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Sleeve sensor versus high-resolution manometry for the detection of transient lower esophageal sphincter relaxations

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Bredenoord, A. J., B. L. A. M. Weusten, R. Timmer, and A. J. P. M. Smout. Sleeve sensor versus high-resolution manometry for the detection of transient lower esophageal sphincter relaxations. *Am J Physiol Gastrointest Liver Physiol* 288: G1190–G1194, 2005. First published January 13, 2004; doi:10.1152/ajpgi.00478.2004.—Transient lower esophageal sphincter relaxations (TLESRs) are the most important mechanism by which gastroesophageal reflux occurs, and sleeve sensor manometry is the gold standard for detection of TLESRs. The aim of this study was to evaluate manometry with closely spaced sideholes (high-resolution manometry) for the detection of TLESRs as an alternative. In 12 patients with gastroesophageal reflux disease, a 90-min postprandial manometry was performed by using a catheter incorporating both a sleeve sensor and closely spaced sideholes in the esophagogastric junction. TLESRs recorded with both techniques were scored. Reflux during TLESRs was detected by using manometry (common cavity), intraluminal impedance, and pH monitoring. A total of 145 TLESRs were detected by using both techniques, 117 with high-resolution manometry and 108 with sleeve sensor manometry [not significant (NS)]. Manometric signs of reflux during TLESRs detected with high-resolution and sleeve sensor manometry were found in 62.4 and 56.5%, NS, respectively, versus 38.5 and 35.2%, NS on pH-metry and 70.1 and 60.2%, NS on impedance monitoring. TLESRs recognized only with high-resolution manometry were more often accompanied by reflux, as detected with manometry (59.5%) and impedance monitoring (67.6%), than TLESRs recognized only with sleeve sensor manometry (32.1 and 28.6%). High-resolution manometry is at least as accurate as sleeve sensor manometry for the detection of TLESRs.

esophageal manometry; transient lower esophageal sphincter relaxation; gastroesophageal reflux; impedance monitoring

BEFORE THE ADVENT OF THE SLEEVE sensor, lower esophageal sphincter (LES) pressure was measured by using a single perfused sidehole or miniature pressure transducer positioned in the lumen of the sphincter. Because of axial movements of the distal esophagus with respect to the pressure sensor, it was difficult to ascertain that a drop in pressure was caused by an LES relaxation. The introduction of the perfused sleeve sensor by Dent in 1976 (11) was an important step forward. The sleeve sensor records the highest pressure along a membrane, thus reducing movement artifacts almost entirely. This technical improvement led to the discovery of relaxations of the LES not associated with swallowing, initially referred to as "inappropriate" LES relaxations, and their important role in the pathogenesis of gastroesophageal reflux disease (GERD) became clear (1, 13, 17, 22, 24). Subsequent studies showed that these inappropriate or transient LES relaxations (TLESRs) are the result of a vagally mediated reflex, triggered by mechanoreceptors in the proximal stomach with the purpose of protecting the stomach against excessive gaseous dilatation (14, 15, 21, 23). TLESRs often facilitate acid reflux, which means that TLESRs are now considered to be a promising target for pharmacotherapy of GERD (2, 6, 18, 33, 35).

New technical developments have led to the introduction of micromanometry (8, 20). Micromanometry catheters contain smaller lumina compared with conventional manometry catheters, and are perfused at very low perfusion rates. This development has made it possible to record pressures at 1-cm intervals without overloading the esophagus with a large quantity of water. This method, known as high-resolution manometry, offers the theoretical advantage above sleeve sensor manometry that more detailed information of the gastroesophageal junction can be obtained (3, 4, 12). Until now it has not been clarified whether TLESRs can be adequately studied by using high-resolution manometry. Therefore, the aim of this study was to compare the detection of TLESRs using high-resolution manometry with the detection of TLESRs using sleeve sensor manometry.

MATERIALS AND METHODS

Subjects. We studied 12 patients (5 men and 7 women, mean age: 50 yr, range: 18–81 yr) with an esophageal acid exposure time of >4.2% of the total time during a recent 24-h pH study. Written informed consent was obtained from all subjects, and the protocol was approved by the medical ethics committee of the University Medical Center Utrecht.

Study protocol. The use of gastric acid inhibitory drugs and drugs that influence gastrointestinal motility was discontinued 5 days before the study. After an overnight fast, the manometry catheter was introduced transnasally. The catheter was positioned such that at least the most distal sidehole recorded gastric pressure and that the high-resolution area of the catheter and the sleeve sensor straddled the LES. After positioning of the manometry catheter, the impedance and the pH catheter were introduced transnasally and positioned based on the manometric findings (see *Intraluminal impedance and pH monitoring*). Subjects were in an upright position, and after an adaptation period of at least 10 min, the experiment was started. Patients were asked to minimize head movements.

After 30 min of recording in the fasting state, the subjects consumed a standardized meal consisting of a hamburger (McDonald's Quarter Pounder consisting of a bun, sauce, meat, pickle and cheese), 20 g of fresh onions, 44 g of potato chips and 475 ml of orange juice (in total 967 kCal). The meal had to be finished in 30 min. After ingestion of the meal, recording was continued for another 90 min.

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Manometric technique. An 18-channel water-perfused silicone rubber catheter (outer diameter: 4.0 mm, length: 75 cm, channel diameter: 0.4 mm) was used for manometric recording (Fig. 1). The proximal part of the assembly incorporated five sideholes at 1-cm intervals. Of these, the sidehole most clearly showing swallow-induced pharyngeal contractions was selected for recording swallows. After selection of this sidehole, perfusion of the other four pharyngeal sideholes was discontinued because it has been suggested that pharyngeal stimulation with water may trigger TLESRs (19). There were four esophageal sideholes at 5-cm intervals and seven sideholes at 1-cm intervals at the distal end of the catheter. In addition, the distal end of the catheter incorporated a 6-cm long reverse-perfused sleeve sensor. The sideholes in the manometry catheter were labeled according to their distance to the midsleeve channel (sidehole 0). All sideholes were perfused at a rate of 0.08 ml/min using a pneumohydraulic perfusion system (Dentsleeve, Wayville, South Australia). The sleeve sensor was perfused at a rate of 0.30 ml/min.

Pressures were measured with external pressure transducers (Abbott, Sligo, Ireland). Pressure data were stored in digital format in two 12-channel dataloggers (Medical Measurement Systems, Enschede, The Netherlands) using a sample frequency of 8 Hz. At the end of the study, all data were transferred to the hard disk of the computer.

Intraluminal impedance and pH monitoring. For intraluminal impedance monitoring, a seven-channel impedance catheter was used [Aachen University of Technology, Forschungszentrum für Eleletro-Magnetishe Umweltverträglichkeit (FEMU), Aachen, Germany]. This catheter (outer diameter: 2.3 mm) enabled recording from seven segments, each recording segment being 2 cm long. The recording segments were located at 0–2, 2–4, 4–6, 8–10, 10–12, 14–16, and 17–19 above the upper border of the manometrically localized LES (Fig. 1). Impedance signals were stored in a digital system (Aachen University of Technology, FEMU) using a sample frequency of 50 Hz (5). Intraluminal pH monitoring was performed with a glass pH electrode (Ingold, Urdorf, Switzerland), and data were stored in a digital datalogger (Orion, Medical Measurement Systems) using a sampling frequency of 2 Hz. The pH glass catheter was positioned 5 cm above the upper border of the LES (Fig. 1). With the use of a cable that connected the pH datalogger with the impedance datalogger, the pH signals were stored on both dataloggers enabling synchronization.

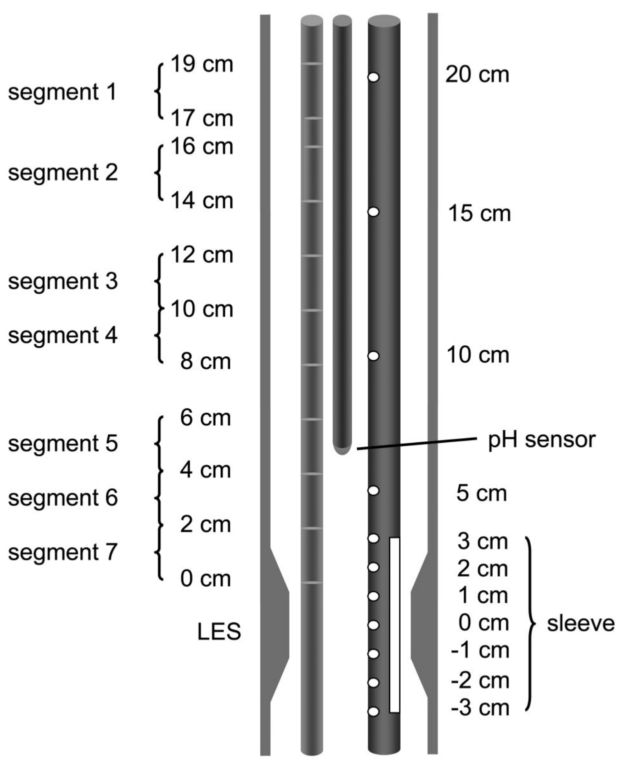

Fig. 1. Impedance (*left*) and pH (*middle*) catheters were positioned with respect to the upper border of the lower esophageal sphincter (LES). The manometry catheter (*right*) was positioned in such a way that the most distal sidehole registered gastric pressure and the sleeve sensor straddled the LES. The sideholes on the manometry catheter were labeled according to their distance to midsleeve.

Data analysis. End-expiratory LES pressure was calculated by using the intragastric pressure as reference. Pressure tracings of the sideholes and sleeve sensor were analyzed on a computer screen. It was possible to obscure signals from individual pressure transducers to blind the observer for these signals. Analysis of TLESRs was thus performed separately with the observer blinded for either the tracings of the sideholes in the high-resolution area (signals of sideholes −2, −1, 0, 1, and 2 not shown on screen) or the sleeve sensor tracings.

In accordance with criteria developed by Holloway et al. (16), a TLESR was defined as a drop in LES pressure with a velocity >0.4 kPa/3 s, time from onset to complete relaxation of <10 s, a nadir pressure of <0.26 kPa, and absence of a swallow in the time window from 4 s before to 2 s after the start of the relaxation. Excluding multiple swallows, LES pressure falls that fulfill the first three criteria but have a duration of >10 s can also be classified as TLESRs regardless of the timing of LES relaxation to swallowing. In the analysis of TLESRs in the high-resolution manometry signals, the signals recorded from the two sideholes with the highest resting pressure had to fulfill the above criteria. An additional criterion was that pressure in adjacent sideholes should not increase simultaneously with the decrease in pressure in the other sideholes. This criterion was added to avoid movement artifacts.

For each TLESR identified, it was observed whether a common cavity phenomenon could be identified. A common cavity was defined as an abrupt increase in intraesophageal pressure to intragastric pressure in at least two distal esophageal recording sites (36).

In the impedance tracings, gas reflux was defined as a rapid (>3,000 Ω/s) and pronounced retrograde moving increase in impedance in two consecutive impedance sites (29). Liquid reflux was defined as a retrograde moving 40% fall in impedance in the two distal impedance sites. Mixed liquid-gas reflux was defined as gas reflux occurring during or immediately before liquid reflux.

In the pH tracings, a decrease in pH of >1 unit or a drop of pH below 4 was considered an indicator of reflux of acid gastric content into the esophagus (34). Analysis of the impedance and pH signals was performed while the investigator was blinded for the results of the TLESR analysis.

Statistical analysis and presentation of data. The χ^2 test was used to compare proportions. Mean TLESR duration was compared by using the Wilcoxon rank sum test. Numbers of TLESRs per subject were compared by using the Wilcoxon signed-rank test. Differences were considered statistically significant when $P \leq 0.05$. Throughout the manuscript, parametric data are presented as means ± SE and nonparametric data as median (interquartile range). Pressures are expressed in kPa (1 kPa = 7.5 mmHg).

RESULTS

In total, 145 TLESRs were identified, either with the sleeve sensor or with high-resolution manometry or with both manometric techniques. The sleeve sensor identified 108 TLESRs; with high-resolution manometry 117 TLESRs could be identified. This implies that the sleeve sensor detected 74.5% of all TLESRs, whereas high-resolution manometry detected 80.7%

(P = 0.2). The median number of TLESRs per patient found with the sleeve sensor was 8 (range, 7–12) and with high-resolution manometry was 9 (range, 8–12), the difference being not statistically significant. High-resolution manometry detected more TLESRs in eight patients, whereas sleeve sensor manometry detected more TLESRs in three patients; in one patient an equal number of TLESRs was found with both techniques.

Median duration of the TLESRs was 17.0 (range, 14.0–22.0) s for sleeve sensor-detected and 18.5 (range, 14.0–22.8) s for high-resolution manometry-detected TLESRs, the difference also being not statistically significant. Proportions of all TLESRs found with either sleeve or high-resolution manometry accompanied by evidence of gastroesophageal reflux as detected by manometry, impedance, or pH monitoring were not significantly different (Table 1). Whereas 80 TLESRs fulfilled the criteria for TLESRs on both sleeve sensor and high-resolution manometry, 28 TLESRs were detected only with the sleeve sensor, and 37 TLESRs were exclusively found with high-resolution manometry (Fig. 2). Significantly higher proportions of TLESRs detected with high-resolution manometry only were associated with reflux, compared with TLESRs only detected with the sleeve sensor ($P < 0.05$).

Several reasons were identified why TLESRs may fulfill the criteria with one of the two techniques and not with the other. TLESRs that fulfilled the Holloway criteria (16) in the sleeve sensor tracing but not in the high-resolution manometry tracings did not meet the criteria for maximum nadir pressure (11 cases), rate of decrease in pressure (6 cases), and relaxation duration (1 case). Sometimes multiple criteria were not fulfilled (10 cases, of which 3 maximum nadir and rate of decrease, 1 maximum nadir and relaxation duration, and 6 all 3 above-mentioned criteria). The TLESRs that only fulfilled the criteria when measured with high-resolution manometry were not recognized in the sleeve sensor signal as a consequence of *1*) a low basal LES pressure (<0.4 kPa) that was not high enough to detect the required rate of decrease in pressure (13 cases), *2*) a too-slow decrease in pressure (9 cases), *3*) a combination of too-high nadir LES pressure and a too-slow pressure decrease (6 cases), *4*) too-high nadir pressure (4 cases), or *5*) the combination of a swallow in the 4 s before and 2 s after the onset of the relaxation and a duration of relaxation shorter than 10 s because of an after-contraction in the distal esophagus that obscured the relaxation of the LES (4 cases) (Fig. 3).

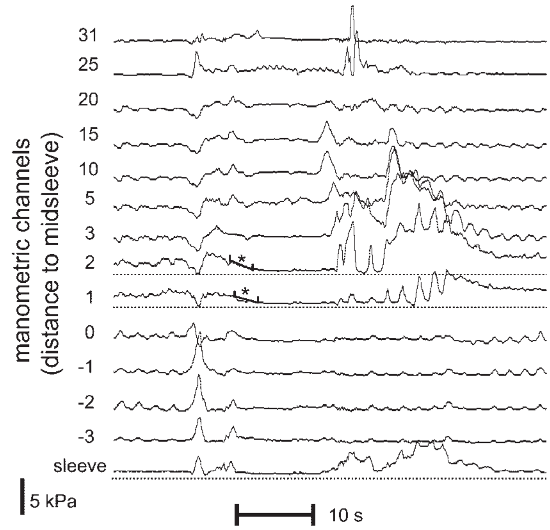

Fig. 2. Transient lower esophageal sphincter relaxation (TLESR). Both the signals from the closely spaced sideholes and the sleeve sensor are shown in this figure. In *channels 1* and *2*, a simultaneous decrease in pressure (*) occurs, the relaxation rate being >0.4 kPa/3 s. In the sleeve sensor signal, a decrease in pressure can be noted, but the rate does not reach 0.4 kPa/3 s because of low baseline LES pressure. Channels −1 to −3 are located in the stomach. The dotted line indicates gastric pressure.

DISCUSSION

To date, TLESRs could only be identified in signals recorded with a sleeve sensor or a sphinctometer. Comparison showed a good concordance between these techniques, but the sphinctometer seems to be inferior to the sleeve sensor when basal LES pressure is low (30, 31). The sleeve sensor with its 6-cm-long membrane overcomes displacement of the pressure sensor out of the esophagogastric junction during respiration and peristalsis and is considered the gold standard (11). This study shows that an array of closely spaced point sensors at the esophagogastric junction is also a reliable tool to identify TLESRs. We found that the TLESR detection rate was not significantly different between high-resolution and sleeve sensor manometry. However, a proportion of the TLESRs that fulfilled the criteria when measured with the sleeve sensor did not fulfill the criteria when measured with high-resolution manometry and vice versa.

Although the criteria of TLESRs were developed on the basis of objective arguments, not all TLESRs are followed by gastroesophageal reflux. Because three independent methods for reflux detection were used (pressure, impedance, and pH

Table 1. *Percentage of TLESRs accompanied by evidence of gastroesophageal reflux*

	TLESRs detected with both methods	all TLESRs detected with sleeve sensor	TLESRs detected with sleeve sensor only	all TLESRs detected with high-resolution	TLESRs detected with high-resolution only
Common cavity	65.00	56.48	32.14	62.39	59.46*
pH drop	40.00	35.19	21.43	38.46	35.14
Impedance, total	71.25	60.19	28.57	70.09	67.57*
Impedance, gas reflux	11.25	12.04	10.71	12.82	16.22
Impedance, mixed gas-liquid reflux	41.25	32.41	10.71	38.46	32.43*
Impedance, liquid reflux	18.75	15.74	3.57	18.80	18.92*

Values are percent. *$P \leq 0.05$ compared with transient lower esophageal sphincter relaxations (TLESRs) only detected with sleeve sensor.

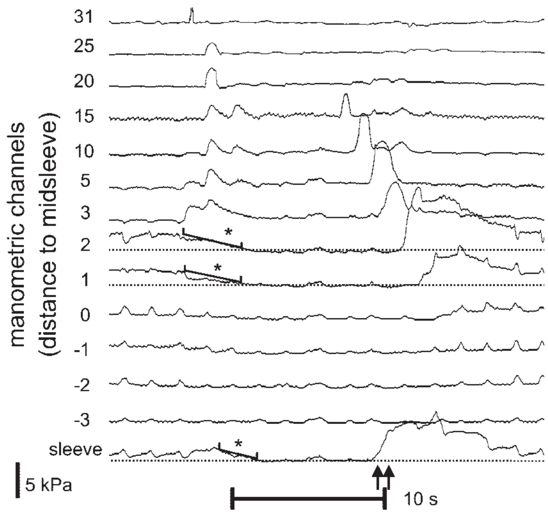

Fig. 3. TLESR. *Channels 1* and *2* and the sleeve show a relaxation to gastric pressure (*) with a relaxation rate of >0.4 kPa/3 s, followed by secondary peristalsis. The increase in pressure in the proximal end of the sleeve (arrows) induced by the peristaltic contraction makes the relaxation last shorter in the sleeve sensor. A swallow is observed in the window between 4 s before and 2 s after the onset of the relaxation, but the relaxation measured with the sideholes lasts longer than 10 s but not as measured with the sleeve sensor. The dotted line indicates gastric pressure.

monitoring), it is unlikely that many reflux episodes were missed in this study. Probably, a proportion of TLESRs are not accompanied by reflux because the gastroesophageal pressure gradient necessary to push gastric contents upward is insufficient even during episodes of complete relaxation of the LES. Both in pathophysiological studies and in the development of new drugs aiming at inhibiting the frequency of TLESRs, one would be more interested to detect those TLESRs that are actually accompanied by reflux (28). The majority of TLESRs observed with both high-resolution and sleeve sensor manometry were accompanied with evidence of gastroesophageal reflux on manometry, impedance, or pH monitoring. However, the TLESRs that fulfilled the Holloway criteria (16) exclusively on high-resolution manometry showed a significantly higher reflux rate than the TLESRs that fulfilled the criteria only on sleeve sensor manometry. Nevertheless, it has to be mentioned that this concerned only a small proportion of the total number of TLESRs detected, and for the majority of the results, the two techniques were comparable.

In this study, most reflux episodes were detected by impedance monitoring followed by manometry, and least reflux was detected by monitoring of esophageal pH. A similar ratio between detection rates was found in a study by Shay and Richter (25). Whereas manometry is not very specific for gastroesophageal reflux, pH monitoring is not able to detect reflux of nonacid gastric substances, has a low sensitivity and specificity for superimposed reflux, and misses virtually all gas reflux episodes. Intraluminal impedance monitoring, however, is thought to detect at least 90% of all reflux episodes (27). Therefore, it is unlikely that with the combination of three reflux detection techniques, many episodes were missed. In the present study, ~70% of the TLESRs were accompanied with evidence of reflux, leaving ~20% that were not. This could in part be due to the fact that the patients were in an upright position during this study, because it is known that more reflux occurs in the right lateral recumbent position (26, 32). The relative position of the stomach with respect to the esophagus and the gastroesophageal pressure gradient are likely to play a role in this phenomenon.

Whereas we show that high-resolution manometry is an accurate device to detect TLESRs, several disadvantages of the technique should be taken into account. First, the equipment of high-resolution manometry is more sophisticated and therefore more expensive. Furthermore, more signals are gathered during high-resolution manometry, which makes interpretation elaborate and analysis of these measurements requires an experienced investigator. Whereas analysis and interpretation is thus more elaborate for high-resolution manometry, various studies describe its benefits. Previously, with the use of high-resolution manometry, topographic analysis of esophageal contraction was made possible, and it was shown that this provided additional information about esophageal function (9, 10). Recently, Fox et al. (12) showed that high-resolution manometry detected clinically relevant esophageal dysfunctions not detected by conventional manometry.

Although a paper by Castell et al. (7) has suggested that a sleeve sensor underestimates the duration of LES relaxation, our data do not support this notion. The observed difference between the durations of LES relaxation measured in our study with high-resolution or sleeve sensor manometry was small and not statistically significant. In the study by Castell et al. (7), comparison was performed between LES relaxations measured with the sleeve sensor and a single sidehole. It is well known now that manometry with a single sidehole is not an adequate technique for measurement of LES relaxation. Furthermore, these observations were made in swallow-induced LES relaxations, i.e., not in TLESRs.

It should be kept in mind, however, that the Holloway criteria (16) were initially developed for detection of TLESRs with sleeve sensor manometry. The criterion of relaxation duration of at least 10 s is necessary to separate TLESRs from swallow-induced LES relaxations. If measurement of relaxation with the sleeve sensor would underestimate duration of relaxation, this 10-s criterion would perhaps not be enough to separate swallow-induced relaxations from TLESRs measured with sidehole manometry. Because TLESRs are much more often accompanied by reflux compared with swallow-induced relaxations of the LES, this would result in a lower reflux rate of the TLESRs measured only with high-resolution manometry. Our data show that this is not the case.

Results from this study imply that besides the currently used sleeve sensor and sphinctometer, high-resolution manometry can also be used to detect and study TLESRs. While the sleeve sensor records the highest external pressure exerted on the membrane, high-resolution manometry registers pressure on different sites in the esophagogastric junction. This study shows that high-resolution manometry is as least as reliable for the detection of TLESRs as the current gold standard sleeve sensor manometry.

GRANTS

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