Mechanics and hemodynamics of esophageal varices during peristaltic contraction

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Mechanics and hemodynamics of esophageal varices during peristaltic contraction. Am J Physiol Gastrointest Liver Physiol 287: G830–G835, 2004; 10.1152/ajpgi.00015.2004.—Our hypothesis states that variceal pressure and wall tension increase dramatically during esophageal peristaltic contractions. This increase in pressure and wall tension is a natural consequence of the anatomy and physiology of the esophagus and of the esophageal venous plexus. The purpose of this study was to evaluate variceal hemodynamics during peristaltic contraction. A simultaneous ultrasound probe and manometry catheter was placed in the distal esophagus in nine patients with esophageal varices. Simultaneous esophageal luminal pressure and ultrasound images of varices were recorded during peristaltic contraction. Maximum variceal cross-sectional area and esophageal luminal pressures at which the varix flattened, closed, and opened were measured. The esophageal lumen pressure equals the intravariceal pressure at variceal flattening due to force balance laws. The mean flattening pressures (40.11 ± 16.77 mmHg) were significantly higher than the mean opening pressures (11.56 ± 25.56 mmHg) (P ≤ 0.0001). Flattening pressures >80 mmHg were generated during peristaltic contractions in 15.5% of the swallows. Variceal cross-sectional area increased a mean of 41% above baseline (range 7–89%, P < 0.0001) during swallowing. The peak closing pressures in patients that experience future variceal bleeding were significantly higher than the peak closing pressures in patients that did not experience variceal bleeding (P < 0.04). Patients with a mean peak closing pressure >61 mmHg were more likely to bleed. In this study, accuracy of predicting future variceal bleeding, based on these criteria, was 100%. Variceal models were developed, and it was demonstrated that during peristaltic contraction there was a significant increase in intravariceal pressure over baseline intravariceal pressure and that the peak intravariceal pressures were directly proportional to the resistance at the gastroesophageal junction. In conclusion, esophageal peristalsis in combination with high resistance to blood flow through the gastroesophageal junction leads to distension of the esophageal varices and an increase in intravariceal pressure and wall tension.

ESOPHAGEAL VARICEAL BLEEDING occurs when an expanding force within the varix exceeds the maximum wall tension. Wall tension is an inwardly directed force opposing an outwardly directed expanding force. Wall tension can be calculated by the Laplace equation. The Laplace equation (WT = pv – pe × r/w) states that the wall tension (WT) is equal to the transmural pressure difference (pv – pe) (where pv is the intravariceal pressure and pe is the esophageal lumen pressure) times the radius of the varix (r) divided by the wall thickness (w). Thus this force is directly proportional to the transmural pressure difference and the radius of the varix and inversely proportional to the wall thickness of the varix.

No methods are presently available that can measure variceal pressures during a peristaltic contraction of the esophagus (1–3, 7, 12). Our hypothesis, based on the data generated in this study, states that variceal pressure and wall tension increase dramatically during esophageal peristalsis as a natural consequence of the anatomy and physiology of the esophagus and of the esophageal venous plexus.

The objective of this study was to estimate variceal pressure and wall tension and to characterize the mechanical and hemodynamic behavior of esophageal varices during peristaltic contractions. This was done through measurements on patients with esophageal varices and in a model varix system that simulates intravariceal pressure generated during peristalsis.

MATERIALS AND METHODS

Patient Studies

This study was approved by the internal review board at Temple University Hospital. Nine patients (8 men and 1 woman with a mean age of 53.1 ± 10.9 yr) with cirrhosis, portal hypertension, and esophageal varices documented on prior outside endoscopy were evaluated in this study. The etiology of the cirrhosis was hepatitis C in two patients, hepatitis B in two patients, alcohol in two patients, hepatitis B and C in one patient, alcohol and hepatitis C in one patient, and cryptogenic in one patient. None of the patients was treated with beta blockers during the study as per the referring physicians. None of the patients had bled from esophageal varices before the study.

Esophageal varices were imaged in cross section with high-frequency endoluminal sonography, using a 20-MHz ultrasonography transducer (Olympus, Tokyo, Japan or Microvasc, Boston Scientific, Boston, MA). The transducer produces a real-time 360° cross-sectional ultrasound image of the esophagus. Real-time images were recorded on Super VHS videotape using a Kayelemetrics swallowing workstation (Kayelemetrics, Lincoln Park, NJ).

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A 3F angiography catheter was glued to the ultrasound catheter to measure pressure in the esophageal lumen. A 1-mm side port was made in the angiography catheter at the same level as the ultrasound transducer. The distal end of the catheter was closed with silicon glue, whereas the proximal end was attached to a water-perfused manometry system (Arndorfer, Milwaukee, WI). Water was perfused at a rate of 0.5 ml/min at a pressure of 15 lb./in.². The manometry system was attached to a Kayelemetrics swallowing workstation, which was then used to synchronize the pressure tracings with the corresponding ultrasound images (Fig. 1).

All studies were performed after an overnight fast with subjects in a supine position and with the patient’s head elevated at 30°. Viscous lidocaine (1%) was administered for nasal anesthesia. The dual 20 MHz ultrasound/manometry catheter was passed transnasally through the esophagus and into the proximal stomach. The dual catheter was then pulled into the esophageal body at a level above the gastroesophageal junction where the varices appeared the largest. The transducer was stabilized in position at this level, and resting esophageal lumen pressure (with breathing) was measured for at least 10 s and then used as the zero baseline. Subjects were asked to repeatedly swallow a bolus of 5 ml of water, with at least 1 min between swallows, while the investigators continuously acquired ultrasound images and simultaneous pressure data.

Still images were digitized and analyzed by using Image Pro Plus software (Media Cybernetics, Silver Spring, MD). Incomplete or inadequate tracings or images due to artifact were not used for evaluation. The maximum cross-sectional area of the varix at rest and at maximum distension was calculated by the Image Pro Plus software, from the outlined still images of the varix. The image of each varix was outlined at the border of the hyperechoic inner variceal wall and the hypoechoic blood within the varix. The readers of the images were blinded to the pressure data. Pressure measurements were read directly from the data stored and presented on the swallowing workstation.

Ultrasound imaging of the varices, during swallowing of water, showed that the varices initially increased in size, then decreased in size, and then flattened, closed, and opened sequentially. Variceal closure was defined as the first point, on the ultrasound image during the peristaltic contraction at which the hypoechoic blood within the varix was no longer visible in the image. Peak closing pressure was defined as the peak esophageal lumen pressure at which a particular varix closed. Variceal flattening was defined as the point at which the exposed (esophageal lumen) side of the varix flattened during the peristaltic contraction (Fig. 2). Because the videotape of the varices can be run in a forward or backward direction, variceal flattening was usually determined by finding the point of variceal closure and then backing the videotape up to the point of variceal flattening. Variceal opening was defined as the first point at which the hypoechoic blood in the variceal lumen was again visible after variceal closing. The points at which the varix closed, flattened, and opened were identified with the corresponding pressures on the esophageal lumen pressure curves. Variceal flattening, closing, and opening pressures were referenced to baseline esophageal pressure in the resting state. Varices were labeled on the ultrasound image to identify the same varix during multiple swallows. The amplitude of the peak esophageal lumen pressure during the peristaltic contraction was recorded and correlated with the variceal closing pressure to determine whether a relationship exists between the force of the peristaltic contraction and the intra-variceal pressure.

![Fig. 1. Simultaneous ultrasound images and manometry pressure curves. A: display screen on the Kayelemetrics workstation with the esophagus at rest. The display screen shows the ultrasound image. Note the large open varix is marked. The esophageal lumen pressure is 12.4 mmHg. B: display screen showing simultaneous ultrasound and manometry during the peristaltic contraction. Note the flattened varix is marked. The esophageal pressure at the point of variceal flattening is 94.4 mmHg. Intravariceal pressure and the esophageal lumen pressure are equal at variceal flattening.](image-url)
The investigators (J. Kim and V. Thangada) measuring the variceal closing, flattening, and opening pressures on the basis of the ultrasound images were blinded to the patient’s clinical status.

Patients were contacted every 6 mo after the initial study to determine whether they experienced any bleeding or were hospitalized for bleeding. If the patients were hospitalized for bleeding, their medical records were reviewed to determine the site of bleeding (variceal vs. nonvariceal) and the time of bleeding with respect to the original simultaneous ultrasound/manometry test. Peak closing pressures in patients that bled were compared with peak closing pressures in patients that did not bleed using an unpaired Student’s t-test.

**Esophageal Variceal Swallowing Models**

The varix model (Fig. 3) consisted of a thin narrow latex balloon, used to simulate a varix, placed inside a thicker and wider polyethylene tube, used to simulate the esophagus. The size, consistency, and material used for the model varix and model esophagus were chosen to simulate an actual esophageal varix and an actual esophagus as closely as possible. The latex balloon was attached to an open hydrostatic reservoir so that the balloon was filled with water at a constant pressure. The resting model varix pressure (pressure in the varix with the varix at rest) was chosen to simulate actual intravariceal resting pressures. A simultaneous ultrasound probe and manometry catheter was placed in the distal portion of the model varix and a pressure transducer was placed in the model esophagus at the same level 1 cm from a plastic electrical tie. The electrical tie was used to narrow the balloon to simulate the resistance due to the palisade vessels at the gastroesophageal junction.

The first varix model was tested at a resting pressure of 16.7 mmHg in the varix. These experiments were performed to determine whether the intraluminal pressure in the esophagus and intravariceal pressure correspond during flattening of the varix. A plastic electrical tie was placed at the distal end of the varix to restrict the varix by 74% of the original cross-sectional area of the balloon. A 1-kg weight was slid over the model esophagus to push a 2-ml gel bolus (a mixture of ultrasound gel and coffee creamer) at a constant velocity of 2.5 cm/s toward the ultrasound and pressure transducers to simulate a fluid bolus swallow and a peristaltic contraction wave. The amplitude and the configuration of the pressure wave closely resembled an actual peristaltic pressure wave in patients. In addition, the velocity of the peristaltic wave was set to simulate the actual propagation velocity of a peristaltic contraction. Fifteen simulated swallows were performed. Simultaneous ultrasound images and pressure data during these swallows were recorded on Super VHS videotape using the Kayelemetrics swallowing workstation. Two blinded readers independently determined when the model varix flattened on the recorded ultrasound image in exactly the same manner as the flattening pressure was determined in actual varices. The pressures within the model varix and model esophageal lumen were recorded at that point.

A second study was performed by using the same varix model to determine the effects of varying the resistance of the distal portion of the varix on the pressure and cross-sectional area of the varix during

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Fig. 3. A: a varix model constructed of a latex balloon (the varix) inside a polyethylene tube (the esophagus). Various restrictions in the distal portion of the balloon were used to simulate the palisade zone. B: enlargement of A.
the simulated peristaltic contraction. The latex (varix) balloon was attached to the open hydrostatic reservoir so that the balloon was filled with water at a stable pressure of 10 mmHg. Four restrictions with electrical ties were used to decrease the cross-sectional area of the distal portion of the model varix (47, 67, 77, and 87% of the cross-sectional surface area of the original latex balloon). An individual balloon model was set up for each restriction. Ten simulated swallows were performed for each restriction. Peak pressures and peak distensions were correlated to the percent restriction in the varix model using a Pearson correlation coefficient.

**Statistical Analysis**

Statistics are reported as means ± SD. Statistical significance is analyzed by using the paired Student’s t-test and Pearson correlation coefficient. P < 0.05 was considered significant.

**RESULTS**

**Clinical Study**

Forty varices and sixty-three swallows were evaluated in nine patients. The mean closing pressure (43.8 ± 23.8) and flattening pressure (40.1 ± 16.8) were significantly higher than the mean opening pressure (11.6 ± 25.6) (P < 0.0001). Flattening pressures >80 mmHg (relative to resting esophageal pressure) occurred in varices during peristaltic contractions in 15.5% of swallows. Flattening pressures >100 mmHg relative to the resting esophageal pressure occurred in 4.5% of swallows. The interobserver variability, between the two blinded readers, for the closing pressure was very low with a correlation coefficient value of r = 0.97.

There was a strong correlation between the peak esophageal lumen pressure and the variceal closing pressure in the seven varices in which three or more swallows could be evaluated (r between 0.78 and 0.99). There was no correlation between variceal closing or flattening pressure and the maximum distension of the varix during the peristaltic contraction (r = 0.10). The varices distended, with a mean peak increase in cross-sectional surface area of 41% (range 7–89%), from a baseline mean of 0.29 cm² to an average maximum of 0.41 cm² during the peristaltic contraction (an increase in average variceal radius of 64%; P < 0.0001; Fig. 4).

On clinical follow-up, four patients (44%) bled from esophageal varices an average of 11.5 ± 7.55 mo after the ultrasound/manometry test. The patients that bled had a significantly higher mean peak closing pressure (83.15 ± 18.38 mmHg) than the five patients that did not bleed (53.2 ± 7.67 mmHg) after a mean of 16.4 ± 0.89 mo (P < 0.04). With the use of 61 mmHg as a cutoff for mean peak closing pressure, the sensitivity, specificity, and positive and negative predictive value for predicting future variceal bleeding were all 100%.

**Varix Model Results**

**Varix model to determine the flattening pressures (74% restriction).** The mean intravariceal pressure at the point at which the varix wall flattened was 63.1 ± 15.4 and 63.1 ± 14.9 mmHg (Fig. 5). The mean esophageal pressure at the point at which the varix wall flattened was 63.4 ± 15.9 and 62.9 ± 14.9 mmHg. The mean percent difference between the actual varix model pressure and the esophageal lumen pressure at the point at which the varix wall flattened was 3.8 ± 2.8 and 4.5 ± 2.8%. The correlation between the model esophageal and model varix pressures at the point at which the varix wall

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**Fig. 4.** Ultrasound images demonstrate an increase in cross-sectional area during peristaltic contraction. *A:* image showing a varix (arrow) while the esophagus is at rest. *B:* image showing the same varix (arrow) during the peristaltic contraction. Note the increase in cross-sectional area during the peristaltic contraction.

**Fig. 5.** Ultrasound images of the varix model during the peristaltic contraction. *A:* ultrasound image showing the varix model at rest. *B:* ultrasound image showing the varix model at the point of flattening during the peristaltic contraction. At the point of flattening, the intravariceal pressure equals the esophageal lumen pressure.
attenuation, the esophageal lumen pressure is equal to the intra-

manometric ultrasound and manometry to evaluate esophageal motility (6, 10, 15, 16).

Simultaneous ultrasound (4, 5, 8, 9, 11, 13, 14) and simultaneous manometry were used in this study to measure variceal pressure during peristaltic contraction. The variceal pressure was found to be significantly higher than the baseline pressure for the 77% restriction, which was 10 mmHg. The mean peak pressure was significantly greater than the baseline pressure for the 77% restriction (i.e., approximately physiological resistance) ($P < 0.00001$). As the restriction in the distal varix increased, the maximum increase in variceal cross-sectional area during the simulated contraction increased in a linear fashion with respect to the restriction ($r = 0.99$) (Fig. 7).

**DISCUSSION**

The simultaneous ultrasound and manometry device, used in this study to measure variceal pressure during peristaltic contraction, is based on prior work using high resolution endoluminal ultrasound (4, 5, 8, 9, 11, 13, 14) and simultaneous ultrasound and manometry to evaluate esophageal motility (6, 10, 15, 16).

Force balance laws explain why, at the point of variceal flattening, the esophageal lumen pressure is equal to the intra-

![Fig. 6](image)

**Fig. 6.** Simultaneous intraluminal pressure tracings of the model varix and model esophagus. Graph shows time on the x-axis and pressure on the y-axis. The intravascular pressure is in black and the esophageal lumen pressure is in gray. Note the peak intravascular pressure occurs well before the flattening pressure (the point at which the lines cross over each other is the point at which the varix flattens). The maximum transmural pressure difference occurs coincidently with the peak variceal cross-sectional area. Thus the wall tension is greatest at this point. The mean flattening pressure was found to always be on the down slope of the variceal pressure curve a mean of 34% less than the mean peak intravascular pressure.

![Fig. 7](image)

**Fig. 7.** A: graph of the %restriction at the gastroesophageal junction vs. and the model mean peak intravariceal pressure. In this graph, variceal restriction is on the x-axis and peak pressure is on the y-axis. The mean peak pressure generated in the distal portion of the varix during the peristaltic contraction was directly proportional to the change in cross-sectional surface area at the gastroesophageal junction ($r = 0.98$). These pressures were significantly higher than the baseline pressures ($P < 0.0001$) at physiological resistances (77%). B: graph of the %restriction vs. the peak varix model cross-sectional area. In this graph %restriction is on the x-axis and peak variceal cross-sectional area is on the y-axis. The maximum change in peak variceal cross-sectional area is directly proportional to the percent restriction in the distal varix during the simulated peristaltic contraction ($r = 0.99$).

Varices, which are tubular vascular structures, run longitudinally in the body of the esophagus. The anatomy of esophageal varices in the body of the esophagus differs dramatically from the anatomy of the varices at the gastroesophageal junction. The venous structure of esophageal varices in the body of the esophagus is truncal. Truncal anatomy consists of a few large columns of varices. The venous structure of esophageal varices at the gastroesophageal junction consists of palisade vessels. The palisade veins consist of numerous tiny vessels. The total cross-sectional area of the varices in the palisade area is ~74%...
less than in the truncal zone of the esophagus as determined previously by Schiano et al. (15).

We suggest that during peristaltic contraction the blood flow in esophageal varices reverses direction. Blood in varices normally flows via the gastric varices through the pyloric vessels at the gastroesophageal junction and into the truncal varices in the body of the esophagus in a caudal to oral direction (distal to proximal in the esophagus). During the peristaltic contraction, a wave of pressure is propagated in an oral to caudal direction (proximal to distal in the esophagus), pushing the blood from the proximal portion of the varix to the distal portion of the varix and effectively reversing the blood flow in the varix. This movement is analogous to fluid being pushed down the lumen of the esophagus toward the stomach during swallowing. The resistance to blood flow at the gastroesophageal junction, due to the relative decrease in vessel cross-sectional area, causes the pressure within the distal truncal varices to rise dramatically during the peristaltic contraction.

The varix model demonstrated excellent correlation between the flattening pressure as measured by the observers from the esophageal lumen pressure at the point of variceal flattening and the actual measured pressure within the model varix. In addition, there was excellent correlation between the observers.

The model varix study in which the distal resistance was varied demonstrated that a small change in the resistance at the distal portion of the varix can have a profound effect on the pressure generated within the varix during the peristaltic contraction. At a physiological resistance of ~77% decrease in cross-sectional area [based on the Schiano study (15)], the pressures generated corresponded very closely to the closing and flattening pressures observed in actual varices.

Another observation demonstrated by the varix model system was that the peak intravariceal pressures during the peristaltic contraction were much higher (an average of 34% higher) than the variceal flattening pressures (Fig. 6). This suggests that the flattening pressures measured in the actual varices probably underestimated the maximum intravariceal pressures generated during the peristaltic contraction. In addition, the varix model demonstrated that the maximum transmural pressure difference occurred coincidently with the maximum variceal distension during the peristaltic contraction, thus maximizing the variceal wall tension.

Although the number of patients in this series was small, it was found that the mean peak closing pressures in patients that experienced future variceal bleeding were significantly higher than the mean peak closing pressures in patients that did not experience variceal bleeding ($P < 0.04$). Patients with a mean peak closing pressure $>61$ mmHg were found to be more likely to bleed. The accuracy of predicting future variceal bleeding in this small series, based on these criteria, was 100%.

In conclusion, taken together, the clinical findings and the findings of the varix model confirm the hypothesis that peristaltic contraction increases the pressure, cross-sectional area, and wall tension in the distal portion of esophageal varices and may have negative consequences in terms of variceal bleeding. It may be possible, in the future, to use this technique to measure variceal pressures during peristaltic contraction to predict future variceal bleeding.

REFERENCES


