Prolonged manometric recordings of oesophagus and lower oesophageal sphincter in achalasia patients

M A van Herwaarden, M Samsom, A J P M Smout

Abstract

Background and aims—Conventional short term manometry is a valuable tool in the diagnosis of achalasia but the technique may fail to detect intermittent motor events. The aim of this study was to investigate the pattern of lower oesophageal sphincter (LOS) and oesophageal pressures during prolonged recording in patients with achalasia.

Methods—Eleven patients with idiopathic achalasia were studied. Prolonged combined oesophageal pH and manometric recordings of the pharynx, LOS, and stomach were performed using a pH glass electrode and a multiple lumen assembly incorporating a Dent sleeve connected to a portable water perfused manometric system.

Results—LOS pressure varied during the day. Postprandial LOS pressures were lower than those recorded preprandially (1.2 v 1.8 kPa; p=0.005) and basal LOS pressures were significantly higher during phase III of the migrating motor complex than during the subsequent phase I (3.3 v 1.8 kPa; p=0.028). Complete LOS relaxations were occasionally observed in seven patients (0.48/h). Complete LOS relaxations were longer in duration than incomplete LOS relaxations (10.8 v 2.8 s; p=0.01) and 57% of complete relaxations fulfilled the criteria of a transient LOS relaxation (TLOSR). Complete LOS relaxations were associated with oesophageal pressure waves with higher amplitudes and longer durations. In addition, a higher proportion of these oesophageal pressure waves were spontaneous (55.6% v 0%; p<0.02) and multipeaked (72.7% v 0%). During prolonged manometry, high amplitude oesophageal pressure waves (>10 kPa) were recorded in six patients and retrograde oesophageal pressure waves in four, phenomena which were not observed during short term manometry.

Conclusion—In contrast with short term stationary manometry, prolonged manometry in achalasia patients revealed the occurrence of complete LOS relaxations, TLOSRs, variations in LOS pressure associated with a meal or phase III, and high amplitude and retrograde oesophageal pressure waves.

(Gut 2001;49:813–821)

Keywords: achalasia; lower oesophageal sphincter; manometry; oesophagus

Achalasia is a rare primary neurogenic motility disorder of the oesophagus and lower oesophageal sphincter (LOS) with dysfunction of the inhibitory innervation as the most prominent feature.1 Neuropathological findings in the oesophagus and LOS of achalasia patients include degeneration and reduction of ganglion cells within the myenteric plexus, reduction of vasoactive intestinal polypeptide and nitric oxide nerve fibres in the myenteric plexus, and degenerative lesions of the vagal nerves and the dorsal motor nucleus of the vagal nerve.2,7 These neuronal abnormalities are associated with non-specific changes in oesophageal smooth muscle.8

Short term stationary manometric recording is the gold standard for the diagnosis of achalasia showing absence of peristalsis and incomplete or absent LOS relaxation in response to wet swallows.9 The simultaneous pressure waves that are seen in the oesophageal body of achalasia patients during conventional manometry usually have a low amplitude.10 Three studies describing the occurrence of complete LOS relaxations in some achalasia patients during short term manometry have cast some doubt on the validity of the traditional manometric criteria for achalasia.11–13 However, in two of these studies LOS pressure was not recorded using a sleeve sensor.11 12 Therefore, it might be that these apparently complete LOS relaxations were an artefact caused by proximal movement of the LOS associated with swallowing, moving the orifice in and out of the LOS. In the third study, undertaken with a sleeve, complete LOS relaxations were defined as a relaxation of >80% and therefore residual LOS pressures were between 0.24 and 0.6 kPa.13

Several short term manometric studies investigated the effects of gastrointestinal hormones on LOS pressures in achalasia.14–19 They showed that these hormones can affect the LOS of achalasia patients, albeit that the magnitude of the effect in achalasia patients is mostly different from that in healthy volunteers. To our knowledge, only one study has been published in which prolonged recording of LOS pressures in achalasia patients was carried out. In this overnight study, a rise in LOS pressure associated with phase III of the interdigestive migrating motor complex (MMC) was observed in two patients.20

Some prolonged manometric studies of the oesophageal body in achalasia patients have been performed.21–23 In contrast with short
Table 1  Patient characteristics and symptoms

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Sex</th>
<th>Age (y)</th>
<th>Age at onset symptoms (y)</th>
<th>Previous treatment</th>
<th>Oesophageal diameter</th>
<th>Dysphagia for solids</th>
<th>Dysphagia for liquids</th>
<th>Retrosternal pain</th>
<th>Regurgitation</th>
<th>Heartburn</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>F</td>
<td>S</td>
<td>F</td>
<td>S</td>
<td>F</td>
</tr>
<tr>
<td>1</td>
<td>F</td>
<td>24</td>
<td>20</td>
<td>PD (1×3+2×1)</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>72</td>
<td>71</td>
<td>None</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>81</td>
<td>71</td>
<td>None</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>37</td>
<td>37</td>
<td>None</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>54</td>
<td>43</td>
<td>PD (2×3)</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>22</td>
<td>16</td>
<td>PD (2×3)</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>21</td>
<td>16</td>
<td>PD (1×3)</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>24</td>
<td>16</td>
<td>PD (2×3)</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>64</td>
<td>54</td>
<td>PD (3×3)+myotomy</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>31</td>
<td>30</td>
<td>PD (1×3)</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>59</td>
<td>43</td>
<td>PD (3×3)+myotomy</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td></td>
<td></td>
<td>3</td>
</tr>
</tbody>
</table>

Oesophageal dilation: 0, not dilated; 1, mild (diameter <0.5 vertebra); 2, moderate (diameter 0.5–1 vertebra); 3, severe (diameter ≥1 vertebra).

Symptom score: frequency (F): 0, never; 1, 1–3/week; 2, 4–6/week; 3, every day; severity (S): 1, mild; 2, moderate; 3, severe.

Prolonged combined oesophageal pH and manometric recordings were performed in 11 patients with symptomatic achalasia (seven men and four women; mean age 46.3 years (range 21–81)) referred to our motility lab. The diagnosis of achalasia had been established by short term manometry using absence of peristalsis in the oesophageal body and absent or incomplete LOS relaxations in response to 10 swallows of 5 ml of water as the most important criteria. Symptoms associated with achalasia were present for an average period of six years (range 0–36) before enrolment. Three patients had never been treated for achalasia. The other eight patients had undergone one or more series of pneumatic dilatations using polyethylene balloons with a diameter of 30–40 mm inflated for a period of three minutes at a pressure of 200 mm Hg. Two patients had undergone a Heller myotomy via laparotomy six and 32 years previous to this study.

Endoscopy excluded other gastrointestinal abnormalities not related to achalasia in all patients. Radiographic examination of the oesophagus was performed which showed a mildly to severely dilated oesophagus in all patients. Severity of dilation was scored on a four point scale in which the diameter of the oesophagus was scored relative to the diameter of the vertebrae: 0, not dilated; 1, mild (diameter <0.5 vertebra); 2, moderate (diameter 0.5–1 vertebra); and 3, severe (diameter ≥1 vertebra).

Methods

PATIENTS

Prolonged combined oesophageal pH and manometric recordings were performed in 11 patients with symptomatic achalasia (seven men and four women; mean age 46.3 years (range 21–81)) referred to our motility lab. The diagnosis of achalasia had been established by short term manometry using absence of peristalsis in the oesophageal body and absent or incomplete LOS relaxations in response to 10 swallows of 5 ml of water as the most important criteria. Symptoms associated with achalasia were present for an average period of six years (range 0–36) before enrolment. Three patients had never been treated for achalasia. The other eight patients had undergone one or more series of pneumatic dilatations using polyethylene balloons with a diameter of 30–40 mm inflated for a period of three minutes at a pressure of 200 mm Hg. Two patients had undergone a Heller myotomy via laparotomy six and 32 years previous to this study.

Endoscopy excluded other gastrointestinal abnormalities not related to achalasia in all patients. Radiographic examination of the oesophagus was performed which showed a mildly to severely dilated oesophagus in all patients. Severity of dilation was scored on a four point scale in which the diameter of the oesophagus was scored relative to the diameter of the vertebrae: 0, not dilated; 1, mild (diameter <0.5 vertebra); 2, moderate (diameter 0.5–1 vertebra); and 3, severe (diameter ≥1 vertebra).

Frequency and severity of dysphagia for solids, dysphagia for liquids, retrosternal pain, regurgitation, and heartburn during the week before the study were scored in each patient using a questionnaire. None of the patients was receiving drugs known to influence oesophageal or gastric motility, or gastric acid secretion. Patient characteristics are presented in table 1.

STUDY PROTOCOL

Prior to the 24 hour study, all patients underwent a conventional short term manometry of the oesophagus in the supine position. Prolonged manometric recording was carried out after a 24 hour period during which patients received a liquid diet followed by an overnight fast. During the 24 hour study, patients were in an upright position during the day and were allowed to consume liquids (beverages and liquid meals) only. To test the effect of a meal on LOS pressure, all patients had one standardised meal consisting of a 200 ml nutrient drink (300 kcal, 13% protein, 39% carbohydrate, 48% fat) (Nutridrink, Nutricia, Netherlands). A single standardised liquid meal was used as we did not wish to jeopardise completion of the test by patients and we wanted to avoid the possibility of prolonged oesophageal retention of solid food particles. Patients were instructed to complete a diary and to use event keys on the data logger indicating the times of meals and occurrence of heartburn and retrosternal pain.

EQUIPMENT

Conventional short term manometric recording of the oesophagus and LOS was performed using the portable perfused manometric system described below or using a seven lumen assembly (OD 4.7 mm, ID 0.74 mm) with an incorporated 6 cm long sleeve (Dentsleeve Pty Ltd, Adelaide, South Australia). Pharyngeal and oesophageal sideholes were localised at 20 and 25 cm and 5, 10, and 15 cm proximal to the sleeve, respectively. Intragastric pressure was measured using a sidehole 1 cm below the sleeve. The assembly was perfused with degassed water at a rate of 0.45 ml/min using a low compliance pneumohydraulic infusion pump and hydraulic flow restrictors (Dentsleeve Pty Ltd).
Manometric recordings of oesophagus and lower oesophageal sphincter

Prolonged manometric recording of the pharynx, oesophagus, LOS, and stomach was performed with a water perfused, micromanometric, 12 channel silicone rubber assembly (Dentsleeve Pty Ltd). The catheter (OD 3.5 mm, ID 0.4 mm) incorporated four pharyngeal sideholes (24, 26, 28, and 30 cm proximal to the proximal border of the sleeve) and three oesophageal sideholes (4, 9, and 14 cm proximal to the proximal border of the sleeve), a reversed perfused sleeve with one sidehole on its proximal border, and one intragastric sidehole (2 cm distal to the sleeve). A guidewire placed in the central lumen of the catheter was used to manoeuvre the flexible catheter through the LOS. The manometric assembly was positioned with the proximal border of the sleeve at 1 cm proximal to the proximal border of the LOS. After correct positioning of the manometric assembly the sidehole on top of the sleeve was capped off and the guidewire was removed. In addition, the two optimal pharyngeal sideholes were detected and the other two were also capped off.

Pressures were recorded using external pressure transducers (Abbott, Chicago, Illinois, USA). Hydraulic flow restrictors were used to reduce water flow to a rate of 0.08 ml/min (Dentsleeve Pty Ltd). The flow restrictors and pressure transducers were mounted on a belt. The system was connected to a locally developed pneumohydraulic low compliance water pump consisting of a small gas cylinder and a water reservoir of 350 ml. The water pump was carried in a backpack. Bench tests showed that the rate of rise of the manometric system was >21.5 kPa/s. Oesophageal pH was recorded using a glass electrode (model LOT 440; Ingold AG, Urdorf, Switzerland) positioned 5 cm above the proximal border of the LOS. Both catheters were connected to a digital data logger (MMS; Enschede, the Netherlands) which sampled pressure signals at a rate of 4 Hz, except for pharyngeal pressure signals which were sampled at a rate of 8 Hz. The pH signal was sampled with a frequency of 1 Hz.

Before the start of the recording, the pH electrode and manometric assembly were calibrated. The pH electrode was calibrated at 37°C using pH 4.0 and 7.0 buffer solutions (Radiometer analytical A/S; Bagsvaerd, Copenhagen, Denmark) and the manometric assembly was calibrated at 0 and 50 cm H2O (0 and 5.0 kPa).

DATA ANALYSIS

Twenty four hour pressure signal sets were visually examined in order to detect complete LOS relaxations, high amplitude oesophageal pressure waves, and retrograde waves. In addition, end expiratory LOS pressure was measured for the 24 hour period, taking visual mean values of consecutive five minute stretches, as described below. In the analysis of the 24 hour data, four periods were distinguished which will be referred to as perprandial, postprandial, fasting, and night time periods. The perprandial period consisted of all periods during drinking; the postprandial period comprised all one hour periods following individual perprandial periods. The fasting period consisted of all remaining periods during the day, and the night time period was the period between retiring and waking up.

LOS PRESSURE MEASUREMENT

Basal end expiratory LOS pressure, referenced to intragastric pressure, was determined at five minute intervals by taking a visual mean value of the tracing during this period after exclusion of relaxations and contractions of the LOS. Recorded LOS pressure was corrected for the changes caused by alterations in body position based on the following results. Bench tests showed identical increments in pressures recorded from the sidehole at the proximal border of the sleeve and the sleeve itself with the assembly in the horizontal and vertical position. A pilot study in four healthy volunteers showed that a change from the supine towards the sitting position increased the pressure in the distal oesophagus (measured by the sidehole at the proximal site of the sleeve) by 0.2 kPa more than the pressure measured by the intragastric sidehole. Therefore, basal end expiratory LOS pressure in the sitting position was defined as the pressure measured in the sleeve relative to the pressure recorded by the gastric sidehole minus 0.2 kPa.

COMPLETE LOS RELAXATIONS

All complete LOS relaxations that occurred during the prolonged recording were detected manually. These were defined as LOS relaxations with a corrected nadir pressure ≤0.2 kPa lasting for at least three seconds. For each patient the mean duration of complete LOS relaxations, defined as the period during which LOS pressure was at the nadir level, was analysed. During each complete LOS relaxation, inhibition of the activity of the crural diaphragm, as recorded by the reversed perfused sleeve, was assessed. Inhibition of the crural diaphragm was defined as a sudden decrease in the amplitude of respiratory oscillations of more than 50%. Complete LOS relaxations were categorised into those that were swallow associated (pharyngeal contraction in a time window from four seconds before to two seconds after the onset of LOS relaxation) and those that were not. In addition, LOS relaxations which fulfilled all of the criteria of a non-swallow related transient LOS relaxation (TLOS) were identified using the criteria of Holloway and colleagues.

The characteristics of oesophageal pressure waves associated with complete LOS relaxations were determined. These were categorised as either associated with a pharyngeal contraction or as spontaneous pressure waves defined as oesophageal pressure waves that occurred in the absence of a swallow in the preceding seven seconds. This definition was based on data obtained from 10 healthy volunteers showing that the mean time ±2 SD for a swallow induced pressure wave in the distal channel was 6.23 seconds (unpublished data). For each detected pressure wave it was determined
whether the contraction was peristaltic, simultaneous, non-transmitted (defined as a wave in one or two channels only), repetitive, or retrograde, using the onset of the pressure wave as the reference point. In addition, the amplitudes and durations of the pressure waves in the proximal, mid, and distal oesophagus were determined (14, 9, and 4 cm above the sleeve). The proportion of oesophageal pressure waves characterised by more than one peak was calculated.

HIGH AMPLITUDE OESOPHAGEAL PRESSURE WAVES

The complete 24 hour recordings were examined in order to identify oesophageal pressure waves with an amplitude >10 kPa. Amplitude, duration, and mode of propagation of these contractions were determined.

EFFECT OF A MEAL ON LOS PRESSURE

To investigate the effect of a caloric nutrient drink on LOS pressure, sphincter pressure during the first hour after the intake of the drink was compared with that recorded during the one hour period before the meal.

RELATIONSHIP WITH PHASE III AND LOS PRESSURE

Participation of the stomach in phase III of the interdigestive MMC is characterised by strong contractile activity of the antrum at the maximum frequency of three per minute. These strong antral contractions can often be detected in pressure recordings from the proximal stomach. In the 24 hour recordings obtained from our patients, all periods suggestive of phase III—that is, short periods with intragastric pressure variations of more than 1 kPa at a frequency of three per minute—were identified. LOS pressures during these periods were compared with LOS pressures during the 15 minute period afterwards (first part of phase I).

INCOMPLETE LOS RELAXATIONS

A randomly selected 30 minute period during fasting was used for detection of incomplete LOS relaxations. It was determined whether these relaxations were swallow associated or spontaneous, and their duration was measured. The same 30 minute period was used to obtain baseline values for amplitude, duration, and association with swallowing of oesophageal pressure waves.

ACID REFLUX

Automated analysis of oesophageal pH data to measure oesophageal acid exposure was expressed as percentage of time with pH <4. Acid reflux episodes were detected visually. These were defined as a drop in oesophageal pH of at least one unit at a rate of >1 pH unit/6 s, and with a duration of >3 s. In addition, pH drifts, defined as a gradual decrease (>6 s/pH unit) to pH <4, were detected. For each event the underlying reflux mechanism was determined.

STATISTICAL ANALYSIS

Data showed a non-parametric distribution and therefore non-parametric tests were used in the statistical analysis. For most comparisons the Friedman ANOVA was used, followed by the Wilcoxon signed rank test in the event of significance. The effect of the nutrient drink on LOS pressure was analysed using the Wilcoxon signed rank test.

Unless stated otherwise, data are expressed as medians and interquartile ranges; p<0.05 was accepted as significant.
Results

During short term manometry all patients showed aperistalsis of the oesophageal body and incomplete LOS relaxations. The short term manometric recording of one patient was lost due to a technical failure. Mean recording time for prolonged manometry was 20.8 hours (range 8.2–23.2). One patient (patient No 11) was excluded from analysis of complete LOS relaxations because of an error during the zeroing procedure. In patient No 9, 3.5 hours of the recording, including the standardised meal, was excluded from the analysis because of technical problems. In one patient (patient No 3), recording was stopped before night time at the patient’s request.

LOS PRESSURE

LOS pressures recorded during the pre-meal period of the 24 hour recording were similar to LOS pressures recorded during short term manometry (1.8 (1.5–2.3) kPa v 2.1 (1.4–2.8) kPa, respectively; NS).

In all patients, LOS pressures were lower after the meal than during the one hour period before the meal (fig 1). LOS pressures during the night were significantly lower than LOS pressures recorded before the meal (1.3 (1.1–1.6) kPa v 1.8 (1.5–2.3) kPa, respectively; p=0.038).

Figure 3 Effect of migrating motor complex (MMC) cycle activity on basal lower oesophageal sphincter (LOS) pressure. LOS pressure was significantly higher during phase III of the MMC cycle than during the 15 minute period afterwards (phase I).

Figure 4 Example of a complete lower oesophageal sphincter (LOS) relaxation. This complete LOS relaxation was associated with a common cavity phenomenon and a high amplitude pressure wave (34.2 kPa) in the distal oesophagus. Several subsequent swallows were not followed by oesophageal pressure waves or LOS relaxation.

Figure 5

Gastric pressure variations suggestive of phase III of the interdigestive MMC were observed in six patients (fig 2). In these six patients a total of 10 of these periods were detected. Basal LOS pressure was significantly higher during these periods than during the 15 minute period afterwards (fig 3).

COMPLETE LOS RELAXATIONS AND ASSOCIATED OESOPHAGEAL PRESSURE WAVES

In seven patients (patient Nos 1, 2, 5, 7, 8, 9, and 10), complete LOS relaxations occurred with a frequency of 0.48 (0.46–0.61) per hour. In total, 113 complete LOS relaxations were observed (fig 4). Inhibition of the crural diaphragm was observed during all of these 113 complete LOS relaxations.

The incidence of complete LOS relaxations was significantly higher during the perprandial period than during the night (0.74/h (0.64–1.63) v 0.13/h (0–0.54), respectively; p<0.05). Similarly, complete LOS relaxations occurred more frequently during the postprandial period than during the night (1.00 (0.87–1.29) v 0.13 (0–0.54), respectively; p<0.05).

Complete LOS relaxations had a significantly longer duration than incomplete LOS relaxations (10.8 s (8.4–12.9) v 2.8 s (2.1–3.0); p=0.01). In addition, complete LOS relaxations lacked an association with a swallow more often than incomplete LOS relaxations (70.0% (45.0–91.4) v 15.6% (14.1–22.4)).

Fifty seven per cent (42.2–80.2%) of complete LOS relaxations not only occurred without a preceding swallow but also fulfilled all other criteria of a TLOSR (fig 5).

In one patient, 44% of complete LOS relaxations were not associated with an oesophageal pressure wave. In the other patients complete LOS relaxations were always associated with an oesophageal pressure wave (fig 4). These pressure waves had significantly higher amplitudes than those recorded during short term manometry and during the 30 minute baseline period of the prolonged manometric recording (fig 6). Mean durations of the oesophageal pressure waves during complete LOS relaxations were also significantly longer than mean durations of the oesophageal pressure waves during incomplete LOS relaxations.
pressure waves during the short term and 30 minute baseline period (table 2).

The proportion of spontaneous oesophageal pressure waves was significantly higher during complete LOS relaxations than during the 30 minute baseline period (55.6% (37.8–68.6) vs 0% (0–6.9), respectively; p<0.02).

Pressure waves associated with complete LOS relaxations were multipeaked more often than pressure waves that were not associated with complete LOS relaxations (72.7% (25.0–82.2) vs 0% (0–0), respectively; p<0.05).

HIGH AMPLITUDE OESOPHAGEAL PRESSURE WAVES

The prolonged manometric tracings of six patients showed oesophageal pressure waves with an amplitude >10 kPa in the proximal, mid, or distal oesophagus. In these patients (Nos 1, 2, 3, 5, 9, and 10), the highest amplitudes were 27.2, 43.2, 50, 33.3, 23.2, and 15.5 kPa, respectively, being 13 (13–13) times higher than the mean amplitude of the oesophageal pressure waves during short term manometry. The median incidence per hour was 2.57 (1.46–4.70). There was no association between the period of the day (perprandial, postprandial, fasted, and night time periods) and the incidence of these pressure waves. Their frequency tended to be higher in patients with mild oesophageal dilatation (p=0.08). In 14.7% (12.7–58.3), these high amplitude oesophageal pressure waves were associated with complete LOS relaxations: 8.8% (7.7–11.4) began within three seconds before the onset of a complete relaxation, 6.4% (0–3.45) coincided with the onset of a complete LOS relaxation, respectively.

RETROGRADE OESOPHAGEAL PRESSURE WAVES

In four patients (patient Nos 1, 5, 9, and 10), retrograde oesophageal pressure waves were detected during the prolonged recording. All of these retrograde pressure waves were characterised by a higher velocity from the distal to mid than from the mid to proximal level (2.3 cm/s (1.8–2.7) vs 0.73 cm/s (0.66–0.90)). All retrograde pressure waves had an amplitude >10 kPa and most of these were associated with a complete LOS relaxation. An example of a retrograde pressure wave is shown in fig 7.

OESOPHAGEAL ACID EXPOSURE

Four patients (patient Nos 2, 4, 5, and 9) showed acid reflux episodes. In the same patients pH drifts were observed. In total, 18 acid reflux events and 21 pH drifts were observed. Ninety five per cent of the acid reflux episodes occurred during the day. In contrast, pH drifts were mainly observed during the night (74%).

In the four patients who had acid reflux, median time with oesophageal pH <4 was 6.4% (4.2–9.3). During the upright and supine periods, the percentage of time with oesophageal pH <4 was 8.5% (5.2–13.6) and 2.8% (0.9–4.4), respectively. Six of the 18 reflux

---

Table 2 Duration of oesophageal pressure waves recorded during short term and prolonged manometry and during complete lower oesophageal sphincter (LOS) relaxations

<table>
<thead>
<tr>
<th></th>
<th>Wet swallow (short term manometry)</th>
<th>Fasting period (prolonged manometry)</th>
<th>Complete LOS relaxations (prolonged manometry)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No patients</td>
<td>10</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Duration proximal (s)</td>
<td>5.4 (4.7–6.9)</td>
<td>4.5 (3.9–5.3)</td>
<td>8.8 (7.5–15.5)*</td>
</tr>
<tr>
<td>Duration mid (s)</td>
<td>5.4 (4.7–6.9)</td>
<td>4.3 (4.2–5.5)</td>
<td>12.1 (9.3–16.5)*</td>
</tr>
<tr>
<td>Duration distal (s)</td>
<td>5.4 (4.7–6.9)</td>
<td>5.2 (4.4–5.4)</td>
<td>14.1 (12.3–17.2)*</td>
</tr>
</tbody>
</table>

*p<0.05 versus short term manometry; *p<0.02 versus prolonged manometry.
Manometric recordings of oesophagus and lower oesophageal sphincter

819

The oesophageal motor activity associated with inhibition of the crural dia-

Discussion

This is the first study in which prolonged manometric recording of the pharynx, oesoph-

achalasia patients by Holloway et al, we observed that complete LOS relaxations prevented the occurrence of acid reflux. Another explanation for the low incidence of reflux events during complete LOS relaxations might be impaired gastric acid secretion in achalasia patients.35 36

In this study we observed that LOS pressure in achalasia patients varied during the day in a manner similar to that described in healthy subjects.37 38 The most striking pressure variations were related to meal ingestion and to phase III of the interdigestive migrating complex. As described previously in two patients by Holloway et al, we observed that LOS pressure was significantly higher during phase III.20 Variations in LOS pressure associated with the MMC cycle have been observed

events were associated with complete LOS relaxations, five with straining, four occurred during incomplete LOS relaxations, and three during low basal LOS pressure.

Although eight of the 11 achalasia patients had been treated previously, all had recurrent complaints of dysphagia and the short term manometric study showed complete aperistalsis of the oesophageal body and incomplete LOS relaxation. Whereas none of the achalasia patients had complete LOS relaxations during the short term manometric recordings, prolonged oesophageal manometry demonstrated the intermittent occurrence of complete LOS relaxations in seven of the 11 patients, with a frequency of 0.5/h. These relaxations were most frequently present during meals and in the postprandial period, which might indicate that complete relaxations of the LOS are provoked by food passage or food retention in the oesophageal body. As with complete LOS relaxations in healthy subjects, all complete LOS relaxations in patients with achalasia were associated with inhibition of the crural diaphragm.30

One could argue that the complete LOS relaxations observed during prolonged record-

achalasia does not result in a complete tension of the oesophageal body as balloon dis-

 LOS relaxations that are not swallow related.

The mechanism through which complete LOS relaxations in achalasia are triggered remains unclear. It is unlikely that complete LOS relaxations are caused by mechanical dis-

tension of the oesophageal body during LOS relaxations. It might be that the oesophageal pressure waves associated with complete LOS relaxations prevented the occurrence of acid reflux. Another explanation for the low incidence of reflux events during complete LOS relaxations might be impaired gastric acid secretion in achalasia patients.35 36

In this study we observed that LOS pressure in achalasia patients varied during the day in a manner similar to that described in healthy subjects.37 38 The most striking pressure variations were related to meal ingestion and to phase III of the interdigestive migrating complex. As described previously in two patients by Holloway et al, we observed that LOS pressure was significantly higher during phase III.20 Variations in LOS pressure associated with the MMC cycle have been observed

www.gutjnl.com

Gut: first published as 10.1136/gut.49.6.813 on 1 December 2001. Downloaded from http://gut.bmj.com/ on June 20, 2022 by guest. Protected by copyright.
in healthy subjects, dogs, and opossums.\textsuperscript{13–16} The increase in LOS pressure during phase III can be blocked by atropine, indicating that cholinergic input is a prerequisite for this phenomenon.\textsuperscript{17} Our observation that in achalasia patients LOS pressure is MMC cycle dependent indicates that the excitatory cholinergic innervation of the LOS is still functional in these patients.\textsuperscript{18,19}

Another new observation was that in achalasia patients LOS pressure decreased in the postprandial period, as in healthy subjects and patients with gastro-oesophageal reflux.\textsuperscript{20–22} Although several neuronal and hormonal mechanisms may play a role in the postprandial decrease in LOS pressure, cholecystokinin release induced by fat in the meal has been put forward as the most important mechanism.\textsuperscript{23,24} However, in patients with achalasia, a paradoxical increase in LOS pressure after cholecystokinin infusion has been reported.\textsuperscript{25} Studies in achalasia patients have shown that LOS pressure is decreased by somatostatin, secretin, vasoactive intestinal polypeptide, and opioids.\textsuperscript{14–17} It might therefore be that one of these or other intestinal hormones or neurotransmitters are responsible for decreased LOS pressure after a meal through inhibition of cholinergic pathways or by acting directly on the LOS.

High amplitude oesophageal pressure waves were observed in six of our 11 patients. This finding was surprising as none of the short term manometric recordings showed pressure waves with amplitudes exceeding 4.5 kPa. Although high amplitude pressure waves tended to occur less frequently in patients with a more severely dilated oesophagus, some of the patients with high amplitude pressure waves had a markedly dilated oesophagus. It is likely that the low incidence of these strong contractions is the most important explanation for these contractions being undetected during short term conventional manometry. It could also be that the nature of the stimulus plays a role as during conventional stationary manometry only 5 ml boluses of water were given, whereas during prolonged recording more substantial liquid meals were taken. This hypothesis is in agreement with a study by Stuart et al who observed high amplitude oesophageal pressure waves in untreated achalasia patients only during a solid meal.\textsuperscript{26} However, we feel that it is unlikely that the observed high amplitude pressure waves were associated with or caused by retention of fluid in the oesophagus because there was an equal distribution over the various periods of the day and oesophageal baseline elevations were rarely seen in association with high amplitude waves. Another unexpected finding was the evidence of retrograde pressure waves in four of the 11 achalasia patients. In their fluoroscopic study, Lu et al occasionally observed retrograde propagation of circular oesophageal contractions in opossums with a dilated oesophagus.\textsuperscript{27} To our knowledge retrograde pressure waves have never been described in achalasia patients. Our observations do not allow conclusions regarding the mechanism underlying this phenomenon. It is likely however that altered innervation of the oesophageal muscle is involved.

In summary, in this study using prolonged water perfused manometry of the oesophagus and LOS, several unexpected manometric findings were made in 11 patients with achalasia which were not observed during short term manometry. Complete LOS relaxations with prolonged duration were found in the majority of patients with achalasia. LOS pressures recorded showed fluctuations during prolonged recording which were related to meals and the MMC cycle, and the oesophageal body of achalasia patients appeared to be able to generate high amplitude and retrograde pressure waves. The importance of our findings for clinical practice needs to be explored in future studies. However, we do not believe that our observations should be interpreted as indicative of the invalidity of established manometric criteria for the diagnosis of achalasia. One should realise that the complete LOS relaxations found in our achalasia patients occurred very infrequently and that it is highly unlikely that a complete LOS relaxation is recorded during standard motility testing.

13 Mearin F, Malagelada JR. Complete lower esophageal sphincter relaxation observed in some achalasia patients is functionally inadequate. Am J Physiol 2000;278:G376–83.
Manometric recordings of oesophagus and lower oesophageal sphincter


