OESOPHAGUS

Studies of acid exposure immediately above the gastro-oesophageal squamocolumnar junction: evidence of short segment reflux

J Fletcher, A Wirz, E Henry, K E L McColl

Background and aims: Oesophageal pH is conventionally recorded from a point 5 cm above the lower oesophageal sphincter. However, the mucosal changes of reflux oesophagitis and intestinal metaplasia tend to affect the segment of oesophagus distal to this and close to the squamocolumnar junction. This study set out to investigate oesophageal acid exposure of squamous mucosa close to the squamocolumnar junction.

Methods: Dual channel 24 hour pH monitoring was carried out in 11 patients with endoscopy negative dyspepsia and no evidence of gastro-oesophageal reflux by conventional oesophageal pH metry. Oesophageal pH was recorded from electrodes positioned 5 mm and 55 mm proximal to the squamocolumnar junction. A novel technique was developed using metal clips to secure the pH catheter to the oesophageal mucosa and maintain these electrode positions. Oesophageal manometry indicated that the distal electrode was within the high pressure zone of the lower oesophageal sphincter.

Results: We found that 24 hour oesophageal acid exposure (per cent time pH <4) was greater 5 mm above the squamocolumnar junction compared with the conventional position 5 cm more proximal (11.7% v 1.8%; p<0.001). The greater acid exposure at the distal versus the conventional site was apparent in both the upright (12.7% v 2.3%) and supine (10.5% v 1.3%) positions, as well as during preprandial (14.2% v 1.6%) and postprandial (21.8% v 2.8%) periods (p<0.001 for each). The number of reflux events recorded close to the squamocolumnar junction was also higher than at the conventional position (168 v 33; p<0.001). There was no correlation between acid exposure at the two sites.

Conclusions: The squamous mucosa of the most distal oesophagus is exposed to substantial acidic reflux, even in patients without evidence of conventional reflux disease. This short segment reflux may explain the high incidence of metaplasia and neoplasia at the gastro-oesophageal junction.

Abbreviations: LOS, lower oesophageal sphincter; TLOSR, transient lower oesophageal sphincter relaxation; PIP, pressure inversion point...
SUBJECTS AND METHODS

Patients
We enrolled 14 patients with chronic dyspepsia and normal upper gastrointestinal endoscopy with no evidence of oesophagitis or a hiatus hernia. The CLO test and antral histology showed no evidence of Helicobacter pylori infection in any patient. All patients had normal 24 hour oesophageal pH monitoring (total per cent time < pH 4: mean 2.7 (range 0.6–4.8)). Mean age was 43 years (range 28–56), and there were six males and five females. All antisecretory therapy was discontinued for three weeks prior to the study. The character of their dyspepsia encompassed a range of upper gastrointestinal symptoms: retrosternal discomfort (n = 5), epigastric discomfort (n = 4), and bloating (n = 2).

Placement of pH catheter
pH monitoring was undertaken with a modified custom made two channel pH catheter (Synectics, Enfield, UK). This catheter incorporated two unipolar antimony electrodes 105 mm and 135 mm from the catheter tip. Three small prolene loops were tied to the catheter, two at 95 mm from the catheter tip and one 200 mm from the tip.

Patients attended the endoscopy unit at 09:00 having fasted, and were given intravenous midazolam to produce conscious sedation. The pH catheter was passed into the oesophagus via the nose. Occasionally grasping forceps were used to position the pH catheter under endoscopic vision. Once the pH catheter was in the stomach it was gently withdrawn until the distal oesophageal electrode was 5 mm proximal to the squamocolumnar junction. An endoscopic clip fixing device (Olympus, Middlesex, UK) was then used to clip one of the prolene loops on the probe to the squamocolumnar junction (fig 1). A second clip was applied to attach the proximal prolene loop in the oesophageal body at approximately 30 cm from the incisors. The prolene loops were small so that after clipping, the pH probe was unable to move by more than 1 or 2 mm around these anchor points.

During the procedure, particular attention was paid to the appearance of the gastro-oesophageal junction. Distances from the incisors to the squamocolumnar junction, proximal end of the gastric folds, and diaphragmatic pinch were measured. At the end of the procedure there were two electrodes in the oesophagus (electrodes 1 and 2). Electrode 1 was positioned 5.5 cm proximal to the squamocolumnar junction and electrode 2 was positioned 5 mm proximal to the squamocolumnar junction. All patients had LOS measured by the station pull through technique with a water perfused manometry catheter. The length of the LOS high pressure zone was measured and the pressure inversion point (PIP) identified. The thoracic/abdominal ratio of the LOS was derived from these measurements. The pinch of the diaphragm at endoscopy was assumed to correspond with the manometric PIP. The distance from the oesophageal pH electrodes to the pinch of the diaphragm was measured and assumed to be equal to the distance to the PIP. From the manometry measurements it was then possible to estimate the distance between the pH electrode and the upper border of the LOS.

On recovery, the patient was monitored for 24 hour pH in the research unit. A standard lunch (soup, sandwich, and rice pudding snack) and dinner (battered cod and French fries) were provided. During the day subjects were seated for most of the time.

Six hours after the probe had been clipped in place, a plain radiograph of the left upper quadrant was obtained to determine the probe alignment in the stomach and confirm that the clips were still in place. The following morning a second endoscopy was undertaken. The probe position was examined to assess the position of the two electrodes and to check any movement of the clips. After the second endoscopy the pH probe was removed. The endoscopic clips were painlessly detached from the oesophageal mucosa with firm traction.

Analyses
pH data were recorded on a digital data logger (Diggitraper MK III; Synectics), downloaded onto a PC, and analysed by oesophagram 5.4 software (Synectics). The postprandial period was defined as the three hours after the evening meal. The preprandial period was defined as the three hours prior to the evening meal. Oesophageal acid exposure was measured as per cent time pH <4 for total, upright, supine, preprandial, and postprandial time periods. The DeMeester score was also calculated. This is a scoring system which is derived from six pH parameters defining the number of reflux events, duration of reflux events, and per cent time pH <4.

The minimum pH recorded during a reflux episode was measured manually in each subject. The median value of these measurements was determined and termed the median pH nadir. A reflux episode was defined as starting when the pH fell below 4 and ending when the pH rose above 4.

Statistical analyses
Values are given as mean and ranges and were compared using the paired Student’s t test.

Ethics
The study was approved by the North Glasgow University NHS Trust and all subjects gave written informed consent.

RESULTS
Three of the recruited patients did not provide results for this study. Two of these were unable to tolerate passage of the pH probe at endoscopy and in a further patient the pH probe dislodged, advancing the oesophageal electrodes into the stomach. Analysis was carried out in the remaining 11 patients.

The proximal oesophageal pH electrode was positioned a mean of 4.4 cm (range 3–6) above the upper border of the LOS and 5.5 cm above the squamocolumnar junction. The distal oesophageal pH electrode was positioned a mean of

![Figure 1](https://www.gutjnl.com)
5 mm above the squamocolumnar junction and 6 mm below the upper border of the LOS (range 1 to −1). Positioning of the electrodes relative to the squamocolumnar junction and LOS is shown in fig 2.

pH measurements revealed that close to the squamocolumnar junction, oesophageal acid exposure was significantly greater than at the electrode position 5.5 cm more proximal. Median total per cent time pH < 4 was 11.7% (range 2.4–36.3) versus 1.8% (range 0.8–4.0) (fig 3). This greater acid exposure of the most distal oesophagus was apparent both in the upright recording period (per cent time pH < 4: 12.7% (range 2.3–32.1) vs 2.3% (range 0.9–4.3)) and during the supine period (per cent time pH < 4: 10.5% (range 1.2–42.9) vs 1.3% (range 0.6–1.1)) (p < 0.001) (table 1). This increased acid exposure in the distal oesophagus was also apparent in the preprandial (per cent time pH < 4: 14.2% (range 1.5–57.6) vs 1.6% (range 0–6.7)) and postprandial (per cent time pH < 4: 21.8% (range 1.0–55.3) vs 2.8% (range 0–9.3)) periods (table 2).

There was no correlation between oesophageal acid exposure close to the squamocolumnar junction and acid exposure measured at the conventional site (r = 0.19).

The number of recorded individual reflux episodes was also higher close to the squamocolumnar junction compared with the conventional position (168 (range 51–350) vs 33 (range 14–53); p < 0.001). Consequently, the DeMeester score (derived from the number of reflux episodes and per cent time pH < 4) calculated from the pH data recorded close to the squamocolumnar junction was significantly greater than at the conventional position (45 (range 12–131) vs 8 (range 4–19); p < 0.001) (table 1). The median pH nadir recorded during reflux episodes was lower close to the squamocolumnar junction than at the conventional site (pH 2.0 (range 1.4–2.6) vs 2.9 (range 1.9–4.0); p < 0.01) (table 3).

The degree of acid exposure just proximal to the squamocolumnar junction was greater during the postprandial period versus the preprandial period with per cent time pH < 4 being 21.8% (range 1.0–55.3) compared with 14.2% (range 1.5–57.6) (p < 0.05) (table 2). Acid exposure just proximal to the squamocolumnar junction was similar during the upright versus the supine period (per cent time pH < 4: 12.7% (range 2.3–32.1) vs 10.5% (range 1.2–42.9)).

There was no significant difference between mean length of reflux episode measured just proximal to the squamocolumnar junction (54 seconds (range 25–91)) compared with the conventional position (50 seconds (range 50–110)). Subjectively, the appearance of reflux episodes on the pH tracing was similar at both recording positions (fig 4A, B). In addition, there was no significant intraindividual correlation between the number of reflux episodes at the distal versus the proximal electrode positions (r = 0.16, NS).

There was no discernable correlation between the location of the pH electrodes relative to the squamocolumnar junction and the high pressure zone of the lower oesophageal sphincter.

DISCUSSION

The present study indicates that oesophageal acid exposure is much greater just above the squamocolumnar junction than 5 cm proximal to it, where reflux is conventionally measured. All parameters of oesophageal acid exposure were substantially higher at the more distal site, generating a much higher DeMeester score of 45 (range 12–131) compared with 8 (range 4–19). Our findings indicate that acid may reflux further into the oesophagus than conventionally measured without extending more proximally. We would suggest that an appropriate term to describe this phenomenon is “short segment reflux”.

Previous studies comparing acid exposure at different positions in the oesophagus have usually examined acid refluxing above the conventional electrode position 5 cm above the upper border of the LOS. Measuring 10 cm above the LOS will result in a 50% reduction in acid exposure compared with the conventional pH recording position.10 11 There is little information on pH measured closer to the LOS or squamocolumnar junction. Weusten et al, using a multichannel pH probe, reported that 43% of reflux events detected at 3 cm above the LOS failed to reach an electrode at 6 cm above the LOS.12 Loughney et al used dual channel 24 hour pH monitoring to compare the pH at the upper border of the LOS with that at the conventional site 5 cm above the upper border of the LOS.13 They studied patients with long segment Barrett’s, patients with short segment (<3 cm) Barrett’s, and patients with reflux symptoms but normal pH studies. In all three groups they showed higher oesophageal acid exposure at the upper border of the LOS than at the conventional site (per cent time pH < 4: 37% v
24%, 13% vs 9%, and 4 vs 2%, respectively). However, this was a relatively modest increase of only 50% compared with the 600% increase in acid exposure seen in our study comparing the conventional site with the most distal oesophageus.

In our study, we positioned the pH electrodes relative to the squamocolumnar junction. Our calculations indicated that the squamocolumnar junction was approximately 11 mm below the upper border of the LOS and thus consistent with that previously reported. Our proximal electrode position was similar to the conventional recording position (4.4 cm vs 5 cm above the upper border of the LOS). The pH data in this study can therefore be usefully compared with previous studies relying on the manometric LOS distance to position the electrodes.

Our study differs from previous attempts to measure distal oesophageal pH in two ways. Firstly, we anchored the pH electrode to the mucosa with clips to avoid electrode movement during oesophageal shortening. Secondly, in our patients the distal oesophageal electrode was below the upper border of the LOS. Our distal oesophageal electrode was therefore likely to be measuring acid exposure for the first time within, rather than above, the LOS.

As well as comparing total acid exposure we were able to examine the pattern of acid exposure at the two sites. Individual reflux episodes were more frequent and produced a lower minimum pH near the squamocolumnar junction than at the conventional site. The pattern of acid exposure near the squamocolumnar junction showed similarities with conventional acid reflux, being increased during the postprandial compared with the preprandial period. However, we found a difference with respect to posture. Conventional acid reflux is less frequent in the supine versus the upright position whereas our acid exposure measured close to the squamocolumnar junction was similar in both positions.

The mechanism of acid exposure at the two sites needs to be considered. The majority of conventional reflux events are confined to the upright position, as might be expected for a TLOS related mechanism. Finally, there was no correlation between the quantity of conventional reflux and short segment reflux measured in each patient.

What other mechanisms might contribute to the high level of acid exposure just above the squamocolumnar junction? We have previously shown that buffering of gastric acid by food is markedly reduced in this region, leading to a pocket of highly acidic (fasting pH) gastric juice at the gastro-oesophageal junction. Further work on the location of this acid pocket has revealed that after a meal it extends from immediately below the squamocolumnar junction to 1–2 cm up onto the squamous epithelium of the distal oesophagus. This postprandial change in pH at and above the squamocolumnar junction may be due to distension of the proximal stomach after a meal. This may cause the LOS to be intermittently prised apart at its distal extent, exposing the oesophageal squamous epithelium to acid.

The mechanism was originally proposed by Oberg and colleagues. This partial opening of the LOS would allow acid to reach an intraspincteric electrode close to the squamocolumnar junction but would not be detected by a conventional pH electrode placed above the upper limit of the LOS. Short segment acid reflux may reflect this process and would be consistent with oesophageal acid exposure just above the squamocolumnar junction being greater during the postprandial versus the preprandial period.

Although short segment reflux was greater in the postprandial period (pH <4: 21.8%), it was also observed under fasting conditions (pH <4: 14.2%). Mechanisms in addition to meal distension therefore need to be considered. The high level of acid exposure just proximal to the squamocolumnar junction might be partly the result of intermittent oesophageal shortening. The latter mainly takes place in the deep muscle layer which is separated from the mucosa by the elastic submucosal layer. If the mucosa does not shorten to the same extent as the deep muscle layer, then the squamocolumnar junction could become located distal to the lower oesophageal sphincter and thus exposed to gastric acid.

The different acid exposure at the two sites might also be due to different neutralising capacities. It is possible that there is more residual saliva present in the lumen above than within the high pressure zone and thus more neutralising capacity.

It is also important to consider the possibility that the increased acid exposure just above the squamocolumnar junction is artefactual and due to the methodology employed. Inadvertent displacement of the clipped pH electrode just above the squamocolumnar junction resulting in the pH catheter separating from the mucosa and moving into the stomach would produce higher levels of detected acid at this electrode. We believe this is unlikely to be the case as we designed the loop and clip to allow only 1 or 2 mm of “play” in the pH catheter. In addition, we repeated endoscopy at the

### Table 1

<table>
<thead>
<tr>
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<th>Conventional reflux</th>
<th>Short segment reflux</th>
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<tbody>
<tr>
<td>% time pH &lt;4 (Total)</td>
<td>1.8% (0.8–4)</td>
<td>11.7% (2.4–36.3)</td>
</tr>
<tr>
<td>% time pH &lt;4 (Upright)</td>
<td>2.3% (0.9–4.3)</td>
<td>12.7% (2.3–32.1)</td>
</tr>
<tr>
<td>% time pH &lt;4 (Supine)</td>
<td>1.3% (0.6–6.1)</td>
<td>10.5% (1.2–42.9)</td>
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</tbody>
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| DeMeester score     | 8 (4–19)            | 45 (12–131)          |

### Table 2

<table>
<thead>
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<th>Conventional reflux</th>
<th>Short segment reflux</th>
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<tbody>
<tr>
<td>% time pH &lt;4 (Preprandial)</td>
<td>1.6 (0–6.7)</td>
<td>14.2 (1.5–57.6)</td>
</tr>
<tr>
<td>% time pH &lt;4 (Postprandial)</td>
<td>2.8 (0–9.3)</td>
<td>21.8 (1.5–55.5)</td>
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| p                   | <0.001              | <0.001               |

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end of the 24 hour study period and were able to confirm that the clips were intact and that the electrode had not moved from its position proximal to the squamocolumnar junction. The methodology also raises concerns about what effect a pH catheter straddling the gastro-oesophageal junction may have on LOS function and oesophageal acid exposure. However, previous studies suggest that oesophageal acid exposure is not influenced by the presence of a pH catheter.19 In addition, other studies by our own group have indicated that the gastro-oesophageal pH step up is not altered by the presence of an endoscopic clip.6

Our observation that the most distal oesophagus has the highest exposure to gastric refluxate is consistent with the anatomical distribution of epithelial damage attributed to reflux.20 Intestinal metaplasia is also more prevalent closer to the gastro-oesophageal junction. Studies of unselected patients undergoing endoscopy found 9–36% with specialised intestinal metaplasia involving less than 3 cm of the distal oesophagus.21–24 The most distal oesophagus is also the site with the highest incidence of adenocarcinoma25–30 and the frequent occurrence of short segment reflux could be an aetiological factor.

### Table 3

<table>
<thead>
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<th>No of reflux episodes</th>
<th>Reflux pH nadir</th>
<th>Mean length of reflux episode (s)</th>
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</thead>
<tbody>
<tr>
<td>Conventional reflux</td>
<td>33 (14–53)</td>
<td>2.9 (1.9–4.0)</td>
<td>50 (19–110)</td>
</tr>
<tr>
<td>Short segment reflux</td>
<td>168 (51–350)</td>
<td>2.0 (1.4–2.6)</td>
<td>54 (25–91)</td>
</tr>
</tbody>
</table>

|                      | p<0.001               | p<0.01          |

![Figure 4](image-url)
Another recent observation has been the high prevalence of intestinal metaplasia of the most distal oesophagus in subjects without any reflux symptoms. Gerson et al reported intestinal metaplasia at the gastro-oesophageal junction or extending less than 3 cm proximal to it in 33% of subjects with no history of reflux symptoms. This intestinal metaplasia is likely to be the precursor of adenocarcinoma of the cardia which also shows little association with reflux symptoms. 11 The majority of subjects in our study had no symptoms of reflux disease. Gastroesophageal reflux is present in subjects without any symptoms of reflux disease. Gerson et al. 12

In conclusion, the most distal oesophagus is exposed to significant amounts of gastric acid, even in subjects without reflux symptoms. This short segment reflux may explain the high incidence of metaplasia and neoplasia of the most distal oesophagus which occurs in the general population.

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