Measuring esophageal distension by high-frequency intraluminal ultrasound probe

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Received 18 March 2002; accepted in final form 24 June 2002

Rhee, Poong-Lyul, Jiaimin Liu, James L. Puckett, and Ravinder K. Mittal. Measuring esophageal distension by high-frequency intraluminal ultrasound probe. Am J Physiol Gastrointest Liver Physiol 283: G886–G892, 2002; 10.1152/ajpgi.00107.2002.—Distension of the esophagus can cause heartburn and chest pain; however, none of the available techniques to study the esophagus measure esophageal distension. We evaluated the technique of high-frequency intraluminal ultrasound probe (HFIUS) to measure the esophageal cross-sectional area (CSA) during gastroesophageal reflux (GER). The following methods were used: 1) the CSA of agarose gel tubes of known dimensions were measured using ultrasound probes; 2) seven normal subjects were studied to evaluate the esophageal CSA during different bolus volumes (1, 5, 10, 15, and 20 ml) of water swallows (WS); and 3) simultaneous pressures, pH, and ultrasound images of the esophagus were recorded in healthy subjects. In vitro studies showed that the HFIUS measured the CSA of the tubes accurately. The maximal CSA of the distal esophagus during WS with boluses of 1, 5, 10, 15, and 20 ml were 54, 101, 175, 235, and 246 mm², respectively. Esophageal contents during 62 episodes of transient lower esophageal sphincter relaxations, 29 pH positive, and 33 pH negative GER episodes revealed that reflux of air into the esophagus occurred more frequently than liquid. The median CSA and estimated diameter of the esophagus during liquid GER was 44.1 mm² and 7.5 mm, respectively. We conclude that HFIUS is a valid technique to measure the CSA of the esophagus in vitro. We then assessed distension of the esophagus during swallows of liquid bolus and during spontaneous GER in normal healthy subjects.

METHODS

HFIUS Technique to Measure the CSA (In Vitro Studies)

We constructed tubes of different diameters (D) from agarose gel. These tubes were filled with water, and the HFIUS probe was placed inside the tube for measurement of the luminal CSA. The ultrasound (US) probe was placed vertically in the center and then at an off-center position in the tube (D = 15.6 mm). We also imaged the tube with the US probe placed at a 15° angle between the side of the tube and the HFIUS probe. The CSA of a large tube (D = 56.8 mm) was also measured with the US probe placed in the center. The US images were recorded in real time using a high-resolution US unit and a videotape recorder (Sony, Tokyo, Japan).

Data Analysis

The US images were digitized on a personal computer equipped with a high-definition video card (DC30 Pro; Pinnacle, Silicon Valley, CA) and analyzed using a commercially available image analysis software package (SigmaScan Pro; Jandel Scientific, San Rafael, CA). Images were displayed on a 17-inch, high-resolution monitor with the pixel size of 640 × 480, which corresponds to an image magnification of approximately ×12 (10 pixels = 1 mm). We selected eight US images recorded from each of the tubes and each probe position inside the tube. The inner circumference of the tube was marked manually using a pointing device and a software

DISTENSION OF THE ESOPHAGUS is a reproducible stimulus to induce heartburn and chest pain in the laboratory setting in humans (2, 3, 14, 18). Distension of the esophagus may also occur during spontaneous gastroesophageal reflux (GER) and could play a role in the causation of esophageal symptoms. Commonly used techniques to study esophageal function do not measure esophageal distension. Esophageal impedance measurement (the most recent technique) can reveal the nature of reflux, i.e., liquid, air, and neutral reflux during spontaneous GER (16, 17, 20). Impedance planimetry can also measure the cross-sectional area (CSA) and thus the diameter of a saline-filled balloon placed inside the esophagus (12, 13). However, impedance planimetry cannot measure the distension of the esophagus during spontaneous GER.

We have used the high-frequency intraluminal ultrasonography probe (HFIUS) to study changes in the esophageal muscle thickness as a marker of muscle contraction (1, 10, 21). We observed that HFIUS is also able to visualize the size and contents of the esophageal lumen. The aim of this study was to determine whether HFIUS could accurately measure the CSA of a tube in vitro. We then assessed distension of the esophagus during swallows of liquid bolus and during spontaneous GER in normal healthy subjects.

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program (artZII, WACOM, Vancouver, WA). Once marked, the image analysis software program automatically calculated the CSA of the tube.

**Subjects**

Esophageal distension during liquid bolus swallow (in vivo studies). These studies were performed in seven healthy volunteers (5 men and 2 women). The age of the volunteers ranged from 21 to 46 yr (median age of 40 yr). Those volunteers with a history of upper gastrointestinal surgery, systemic diseases known to influence gastrointestinal motility, and medication that may affect the esophagus were excluded from the study. All subjects gave informed consent before participating in the study. The Human Research Protection Program at the University of California, San Diego, approved the protocol for the study.

**Study protocol.** Subjects fasted overnight, and recordings were performed with the subjects in the recumbent position. The esophageal pressure and HFIUS images were recorded simultaneously with a catheter assembly consisting of a 4.5-mm-diameter water-perfused manometry catheter, a 6-Fr silicon tube for water injections in the esophagus, and a 2.3-mm US probe (UM-3R Olympus). The US probe was equipped with a 20-MHz transducer.

The nasal cavity and oropharynx were anesthetized with 1% lidocaine gel and 1% benzocaine spray. The catheter assembly was positioned via the nose in the esophagus and stomach. A standard pull-through procedure was performed, and the US probe was positioned at 5 cm above the upper end of the lower esophageal sphincter (LES; distal). Subjects swallowed water of various volumes (1, 5, 10, 15, and 20 ml) at 60-s intervals. Subjects were instructed to hold swallowing in between water swallows. Each volume was repeated two to three times. After water swallows, different volumes of water (1, 5, 10, 15, and 20 ml) were injected in the esophagus, 5 cm proximal to the HFIUS probe. At the completion of each injection, subjects were asked to swallow to clear the water from the esophagus. Again, 60 s were allowed in between each water injection. Each volume was repeated two to three times. The US transducer was then repositioned 3–5 cm below the lower end of the upper esophageal sphincter (proximal). The water swallows (same volumes as described earlier) and water injections just above the US probe were repeated.

The pressure tracings were recorded on a computer through a PC polygraph (Medtronic Synectics, Shoreview, MN), and US images were recorded on a videotape (Sony). The pressure and US recordings were synchronized using a time code device (Thalaner Electronics, Ann Arbor, MI).

**Data analysis.** The water swallows and water injection sequences were visualized on a high-resolution monitor, and the US image corresponding with the maximal dimension of the esophagus was selected for analysis. The liquid-filled lumen and the inner mucosal margin of the esophagus were clearly visualized in these US images. The interface between the water and the mucosa was marked manually using the pointing device to allow the computer software program to calculate the CSA of the lumen of the esophagus (Fig. 1). From the measured value of the CSA, the diameter of the

**Fig. 2.** The esophageal CSA during 1, 5, 10, 15, and 20 ml of water swallows in the distal and proximal esophagus. There is a linear increase in the esophageal CSA with the increase in the volume of the swallowed bolus in both the distal ($R = 0.75, P < 0.05$) and proximal ($R = 0.78, P < 0.05$) esophagus. In the distal esophagus, there is no difference in the CSA between 15 and 20 ml [ANOVA on ranks, *P* not significant (NS)].
esophageal lumen was calculated based on the equation $D = 2 \cdot \sqrt{CSA/\pi}$.

Subjects

Analysis of esophageal contents and dimension during transient lower esophageal sphincter relaxation. Twelve healthy volunteers, six males and six females, ranging in age from 18 to 53 yr (median age of 27.5 yr) were evaluated to determine the distension of the esophagus caused by physiological GER. This study was conducted previously to evaluate the usefulness of the sphinctometer in the detection of transient lower esophageal sphincter relaxation (TLESR; the data were reported earlier; see Ref. 9). None of these volunteers had any upper gastrointestinal symptoms or history of abdominal surgery. All subjects signed informed consent before participating in the study.

Study protocol. Studies were performed after an overnight fast. Subjects were asked to stop smoking and refrain from drinking alcohol for 24 h before the study. The LES, esophageal and gastric pressures, esophageal pH, and HFIUS images were recorded simultaneously. The catheter assembly consisted of a sphinctometer catheter (Sentron), a pH probe (Synectics Medical), and an US probe with a 20-MHz transducer (UM-3R Olympus). The sphinctometer was part of a solid-state catheter system (Synectics Medical) that also had three solid-state esophageal pressure transducers. These transducers were located at 3, 8, and 13 cm proximal to the upper edge of the sphinctometer device. This particular design of the sphinctometer has a pressure transducer located in the middle of a 6-cm sealed “balloon-like” sleeve system. The sleeve system is filled with oil and is designed to measure LES pressure over its entire length. The three catheters were taped together with a paraffin film. The sphinctometer was calibrated at 0 (atmospheric pressure) and 50 mmHg at room temperature. Subject’s nares and pharynx were anesthetized with 5 ml of 1% viscous lidocaine gel and topical lidocaine spray, respectively. After a standard pull-through technique, the catheter assembly was placed in such a fashion that the sphinctometer straddled the LES. The pH sensor was positioned at 5 cm above the LES, the esophageal pressure transducers were placed at 5, 10, and 15 cm above the LES, and the US transducer was positioned at 5 cm above the LES. Three to five wet swallows of 5 ml of water at room temperature were performed at the beginning of each recording period. Subjects were asked to refrain from spontaneous swallows for at least 30 s before and after each induced wet swallow. Recordings were then performed for 1 h in the fasting state and for an additional 2 h after the ingestion of a standard meal, consisting of a sandwich and a soft drink (1,000 kcal, 40 g carbohydrate, 40 g protein, and 20 g fat). All recordings were performed with the subjects in the left recumbent position during the study (mean observation time, 3 h 22 min). The pressure and pH were recorded through the PC polygraph (Synectics Medical) on a computer with a sampling frequency of 8 Hz. The US images were recorded in real time on a videotape recorder (Sony), and the pressure and US recordings were synchronized using a time code device (Thalanner Electronics).

Data analysis. Water swallows were analyzed as described earlier. The LES pressure record was screened for TLESRs. The US images during TLESR were visually analyzed to determine the nature of the refluxed material (predominantly liquid, predominantly air, and a mixture of liquid and air). The US image, corresponding to the maximal dimension of the esophageal lumen during TLESR, was selected for the CSA measurement and the estimation of the diameter.

Statistical Analysis

The data are shown as median with the upper and lower limits. The statistical differences were estimated using ANOVA on ranks or linear regression for in vitro and in vivo validation studies. The Chi square test was used for the analysis of patterns of the esophageal luminal contents, and the Mann Whitney rank sum test was used for analysis of esophageal distension during swallows and TLESR.

RESULTS

Validation of the HFIUS Probe In Vitro

The CSA of the agarose probe (D = 15.6 mm) was measured from the HFIUS probe images, with the US probe placed at the center of the tube, off-center, and at a 15° oblique angle. The percentage difference between the US-measured CSA and the actual CSA was 3.3% for the central location (range 2.1–4.7), 3.2% for the off-center location (range 0.5–6.5), and 2.4% for the 15° oblique angle (range 1.7–3.7) location. The difference between the actual and the measured CSA of the agarose tube of 56.8 mm was 4.5% (range 4.3–4.6).

The Nature of the Swallowed Material: In Vivo Swallow and Injection of Water

The swallow of liquid bolus was associated with the passage of air and liquid through the esophagus. In the majority of swallowing, the liquid was seen first, followed by air. The injection of water directly in the esophagus was also associated with the passage of liquid first, followed by air through the esophagus.

CSA of the Esophagus In Vivo During Swallows

The CSA during 1-, 5-, 10-, 15-, and 20-ml bolus swallows in the distal esophagus (5 cm above the LES) are shown in Figs. 1 and 2. There was a linear increase in the CSA of the esophagus with an increase in bolus volumes up to 15 ml ($R = 0.75$, $P < 0.05$). The esophageal CSA between 15- and 20-ml swallows were not different (Fig. 2).

The relationship between the volume of swallowed bolus and the CSA of the proximal esophagus was also linear ($R = 0.78$, $P < 0.05$, Fig. 2). The median CSA during 15-ml water swallows in the distal esophagus was greater than that of the proximal esophagus ($P < 0.05$). The maximal estimated diameter during water swallows at the distal and proximal esophagus were 22 and 21 mm, respectively.

Esophageal Distension by Injection of Water in the Esophagus

The esophageal CSA during intraesophageal water injection increased in a linear fashion with an increase of the injected water volume ($R = 0.76$, $P < 0.05$). The CSA of the proximal esophagus during 1, 5, 10, 15, and 20 ml of water injection was 65 mm$^2$ (range 34–90), 76 mm$^2$ (range 49–153), 129 mm$^2$ (range 58–185), 170 mm$^2$ (range 69–272), and 202 mm$^2$ (range 71–307), respectively ($R = 0.68$, $P < 0.05$, Fig. 3). There was no difference in the CSA between the distal and proximal
esophagus during injection-induced esophageal distension. The maximal estimated diameters during water injection in the distal and proximal esophagus were 23 and 20 mm, respectively.

Nature of Esophageal Contents and CSA of the Esophagus During Swallows and TLESR

Forty-six 5-ml water swallows and 62 episodes of TLESR were analyzed in the 12 normal subjects. Acid reflux was detected during 29/62 TLESR episodes (defined as an intraesophageal pH drop to <4, lasting >5 s). The US images during swallows and TLESR were analyzed to determine the opening of the esophageal lumen and the nature of the esophageal contents. The following patterns of esophageal luminal contents were noted: 1) no luminal opening; 2) luminal opening with predominant liquid only; 3) luminal opening with predominant liquid followed by air; 4) luminal opening with predominant air followed by liquid and; 5) luminal opening with predominant air only (Fig. 4).

During water swallows, the passage of “liquid followed by air” was the most frequent pattern (67%). There were no episodes of “failed esophageal luminal opening.” The most frequent pattern during TLESR was the passage of “air only” (58%). The frequency of other patterns was as follows; “air followed by liquid” (21%), “failed luminal opening” (15%), and liquid followed by air (7%; Fig. 5). The patterns of the esophageal contents during positive pH drop and negative pH drop episodes were not different. During 17 of the 29 acid reflux positive episodes (59%), no liquid material was seen in the esophagus (Fig. 6).

The CSA of the esophagus could be measured during 43 of the 46 water swallows but only during 17 of the 62 TLESR episodes. In the remainder, either there was no opening of the esophageal lumen or the presence of too much air in the esophagus precluded the CSA measurements. The median CSA of the esophagus during these 17 reflux episodes was 44 mm² (range 24–187). In the same subjects, the median CSA of the esophagus during 5-ml water swallows was 53 mm² (range 25–158). There was no difference between the CSA during 5-ml swallows and liquid GER episodes (P = not significant, Fig. 7). Furthermore, no difference was detected in the CSA of the esophagus during acid reflux-positive and acid reflux-negative GER (44 vs. 44 mm²).
Our in vitro studies show that the HFIUS probe can measure the CSA and thus the diameter of a tube fairly accurately. In vivo measurements of the esophagus during water swallows reveal that adequate images of the esophagus are obtained as the liquid bolus traverses through the esophagus. The CSA of the esophagus increases in a linear fashion as the volume of swallowed bolus increases, with a peak esophageal diameter of 22 mm at 15-ml water swallows. The CSA of the distal esophagus was larger than that of the proximal esophagus. Interestingly, the CSA and the diameter of the esophagus during spontaneous liquid GER in healthy, asymptomatic subjects is small, comparable to a 5-ml swallow. Finally, the nature of the esophageal contents, i.e., air, liquid, acidic, and neutral reflux, can be detected by the technique of simultaneous pressure, pH, and US image recordings.

**In Vitro Validation**

For in vitro studies, we tested the tubes of different CSAs that are relevant to the in vivo dimensions of the human esophagus. Our data show that the US probe can measure the CSA of tubes up to 50 mm in diameter fairly accurately. We also tested other possibilities, i.e., movement of the US transducer from the center to an off-center position and the possibility that the US transducer may not be perpendicular to the wall of the esophagus. The angle between the probe and esophageal wall depends on the diameter and the length of the esophagus. Based on geometrical principles, the maximal angle in a 20-cm-long tube with a diameter of 1.0 cm is 2.86° [tan⁻¹ (1.0 cm/20.0 cm)]. The same angle in a tube with a lumen measuring 5 cm in diameter will be 14°. Our data show the off-center position and probe angles of less than 15° do not affect the CSA measurement accuracy.

**In Vivo Measurements of the Esophagus**

The CSA of the proximal and distal esophagus, using a 10-ml liquid bolus, have been reported using the technique of an ultrafast computed tomography (CT) scan (11). It is noteworthy that the measurements reported in that study are similar to our findings. The ultrafast CT scanning, unlike HFIUS imaging, cannot be used for long-term recordings. Our in vivo studies show that the esophageal CSA increases as the volume of ingested bolus increases. The maximal CSA was recorded with swallowed and injected boluses of 15 ml of water. From these CSA measurements, we estimated that the maximal diameter of the distal esophagus during physiological swallows is <23 mm. Several studies report that the proximal esophagus is less compliant than the distal esophagus (6, 7), and we find the same, i.e., at higher ingested volumes, the CSA of the proximal esophagus is lower than the distal esophagus.

**Patterns of Liquid and Air Contents in the Esophagus During Swallows**

The air residing in the oropharynx is ingested along with other oral contents during a swallow. Ultrafast CT scan studies show that a normal subject ingests ~10–15 ml of air with each swallow (11). Our study confirms that air is ingested along with the liquid during water swallows. The difference between CT studies and our US studies, however, is that we noticed liquid traversing ahead of the air during the majority of swallows. On the other hand, CT studies revealed the transit of air through the esophagus first, followed by liquid. The reason for the difference in the two studies may be related to the manometry technique used in our studies, which requires infusion of water in the esophagus. The infused water will be expected to move ahead of the air entering the esophagus from the pharynx. The slight difference in the position of the subject may also make a difference, because in the upright position, with air being lighter than water, the...
air will be expected to rise and move behind the liquid bolus.

**Patterns of Gas and Liquid Reflux**

The patterns of gas and liquid reflux during TLESRs have been reported in several recent studies using the technique of impedance measurements (16, 17). The air only was the predominant pattern (58%) of reflux in our study. Impedance studies show similar findings, even though the incidence of air only reflux was 18% (17). The physical posture of the subject seems to be a major determinant of the nature of the material that refluxes in the esophagus. We studied our subjects in the left lateral position, a position in which reflux of air occurs more frequently than the liquid reflux. On the other hand, reflux of liquid dominates in the right lateral position (15, 19). Therefore, to determine esophageal distension by US imaging, the right lateral position of the subject may be ideal because liquid reflux in this position will allow adequate US images for distension measurements.

We detected a large number of reflux episodes in which the pH probe registered acid reflux, but no liquid was seen in the esophagus on the HFIUS images. Similar observations have been made with the impedance measurement technique (17). We suspect that similar mechanisms are at work here.

Distension associated with GER is very small. It results from the ingested vs. the refluxed esophageal contents during these periods. Because TLESR is the major mechanism of GER in normal subjects, the esophageal contents during these periods can only be related to GER (5, 8, 9). Second, the HFIUS technique can not measure the esophageal CSA during predominant air reflux episodes. Finally, esophageal distension can only be measured at one site in the esophagus using one transducer. Withstanding these limitations, HFIUS is a valid technique to measure the CSA of the esophagus and the esophageal distension in vivo during liquid swallows and liquid reflux episodes. The maximal diameter of the esophagus under physiological liquid GER is ~4–5 mm. Future studies in patients with symptomatic GER disease should be able to address whether heartburn and esophageal pain are related to the GER-related distension of the esophagus.

**REFERENCES**


