Lower esophageal sphincter monitoring with sphinctometer: in vitro and in vivo studies

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Pehlivanov, Nonko, Jianmin Liu, Tania Arora, Yoshihiro Yamamoto, and Ravinder K. Mittal. Lower esophageal sphincter monitoring with sphinctometer: in vitro and in vivo studies. Am. J. Physiol. 277 (Gastrointest. Liver Physiol. 40): G577–G584, 1999.—The sphinctometer is a solid-state device system for prolonged ambulatory recordings of the lower esophageal sphincter (LES) pressure. The aims of this study were to determine 1) the pressure sensitivity and the latency of sphinctometer responses in vitro, 2) if the sphinctometer can record transient LES relaxations (TLESRs) in vivo, and 3) if the currently accepted criteria for TLESRs are applicable to sphinctometer recordings. Different segments of the sphinctometer were positioned in a chamber at known pressures to assess the sphinctometer readings as well as the latency of the response. Ten healthy subjects were investigated with the use of a solid-state transducer sphinctometer assembly and a pH probe for 4 h. The LES pressure was analyzed during baseline periods, swallow-induced LES relaxations (SILESRs), and LES relaxations associated with acid reflux episodes (pH < 4) (presumed TLESRs). Our results showed that sphinctometer readings were linearly related to the chamber pressure and the length of the segment exposed to the pressure; however, the latter was considerably underestimated. We also found that sphinctometer segments of equal length but at different levels showed different pressure readings, the mean response time of sphinctometer was 0.25 s, and sphinctometer output was susceptible to temperature changes of the environment. In humans, only 25 of 45 episodes (64%) and 17 of 22 episodes (77%) were detected by the sphinctometer as being SILESRs and TLESRs, respectively. The pattern of the LES pressure during acid reflux events resembled classical TLESRs. We concluded that the sphinctometer is a useful device for determining qualitative changes in LES pressure. However, its major limitations are pressure underestimation, different sensitivity of various segments, pressure drifts, and underscoring of LES relaxations.

METHODS

The sphinctometer (Sentron, Roden, The Netherlands) was mounted on a solid-state catheter system (Synectics Medical, Stockholm, Sweden). This catheter system, in addition to a sphinctometer, has three solid-state esophageal pressure transducers. These transducers are located at 3, 8, and 13 cm proximal to the upper edge of the sphinctometer sleeve. This particular design of the sphinctometer has a pressure transducer located in the middle of the 6-cm sealed “balloonlike” sleeve system. The sleeve system is filled with oil and is designed to measure LES pressure over its entire length.

In Vitro Studies

In vitro studies were designed to assess 1) the response to pressure at different segments of the sphinctometer and also the response of its entire length against a known pressure, 2) the response time, which was defined as the latency of the sphinctometer response to the applied pressure, and 3) the susceptibility of the sphinctometer to the drifts in pressure over time and to changes in the temperature. A chamber similar to the one described by Gotley et al. (8) (Fig. 1) was used for these experiments. This chamber has two glass rods to hold the catheter, a pressure gauge, and a manual pump for pressurization of the chamber. A piece of fresh rabbit small intestine was secured between the two glass rods. A plastic tube with an inner diameter slightly larger than the sphinctometer was inserted into one of the rods in such a fashion that, when the sphinctometer was passed through the plastic tube and the rabbit’s intestine, it was possible to expose

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different lengths of the sphinctometer at different places by moving the plastic tube and/or the sphinctometer. The sphinctometer pressure was monitored using a PC polygraph (Synectics Medical) and a computer.

The sphinctometer was calibrated against two known pressures of 0 and 50 mmHg at room temperature with the entire length of the device placed in the calibration chamber. To test the different segments of the sphinctometer, its length was divided into six 1-cm segments separated by centimeter marks, beginning from the distal end. The following segments of the sphinctometer, confined between the following marks on the sleeve, were tested:

1. 1-cm segments at 0–1, 1–2, 2–3, 3–4, 4–5, and 5–6 cm;
2. 2-cm segments at 0–2, 2–4, and 4–6 cm, respectively;
3. 3-cm segments at 0–3, 2–5, and 3–6 cm, respectively;
4. 4-cm segments at 0–4, 1–5, and 2–6 cm, respectively; and
5. 5-cm segments at 0–5 and 1–6 cm, respectively. The whole length of the sphinctometer (6 cm) was also tested. The sphinctometer was tested in the following manner: 1) parts with different lengths of 1, 2, 3, 4, and 6 cm were exposed to pressures ranging from 10 to 60 mmHg with 10-mmHg increments and returning to 0 mmHg between increments, and 2) parts of equal length but at different levels along the sphinctometer sleeve were tested against pressure in the same fashion. Average results of the three measurements of the response time and pressure reading were obtained at each increment of the applied pressure. The differences between the chamber pressure and the sphinctometer output were assessed.

Finally, to test the sphinctometer’s susceptibility to pressure reading drifts, we performed two 24-h recordings, at 0 and 30 mmHg, in the calibration tube at room temperature. We also tested the influence of temperature changes on the pressure reading. The sphinctometer was calibrated at 22°C and submerged in a water bath, which was gradually heated to 37°C and then cooled to 22°C. The changes in the pressure reading with each 1°C increment were recorded on a computer and processed afterward.

**In Vivo Studies**

Ten healthy volunteers, 3 males and 7 females, mean age 31.9 ± 14.06 yr (range 18–53), entered the study. None of these volunteers had any upper gastrointestinal symptoms or history of abdominal surgery. Studies were performed after an overnight fast and 24-h cessation of alcohol and tobacco. The Human Investigation Committee of the University of Virginia approved the protocol, and each volunteer signed an informed consent before participation in the study.

The in vivo studies were performed using the sphinctometer pressure catheter and a pH probe (Synectics Medical) attached 3 cm above the proximal edge of the sphinctometer. The sphinctometer was calibrated at 0 (atmospheric pressure) and 50 mmHg at room temperature. Subjects’ nares and pharynges were anesthetized with 5 ml of 1% viscous lidocaine gel and topical lidocaine spray, respectively. After a standard pull-through technique, the catheter assembly was placed in such a fashion that the proximal end of the sphinctometer was located 2 cm above the upper edge of the LES, pH probe at 5 cm above the LES, and pressure ports at 5, 10, and 15 cm above the LES. The subjects remained in the left recumbent position from 2 h before until 2 h after the ingestion of a standard meal, consisting of a sandwich and a soft drink (1,000 kcal, 40% carbohydrate, 40% protein, and 20% fat). Five wet swallows of 5 ml of water at room temperature were performed by each volunteer at the beginning of the investigation. Subjects were asked to refrain from spontaneous swallows for at least 30 s before and after each induced wet swallow. The pressure and pH were recorded through the PC polygraph (Synectics Medical) onto a computer with a sampling frequency of 8 Hz.
Data Analysis

All of the tracings were read by one investigator (N. Pehlivanov). The sphinctometer readings were expressed in sphinctometer units (SU). Ten SU was the reading when the entire length of the sphinctometer (6 cm) was exposed to a 10-mmHg calibration pressure.

In vitro data analysis. For the purposes of comparison, sphinctometer readings and pressure recordings of the test chamber were digitized and processed at a sampling rate of 1 Hz. For the latency of the sphinctometer response studies, the sampling rate was 8 Hz. The response time was defined as the difference between the initial pressure rise recorded by the sphinctometer and the applied chamber pressure.

In vivo data analysis. In normal subjects, the majority of acid reflux episodes occurs during TLESR (5). Therefore, we selected LES pressure profiles at the time of acid reflux as indicative of TLESR. Acid reflux was defined as an intraesophageal pH drop to <4 that lasted longer than 5 s. The atmospheric pressure was used as the zero pressure reference for calculations of the intraesophageal pressure. The LES baseline pressure was defined as the end-expiratory LES pressure above the atmospheric pressure. Two main patterns of resting LES pressure were recognized: end-expiratory and inspiratory (Fig. 2). The inspiratory pressure pattern consisted of either a monophasic or a biphasic wave. The latter consisted of a positive and a negative pressure wave during the same inspiration phase. The baseline LES pressure was calculated as the mean end expiratory pressure during a 10-min period after a short stabilizing interval following the catheter placement and for 10–20 s before each swallow-induced LES relaxation (SILESR) as well as TLESR. Inspiratory pressure in the LES records was calculated as the mean of peak values of inspiratory waves. In the case of biphasic inspiratory waves, the inspiratory pressure was measured at the peak of the inspiratory wave, and the end-expiratory pressure was measured at the point of intersection between the LES pressure trace and an extrapolated line connecting the peak expiratory pressure points in the esophageal leads. Inspiratory pressure amplitude of LES was estimated between the points of end-expiratory and peak inspiratory pressure waves. The duration of LES relaxation was the time between the point at which the LES tracing crossed the horizontal line connecting the end-expiratory pressure points before the relaxation and the point of intersection of this line with the LES contraction wave after the relaxation. The time needed to complete LES relaxation was estimated between

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<th>Table 1. Classical criteria for TLESR as defined in studies using water-perfused catheter systems and corresponding findings according to the present study</th>
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<td>Classical Criteria for TLESR Based on Water-Perfused Catheter System</td>
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<td>1. Duration of LES relaxation &gt; 10 s</td>
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<td>2. Loss of inspiratory LES pressure oscillations (crural diaphragm inhibition)</td>
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LES, lower esophageal sphincter; TLESR, transient LES relaxation; SU, sphinctometer units.

In vitro data analysis

The pressure readings in each test segment were linearly related to the pressure in the test chamber (r = 0.99; P < 0.05) (Fig. 3).

Effect of sphinctometer length on the recorded pressure. The pressure recorded by the sphinctometer was linearly related to the length of the sphinctometer segment exposed to the pressure chamber (Fig. 3). The larger the length of the sphinctometer exposed to the chamber, the closer was the device’s reading to the applied pressure. The readings of sphinctometer segments with lengths of 4 cm or more were fairly close to the applied pressure, ranging from 82% to 100% of the applied pressure. On the other hand, segments of 1–3 cm indicated pressures of 45–79% of the actual chamber pressure.

Effect of different segments of the sphinctometer on the recorded pressure. Sphinctometer segments of equal length but at different levels showed different pressure

Fig. 2. Schematic representation of characteristics of lower esophageal sphincter (LES) relaxation.
readings for a given chamber pressure (Fig. 4). When the 1-cm segment of the sphinctometer was exposed to the chamber pressure at different levels along the sleeve, the output varied from 31% to 89% of the chamber pressure. The most accurate pressure readings were measured from the two 1-cm segments proximal to the center of the device, between the 3rd- and 5th-cm marks. The two 1-cm segments with the lowest pressure sensitivity were at the two ends of the device.

Effect of different pressures on the sphinctometer output. Sphinctometer output was closer to the chamber pressure when a low pressure was applied, i.e., for 4-cm segments and 10 mmHg pressure the output varied from 8.71 SU (87.15%) to 10 SU (100%) for different segments of the device. For 60 mmHg, the readings ranged between 40.61 SU (67.68%) and 58.95 SU (98.25%). When the 3-cm segment was exposed, the readings ranged between 6.47 SU (64.74%) and 8.91 SU (89.17%) for 10 mmHg and between 36.1 SU (60.25%) and 47.4 SU (79.01%) for 60 mmHg applied pressure.

Latency in sphinctometer pressure response. Response time varied according to the length of the tested segments and their position along the sphinctometer sleeve. For 1-cm segments, the quickest response was achieved from the segment between 1st- and 2nd-cm marks (latency 0.19 s), and the slowest response (0.43 s, P < 0.05) was given by the segment between the 0- and 1st-cm mark. The latency response for the 3-cm and 4-cm segments was 0.24 ± 0.13 and 0.19 ± 0.07 s, respectively. Overall, the averaged response time of all segments was 0.24 ± 0.10 s.

Drift susceptibility of the sphinctometer to time and temperature. The in vitro drift tests at 0 and 30 mmHg showed only a slight difference of 2–3 SU between the sphinctometer output and the pressure in the calibration cylinder during a 24-h recording period at room temperature. However, the sphinctometer output was influenced by temperature. The readings showed a gradual drop of up to 22 SU at 37°C (Fig. 5). During the cooling period, the pressure reading curve lagged behind compared with the one during the heating period.

In Vivo Studies

Baseline LES pressure. An LES baseline pressure reading drift occurred in 9 of 10 subjects. The LES pressure readings in eight subjects fell below the atmospheric zero pressure shortly after the placement. In one case, the baseline pressure gradually increased to 58 SU above zero and LES relaxation never reached zero, suggesting that the baseline reading most likely drifted in the positive direction. In 9 of 10 cases, the baseline pressure readings became stable within 10–15 min after the insertion of the sphinctometer. After this initial period of drift, the baseline pressure readings did not change dramatically throughout the rest of the study.

Fig. 3. Effects of sphinctometer length exposed to the chamber pressure on the recorded output. Chamber pressures vs. sphinctometer outputs were recorded by different segments of the sphinctometer. Note that the longer a sphinctometer segment was exposed to the chamber pressure the more accurate was the sphinctometer output. SU, sphinctometer units.

Fig. 4. Effects of different segments of sphinctometer exposed to the chamber pressure on the sphinctometer output. One-centimeter segments along the sphinctometer were exposed to the chamber pressure. Note that the most sensitive pressure segments were in the center of the sphinctometer.
investigation. In these nine cases, zero line adjustments were made based on the lowest pressure achieved during SILESR relaxations and/or TLESRs. Mean adjustment for the cases with baseline pressures below zero line was $-3.87 \pm 3.24$ SU (range from $-0.9$ to $-11$ SU). In the case with an elevated baseline, a new zero line was set at 43.1 SU, the nadir pressure during the LES relaxations.

The mean end-expiratory baseline pressure was measured during 10-min periods after the pressure readings were already stable and was $7.15 \pm 4.25$ SU. It did not differ significantly from the mean baseline pressures before SILESRs ($6.02 \pm 2.46$ SU, $P > 0.05$) and TLESRs ($6.0 \pm 2.57$ SU, $P > 0.05$), which were measured later during the recordings. The LES pressure during inspiration usually demonstrated a monophasic wave pattern. However, biphasic pressure waves with a sharp initial positive and then a negative deflection were observed in some records (before and after the TLESR, Fig. 6, right). The incidence of biphasic waves varied in a given subject as well as among different subjects.

SILESR. A total of 45 swallows in nine subjects were analyzed for SILESRs (mean of 3.2 per subject, range of 2–5). A drop in LES pressure, i.e., LES relaxation, was observed in 29 of the 45 swallows (64.44%). Each of these swallows was accompanied by a normal peristaltic wave in the esophageal body. In the remaining 16 (35.56%) swallows, no LES relaxations were visualized, although peristaltic waves were present in the esophagus. Data from 29 wet swallows with SILESRs were used to measure the duration of relaxation, end-expiratory, and inspiratory pressure in LES before and during the SILESR. Mean duration of SILESRs was
LES relaxations of durations longer than 10 s were registered in three cases. Mean end-expiratory LES pressures before and during SILESRs were 6.02 ± 2.46 and 1.86 ± 1.68 SU, respectively, and represented an average decrease of 67.4% (range of 9.87–100%) of the initial pressure. The results for mean inspiratory LES pressure amplitude before and during SILESRs were 5.21 ± 2.33 SU and 3.0 ± 2.44 SU, respectively, or an average of 41.5% (range of 5–100%) reduction in the pressure amplitude.

TLESRs. Three volunteers did not reveal any acid reflux episodes. In the remaining seven subjects, 22 episodes of acid reflux were identified (mean of 2.43, range of 1–5 per subject). All of these reflux episodes occurred in the postprandial period. The LES pressure profiles around the time of acid reflux were characterized during these 22 episodes. The LES pressure showed a drop in 17 of these 22 (77.27%) episodes, which were regarded as TLESRs. The mean duration of the TLESRs was 19.3 ± 5 s (range 8.88–30.49) (Table 1) with only one episode lasting <10 s. The mean end-expiratory LES pressures before and during TLESRs were 6.0 ± 2.57 SU and 1.1 ± 1.06 SU, respectively, an average decrease of 78.9% (range of 28.5–100%) of pressure. The mean end-expiratory pressures during TLESRs and SILESRs did not differ significantly (P = 0.183). Mean inspiratory LES pressure amplitudes before and during TLESRs were 4.59 ± 4.22 SU and 2.43 ± 1.22 SU, respectively, an average decrease of 33.2% (range of 6.1–74.1%). Mean time from the onset of TLESR to complete relaxation was 5.01 ± 3.28 s (range of 1.06–10.63). The rate of LES relaxation was 2.07 ± 1.83 SU/s (range of 0.41–4.75). Only two episodes showed a rate of LES relaxation <1 SU/s. TLESRs were associated with a common cavity pressure in 14 of 17 (82.35%) of the instances. Simultaneous esophageal pressure waves at the onset of TLESRs were seen in nine (52.94%) and peristaltic esophageal contraction waves were identified at the end of TLESR in 16 of 17 (95.88%) of the episodes.

**DISCUSSION**

The main purposes of the current investigation were to validate the sphinctometer in vitro and to determine its ability to detect baseline LES pressure as well as LES relaxations associated with swallows and acid reflux episodes (presumed TLESR).

Water-perfused systems measure pressure by converting the resistance to flow into an electrical signal (17). The Dent-sleeve system works as a Starling resistor and measures the highest pressure applied anywhere along its whole length. The length of the sphincter and its relative position on the sleeve do not affect the pressure output of this sensor. The sphinctometer, on the other hand, uses a solid-state transducer, which is encased in a silicone sleeve like membrane tube filled with oil for conductivity of the pressure along the sleeve length. Although the pressures measured by the sphinctometer were different from the applied pressures, there was a strong correlation between the two (r > 0.99). Our data showed that the sphinctometer clearly underestimates the pressure, confirming the previously published reports of the in vitro as well as in vivo studies (3, 8, 18). Unlike the Dent sleeve, the sphincter length, as well as its position on the sphinctometer, affects the readings of the sphinctometer. In normal physiological conditions, the LES is ~4 cm in length (9). Our in vitro studies indicate that if the high-pressure zone involves more than 4 cm of the sphinctometer length then it is more likely to record the true pressure (>80%). On the other hand, if the high-pressure zone is ≤3 cm in length, the sphinctometer output would represent <79% of the real pressure. Therefore, the longer the high-pressure zone of the esophagus, the more accurate the sphinctometer. Our data also showed that lower pressures (10 mmHg) were more accurately read by the sphinctometer than higher pressures, especially when a longer part of the device was involved.

The present investigation also established that there were differences in the pressure sensitivity along the different parts of the sphinctometer. The pressure output derived from 1-cm segments varied from as low as 31% to as high as 89% of the applied pressure, depending on the location along the sphinctometer sleeve. This variability may be due to the physical structure of the sphinctometer. Because the pressure transducer is located in the center of the sphinctometer, the high-pressure zone located on the transducer itself is most likely to record an accurate pressure. On the other hand, a high-pressure zone located at sites other than the transducer itself is more dependent on the transmission of its pressure through the liquid medium and the compliance of the encasement assembly. Our in vitro data showed that the most sensitive segment of the sphinctometer was indeed located in the middle of the sphinctometer.

In normal physiological settings, the esophagogastric junction pressure is due to the contributions from the LES, ~4 cm long, and crural diaphragm, ~2 cm long (9). The latter surrounds the proximal half of the LES. The end-expiratory pressure is due to the smooth muscle LES, and the apparent increase in LES pressure during inspiration is due to the contraction of the crural diaphragm, which can reach up to 68 ± 5 mmHg during forced inspiration (9). Such an uneven distribution of the pressure along the high-pressure zone could also influence the pressure output depending on the fidelity of the recording device. Furthermore, the LES moves relative to the sphinctometer sleeve due to contraction of the diaphragm during inspiration and expiration (6). The variability of the inspiratory waveforms, ranging from monophasic to biphasic waves in our recordings, is most likely due to changes in the relative position of the LES and crural diaphragm to the sphinctometer sleeve and the variability of the responsiveness of different segments of the sphinctometer to applied pressure. Occurrence of pressure artifacts during biphasic waves (negative deflections to below zero line) could also be due to the fact that the sphinctometer recorded pressures from two different
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environments with different pressures, i.e., abdominal and chest cavities, during one respiratory cycle (6, 7).

Our in vitro study showed a lag in the response time of sphinctometer output compared with the chamber pressure. However, this latency usually did not exceed 0.25 s and thus is most likely sufficiently small for the clinical LES motility investigations.

In contrast to the lack of significant reading changes during a 24-h test for drift at room temperature, we found that heating of the device to a body temperature level influenced the sphinctometer output. The pressure readings at the calibration values at room and body temperature can differ up to 22 SU. Moreover, when the temperature was gradually changed, the sphinctometer reading curve obtained during warming differed from the curve obtained during cooling of the device. The difference in the reading curves during heating and cooling is also known in the technical language as hysteresis. The effect of temperature on the sphinctometer output could be explained on the basis of changes in the sleeve material, the physical characteristics of the sphinctometer, the oil, and probably the pressure transducer. The cause of the pressure reading drift in the initial 10–15 min of the in vivo recordings is most likely due to differences in room and body temperatures. The LES baseline pressure readings stabilized and remained practically unchanged during the rest of the procedure, which allowed setting of new zero lines that corresponded to the lowest LES pressure during its relaxations. However, we could not explain the positive drift in pressure in one case.

The in vivo part of the present study established lower basal end-expiratory LES pressure readings in normal subjects (7.15 ± 4.25 SU) compared with similar measurements made with the water perfused systems (3, 10, 12). However, our sphinctometer pressure findings were similar to the results reported by others (3, 18).

The sphinctometer detected SILESR and TLESR in 68% and 77% of the cases, respectively. Our data had a relatively higher detection rate of TLESR compared with other reports (18). The duration values of both types of relaxations in this investigation were similar to the ones reported in studies using water-perfused systems (14). The mean duration of TLESR in our study (19.3 ± 5 s) was slightly longer than the duration established in another study using the sphinctometer (18). We found significant decreases of end-expiratory pressure of 67.4% during SILESR and 78.9% during TLESR. However, the mean inspiratory pressure amplitude during TLESRs remained higher in comparison to the water-perfused systems (13), although it was diminished to ~ 33%. The rate of LES relaxation and the time from the onset to complete relaxation were similar to those in published studies that used water-perfused systems (Table 1). Similar to other studies, the other features of the TLESR, e.g., common cavity pressure during TLESR, simultaneous esophageal contractions at the onset, and peristaltic contractions at the end of TLESR, were detected in this study and indicated that the events we observed were indeed true TLESRs (15).

We conclude that the sphinctometer in the currently available form has a number of limitations. Unlike the Dent-sleeve system, it does not measure absolute LES pressures. Relative movement of the high-pressure zone along the sphinctometer length creates pressure artifacts; it is sensitive to the changes in temperature, resulting in baseline reading drifts. Other limitations are pressure underestimation, different sensitivity to pressures at different sites along the length of the sleeve, and underestimation of LES relaxations. Despite limitations, the sphinctometer can record TLESRs in the ambulatory setting in two-thirds of the instances. Furthermore, most of the currently accepted criteria for TLESR are applicable to sphinctometer records. Further improvement in sphinctometer technology is needed before it can be recommended for routine clinical use.

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