Mechanical properties in the human gastric antrum using B-mode ultrasonography and antral distension

H. GREGERSEN,1 O. H. GILJA,2 T. HAUSKEN,2 A. HEIMDAL,2 C. GAO,1 K. MATRE,2 S. ØDEGAARD,2 AND A. BERSTAD2
1Department of Gastrointestinal Surgery, Aalborg Hospital, DK-9100; and Center for Sensory-Motor Interaction, Aalborg University, DK-9220 Aalborg, Denmark; 2Institute of Medicine, Haukeland University Hospital, 5021 Bergen; and 3Department of Informatics, University of Oslo, 0316 Oslo, Norway

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The function of the gastric antrum is to a large extent based on mechanical properties. Contents received from the corpus of the stomach are propelled through the pylorus into the proximal part of the small intestine, where the content is further digested. Methods traditionally used for clinical or basic investigations of the antrum are endoscopy, manometry, and radiographic examinations (4, 26–28). Although these methods provide important data on antral motor function and gastric emptying, little attention has been paid to the biomechanical properties of the wall and to determination of the wall stress. During recent years, there has been more interest in studying gastrointestinal physiology with ultrasound and in clinical evaluation of the stomach.

Transabdominal ultrasonography is a noninvasive and safe method that has proven applicable in the study of antral motility in patients with functional dyspepsia (3, 21). Two-dimensional (2D) ultrasonography has been used to assess gastric emptying (3, 6). Furthermore, Hausken et al. (22–24) have used Doppler for the study of gastroduodenal flow and Gilja et al. developed 2D and three-dimensional ultrasonographic methods to study accommodation of the proximal stomach (10, 11, 13) and gastric volumes (9, 12, 14, 25). Moreover, Ahluwalia et al. (1, 2) evaluated the post-prandial changes in antrum circumference by using ultrasound in volunteers and patients with dyspepsia. Despite these developments and the fact that the mechanical wall properties are important for normal function of the antrum, the biomechanical properties of the antrum in vivo are still largely unknown. In this study, we intended to gain a better understanding of antral biomechanical function.

In distensible biological tubes, the circumferential wall stress is of principal interest because the tensile stress is largest in that direction during distension (18). There are several reasons for studying the stresses and strains in intact hollow organs: 1) wall stress and strain data give valuable information on the elastic properties (8, 18), 2) mechanoreceptors do not respond directly to changes in pressure or volume but rather to changes in stress or strain (18), 3) it is important to differentiate active properties such as phasic contractions and smooth muscle tone from passive tissue properties in pharmacological and biomechanical studies (16, 17), and 4) intact organs maintain normal geometry in contrast to the tissue strips often used for length-tension measurements in physiological and pharmacological studies (7, 18).
In this study, we aimed to develop a new method for investigation of the biomechanical properties, including active and passive wall stresses, in the human antrum in vivo. The method is based on distension of a bag placed in the antral lumen with concomitant measurement of the distension pressure and the antral geometry in a selected cross-sectional plane by means of transabdominal real-time B-mode ultrasound.

MATERIALS AND METHODS

Seven normal volunteers (3 females, 4 males) were included in the study. The age, weight, and height ranges were 22–28 yr, 54–77 kg, and 163–181 cm, respectively. The volunteers did not take any drugs and did not suffer from illnesses or abuse of alcohol. The regional ethics committee approved the study protocol, and the experiments were conducted in accordance with the revised Declaration of Helsinki. All volunteers were asked to give a written, informed consent to participate in the trial.

Probe design and equipment. A specially designed distension probe was constructed. The probe was 120 cm long and contained a 30-μm-thick polyester urethane bag 10 cm from the tip of the probe. The cylindrical bag was 5 cm long and could be inflated with fluid through an infusion channel of 3.5 mm to a diameter of 40 mm without stretching the bag wall. The size of the bag was chosen on the basis of previous experience from ultrasonographic studies of the antrum (25). The probe contained a metal clip in the middle of the bag as a marker for ultrasound. Two side holes for pressure measurements were placed in the middle of the bag and 2 cm proximal to the bag. The lumens and side holes both had diameters of 0.5 mm. The perfusion rate for the pressure channels was 0.1 ml/min. The pressure was measured by a low-compliance perfusion system connected to external channels was 0.1 ml/min. The pressure was measured by a low-compliance perfusion system connected to external transducers (Medex). The pressure data were amplified and analog-to-digital converted at a sampling rate of 10 Hz by using a motility data acquisition system from Gatehouse (Nørresundby, Denmark). The digitized data were stored on a PC for later analysis.

The ultrasound equipment for 2D scanning of the antrum was a digital sector scanner (System Five; GE Vingmed Ultrasound, Horten, Norway) with a 5- to 8-MHz linear array transducer. The resolution in the focus point was for 5.0 focused linear array (FLA) (axial, 0.4 mm; lateral, 0.6 mm; slice thickness, 1.4 mm). This system allowed measurement of the cross-sectional area (CSA) of the antrum during resting conditions and distension.

Experimental procedure. The volunteers were scanned after an overnight fast and were sitting in a chair, leaning slightly backwards. The probe was passed into the stomach via the nostrils after calibration of the pressure-measuring system. The ultrasound transducer was placed in the epigastrium. The depth of scanning was 4–8 cm during the experiments. The positioning of the probe was guided by ultrasound imaging, and the middle of the bag was placed ~3 cm proximal to the pylorus. The zero pressure level for the distension series was determined.

The distension protocol was performed as a volume-controlled series. The distensions were started in antral phase 1 or early phase 2. The fluid volume of the bag was changed intermittently, with volumes ranging from 5 to 60 ml for 1-min periods, by using a hand-held syringe. The stepwise volume infusions were done at an infusion rate of 10 ml/sec. The distensions were separated by 2-min resting periods, i.e., the volume was withdrawn from the bag and the bag pressure was kept slightly negative during these periods to ensure complete emptying of the bag. During this period, the subjects were asked to report any visceral perception resulting from the previous distension. The ascending method of limits is vulnerable to psychological bias in sensory assessment (33), and it is important to obtain reproducibility data for the mechanical measurements. Therefore, we used a pseudorandom sequence with lower-intensity stimuli interspersed within the ascending volumes, i.e., the volumes of 10 and 30 ml were infused twice to study reproducibility. An ultrasonographic image was obtained when a steady state was reached after 1 min of distension, and a mark was inserted in the file containing the pressure data. Thus the pressure could be evaluated at the same point in time. All selected ultrasound images were scanned in expiration, and standardized image sequences were frozen before digital storage. A mark on the skin as well as the localization of the metal marker on the probe ensured that the same section was scanned each time. One-minute distension periods were chosen from previous experiments, demonstrating that steady-state CSA would always be obtained within this period. In three volunteers, another distension series was performed after administration of 20 mg butylscopolamine intravenously. The drug administration was repeated after 15 min to ensure continuous smooth muscle relaxation. None of the volunteers experienced side effects such as double vision due to the anticholinergic action of the drug. The total investigation time never exceeded 3 h.

Data collection and analysis. The collection of personal data was performed by interview and recorded onto a registration form. Furthermore, the volunteers were asked to report any symptom that arose during the experiments.

Analyses of the pressure recordings were done by means of computer software (Openlab version 2.11; Gatehouse).

In most cases, five layers of the gastric wall could be visualized in the anterior part of the antrum. The thickness of the wall was defined as the radial distance from serosa to the inner hypoechoic layer, representing the mucosa. The balloon wall usually did not appear on the images. All selected ultrasound images were frozen before digital storage on the scanner and transferred to a PC workstation. A designated software package (EchoPAC-3D; GE Vingmed Ultrasound) installed on a separate workstation equipped with Windows NT 4.0 software was used for measurement of gastric sizes. The tracing algorithm was previously evaluated and demonstrated good agreement as well as low intra- and interobserver errors (12, 14, 25). The inner echogenic layer of the stomach, corresponding to the interface between the bag and the mucosa of the gastric wall, was outlined. Then, the major and the minor diameters of the antral lumen were measured. Ultrasound images were acquired in a sagittal section of the antrum, in the region where the aorta and the mesenteric vein were visualized. The thickness of the wall was estimated three times, and the mean value was recorded.

The steady-state pressure, diameters, CSA, and wall thickness values at each volume distension step were used for the computation of stretch ratios, strain, and wall stress.

The circumferential strain ad modum Cauchy was computed as the fractional change in radius

$$
\varepsilon = \frac{r - r_0}{r_0}
$$

where r is the hydraulic midwall radius at a given distension, i.e., the average of the minor and major radii; r_0 is the reference radius determined for each subject as the radius at stress = 0 by using linear regression in a radius-stress plot.
The stretch ratio \( \lambda \) was determined for the circumferential (\( \theta \)), radial (\( r \)), and longitudinal (\( z \)) directions. The stretch ratio is defined as the length at loaded conditions (\( L \)) divided by a reference length at unloaded conditions (\( L_0 \)), i.e., \( \lambda = L/L_0 \). For circumferential and radial directions, the stretch ratios could be determined from the experiments by using the same principle as for the strain calculation. The stretch ratio in longitudinal direction \( \lambda_z \) was determined from knowing the two other stretch ratios and using the incompressibility assumption, i.e., \( \lambda_\theta \lambda_r \lambda_z = 1 \) (8, 18).

The circumferential wall stress \( \sigma_\theta \) was computed according to Laplace’s law for circular pressure vessels as

\[
\sigma_\theta = \frac{\Delta P r}{h} \quad (2)
\]

This stress is also called the Cauchy stress or hoop stress, \( \Delta P \) is the transmural pressure (antrum pressure minus abdominal pressure), and \( h \) is the wall thickness. The bag pressure at the lowest volume was assumed equal to the resting pressure of the antrum, i.e., the intra-abdominal pressure. Hence, the transmural pressure during distension was considered to be equal to the difference between the bag pressure and the resting pressure; \( r \) is the hydraulic radius of the antrum. The circumferential stress was plotted as the function of the circumferential stretch ratio. To test whether the curves followed an exponential form, the data were fitted to the function given by Fung (8)

\[
\tau = (\tau^0 + \beta) e^{\alpha(\varepsilon - \varepsilon^*)} - \beta
\]

and the \( \alpha \) and \( \beta \) constants as well as the regression coefficient were derived. The starred quantities denote a reference stress and strain in the physiological range.

The wall stress was decomposed into active and passive components. The total wall stress (\( \sigma_{\text{total}} \)) reflects both active and passive tissue properties and was determined from the distension test without the administration of butylscopolamine. The readings were done when phasic contractions were not present. The passive stress (\( \sigma_{\text{passive}} \)) only results from passive components such as the extracellular collagen and was obtained from the test done during butylscopolamine. The active stress (\( \sigma_{\text{active}} \)) contributed by tonic smooth muscle activity was computed by using the equation

\[
\sigma_{\text{total}} = \sigma_{\text{active}} + \sigma_{\text{passive}}
\]

These wall stresses were plotted as a function of the distending volume to represent an in vivo smooth muscle length-tension diagram similar to the well-known length-tension diagram obtained from muscle strips in vitro (7, 8).

**Statistical analysis.** The results are expressed as means \( \pm \) SE. Analysis of variance was used to evaluate the variation of the various parameters as function of the distension volume and to compare the values obtained in the distension during or without the administration of butylscopolamine. Differences were considered significant if \( P < 0.05 \).

**RESULTS**

The introduction of the probe did not cause any significant discomfort to the volunteers. Stepwise volume inflation of the bag resulted in a consistent mechanical response. The distensions induced phasic contractions in the antrum but seemed not to alter the antral phase between the distensions. The frequency and pressure amplitude of the evoked contractions are given in Fig. 1. The induced contractions propagated in distal directions. Phasic contractions were not observed on the pressure recording or on the ultrasonographic images during the administration of butylscopolamine. Figure 2 shows a B-mode image during distension. The selected range of distensions did not cause significant symptoms or discomfort. Sensation of fullness was the symptom most often reported. Pain was only infrequently reported and not in a consistent way (only in two volunteers at a few distension steps).

The pressure and morphometric data in terms of CSAs, wall thickness, and diameters are shown as functions of the distension volume without administration of butylscopolamine in Fig. 3. The pressure increased significantly as function of volume [Fig. 3A; variance ratio (\( F \) = 8.77, \( P < 0.001 \)]. The pressure increase was relatively minor until a volume of 45 ml. The CSA increased (Fig. 3B; \( F = 20.97, P < 0.001 \)), and the wall thickness decreased (Fig. 3C; \( F = 2.99, P < 0.01 \)) as a function of bag volume. Figure 3B shows the CSA as measured directly on the ultrasound monitor. The CSA could also be calculated from the major and minor diameters assuming an ellipsoidal geometry. The measured CSA was 5–10% larger than the calculated CSA, indicating a small deviation from the ellipsoidal shape. The major and minor diameters increased as a function of volume (Fig. 3D; \( F = 7.45, P < 0.001 \) and \( F = 16.96, P < 0.001 \)). The ratio between the major and minor diameters was \( \approx 1.5 \) at low volumes and decreased to 1.2 at the highest volumes (Fig. 3E; \( F = 3.78, P < 0.001 \)). The bag pressure and the morphometric measures (diameters, CSA, and thickness), were reproducible, i.e., when a volume step was repeated in the pseudorandom sequence, there was no
stress was plotted as functions of the distending volume (Fig. 5). The passive and total stresses were exponential-like, whereas the active stress reached a maximum at 50-ml volume, corresponding to a stretch ratio of ~1.5 (the optimum length for muscle force generation). Hence, it was possible to reproduce the well-known length-tension diagram from in vitro studies of gastrointestinal smooth muscle strips. However, it must be emphasized that the active stress in this study is not under maximally stimulated conditions, as usually done in muscle strip studies. Rather, it represents a tonic state of the antral smooth muscle. The active stress during phasic contractions was up to 12 times higher than the stresses observed during tonic contractions.

**DISCUSSION**

**Methodological aspects.** Only a few methods exist for determination of the mechanical properties in the gastrointestinal tract in vivo. In a cylinder-shaped organ, such as the gastric antrum, where the largest tensile (hoop) stress is in the circumferential direction, it is important to determine stress-strain properties in selected cross-sectional planes. Several reasons for studying stresses and strains are provided in the introduction. In addition, it has been found in other tissues, such as in the cardiovascular system, that tissue growth is stress dependent (Fung’s stress-growth law) and that the baroreceptors depend on strains (the deformation in the vicinity of the receptors) (8). It is likely that stresses and strains regulate similar physiological functions in the gastrointestinal tract.

Pressure-volume measurements have been used extensively for distension purposes in the gastrointestinal tract but suffer from errors up to 30% due to elongation of the bag (15). The error caused by bag elongation was overcome by the impedance planimetric method that provides measures of pressure and bag CSA during distension. Impedance planimetry has been successful for determination of smooth muscle tone and tension-strain relations in various parts of the human gastrointestinal tract (16, 19, 20). However, the impedance planimetric method seems never to have been used in the antrum. Furthermore, in biomechanical studies it is more useful to compute wall stress than tension and to derive material constants from the stress-strain data. The wall thickness of the organ must be known to compute stress rather than tension (8). It is likely that stresses and strains regulate similar physiological functions in the gastrointestinal tract.

The real-time B-mode ultrasonography principle is well known and used daily in clinical work. Ultrasound
of the gastric antrum is widely applied to study gastric emptying, configuration, and contractility. Possible sources of error related to the specific protocol in this study were dislocation of the scanned plane in relation to the bag. To ensure that recordings were done at the middle location on the bag each time, we inserted a metal clip on the probe that would give a reflection in the image. We were also careful to locate the scanning head at the same epigastric location each time and with the same orientation of the scan plane.

The combined manometric and ultrasonographic technique made the derivation of several biomechanical parameters possible from the measurements of pressure, diameters, CSA, and wall thickness. Since ultrasound provides a valid measure of organ geometry, including the radius and the wall thickness, it is, with a few assumptions, the basis for measurement of the circumferential wall stress according to Laplace’s law. The estimation is valid only at a constant transmural pressure and at equilibrium. Furthermore, a circular lumen must be assumed, although it is seldom encountered in biological systems, and the antrum wall must be in close contact with the bag wall. The ultrasonographic investigations demonstrated that contact with the wall was achieved during distension. The lumen was elliptical, with a major-to-minor diameter ratio of 1.5 at small volumes and 1.2 at large volumes. Therefore, it must be emphasized that the stress is an average stress (computed from the hydraulic radius) and that small variation can occur along the circum-

Fig. 3. Bag pressure (A) and morphometric (B–F) data from the human antrum. Cross-sectional area (CSA) measured directly from the ultrasound image (B), wall thickness (C), minor (min) and major (max) diameters (D), and ratio between the diameters (E) are illustrated as a function of volume. All data in A–E were obtained without administration of butylscopolamine. F: CSA measured directly from the ultrasound image as a function of volume both without and during administration of butylscopolamine. CSA was largest during administration of butylscopolamine [variance ratio ($F$) = 15.13, $P < 0.001$]. Means ± SE are shown.
ference. Due to the initial zero setting of the pressure recording, it was assumed that the balloon pressure was equal to the transmural pressure. This assumption seemed reasonable considering the anatomic relations of the antrum in the abdominal cavity. The strain measurement was considered valid due to the ease of determining the inner and outer dimensions of antrum during distension. The reference for the strain measurement was also considered valid since the antrum was not collapsed when the transmural pressure was zero, as found in this and other studies (21, 25).

Physiological and biomechanical aspects. Besides providing numerous geometric and morphometric data on the antrum with the combined distension and ultrasonographic techniques, the major findings in this study were that 1) the circumferential stress-strain curves exhibited an exponential behavior, 2) the active and passive tissue behavior could be differentiated by using the antimuscarinic drug butylscopolamine, and 3) the smooth muscle cells at the site of distension exhibited tonic as well as phasic contractions.

When the gastrointestinal tract is pressurized, it is subjected to distension in all directions. The major tensile stress during distension is in the circumferential direction (18). It is well known that the passive elastic behavior of the gastrointestinal tract and other visceral organs is nonlinear and that the deformation is large (5, 8, 18). The stress-strain curve in Fig. 5 shows for the first time that the passive elastic behavior of antrum in vivo is also exponential. The exponential behavior protects the tissue against overdistension and damage at high luminal pressure loads while distending easily and facilitating flow in the physiological pressure range.

The administration of the antimuscarinic drug butylscopolamine allowed us to investigate active and passive tissue behavior, though we cannot be sure that butylscopolamine in the doses administered fully relaxed the smooth muscle in this in vivo study. Furthermore, a noncholinergic component contributing to the tone in the antrum may exist. It was clear from the data that phasic as well as tonic muscle contractions were elicited in response to the distension. Both types of contractions seem to be mediated, at least in part, by the muscarinic pathways since butylscopolamine abolished the phasic contractions and increased the luminal CSA. The antral CSA values obtained before and during administration of butylscopolamine were significantly different, i.e., the antrum was larger during butylscopolamine administration. Because the antrum is a reasonably uniform cylinder in the portion we studied, essentially a deformable tube, it makes geometric sense to define tone as a sustained active stress tending to produce strain that leads to a reduction in luminal CSA and circumference or surface area (17). This stress represents the activation of the smooth muscle in the walls of the cylinder. This definition is in accordance with the definition of tone in urological and cardiovascular physiology. The distension protocol can be considered isometric in the sense that the bag vol-

Fig. 4. Biomechanical data. A: stretch ratios in circumferential, radial, and longitudinal directions as a function of volume. The former two were obtained from direct measurements, whereas the longitudinal stretch ratio was computed from the other stretch ratios assuming incompressibility. Means ± SE are shown. B: wall thickness-to-radius ratio as a function of volume. The sum of the minor (r) and major (R) radii is used in the plot. C: circumferential stress-strain relation obtained without and with the administration of butylscopolamine.

Fig. 5. The stress-volume diagram in which stress is decomposed into total, active, and passive components. See text for computation of stress. It is clearly shown that the active stress reaches a maximum after the force generation but decreases again. Means ± SE are shown.
volume was controlled in a stepwise manner. The length-tension test reproduced the well-known length-tension diagrams obtained in smooth muscle strips from various organs (7, 29, 31). The strip model has been used extensively in physiology and pharmacology research. The model proposed in this study has the advantage that it is performed under in vivo conditions and with preserved organ geometry. The shape of the active component of the stress-strain curve showed a maximum stress development followed by a decline with further stretch. The maximum active stress appeared at a volume of 50 ml, corresponding to a stretch ratio of 1.45. The maximum active stress is presumably reached at a level of optimum overlap between the sliding filaments in the smooth muscles. At strains above the maximum active stress, the tissue elastic behavior is determined mainly by the passive tissue properties, whereas at low strains, i.e., in the physiological range, the active stress also contributes significantly to the tissue behavior, facilitating bolus transport. Thus the distensibility in vivo depends not only on the passive properties but also on the physiological state of the smooth muscle. However, the method may be further developed, e.g., to incorporate the stress development during phasic contractions and the muscle properties in the longitudinal direction. Furthermore, other parts of the gastrointestinal tract such as the pylorus should be studied in the same manner due to the coordinated regulation of the function of the antropyloric region during gastric emptying.

Conclusions and future clinical applications. It was possible to reproduce the length-tension diagram known from muscle strip studies. Administration of drugs such as butylscopolamine provided a simple method for differentiation between passive and active tensions of the antrum in vivo. The new test may have applications in testing the effects of drugs on gastrointestinal motor function.

The present study attracts attention in relation to patients with gastroparesis, diabetic autonomic neuropathy, and functional dyspepsia in whom gastric motor disturbances have been detected. Although the volume distensions in this study were too small to elicit significant symptoms in healthy controls, the distension volumes could have been sufficient to induce symptoms in dyspeptic patients. On this background, there is an obvious need to carry out research to enhance our understanding of the pathophysiology underlying the symptom induction in dyspeptic patients.

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