Common cavity pressure during gastroesophageal reflux: reassessment using simultaneous pressure, impedance, and ultrasound imaging

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Tipnis, Neelesh A., Jianmin Liu, James L. Puckett, and Ravinder K. Mittal. Common cavity pressure during gastroesophageal reflux: reassessment using simultaneous pressure, impedance, and ultrasound imaging. Am J Physiol Gastrointest Liver Physiol 290: G1149–G1156, 2006—An increase in intraesophageal pressure during transient lower esophageal sphincter (LES) relaxation [referred to as common cavity (CC) pressure] is thought to be a marker of gastroesophageal reflux (GER). Multimodal impedance (MII) measurement is a sensitive marker of reflux entry into the esophagus during GER. We recorded GER using esophageal pressure, pH, impedance, and intraluminal ultrasound (US) images to understand the genesis of the esophageal CC pressure. Nine normal subjects underwent simultaneous MII/pH/pressure and US image recording of the esophagus for 2 h following a standardized meal. MII and pressure transducers were located at 5 and 15 cm above the LES. The US transducer and pH sensors were also placed at 5 cm above the LES. Reflux entry into the esophagus by MII criteria was determined relative to the onset of CC pressure wave. Esophageal lumen cross-sectional area (CSA) and muscle CSA during GER were determined from the US images. Eighty liquid GER episodes identified using MII criteria, of which 55 were clearly associated with CC pressure waves, were analyzed. The GER reached 15 cm above LES in 49 of 55 (89%) by MII criteria, but the CC pressure wave was observed at 5 and 15 cm during all episodes. The propagation of the CC pressure wave was simultaneous between 5 and 15 cm during 49 of 55 (89%) of the GER episodes, but reflux entry by MII criteria was retrograde during 53 of 55 (96%) of these episodes. During 5 air-reflux episodes, MII showed a simultaneous reflux entry between the 5- and 15-cm site, however, the CC pressure wave preceded reflux entry during all of these episodes. There was poor correlation between the luminal CSA and the magnitude of CC pressure (R2 = 0.144). US images revealed a close temporal correlation between CC pressure and the increase in esophageal muscle thickness and muscle CSA (markers of longitudinal muscle contraction). Dissociation between CC pressure and MII-detected reflux suggests that the onset of CC pressure is not due to GER. We speculate that the increase in esophageal muscle contraction plays an important role in the genesis of CC pressure.

intraluminal impedance; ultrasound imaging of the esophagus

MCCNELLY ET AL. (5) were the first to observe an increase in esophageal pressure in association with belching and gastroesophageal reflux (GER). Several investigators (1, 2, 4, 15, 26) since then have reported the same association with GER. Dent and colleagues (2, 4) felt that the increase in intraesophageal pressure in association with transient lower esophageal sphincter (LES) relaxation (TLESR) is due to movement of gastric contents into the esophagus (GER) and referred to it as the common cavity pressure wave. Common cavity pressure wave is currently felt to be a surrogate marker of GER (3, 12, 15, 26). Under normal physiological conditions, end-expiratory gastric pressure is 4–6 mmHg higher than the esophageal pressure, and therefore, it is possible that at the time of complete LES relaxation, the esophagus and stomach become one cavity, a common cavity, resulting in equalization of stomach and esophageal pressures due to movement of stomach contents (liquid, air, or combination) into the esophagus.

Intraluminal impedance is a novel technique to record physical movement of gastric contents into the esophagus, i.e., GER. The combined impedance and pH catheter technique can record all types of reflux episodes, i.e., air, liquid, acid, and neutral (16, 18, 19, 22–25). The technique is based on the measurement of electrical impedance between closely spaced electrodes positioned in the esophagus. Intraluminal multipole-site impedance recordings reveal that changes in impedance during GER occur in a retrograde fashion, from the distal to the proximal site in the esophagus. In fact, impedance recordings show that retrograde movement of air or liquid in the esophagus represents GER, and antegrade movement is the result of a swallowed bolus. We observed that the common cavity pressure wave seen in association with GER occurs simultaneously along the length of the esophagus during most of the instances. If common cavity pressure and changes in impedance are indeed markers of GER (physical movement of gastric contents, liquid, or air into the esophagus), it is not clear why the impedance wave should spread though the esophagus in a retrograde fashion and the common cavity pressure wave occurs simultaneously. We recorded GER using esophageal pressure, pH, impedance, and intraluminal ultrasound (US) imaging in normal subjects to better understand the genesis of the common cavity pressure wave associated with GER.

METHODS

The Human Research Protection Program at the University of California San Diego approved this study. The study population consisted of nine healthy individuals (7 males, ages 18–64 yr) with either no or minimal symptoms of GER disease (no more than 1 time/mo, no nocturnal symptoms, and no symptoms requiring H2 receptor antagonist or proton pump inhibitors for control). None of these subjects was taking any medicines or antacids for relief of heartburn.

Catheter assembly. A customized catheter assembly consisting of a 2-mm diameter, 4-channel solid-state pressure transducer catheter (Galtect, Ilse of Skye, Scotland), a 1.5-mm diameter Comfortec multimodal impedance (MII)-pH impedance-pH probe (Sandhill Scientific, Highlands Ranch, CO), and a 1.2-mm 30 MHz high-frequency...
common cavity pressure wave criteria were determined. The time movement, from 5 to 15 cm above the LES, by impedance criteria and reduction in the baseline impedance value. Velocity of refluxate

The MII criterion for refluxate entry into the esophagus is a 50% decrease in the expiratory esophageal pressure of the common cavity was defined as a sharp and sustained rise in end-expiratory esophageal pressure of ≥4 mmHg in 2 consecutive leads in association with GER (6). The onset of the esophageal common cavity was defined as the inflection point at the onset of the increase in the muscle CSA during GER (identified from physiological tracings) was digitized at a frequency of 100 ms using a digital video-editing system (Pinnacle DV500 and Adobe Premiere 6.0, Adobe Systems, Mountain View, CA). These US images were analyzed for 1) opening of the esophageal lumen (as a marker of GER bolus entry into the esophagus); and 2) cross-sectional area (CSA) of the lumen (as a marker of degree of esophageal distension during reflux) at the peak of distension. In addition, CSA of the muscularis propria of the esophagus (as a marker of longitudinal muscle contraction) (8, 9) was measured during randomly selected liquid reflux episodes. The time of lumen opening was identified as the first frame at which the mucosa separated from the edges of the catheter assembly for at least four consecutive frames. The luminal CSA at the peak esophageal distension was measured using graphing software (Sigma Scan Pro, Jandel Scientific, San Rafel, CA). The reflux entry into the esophagus and lumen CSA were determined for all reflux episodes, but the muscle CSA during GER was determined from the 10 randomly selected liquid GER sequences in which the entire circumference of the esophagus was clearly visualized on the US images. The time of onset of muscle CSA increase was when it increased at least 50% of the baseline value for at least 1 s. The muscle CSA was plotted against the esophageal pressure at 5 cm above the LES to determine the temporal correlation between the two. The duration of common cavity and the duration of increase in the muscle CSA during common cavity were determined. Differences in the time of bolus entry by impedance at 5 and 15 cm above the LES and onset of common cavity pressure at 5 and 15 cm above the LES were determined.

Statistical analysis. Synchrony between various physiological events was determined by comparing the time offset between various events against a test value of 0 s (simultaneously occurring events)

Data analysis. GER episodes were identified from the physiological recordings obtained in the postprandial period with either pH or MII criteria using Bio-view Analysis software, (Sandhill Scientific). Confirmation of reflux episodes was performed manually. Esophageal common cavity was defined as a sharp and sustained rise in end-expiratory esophageal pressure of ≥4 mmHg in 2 consecutive leads in association with GER (6). The onset of the esophageal common cavity was defined as the inflection point at the onset of the increase in the pressure. The computerized automated analysis software determined the time of GER entry into the esophagus from the MII recordings. The MII criterion for refluxate entry into the esophagus is a 50% reduction in the baseline impedance value. Velocity of refluxate movement, from 5 to 15 cm above the LES, by impedance criteria and common cavity pressure wave criteria were determined. The time

Study protocol. The catheter assembly was placed transnasally, and the LES was identified using the station pull-through method. Subjects were studied for at least 2 h following ingestion of a standardized, mixed liquid/solid meal in a semirecumbent, right decubitus position. Subjects were required to maintain quiet during the study and were not allowed to sleep.

Fig. 1. Schematic of combined high-frequency intraluminal ultrasound, multiluminal impedance (MII), pH, and manometry catheter assembly. The catheter is assembled such that the ultrasound transducer, pH sensor, and 1 pressure transducer are located at the same level, 5 cm above the lower esophageal sphincter (LES). Impedance electrodes are located at 2, 4, 6, 8, 10, 14, 16, and 18 cm above the LES. Also note the location of the other pressure sensors.
using the single-value Student’s t-test. A paired t-test was used to compare the velocity of bolus movement from 5 to 15 cm above the LES as determined by impedance and common cavity pressure. The duration of the common cavity pressure wave with the duration of the longitudinal muscle contraction events were evaluated by a paired-samples t-test. The Pearson’s correlation coefficient was used to evaluate the relationship between luminal CSA and common cavity pressure individually in subjects with three or more GER episodes and the onset of the common cavity pressure wave with the onset of the increase in muscle CSA. Data are shown as means ± SE.

RESULTS

Eighty episodes of GER were identified using conventional MII and/or esophageal pH criteria and analyzed for this study (Fig. 2). A discrete common cavity during GER was identified during 55 (69%) of the GER episodes. In the other 25 episodes, the onset of a common cavity pressure was not discrete (14) or the pressure morphology did not meet study criteria for a common cavity pressure wave (11). On the basis of the MII criteria, 51 of 55 (92%) were predominantly liquid reflux episodes, 2 (4%) were air reflux, and another 2 (4%) were mixed air and liquid. Of the 55 GER episodes associated with a common cavity, 45 (82%) were acid, 7 (13%) were nonacid, and 3 (5%) were minor acid reflux episodes. US images identified esophageal lumen opening during 78 of the 80 GER events detected by the MII and/or pH criteria and during all 55 GER events associated with a common cavity pressure wave. Three additional air-reflux episodes that occurred during the meal period were evaluated but were not included in postprandial analysis.

Morphology of esophageal pressure during the common cavity. The esophageal pressure shows negative pressure oscillations with the inspiratory phase of the respiratory cycle, which is due to the transmission of intrathoracic pressure into the esophagus. The amplitude of negative esophageal pressure waves in the absence of common cavity ranged from 5 to 9 mmHg (Fig. 3). During the common cavity, the inspiratory negative pressure oscillation was diminished to <2 mmHg in 45 of 55 (82%) of the instances.

Time of onset of GER entry by common cavity pressure and MII. The onset of GER (liquid or air) entry, as defined by the MII and the onset of common cavity pressure wave, was compared at 5 and 15 cm above the LES (Fig. 3). At the 5- and 15-cm sites, the onset of common cavity pressure and GER entry by MII criteria occurred at the same time only 20% and 7% of the times, respectively. During all other times, there was disassociation between the onset of GER entry and the onset of common cavity pressure event. The pressure wave occurred before impedance wave during 34% and 64% of the times at 5 and 15 cm above the LES, respectively. On the other hand, pressure waves occurred later than impedance wave during 46% and 18% of the times at the 5- and 15-cm sites, respectively. The mean time difference between the onset of the common cavity pressure wave and the onset of the GER entry by MII criteria was 1.5 ± 0.3 s and 2.2 ± 0.4 s at 5 and 15 cm, respectively (P < 0.001 compared with no difference).

Progression of the common cavity pressure and impedance in the esophagus. The relationship between the progression of common cavity pressure and GER entry by MII criteria along the length of the esophagus, when both were present, was assessed during 55 GER episodes. Common cavity pressure reached the 15-cm site in all 55 episodes, but on the basis of the MII criteria of refluxate entry, GER failed to reach the 15-cm site during six (11%) episodes. Common cavity pressure waves occurred at the same time (simultaneously) between the 5- and 15-cm sites (Fig. 3) above the LES during the majority, 48 of 55 (79%), of GER episodes (time resolution, 0.1 s). On the other hand, GER (by MII criteria) arrived at 5- and 15-cm sites in the esophagus in a retrograde fashion (Fig. 3) in the majority, 47 of 49 (96%), of GER episodes with a mean time interval of 2.4 ± 1.8 s between the two sites. Only 6 of the 55 (11%) common cavity pressure waves were retrograde. However, the velocity of the retrograde movement of the GER bolus, as measured by the MII, was significantly slower than the retrograde velocity of pressure waves (10 ± 13 vs. 30 ± 20 cm/s; P < 0.05). One of the six MII episodes that failed to reach the 15-cm site occurred during the retrograde common cavity events.

Relationship between common cavity pressure and longitudinal muscle contraction of the esophagus. Synchronized M-mode US images and physiological tracings are shown in Fig. 3. A and B. In both figures, an increase in muscle thickness (a marker of longitudinal muscle contraction) coincides with the onset of common cavity pressure wave. The temporal correlation between common cavity pressure wave at 5 cm above the LES and contraction of the longitudinal muscle of the esophagus (changes in muscle CSA) at the same site was determined during 10 GER episodes (Fig. 4). In all of these episodes, there was a close temporal correlation between the onset of the common cavity pressure wave and the increase in esophageal muscle CSA (mean time difference < 0.1 s; Pearson’s correlation coefficient = 1; P = 0.01). The muscle CSA remained elevated during the entire duration of the common cavity pressure wave, and it returned to the baseline with the termination of the common cavity (usually by an esophageal contraction wave). The duration of common cavity pressure was the same as the duration of the longitudinal muscle contraction (15.65 ± 2.58 vs. 15.81 ± 2.57; P = 0.061).

Relationship between common cavity pressure and CSA of the esophageal lumen. The mean common cavity pressure was 6 ± 1.8 mmHg. Six subjects had three or more GER episodes in which the common cavity pressure and lumen CSA could be compared in each subject. In all subjects, there is a poor...
Fig. 3. A and B: representative manometry, MII, and pH tracings of GER events. Note the onset of common cavity pressure waves (△) occurs simultaneously as shown in the above 2 tracings. On the other hand, the arrival of the GER bolus (as seen by MII recordings) occurs in a retrograde fashion (arrow). The onset of the common cavity precedes GER bolus entry in A, and it occurs after the GER bolus entry in B. Synchronized M-mode ultrasound images of the GER episodes at 5 cm above the LES are displayed above the physiological tracings. The dashed lines depict GER bolus entry at 5 cm above the LES and the onset of common cavity. Note an increase in muscle thickness coincident with the onset of the common cavity wave. Furthermore, a gradually increasing common cavity pressure is associated with a gradually increasing muscle thickness.
correlation between the common cavity pressure and lumen CSA (Pearson’s correlation range, \(-0.617\) to \(0.684\), and \(P\) values \(0.062–0.894\)).

**Simultaneous GER entry and common cavity pressure during air reflux.** Five episodes of air reflux, as determined by MII criteria, were observed in three subjects. Three of these episodes occurred during the meal phase of the study and were not part of the postprandial data analysis. During all five air-reflux episodes, air arrived at the 5- and 15-cm sites simultaneously (as recorded by MII), and the onset of pressure wave at the two sites was also simultaneous. However, the onset of common cavity pressure wave occurred earlier than the arrival of air at the corresponding MII recording site during all of these air-reflux episodes. In all five episodes, US images revealed that first, there is an increase in the muscle thickness and muscle CSA, which is then followed by air entry into the esophagus (Fig. 5). Air entry into the esophagus resulted in a loss of US esophageal image during all of these episodes. The onset of common cavity pressure coincided with the increase in muscle thickness and muscle CSA rather than the entry of air into the esophagus.

**DISCUSSION**

Our data show 1) the common cavity pressure seen in association with GER is not associated with liquid or air entry into the esophagus as detected by the MII criteria during most instances; 2) during the majority of GER episodes, a common cavity pressure wave occurs simultaneously along the length of the esophagus, but GER entry by MII criteria occurs in a retrograde fashion; 3) there is a poor correlation between the amplitude of common cavity pressure and the degree of esophageal distension during liquid GER; and 4) a close temporal correlation exists between the contraction of the longitudinal muscle of the esophagus and common cavity pressure wave in the esophagus.

The common cavity pressure wave is widely felt to be a marker of GER. It is thought to be the result of equalization of gastric pressure with esophageal pressure during GER. However, the equalization of pressure between the two cavities can only occur if there is physical movement of contents between the two cavities. During GER, movement of either air or liquid will be required to equalize pressures between the esophagus and the stomach. MII monitoring is a very sensitive technique to record air as well as liquid reflux. Our findings indicate that there is a significant difference between the onset of common cavity pressure and refluxate entry by MII criteria, arguing against common cavity pressure being directly related to the GER entry into the esophagus.

Could the differences in the timing of pressure and MII waves be related to the fidelity response of sensors and the definition of MII criteria of refluxate entry used in our study? The pressures were measured using solid-state pressure transducers that have high-fidelity response times. Similarly, the MII technique is based on the changes in electrical impedance, which has a high-fidelity response. The frequency of data acquisition was fairly fast, 30 Hz. We used a 50% reduction rather than the onset of reduction of electrical impedance as the MII criteria for the bolus entry in our study, as suggested by the simultaneous fluoroscopic and impedance recording studies of Silny and colleagues (21). It is possible that the MII criteria for refluxate entry may have contributed to the difference in the temporal correlation between the impedance and pressure.

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**Fig. 4.** M-mode ultrasound (US) images of the esophageal wall (A) and esophageal muscle cross-sectional area (CSA; B) during a common cavity event. Note, a close temporal correlation between muscle CSA (a marker of longitudinal muscle contraction of the esophagus) and common cavity pressure wave. US images also reveal a close temporal correlation between the increase in esophageal muscle thickness and the common cavity pressure wave. CM, circular muscle; LM, longitudinal muscle.
waves. Changing the MII criteria for bolus entry (e.g., using 10% reduction in impedance signal) would shift the timing of bolus entry backward. The number of events where the impedance and pressure changes occur simultaneously would simply shift to where the onset of the impedance wave occurs before the onset of the pressure wave. Thus the change in MII criteria of determining the onset of bolus entry would further decrease or have little effect on the number of synchronous impedance and pressure reflux events. Furthermore, the observation that common cavity pressure occurs simultaneously, but the MII wave spreads in a retrograde fashion along the length of the esophagus during the majority of the instances, argues against common cavity pressure being related to the movement of gastric contents into the esophagus. It is possible that a small amount of air reflux preceded liquid reflux into the esophagus, which could account for the time differences observed between the propagation of the pressure wave compared with the fluid entry wave by the MII criteria. We think it is unlikely because 1) MII tracings were carefully scrutinized to assess for presence of air in the GER refluxate; 2) we studied subjects in the right decubitus position, which is associated with predominantly liquid reflux (13); and 3) we did not see air reflux preceding liquid reflux on our US images; the latter is very sensitive in detecting air in the esophagus. The choice of subject position in our study also explains the differences in the frequency of air reflux between ours and other studies. MII records reveal that the GER entry into the esophagus during air-reflux episodes can occur simultaneously along the length of the esophagus, which is most likely due to a rapid spread of air along the length of the esophagus compared with the liquid reflux contents. However, even during these air-reflux episodes, the onset of common cavity pressure wave and increase in muscle thickness precedes MII criteria of refluxate entry, further supporting our contention that the onset of common cavity pressure is not related to reflux of gastric contents into the esophagus.

Additional evidence that the common cavity is not due to equalization of gastric and esophageal pressure comes from the close inspection of the manometric recording in which LES pressure was recorded for extended periods of time using a sleeve sensor to determine the mechanism of GER (8, 9). These recordings show that the onset of common cavity pressure wave may precede complete relaxation of the LES by 1–2 s. Complete LES relaxation would be required if the common cavity were indeed related to equalization of gastric and esophageal pressures unless there is an increase in gastric pressure (stress reflux) during GER, which is not the case during majority of reflux episodes in normal subjects.

If common cavity pressure was related to the physical movement of reflux contents into the esophagus, principles of physics dictate that there would be a direct relationship between the volume of GER and the amplitude of common cavity pressure. We could not measure GER volume using our recording techniques but the CSA of the lumen of the esophagus is likely to be a surrogate for the volume of GER. We did not find a linear relationship between the common cavity pressure and the CSA of the esophagus during GER episodes either in the individual subjects or in the group data. These findings

Fig. 5. M-mode US images of the esophageal wall (A) during a common cavity event associated with an air-reflux episode (B). Note, a simultaneous increase in impedance (suggestive of air reflux) along the length of the esophagus. The onset of the common cavity pressure wave correlates with the onset of thickening of the muscularis propria (solid lines). The onset of the common cavity wave (solid vertical black line) precedes the onset of air entry (dashed lines shown on the physiological tracing and ultrasound image). Equalization of pressures is seen at air entry. US images are lost with the entry of air into the esophagus and reappear with the clearing esophageal contraction wave.
further argue against common cavity pressure being due to physical movement of gastric contents into the esophagus. If it is not the movement of GER contents, then what causes the so-called “common cavity pressure wave”? We found a close temporal correlation between changes in common cavity pressure waves and the thickness as well as the CSA of the muscularis propria, both of which are measures of longitudinal muscle contraction (7, 11). A gradual increase in muscle thickness with a gradual increase in esophageal pressure seen during some GER episodes also supports our hypothesis that longitudinal muscle contraction is the cause of the increase in esophageal pressure. Longitudinal muscle contraction at the onset of TLESR has been described in several recent reports (17, 20). Because TLESR is the major mechanism of reflux in normal subjects, our finding of longitudinal muscle contraction with the common cavity pressure wave is consistent with those reports. Longitudinal muscle contraction at the onset of a common cavity pressure wave suggests at least two other possibilities as to the cause of the common cavity pressure wave: 1) the esophagus is a closed chamber between the upper and lower esophageal sphincters. The product of pressure and volume is constant in a closed chamber, and as the volume decreases, the pressure will increase (Boyle’s Law) (10). Axial shortening of the esophagus as a result of longitudinal muscle contraction would be predicted to increase esophageal pressure. It may be that the change in the dimension of the esophagus, either before or during GER, could cause changes in its pressure. Second, the esophagus is a relatively compliant organ and, as a result, its pressure reflects intrathoracic pressure at rest. It may be that the contraction of longitudinal muscles renders the esophagus relatively less compliant and thereby prevents transmission of intrathoracic pressure to the lumen of the esophagus. Others and we have observed that the inspiratory negative pressure waves during common cavity are smaller in amplitude than either before or after the common cavity events, which would also support our theory of the effects of longitudinal muscle contraction on the compliance of the esophagus. We cannot be sure as to which mechanism is the cause of common cavity pressure, but our data strongly support that the onset of common cavity pressure seen in association with GER is not due to the entry of refluxate into the esophagus. To be technically correct, the term common cavity implies that the esophagus and stomach are one cavity with the same pressures. Our data suggest that the term common cavity pressure, as is being used in the current literature, is technically incorrect because an increase in intrathoracic pressure in association with GER may occur due to reasons other than the true common cavity.

We do not intend to imply that physical movements of gastric contents into the esophagus (GER) cannot increase esophageal pressure. Our data only suggest that the onset of common cavity pressure waves seen in association with GER, in normal subjects, is not due to physical movement of gastric contents into the esophagus. However, it is possible that in patients with GER disease, in whom volume of reflux may be greater than normal subjects (14), some of the common cavity pressure waves might be related to GER. We propose that the common cavity pressure, observed on pressure recordings, cannot be used as a surrogate marker of GER.

GRANTS

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