and the area, $t_e \times 1$, of the two wall sections. At equilibrium the forces balance, thus:

$$2Pr = 2T_e t_e$$

or

$$Pr = T_e t_e = F.$$

The force, F, is thus also equal to the product of the measured pressure and the radius of the measuring probe (Pr). Using this equality we can estimate the force exerted by 1-cm wide esophageal strip, without any knowledge of the thickness of the esophageal wall.

(*b*) *Circular muscle tension.* A similar reasoning can be applied to the circular muscle layer. If we let P_m be the pressure exerted by the mucosa against the circular muscle, we write

$$P_m r_m = T_m t_m$$

or

$$T_m = P_m r_m / t_m. \tag{3}$$

Assuming that the pressure, P_m, between the mucosa and the circular muscle is the same as the intraluminal pressure, P, Eq. 3 and 1 are equivalent. T_m can be calculated from Eq. 1 if r_m and t_m are known. Depending on the position of the olive with respect to the point of respiratory reversal, sphincter pressures fall to abdominal or thoracic pressures in response to swallowing. Thus, it appears that in the range tested, sphincter pressure is generated entirely by circular muscle contraction with no contribution by the mucosa or adjacent structures. Furthermore, the inner perimeter of the mucosa in six sphincter frozen sections was found to be 4.2±0.5 cm (mean±SE), corresponding to a diameter of 1.3 cm. It would therefore require a 1.3-cm probe to distend the mucosa, a value which exceeds the largest probe diameter used. Contribution of the muscularis mucosa to sphincter closure and relaxation, if any, was neglected.

(*c*) *Changes in esophageal and LES dimensions with probe diameter.* The change in the ratio t_m/r_m due to the presence of olives in the LES and esophagus can readily be determined for each olive if we assume that the volume and length (and hence the cross-sectional area) of tissue remain unchanged during deformation. Incompressibility of tissue is characteristic of many biological materials (3, 11). It has been shown in Fig. 3 (top) of reference 3 that the cross-sectional areas of rat esophagus and LES calculated from experimental points remain constant when stretched by probes of various diameters. When an olive is introduced into the esophagus the area enclosed by the circular muscle equals the sum of the cross section areas of the mucosa and the olive (Fig. 3).

The ratio t_m/r_m can be written as:

$$\frac{t_m}{r_m} = \frac{R - r_m}{r_m} = \frac{R}{r_m} - 1, \tag{4}$$

and in terms of the areas:

$$\frac{t_m}{r_m} = \sqrt{\frac{A_o + A_c + A_m}{A_o + A_c}} - 1. \tag{5}$$

Using Eq. 5 we calculated the ratio t_m/r_m for the case of a collapsed lumen (no olive) and the four cases where olives of diameters 0.25, 0.5, 0.75, and 1.0 cm are placed in

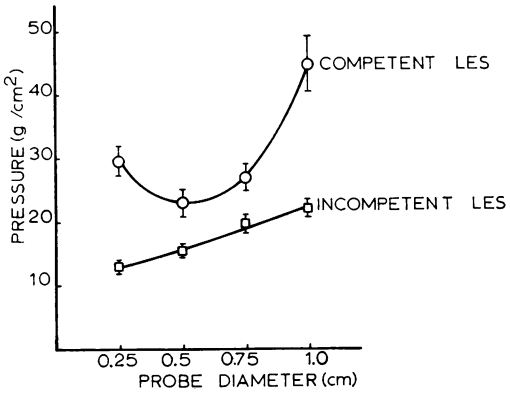

FIGURE 4 P-D curves of competent and incompetent LES. Values are means±SE. 1 g/cm² = 1 cm H_2O = 0.74 mm Hg.

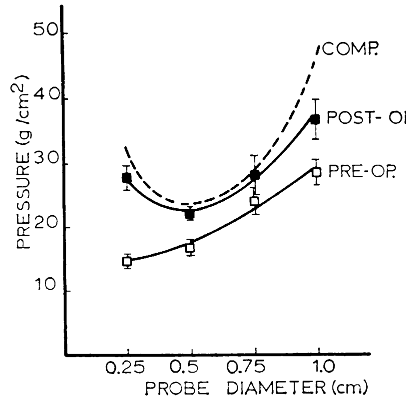

FIGURE 5 P-D curves of five patients with incompetent sphincters before and 1 yr after a successful fundoplication. The mean P-D curve of competent sphincter (broken line) is plotted for comparison. Values are means±SE. 1 g/cm² = 1 cm H_2O = 0.74 mm Hg.

the lumen. Areas A_o and A_m are obtained from frozen sections of normal esophagi taken from cadavers. Thus, the use of Eq. 5 to calculate t_m/r_m in healthy subjects and patients with reflux esophagitis neglects possible differences in mucosal volume and may affect the accuracy of the calculated circular muscle tension (Eq. 1). The force of closure, however, is independent of esophageal dimensions and is therefore used to compare competent and incompetent LES and to determine the effect of hiatus hernia repair on LES circular muscle function.

RESULTS

P-D characteristics of the LES. Fig. 4 shows that competent sphincters exhibit higher pressures (31.8±2.3 g/cm²) with olives 0.25 cm in diameter, with lower pressures (23.0±2.2 g/cm²) at 0.5 cm, and a gradual increase as the olive diameter increases to 0.75 and 1.0 cm (27.1±2.3 and 45.7±4.9 g/cm², respectively). Incompetent sphincters are characterized by lower pressures at all diameters studied. Mean sphincter pressures of 12.9±0.9 g/cm² observed at 0.25-cm diameter increased gradually to 14.7±1.1, 20.5±1.6, and 22.7±1.8 g/cm² with increasing diameter of the probe to 0.50, 0.75, and 1.0 cm, respectively. Sphincter pressures were significantly different ($P < 0.02$ to $P < 0.001$) when measured pressures of competent and incompetent sphincters were compared at various probe diameters. Measured pressures of competent sphincters were not different only with probes between 0.50 and 0.75 cm ($P > 0.05$).

Fundoplication changed the magnitude and shape of the P-D curves of the incompetent sphincter. As shown in Fig. 5, the P-D curves of the incompetent sphincters, performed in the same group of patients before and 1 yr after a successful fundoplication, changed to a curve similar in magnitude and shape to that of competent ones. The sphincter pressures increased at all diameters. Further, before fundoplication, the mean±SE of the absolute value of sphincter pressures during swallow was 3.4±0.7 below and 0.5±0.5 g/cm² above the point of respiratory reversal. These values remained unchanged after fundoplication (2.5±1.0 and 0.5±0.5 g/cm², respectively).

Effect of anticholinergic and cholinergic drugs on P-D curves. The effect of intravenous Pro-Banthine (15 mg) on P-D characteristics of competent sphincters is shown in Fig. 6*a*. Pro-Banthine changed the magnitude and shape of the curve, which became very similar to that observed in the incompetent sphincter. Conversely, 5 mg of subcutaneous Urecholine stimulated pressures of incompetent sphincters and the P-D curve became very similar in magnitude and shape to the curve of competent sphincters (Fig. 6*b*). However, stable and reproducible pressures could not be obtained with olives 1.0 cm in diameter since the olives could

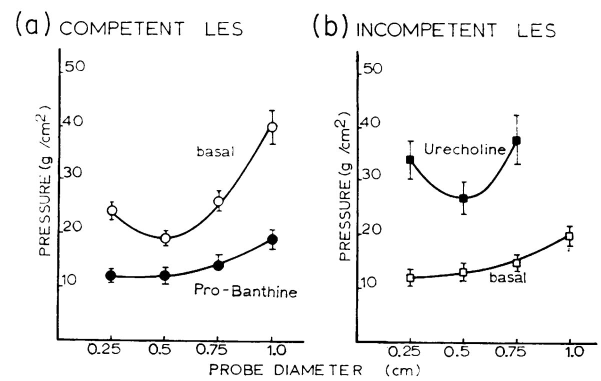

FIGURE 6 (*a*) P-D curves of competent sphincter (○) before and after the intravenous administration of 15 mg of Pro-Banthine. (*b*) P-D curves of incompetent sphincter (□) before and after the subcutaneous administration of 5 mg of Urecholine. Values are means±SE. 1 g/cm² = 1 cm H_2O = 0.74 mm Hg.

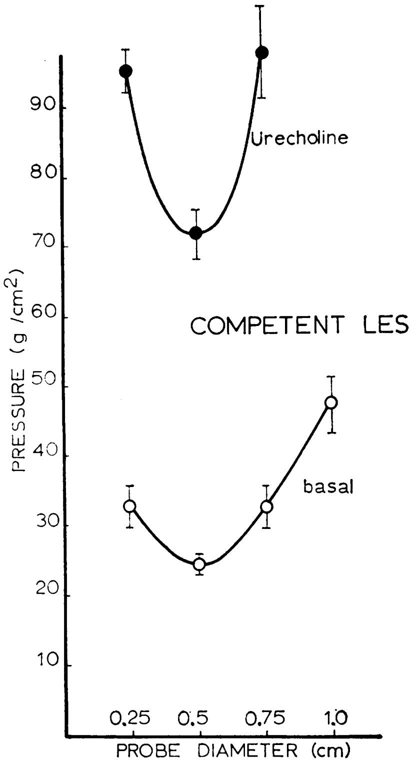

FIGURE 7 P-D curves of competent sphincter before and after subcutaneous administration of 5 mg of Urecholine. Values are means±SE. 1 g/cm² = 1 cm H_2O = 0.74 mm Hg.

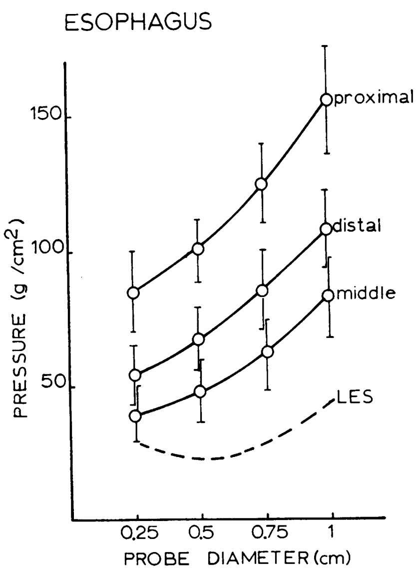

FIGURE 8 P-D curves of the esophagus. Peak esophageal pressures in response to swallows were measured at 20 cm (proximal), 30 cm (middle), and 40 cm (distal) from the incisors. Competent LES P-D curve is shown for comparison (broken line). Values are means±SE. 1 g/cm² = 1 cm H_2O = 0.74 mm Hg.

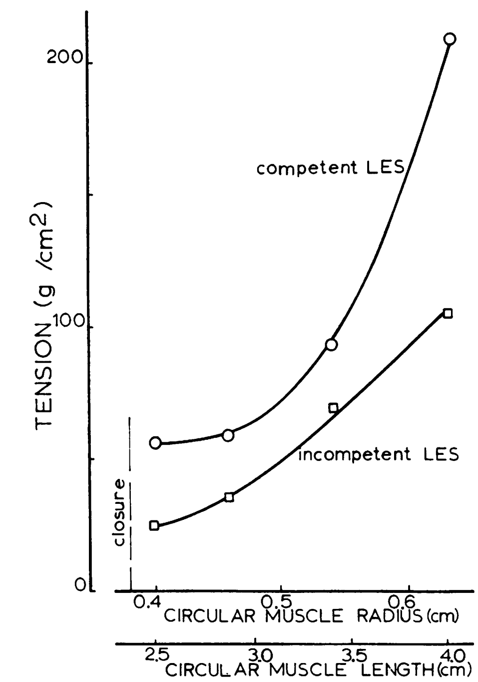

FIGURE 9 Length-tension characteristics of competent and incompetent LES. The tension was calculated from pressure measurements according to Eq. 1. The radius of the circular muscle was calculated for each probe, according to Fig. 3. Circular muscle length equals muscle radius times 2π. At closure the radius of the circular muscle is 0.38 cm as indicated by the broken lines.

not be held in place for a sufficient period of time. Furthermore, 5 mg of subcutaneous Urecholine also caused a threefold increase in sphincter pressures of four normal subjects with a competent sphincter (Fig. 7).

P-D characteristics of the esophagus. Peak esophageal pressures in response to swallowing increase with larger probe diameter. In the proximal esophagus (at 20 cm from the incisors) the pressures were highest. They were lowest in the mid-esophagus (at 30 cm). The pressures in the distal esophagus (at 40 cm) fell in between. No difference in the shape of the curves or in the amplitude of the esophageal contractions was observed in normal subjects and patients with reflux esophagitis. The curves shown in Fig. 8 are the mean pressures of both groups.

LES and esophageal circular muscle tension. The length-tension relationship of the circular muscle of competent and incompetent sphincters is shown in Fig. 9. As opposed to the P-D curves of the competent LES, tension increases continuously as the diameter increases for competent and incompetent sphincters. The tension of the circular muscle of the incompetent LES is of lower magnitude. Likewise, the tension of the circular muscle of the esophagus increases with larger probe

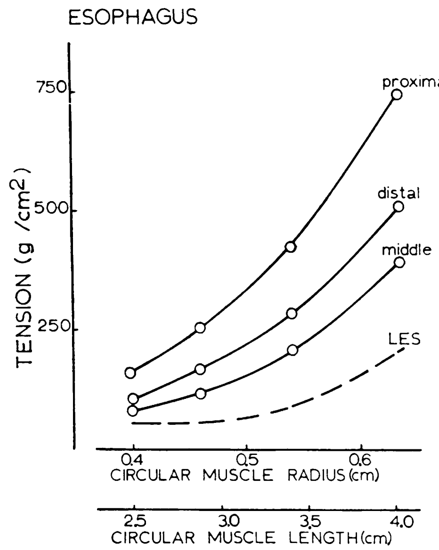

FIGURE 10 Length-tension curves produced by esophageal contractions in response to swallowing at three different levels in the esophagus. Tension is calculated according to Eq. 1 from the pressure data in Fig. 8. The length-tension curve of competent sphincters (broken line) is plotted for comparison.

diameter on all three levels, and as shown in Fig. 10 it was lowest in the mid-esophagus (at 30 cm). During swallowing the esophageal circular muscle generates over twice the LES tension, even in the mid-esophagus.

LES force of closure. Circular muscle tension and force of closure of competent and incompetent sphincters are shown in Fig. 11. Force and tension curves are quite similar in each type of sphincter, although the scales for tension and force of closure are dimensionally

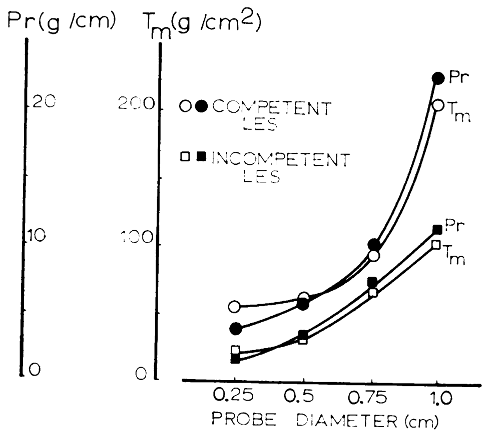

FIGURE 11 Comparison of circular muscle tension, T_m, and force of closure, *Pr*, for competent and incompetent LES. The muscle tension expressed in grams per square centimeter is approximately 10 times larger than the force of closure expressed in grams per centimeter for all diameters larger than 0.4 cm.

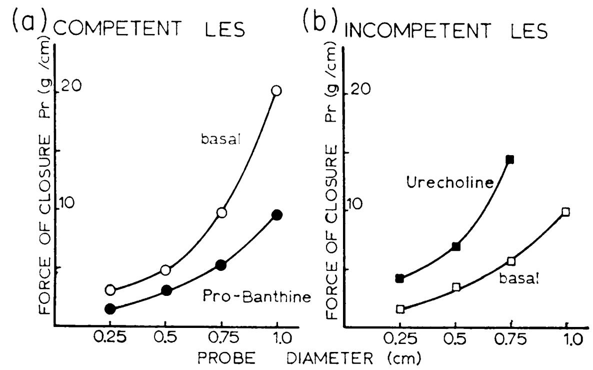

FIGURE 12 Force of closure of competent and incompetent LES. Pro-Banthine reduces the force of closure of competent LES; Urecholine increases the force of closure of incompetent LES.

and numerically different. The tension can be approximated by multiplying the force of closure by a dimensional factor of 10 cm^{-1}. Force of closure of competent and incompetent sphincters also increases with increasing probe diameter. Pro-Banthine markedly reduced the force of closure of competent sphincters (Fig. 12*a*) whereas Urecholine increased the force of closure of incompetent sphincters (Fig. 12*b*). Force of closure was also increased by fundoplication. The force of closure-diameter relationship was shifted to the left by fundoplication (Fig. 13).

DISCUSSION

Competent and incompetent sphincters have distinctly different P-D characteristics. As the diameter decreases and the sphincter approaches closure conditions, the pressure increases in the competent and decreases in the incompetent sphincter. Thus, commonly used motility catheters, which are frequently around 0.5 cm in

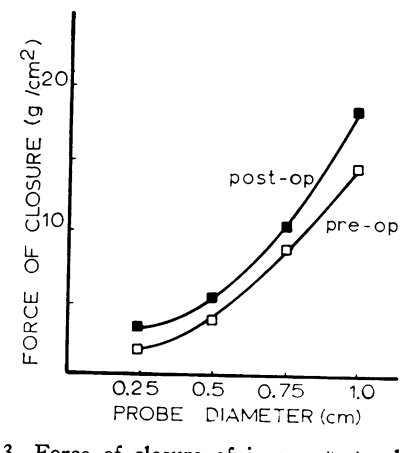

FIGURE 13 Force of closure of incompetent sphincters before and 1 yr after a successful fundoplication. Values are means.

diameter (7), will underestimate closure pressures of competent sphincters and overestimate those of incompetent ones. Since at this diameter the difference in pressure between both sphincters is relatively small, this could in part explain the pressure overlap sometimes found between patients with reflux esophagitis and normal subjects (12, 13). The fall in pressure in competent sphincters as the lumen is stretched open may also explain the observation that gastric intubation renders the sphincter incompetent and induces gastroesophageal reflux (14, 15).

In contrast to the P-D curves, competent and incompetent sphincters have similar force of closure and tension characteristics. The force of closure and tension increase with increasing probe diameter, but have lower magnitude for incompetent sphincters. Because force of closure and tension continue to increase within the range tested, the diameter of optimum tension development is larger than 1 cm and far from closure. These observations are in complete agreement with the data obtained in the rat LES (3).

Since force of closure is given by the product of intraluminal pressure and radius of the manometric probe (Pr), it can be measured without knowledge of muscle and mucosal thickness, which could vary in different experimental conditions. Thus, force of closure could be used in the study of the mechanisms whereby fundoplication increases resting sphincter pressures (10). Fundoplication changed the shape of the P-D curve of incompetent sphincters and increased their force of closure. The increase in force of closure was due to a shift of the force of closure-diameter relationship to the left. After fundoplication the force of closure measured at 0.25 cm in diameter was the same as the force of closure at 0.50 cm diameter in the preoperative, incompetent sphincter. This shift in force of closure could result from shortening of the circular muscle layer as the fundus is sewn on the wall of the esophagus (16).

The relation between intraluminal pressures and circular muscle tension is given in Eq. 1. Intraluminal pressure equals the product of the average muscle tension (T_m) and the ratio of circular muscle thickness (t_m) and inner radius of the circular muscle layer (r_m). The ratio t_m/r_m increases rapidly with decreasing diameter as closure is approached. Since the length-tension curve of the competent sphincter becomes almost flat as closure is approached, the increase in t_m/r_m ratio is sufficient to offset the slight decrease in tension. Thus, for the competent sphincter pressure increases near closure.

In the rat LES (3) or in the human competent LES, the tension curves become flat at very small diameter. The rat LES is capable of developing active tension when its diameter is reduced to 15% of the diameter of optimal tension development, indicating that, in a limited range near closure, tension is somewhat independent of intraluminal diameter. We suggest that the ability to develop a relatively constant tension at very small diameter characterizes the normal LES circular muscle, whose function is to keep the lumen collapsed. A similar behavior has been used by Burton (17) to explain the existence of a "critical closing pressure" in small blood vessels. Other smooth muscles can develop tension at very short length, such as the trachealis muscle of the dog, which can develop tension when shortened by 87% of the length of optimal tension development (18).

The factors that determine the P-D curve of the incompetent sphincter, however, are not entirely clear. If the t_m/r_m ratio is the same as for the competent sphincter, the flatness of the P-D curve may be caused by a more rapid fall in tension as closure is approached. Since the t_m/r_m ratio was measured in the postmortem specimens taken from normal esophagi, it is possible that incompetent sphincters may have a lower t_m/r_m ratio near closure. An increase in radius due to mucosal edema as well as a decrease in the thickness of the muscle layer could lower the ratio.

In the esophagus, although the t_m/r_m ratio is similar to that of the sphincter and the peak tension in response to swallowing is much higher than the resting tension of the competent sphincter, pressure decreases near closure. A rapid fall in circular muscle tension as closure is approached, similar to that observed with the incompetent sphincter, may not be offset by the increase in the t_m/r_m ratio, and thus, pressures fall despite high peak tension during esophageal contraction.

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