# Three-dimensional Imaging of the Lower Esophageal Sphincter in Gastroesophageal Reflux Disease

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**The resistance of the lower esophageal sphincter to reflux of gastric juice is determined by the integrated effects of radial pressures exerted over the entire length of the sphincter. This can be quantitated by three-dimensional computerized imaging of sphincter pressures obtained by a pullback of radially oriented pressure transducers and by calculating the volume of this image, in other words, the sphincter pressure vector volume. Validation studies showed that sphincter imaging based on a stepwise pullback of a catheter with four or eight radial side holes is superior to a rapid motorized pullback. Compared with 50 healthy volunteers, the total and abdominal sphincter pressure vector volume was lower in 150 patients with increased esophageal acid exposure ($p < 0.001$) and decreased with increasing esophageal mucosal damage ($p < 0.01$). Calculation of the sphincter pressure vector volume was superior to standard techniques in identifying a mechanically defective sphincter as the cause of increased esophageal acid exposure, particularly in patients without mucosal damage. The Nissen and Belsey fundoplication increased the total and intra-abdominal sphincter pressure vector volume ($p < 0.001$) and normalized the three-dimensional sphincter image. Failure to do so was associated with recurrent or persistent reflux. These data indicate that three-dimensional imaging of the lower esophageal sphincter improves the identification of patients who would benefit from an antireflux procedure. Analysis of the three-dimensional sphincter pressure profile should become the standard for evaluation of the lower esophageal sphincter.**

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THE LOWER ESOPHAGEAL sphincter is the primary barrier against reflux of gastric juice into the esophagus. The function of the sphincter depends on the resistance it imposes to the flow of gastric contents from the positive intra-abdominal pressure environment into the negative-pressure environment of the chest. Manometric evaluation of the high-pressure zone at the gastroesophageal junction usually is performed by measuring its peak resting pressure or the pressure at the respiratory inversion point and assuming that this reflects sphincter resistance.[1,2] Various studies have confirmed that this single pressure measurement is lower in patients with increased esophageal exposure to gastric juice than in controls and decreases with increasing severity of mucosal injury.[3,4] Despite this correlation this method has been shown to be inadequate to identify individual patients with mechanically defective sphincters because of the large overlap with normal subjects.[5] There remained a large number of patients with adequate sphincter pressure who had increased esophageal acid exposure on 24-hour esophageal pH monitoring.

Subsequent investigations have shown that the position of the sphincter, in other words, how much of the sphincter is exposed to the positive intra-abdominal pressure environment, and the overall length of the sphincter, also contribute to its resistance in that an overall length or abdominal length below the fifth percentile of normal could nullify a normal sphincter pressure.[6,7] Patients with low normal values of each of these components, however, still could have an incompetent sphincter.[5] Consequently the simple measurement of the sphincter's resting pressure, overall length, and abdominal length was still insufficient to identify subtle mechanical defects of the sphincter that may result in increased esophageal acid exposure.

From a mechanical standpoint, the pressures exerted at each point over the entire length and around the circumference of the sphincter must be taken into account as contributing to the overall resistance of a sphincter. Bombeck and co-workers[8] have applied this concept of resistance to the lower esophageal sphincter using a manometry catheter with radially oriented side holes. They

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showed that the volume circumscribed by radial pressures measured over the entire length of the sphincter allowed integration of sphincter length and pressure into one parameter, termed the sphincter pressure vector volume. The sphincter pressure vector volume was found to be superior to all individual parameters in predicting patients with gastroesophageal reflux disease who would not respond to medical therapy.

The rapid pullback technique used by Bombeck et al. to obtain the sphincter pressure vector volume has several shortcomings. First it is cumbersome because it requires the use of a custom-made motor to perform the pullback at a constant speed and sophisticated computer hardware and software for acquisition and analysis of the data. Second, in contrast to a stepwise pullback, it is unable to measure the amount of sphincter affected by the positive intra-abdominal pressure environment. This is because the patient is requested to hold his breath during the pullback. Consequently the contribution of the intra-abdominal portion of the sphincter to its resistance can not be evaluated. Finally the rapid pullback technique requires a special catheter assembly with radially oriented transducers located at the same level to obtain a three-dimensional sphincter image. This does not allow the evaluation of esophageal body function in the same setting, and the patient must go through the inconvenience of being reintubated with a second catheter assembly to complete the esophageal evaluation.

In a validation study, we compared sphincter pressure vector volumes obtained by a rapid and stepwise pullback of a catheter with eight radially oriented side holes located at the same level, and a stepwise pullback of a catheter with four sequential side holes oriented radially at 5-cm intervals. In the latter situation, esophageal body function could be evaluated concomitantly. Based on the validation study, we selected the technique that provided the best discrimination of patients with increased esophageal acid exposure from control subjects. We then compared the sphincter pressure vector volume with standard sphincter analysis in a large number of patients with increased esophageal acid exposure and various degrees of mucosal damage. The effect of the Nissen and Belsey fundoplication on the three-dimensional sphincter pressure profile also was evaluated.

## Materials and Methods

### *Populations and Study Design*

The validation population consisted of 15 healthy normal volunteers and 27 symptomatic patients, 17 with normal esophageal acid exposure and 10 with increased esophageal acid exposure documented by 24-hour ambulatory esophageal pH monitoring. All 10 patients with increased esophageal acid exposure had at least 6 months of aggressive acid suppression therapy before the studies and were classified by the referring physician as having gastroesophageal reflux disease unresponsive to medical treatment. On endoscopy 3 of these 10 patients had no mucosal injury, 5 had esophagitis, and 2 had Barrett's esophagus. All volunteers and patients in the validation study underwent three manometric studies to measure the sphincter pressure vector volume, in other words, a rapid and stepwise pullback using a catheter dedicated to measure radial sphincter pressures consisting of eight radially oriented side holes located at one level, and a stepwise pullback using a standard manometry catheter with four sequential side holes oriented radially at 5-cm intervals. The latter catheter is routinely used in manometric studies and allows evaluation of the esophageal body in the same setting. The data obtained were used to assess whether the sphincter pressure vector volume can be reliably obtained with the standard manometry catheter and to identify the best manometric technique to differentiate patients with increased esophageal acid exposure from control subjects.

The method for three-dimensional sphincter imaging selected in the validation study was subsequently compared with standard manometry of the lower esophageal sphincter in a study population consisting of 50 normal healthy volunteers and 150 consecutive patients with increased esophageal acid exposure on 24-hour esophageal pH monitoring. On endoscopy 57 of 150 patients had no mucosal injury, 42 had esophagitis, 20 had a stricture, and 31 had Barrett's esophagus. Thirty-two of these patients also had follow-up studies 1 to 10 years after a Nissen (n = 28) or Belsey (n = 4) fundoplication. The demographic data of the study populations are given in Table 1.

Approval by the local Human Research Ethic Committee was obtained to study the subjects in the validation

TABLE 1. *Demographic Data of the Study Population*

| Study | Number | Mean Age (Range) | Male/Female Ratio |
|---|---|---|---|
| Validation study | | | |
| Normal volunteers | 15 | 32.2 (22–48) | 6/9 |
| Patients, no GERD | 17 | 55.3 (32–69) | 10/7 |
| Patients, GERD | 10 | 52.7 (28–68) | 6/4 |
| Main study | | | |
| Normal volunteers | 50 | 35.2 (23–71) | 20/30 |
| Patients with GERD | | | |
| No mucosal injury | 57 | 46.2 (16–69) | 27/30 |
| Esophagitis | 42 | 48.2 (17–72) | 22/20 |
| Stricture | 20 | 59.0 (17–78) | 13/7 |
| Barrett's | 31 | 53.1 (25–76) | 19/12 |
| Patients s/p antireflux surgery | | | |
| Nissen fundoplication | 28 | 51.3 (25–72) | 16/12 |
| Belsey fundoplication | 4 | 58.2 (44–72) | 2/2 |

GERD, gastroesophageal reflux disease.

study and the 50 normal volunteers. Written informed consent was obtained from all subjects before the study.

### *Manometry of the Lower Esophageal Sphincter*

Manometry of the lower esophageal sphincter was performed after an overnight fast. Medications known to interfere with gastrointestinal secretory or motor function were discontinued at least 48 hours before the study. Various catheter assemblies with an outer diameter of 4.8 mm and four to eight lateral openings of 0.8 mm diameter were used. The catheters were perfused with distilled water at a constant rate of 0.6 ml/min using an Arndorfer pneumohydraulic low-compliance perfusion pump. Each tube was connected to an external pressure transducer positioned at the midaxillary level. Before each test the transducers were calibrated using a mercury-filled manometer so that a change in pressure of 1 mm Hg corresponded to 0.5 mm on the recording paper. The pressures measured were printed by a Gould ES1000 16-channel recorder on paper running at a velocity of 5 mm/second. A belt pneumograph was positioned around the chest to record respiratory excursions. A piezoelectric transducer was taped to the neck at the level of the cricoid cartilage to indicate pharyngeal swallows. The catheter assembly was passed through an anesthetized nostril into the stomach, and the gastric pressure pattern was confirmed. All pressure measurements were read with the gastric baseline pressure as reference point.

### *Three-dimensional Imaging of the Lower Esophageal Sphincter*

Three-dimensional manometric imaging of the lower esophageal sphincter was performed with a rapid and stepwise pullback of various catheters illustrated in Figure 1.

Rapid motorized pullback manometry was performed using a catheter assembly with eight radially oriented side holes located at the same level in 45-degree angles to each other. The side holes were withdrawn through the gastroesophageal junction at a constant speed of 3.3 mm/second by a custom-made high-torque hysteresis synchronous motor. The subjects were instructed to hold their breath in the end-expiratory position during the pullback. The mechanical pullbacks were repeated until three satisfactory readings were obtained. Sphincter pressures in all eight radial channels were measured manually at 0.5-cm intervals beginning with the rise of pressure above gastric baseline until the recorded pressures in all channels fell below gastric baseline. Because the breath was held during the motorized pullback, the respiratory inversion point and consequently the abdominal portion of the sphincter could not be identified by this technique.

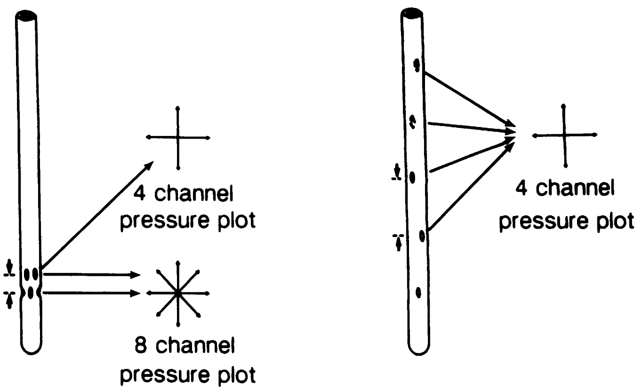


FIG. 1. Catheters used to obtain a three-dimensional sphincter image. (A) A catheter with eight radial side holes at one level oriented in 45° angles to each other. Three-dimensional spincter images were obtained using a rapid and stepwise pullback technique. The sphincter pressure vector volume was calculated based on eight or four radial side holes placed over the length of 1 cm (between arrows). (B) A standard esophageal motility catheter with five side holes spaced at 5-cm intervals (between arrows). The four proximal side holes are oriented in 90° angles to each other. A stepwise pullback of the four proximal side holes through the lower esophageal sphincter was used to construct a three-dimensional sphincter image and calculate the sphincter pressure vector volume.

Stepwise pullback manometry was performed using the catheter assembly with eight radially oriented side holes located at one level in 45-degree angles to each other and the second assembly containing four sequential side holes spaced in 5-cm intervals and oriented radially in 90-degree angles to each other. The latter catheter was identical to the catheter routinely used for standard manometric evaluation of the lower esophageal sphincter and esophageal body. The catheter assembly was withdrawn from the stomach in 1-cm increments every 20 seconds until all transducers had passed through the gastroesophageal junction. The patient was instructed to breathe normally but to avoid swallowing. The stepwise pullback of the catheter with eight radial channels was repeated three times. End-expiratory sphincter pressures in all radial channels were measured manually at 1-cm intervals from the rise of the end-expiratory pressure above gastric baseline until the recorded end-expiratory pressures in all channels fell below gastric baseline. The respiratory inversion point, in other words, the level when the positive deflections in the pressure curve caused by inspiration within the abdomen changed to negative within the chest, was located in each channel and used to identify the intra-abdominal portion of the sphincter.

Three-dimensional images of the lower esophageal sphincter were constructed by a computer program developed by one of us (REP). Pressures measured at each station of the pullback were plotted radially around an axis representing gastric baseline pressure with the program, accounting for the longitudinal spacing of the side holes on the catheter (Fig. 2). For visual purposes the three-dimensional reconstruction of the sphincter pressure

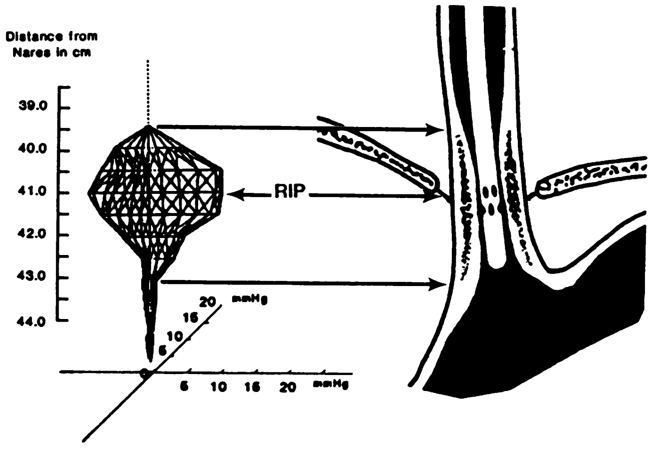


FIG. 2. Computerized three-dimensional imaging of lower esophageal sphincter. A catheter with four to eight radial side holes is withdrawn through the gastroesophageal junction. For each level of the pullback, the radially measured pressures are plotted around an axis representing gastric baseline pressure. When a stepwise pullback technique is used, the respiratory inversion point (RIP) can be identified.

image was enhanced by applying a cubic curve-smoothing interpolation, which retains the original data points while adding intermediate ones to give a smoother surface to the three-dimensional sphincter image and improve its readability. This interpolation was performed for imaging only, whereas all mathematical calculations were made solely with the primary data. The three-dimensional image can be rotated on the computer screen and inspected from various angles (Fig. 3).

The volume circumscribed by the three-dimensional sphincter pressure profile was measured by calculating the cross-sectional radial pressure areas at each measured level, in other words, 5-mm intervals for the rapid pullback and 10-mm intervals for the stepwise pullback, using the trigonometric formula for an irregular octagon or tetragon. Each cross-sectional sphincter pressure area, expressed as square millimeters of mercury, then was multiplied by the length of the section. The sum of all cross-sectional sphincter pressure areas integrates radial pressures exerted over the entire length of the sphincter into one number, the total sphincter pressure vector volume expressed in units of $mmHg^2 \times mm$. With the stepwise pullback technique, which allowed identification of the respiratory inversion point, the intrathoracic and intra-abdominal portions of the sphincter pressure vector volume, in other words, the portions of the sphincter pressure vector volume located above and below the respiratory inversion point, also were determined. The pressure vector volume was calculated from data obtained by (1) a rapid and stepwise pullback of a catheter with eight radial side holes located at the same level; (2) a rapid and stepwise pullback of four radial side holes located at the same level; and (3) a stepwise pullback of a catheter with four sequential side holes oriented radially and spaced in 5-cm intervals. Measurement 2 was obtained from recordings made with the eight-channel catheter by ignoring every other channel (Fig. 1). A sphincter was defined as mechanically defective when the total or abdominal sphincter pressure vector volume was below the fifth percentile of that measured in 50 normal volunteers.

## *Standard Manometry of the Lower Esophageal Sphincter*

Standard manometric evaluation of the lower esophageal sphincter was performed using a catheter with five lateral side holes placed at 5-cm intervals from the distal end of the catheter and oriented around the circumference. The catheter was withdrawn from the stomach at 1-cm increments every 20 seconds until all side holes had passed through the gastroesophageal junction. The patient was instructed to breathe normally but to avoid swallowing. Overall length, abdominal length, in other words, length below the respiratory inversion point, and resting pressure of the lower esophageal sphincter were measured as previously described.[5] Based on extensive studies in normal volunteers and patients with increased esophageal acid exposure, the lower esophageal sphincter was defined as mechanically defective if, on the mean of five pullbacks, the resting pressure was below 6 mm Hg, the overall length was less than 2.0 cm, or the abdominal length was less than 1.0 cm.[5,9]

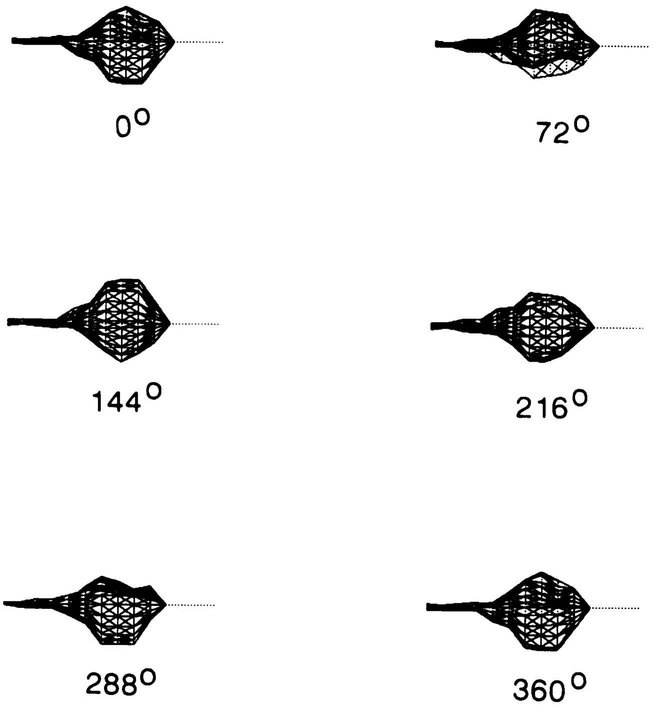


FIG. 3. The three-dimensional sphincter pressure image of a normal volunteer shown from various angles. This effect is achieved by rotating the image around an axis representing gastric baseline. Note the marked asymmetry of the sphincter.

### *Ambulatory 24-hour Esophageal pH Monitoring*

Outpatient 24-hour esophageal pH monitoring was performed using a combined Ingold glass electrode with a built-in reference electrode. The probe was calibrated in standard buffer solutions at pH 7 and 1 before and after the study. Only recordings with an electrode drift of less than 0.2 pH units over the 24-hour monitoring period were accepted. The electrode was passed transnasally and placed 5 cm above the upper border of the lower esophageal sphincter. The electrode was connected to a portable digital data recorder, which stored pH readings every 4 seconds (Synectics, Irving, TX). After placement of the probe, the subjects were sent home and instructed to remain in the upright or sitting position until they retired for the night, to perform normal daily activity but to avoid strenuous exertion, and to follow a diet restricted to three meals composed of food with a pH between 5 and 6. Only water was permitted between meals. A diary was kept of food and fluid intake, symptoms experienced during the monitored period, the time when the supine position was assumed in preparation for sleep, and the time of rising in the morning. All medications known to interfere with foregut motor or secretory function were stopped at least 48 hours before the study. The amount of esophageal exposure to gastric juice ($pH < 4$) was quantitated using a composite scoring system.[9,10] A patient was considered to have increased esophageal exposure to gastric juice if the composite score exceeded the 95th percentile of 50 normal healthy volunteers, in other words, a score value above 14.8.

### *Endoscopy*

Upper gastrointestinal endoscopy was performed in all patients by the senior author (TRD), who was unaware of the results of manometry and pH monitoring at the time of endoscopy. The presence of esophagitis was recognized by mucosal erythema (grade 1), linear erosions and friability (grade 2), or coalescent erosions, the so-called cobblestone mucosa (grade 3). An esophageal stricture was identified by the inability to pass a 12-mm endoscope with ease. Biopsies were performed on all strictures to exclude malignancy, and they were dilated to 50 French before manometry and pH monitoring. There was an intervai of at least 1 week between dilatation and esophageal function tests. Barrett's esophagus was diagnosed by histologic documentation of columnar epithelium lining the esophagus at least 3 cm above the endoscopic gastroesophageal junction.

### *Statistical Methods*

The sphincter pressure vector volumes obtained with various techniques in the validation population were compared with each other using Spearman's rank correlation coefficient. The ability of the various techniques to discriminate patients with increased esophageal acid exposure from control subjects was evaluated using analysis of variance and comparison of the confidence intervals.

Standard nonparametric tests for unpaired and paired data sets were used to compare the sphincter pressure vector volumes between or within subject groups of the study population. The prevalence of a mechanically defective sphincter was compared between groups using the Fisher's exact test of proportion. A $p\text{-value} < 0.05$ was considered significant. Unless otherwise stated, all data are expressed as mean ± standard error of the mean (SEM).

## Results

The validation study showed that measurements of the sphincter pressure vector volume with eight radially oriented side holes at one level compare well with those made with four radial side holes at one level (Table 2). Measurements obtained with the stepwise pullback of a catheter with four or eight radial side holes located at one level were similar to those obtained with a standard manometry catheter having four sequential radial side holes placed in 5-cm intervals (Table 2). This gave confidence in the use of the standard manometry catheter to measure the sphincter pressure vector volume.

Figure 4 shows the individual measurements of the sphincter pressure vector volume made with a rapid and stepwise pullback of the catheter with eight radial side holes at one level and a stepwise pullback with the standard motility catheter. Both stepwise pullback techniques provided a better discrimination of subjects with increased esophageal acid exposure than a rapid pullback. This was reflected also by a higher significance level and a smaller overlap in the confidence intervals between those subjects with and without increased esophageal acid exposure (Table 3).

TABLE 2. *Comparison of Various Techniques to Calculate the Sphincter Pressure Vector Volume*

| Technique | Spearman's Rank Correlation Coefficient | p |
|---|---|---|
| RP (8 channel) *vs.* RP (4 channel) | 0.86 | <0.0001 |
| SP (8 channel) *vs.* SP (4 channel) | 0.91 | <0.0001 |
| SP (8 channel) *vs.* SSP (4 channel) | 0.81 | <0.0001 |
| SP (4 channel) *vs.* SSP (4 channel) | 0.82 | <0.0001 |

RP, Rapid motorized pullback of radial transducers located at one level.

SP, stepwise pullback of radial transducers located at one level.

SSP, stepwise pullback of radial transducers located at 5-cm intervals.

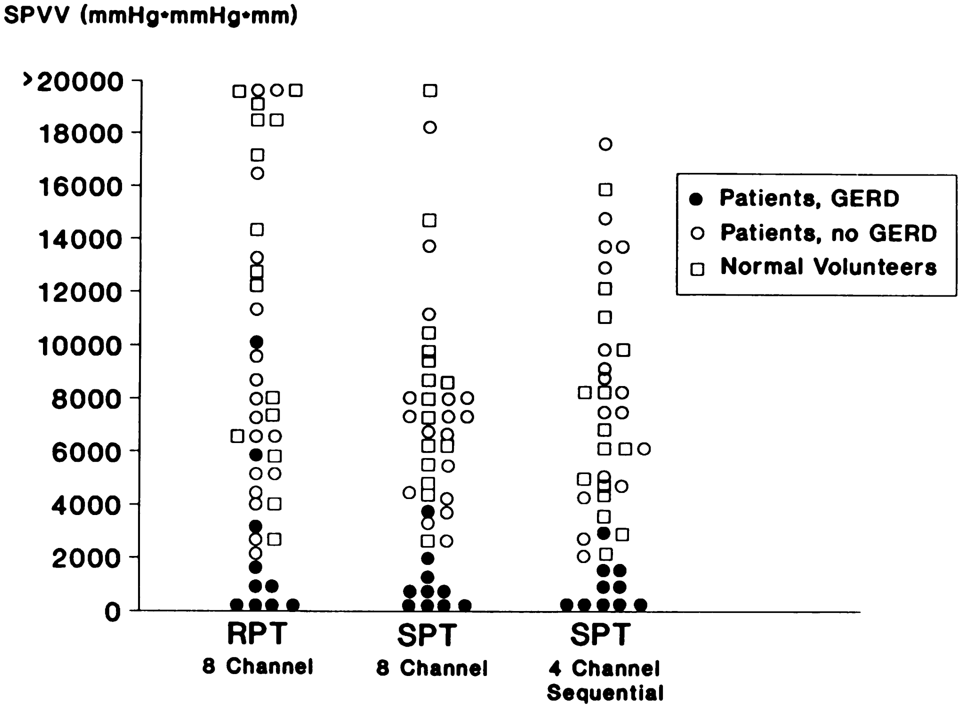


FIG. 4. A plot of the individual sphincter pressure vector volumes (SPVV) obtained with a rapid or stepwise pullback (RPT or SPT) of a catheter with eight radial side holes at one level and a stepwise pullback of a catheter with four sequential radial side holes placed at 5-cm intervals. Both stepwise pullback techniques provided a better discrimination of patients with gastroesophageal reflux disease (GERD) from control subjects than the rapid pullback technique.

Normal values for the total sphincter pressure vector volume, and the intra-abdominal and intrathoracic components obtained in 50 normal volunteers with a stepwise pullback of the standard manometry catheter are given in Table 4. Figure 5 shows that total and intra-abdominal sphincter vector volumes obtained with this technique are significantly lower in patients with increased esophageal exposure to gastric juice as compared with normal volunteers ($p < 0.001$), and decrease with increasing severity of mucosal injury ($p < 0.01$).

TABLE 3. *Mean Sphincter Pressure Vector Volumes and Confidence Intervals in Subjects With and Without Increased Esophageal Acid Exposure*

| Technique to Measure SPVV | Normal Esophageal Acid Exposure (N = 27) Mean (99.99% CI) | Increased Esophageal Acid Exposure (N = 10) Mean (99.99% CI) | p |
|---|---|---|---|
| Rapid pullback (8 radial side holes at one level) | 10841 (6866–14816) | 2340 (0–9451) | 0.001 |
| Stepwise pullback (8 radial side holes at one level) | 7925 (5485–10366) | 872 (0–5237) | 0.00001 |
| Stepwise pullback (4 radial side holes located at 5-cm intervals) | 7403 (4950–10724) | 673 (0–4802) | 0.00001 |

SPVV, sphincter pressure vector volumes; CI, confidence interval.

Figure 6 compares the prevalence of a mechanically defective sphincter based on analysis of the three-dimensional sphincter image, in other words, total and intra-abdominal sphincter pressure vector volume, with standard techniques of sphincter analysis, in other words, sphincter pressure at the respiratory inversion point, overall length, and abdominal length, in patients with increased esophageal exposure to gastric juice and various degrees of mucosal injury. Both techniques show an increasing prevalence of a mechanically defective sphincter with increasing severity of mucosal injury. In patients with increased esophageal exposure to gastric juice but no mucosal injury, analysis of the three-dimensional sphincter image identified a significantly higher prevalence of a defective sphincter as compared with standard techniques ($p < 0.05$). The differences between the two techniques in patients with complications of gastroesophageal reflux disease, in other words, esophagitis, stricture, or Barrett's esophagus, were not significant.

The effect of an antireflux procedure on the three-dimensional sphincter pressure profile in a patient with Barrett's esophagus is shown in Figure 7. Nissen fundoplication restored the sphincter image to normal. Figure 8 displays the mean sphincter pressure vector volume in 32 patients with gastroesophageal reflux disease before and after a Nissen or Belsey fundoplication. Both procedures markedly increased the total and intra-abdominal sphincter pressure vector volume ($p < 0.001$). The total

TABLE 4. *Normal Values for Sphincter Pressure Vector Volume (SPVV) Obtained with a Stepwise Pullback of Four Radially Oriented Transducers Placed at 5-cm Intervals*

| SPVV | Mean | Standard Error | Median | 5th Percentile | 95th Percentile |
|---|---|---|---|---|---|
| Intraabdominal | 3613 | 531 | 2012 | 684 | 12918 |
| Intrathoracic | 2050 | 319 | 1452 | 476 | 6022 |
| Total | 5723 | 843 | 3667 | 1212 | 16780 |

sphincter pressure vector volumes before and after antireflux surgery for the individual patients are shown in Figure 9. Preoperatively 26 of 32 patients had a defective total sphincter pressure vector volume, whereas three of six of the remaining patients had an isolated defect in the intra-abdominal pressure vector volume. Subjective and objective control of reflux was associated with a normalization of the sphincter pressure vector volume in 28 patients. Four patients had persistent or recurrent reflux on 24-hour esophageal pH monitoring after the antireflux procedure. In three fourths of these patients, the postoperative sphincter pressure vector volume was below the 5th percentile of normal volunteers.

## Discussion

Gastroesophageal reflux disease is a common foregut disorder that is complicated by esophagitis, stricture, or Barrett's esophagus in about 50% of affected patients.[9] A mechanically defective lower esophageal sphincter is the cause of increased esophageal acid exposure in the majority of patients with complications of the disease.[11] Medical therapy in this situation is plagued by high failure and relapse rates.[12,13] This is because medical therapy is aimed at suppression of acid secretion while allowing other noxious ingredients of gastric juice like pepsin, trypsin, and bile salts to reflux unabated through the defective sphincter, resulting in persistent mucosal injury. Even if medical therapy is effective in healing mucosal damage, the mechanical defect of the sphincter persists and mucosal injury recurs as soon as medical therapy is discontinued.[12-14] Conversely antireflux surgery is designed to correct a mechanically defective sphincter and can effectively prevent reflux of any gastric content.[15] It is important to identify the patients with a mechanically defective lower esophageal sphincter before the development of complications to avoid the loss of esophageal body function, which is known to occur as mucosal injury progresses.[16] In such patients surgery should be performed before the loss of esophageal body function occurs.[17,18] The present study shows that measuring the sphincter pressure vector volume is superior to standard techniques in identifying a mechanically defective lower esophageal sphincter as the cause of increased esophageal acid exposure, particularly in patients with no mucosal injury.

Radial manometric evaluation of lower esophageal sphincter pressures is not new. Using a stepwise pullback of a catheter with radial side holes, Winans[19] demonstrated a marked cross-sectional asymmetry of the lower esophageal sphincter in normal volunteers. Three-dimensional images of the lower esophageal sphincter in healthy volunteers obtained by a rapid pullback of a catheter with eight radial side holes were recently presented by Bemel-

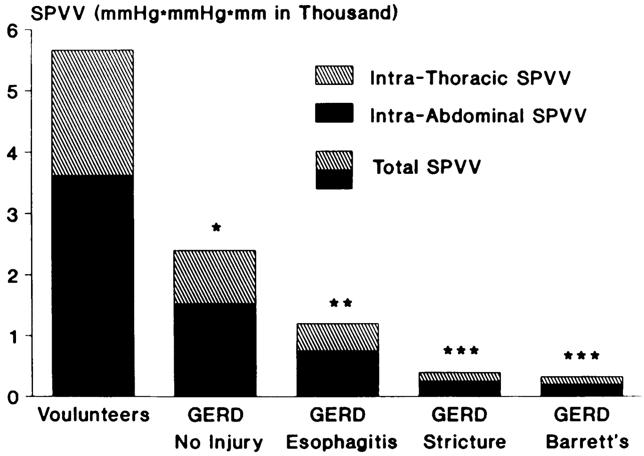


FIG. 5. Mean total and intra-abdominal SPVV in 50 healthy volunteers and 150 patients with gastroesophageal reflux disease GERD and various degrees of mucosal damage. The p values are given for total and intra-abdominal SPVV. $*p < 0.01$ *versus* volunteers; $**p < 0.01$ *versus* volunteers and GERD patients with no mucosal injury; $***p < 0.01$ *versus* all other groups.

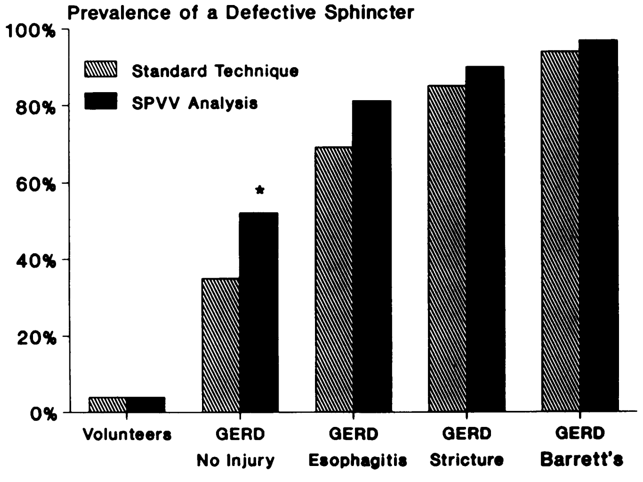
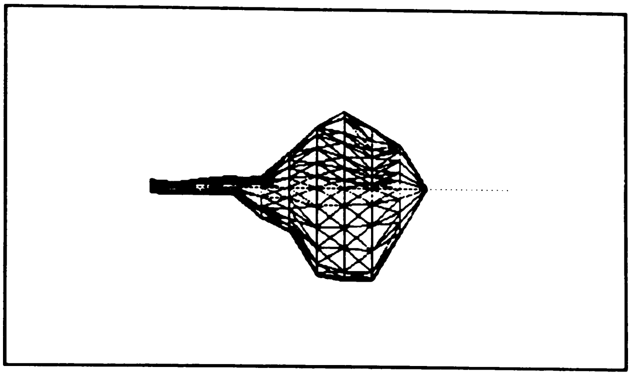
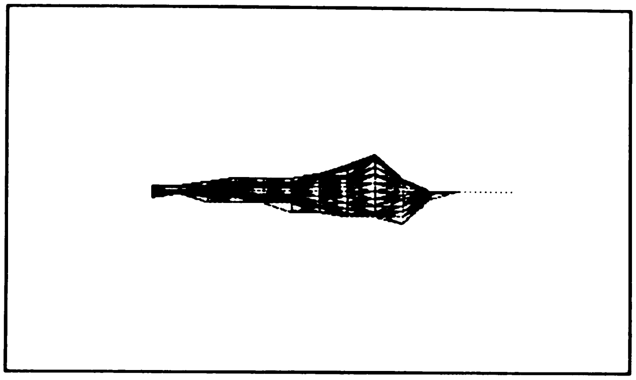


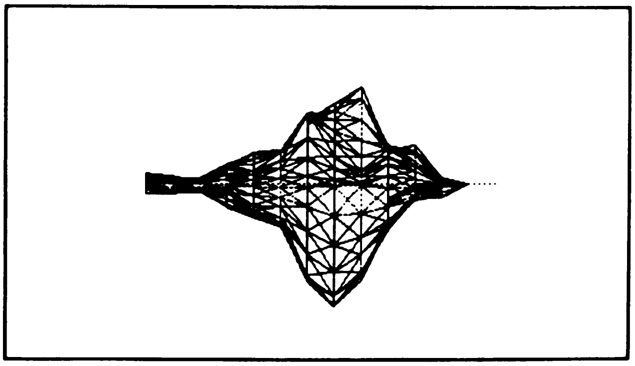
FIG. 6. Comparison of standard manometric techniques and SPVV analysis in the identification of a mechanically defective lower esophageal sphincter. $*p < 0.05$ *versus* standard manometry.



Normal



Barrett's Preop



After Nissen

FIG. 7. The three-dimensional sphincter pressure image in a normal volunteer, a patient with Barrett's esophagus, and the same patient after Nissen fundoplication.

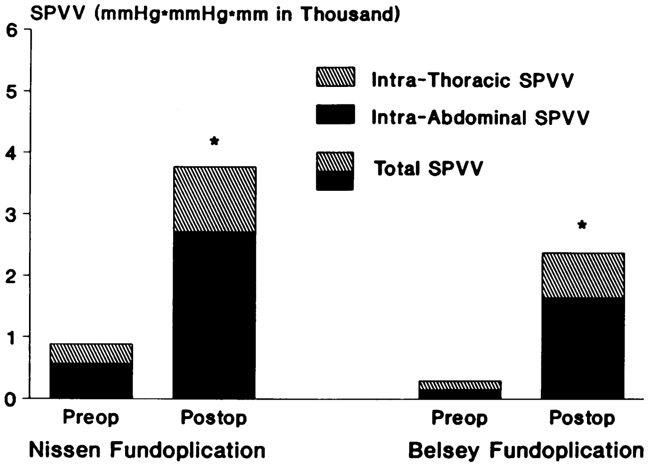


FIG. 8. Effect of the Nissen (N = 28) and Belsey (N = 4) fundoplication on the SPVV. *p < 0.001 *versus* preoperative values. SPVV, sphincter pressure vector volume.

man et al.[20] The use of radially measured sphincter pressures in the assessment of patients with gastroesophageal reflux disease was first reported by Bombeck et al.[8] Applying sophisticated computer technology, he and his coworkers analyzed the three-dimensional sphincter pressure profile obtained by a rapid pullback of a catheter with four to six radial side holes located at one level. They introduced the "sphincter pressure vector volume" as a parameter that integrates sphincter pressures exerted around the circumference and along the entire length of the sphincter into one value representing lower esophageal sphincter resistance. In all these studies, radial sphincter pressures were measured with a dedicated catheter assembly that did not allow the concomitant assessment of esophageal body function. The present study showed that four radially oriented side holes are sufficient to reliably evaluate the sphincter pressure vector volume and that a stepwise pullback technique with a catheter containing radial side holes located at the same level or placed se-

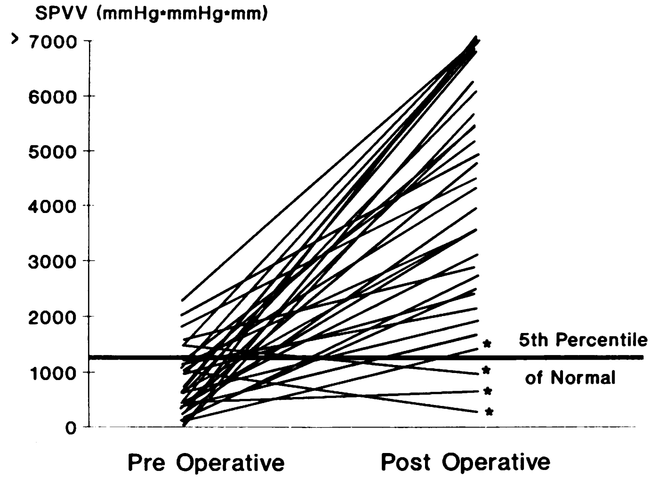


FIG. 9. Individual preoperative and postoperative sphincter pressure vector volumes (SPVV) in 32 patients undergoing antireflux surgery. *Patients with persistent or recurrent reflux. The six preoperative values above the 5th percentile line are six patients who had isolated abnormality in their abdominal SPVV but a normal total SPVV.

quentially in 5-cm intervals is superior to a rapid pullback in discriminating patients with gastroesophageal reflux disease from control subjects. Consequently a stepwise pullback of a catheter assembly with four sequential radial side holes was used in all subsequent studies. This catheter assembly allows evaluation of esophageal body function in the same setting. In addition calculation of the sphincter pressure vector volume by this technique is less complex and does not require the sophisticated computerized data acquisition and analysis systems used by other groups.

Evaluation of the three-dimensional sphincter pressure profile in a large population of patients with increased esophageal acid exposure showed that both total and abdominal sphincter pressure vector volume were markedly lower compared with 50 healthy volunteers, and decreased with increasing severity of mucosal injury. Although it is tempting to ascribe the loss of sphincter function to inflammation or tissue damage, the observation of a low sphincter pressure vector volume in the absence of mucosal damage suggests that the loss of sphincter resistance is primary and probably due to smooth muscle abnormalities.[21]

Standard techniques to assess sphincter resistance and calculation of the sphincter pressure vector volume showed an increasing prevalence of a mechanically defective sphincter with increasing severity of mucosal injury. Calculation of the sphincter pressure vector volume did not have a significant advantage over standard manometric techniques in detecting a defective sphincter in patients with advanced complications of gastroesophageal reflux disease, but significantly increased the sensitivity of manometry in identifying a mechanically defective sphincter in patients with increased esophageal acid exposure but no mucosal damage. This indicates that standard techniques, in other words, measurement of sphincter pressure, overall length, and abdominal length, can reliably identify gross sphincter defects but are insufficient to detect subtle sphincter abnormalities.

Despite the advance of three-dimensional sphincter imaging in assessing sphincter resistance, there still remains a number of patients with increased esophageal acid exposure and an apparently normal lower esophageal sphincter. A marked asymmetry of the sphincter, which is not taken into account when calculating the sphincter pressure vector volume, may be responsible for reflux in some of these patients.[22] In the remainder other causes of increased esophageal exposure to gastric juice are likely to be present. In such patients a careful evaluation of esophageal body function, gastric emptying, gastric acid secretion, and duodenogastric reflux should be performed.[9]

In patients with increased esophageal acid exposure due to a mechanically defective lower esophageal sphincter, reconstruction of a functional sphincter by an antireflux procedure provides the only rational therapy in that it effectively abolishes reflux of any gastric contents in over 90% of patients.[15] Our study demonstrates that this is achieved by increasing the total and abdominal sphincter pressure vector volume to normal. This is further emphasized by the observation that failure to restore the three-dimensional sphincter pressure profile to normal was associated with persistent or recurrent reflux.

In summary the present study shows that the analysis of the three-dimensional sphincter pressure profile obtained with a stepwise pullback is superior to a rapid pullback technique in the ability to differentiate between subjects with or without increased esophageal acid exposure. Calculation of the sphincter pressure vector volume increases the sensitivity of manometry to identify a mechanically defective lower esophageal sphincter as the cause of increased esophageal acid exposure, particularly in patients with no mucosal injury. The effect of an antireflux procedure in controlling reflux is dependent on restoration of the sphincter pressure vector volume to normal. Calculation of the sphincter pressure vector volume allows identification of patients who would benefit from an antireflux procedure before the development of mucosal injury and loss of esophageal body function. Consequently this manometric technique should become the standard for the evaluation of the lower esophageal sphincter in patients with gastroesophageal reflux disease.

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## DISCUSSION

DR. EDWARD W. HUMPHREY (Minneapolis, Minnesota): Dr. Stein has presented us with a method of mathematically modeling the lower esophageal sphincter area. I have long admired the efforts of Dr. DeMeester's group to raise the work on the lower esophageal sphincter from the realm of metaphysics to that of real science, and this paper is no exception.

I do have three questions on this work. The first is, what is the reproducibility of the sphincter pressure vector volume with time in the same individual? If it is good, it might permit the longitudinal studies to finally learn whether the motor abnormalities seen with esophagitis are the cause or effect of the abnormal reflux.

Secondly I made some extrapolations from the graphs in your manuscript. I found that although the absolute value of the abdominal portion of the pressure vector volume is less in the patients with esophagitis and the total volume is less, the proportion is the same. In patients with esophagitis, 67% of the total volume is below the diaphragm and thus in the abdomen; in your volunteers it was 63%. With the error in my extrapolation, those are essentially the same, and I wonder if you can explain that? Because 80% to 85% of patients with abnormal reflux have a hiatus hernia, I would have expected the abdominal portion to be considerably smaller in patients with esophagitis.

Third have you noted any differences that will predict which of the patients will be in the 10% to 15% that have a poor result from a fundoplication? If you could do that with this method, it would be a significant advance.

Thank you very much.

PROFESSOR MARTIN ALLGOWER (Basel, Switzerland): I have four questions (they are rather naive) and one comment. The Basel anatomist was telling us surgeons that we have a very astounding capacity to name and to cut structures he had never seen. I think it is the merit of Doris Lieberman to describe the anatomic reality of the lower esophageal sphincter.

My first question is, whether sphincter pressure vector volumes in a way do mirror the anatomic findings that Lieberman has been describing? Naturally the actual clinical application of the Lieberman procedure would be somewhat devastating to the patient! I wonder whether you agree that your quantification of LE-function constitute an interesting confirmation of Doris Lieberman's findings.

Second the merits of your three-dimensional imaging are to a large extent validated by their conformity with the increased esophageal acid exposure. Now my question is, what is the additional information with regard to therapeutic decisions taken from your values?

Thirdly the reflux disease without mucosal lesions seems to be the main real case for your method. Now could it be that your method picks out the known hypersecreters who would probably benefit from an early antirefluxplasty?

And fourthly one "philosophical" question: Does not the "amount of subjective suffering" constitute an important element of an indication for operation?

I enjoyed so very much to see Bombeck's finding substantiated and made more easily applicable.

Naturally I was particularly happy to see that the Nissen procedure really has stood the test of time. Thank you very much for this very good paper.

DR. PHILIP DONAHUE (Chicago, Illinois): My only slide—may I see it now, please?—illustrates a concept of the vector volume and introduces my three questions. This is actually one of Tom Bombeck's slides from his presentation here in 1987. A "full-bodied" sphincter is normal; "skinny, abnormal-looking" sphincters, are abnormal. After fundoplication, the contour of the sphincter is more normal.

My first question relates to vector volume: The computer program converts multiple virtual areas of segments of the sphincter into a volume, by multiplying an average area times the length. The radius of that cylinder is the critical factor, and I am concerned about the station pullback technique that you have used. You thought that it was better than rapid pullback technique, but we believe the rapid pullback eliminates subjective factors in estimating the average pressure along sphincters. When station pullback is employed, bias is introduced.

How do you avoid subjective bias in estimating pressures?

Secondly we have found that asymmetry of the sphincter is an important concept (Probably affecting only patients with marginal pressures). Can you tell us whether you have noted the presence of asymmetry in any of your patients with failed sphincter?

Finally the vector volume concept still does not identify 20% of patients who require surgery, because 20% of the patients you operated on had a normal study; we believe that abnormal (but as yet unmeasurable) aspects of gastric components of the reflux barrier can help explain reflux disease in some of these patients. I invite your comments about this possibility.

DR. HUBERT J. STEIN (Closing discussion): Thank you very much for those kind remarks. I would like to answer Dr. Humphrey's questions first. He addressed the reproducibility of the measurement over time. We performed reproducibility measurements within the same subject within 2 or 3 hours. Within this short period, all of the measurements, in other words, the rapid and stepwise pullback, were highly reproducible. We do not have long-term reproducibility studies yet, but it would certainly be interesting to see what they would show.

Why was the percentage of the intra-abdominal segment of the sphincter similar in volunteers and in the patients with esophagitis, even though many of the latter had a hiatal hernia? We have previously shown that the presence of a hiatal hernia does not necessarily mean that there is no intra-abdominal segment of the lower esophageal sphincter. The length of the intra-abdominal segment is determined by the insertion of the phreno-esophageal membrane, and even in patients with a large hiatal hernia, intra-abdominal pressure can be exerted on the sphincter through the hiatus. Patients with esophagitis frequently had an isolated defect in their intra-abdominal segment, however, but there were others in the same group of patients with a normal intra-abdominal segment but a short overall length of the sphincter and a defective total sphincter pressure vector volume.