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Location of the lower oesophageal sphincter and the squamous columnar mucosal junction in 109 healthy controls and 778 patients with different degrees of endoscopic oesophagitis

A Csendes, F Maluenda, I Braghetto, P Csendes, A Henriquez, M S Quesada

Abstract

In this study the location of the lower oesophageal sphincter measured by manometry and the location of the squamous columnar junction measured by endoscopy were determined in 109 healthy controls and 778 patients with different degrees of endoscopic oesophagitis. No significant differences in the prevalence and severity of the heartburn and regurgitation were observed when different degrees of oesophagitis were compared but dysphagia was more common and severe in patients with complicated Barrett's oesophagus (p<0.001). This group also showed a male predominance and older age compared with other groups. The total length of the oesophagus, measured by the location of the distal end of the lower oesophageal sphincter was similar in all patients; however, the location of the squamous columnar junction extended more proximally and was related to the increasing severity of endoscopic oesophagitis. The manometric defects at the cardia were more frequent in severe oesophagitis (p < 0.001). These results suggest that, during the course of oesophagitis, the squamous columnar junction is displaced proximally. This displacement is limited to the mucosa, however, and does not involve the muscular layer, because the lower oesophageal sphincter undergoes no dislocation.

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There is controversy over the precise location of the true oesophagogastric junction or 'cardia' in patients with reflux oesophagitis.12 For many endoscopists, the squamous columnar junction is considered as the representative of the oesophagogastric junction and the segment distal to it is frequently thought of as a 'hiatal hernia', because of the presence of gastric mucosa.13-5 For radiologists, it is difficult to be precise because when contrast medium is passing through the distal oesophagus, the lower oesophageal sphincter is relaxed and it is impossible define.167 For gastroenterologists and surgeons who perform manometric studies, the distal end of the lower oesophageal sphincter, which has an abdominal portion of 1 to 2 cm long, is the true oesophagogastric junction. 128-10 These different criteria have led to confusion in the diagnosis of the tubular or dilated segment distal to the mucosal junction. Is it a hiatal hernia or a portion of oesophagus lined by columnar epithelium? This discrepancy is in part, caused by the many reports in which patients with reflux oesophagitis are taken as a single group, without separating them according to the degree or severity of the injury to the oesophageal mucosa, and in part by the lack of manometric studies in the same patients.

The purpose of the present prospective study was to analyse 109 controls and 778 patients with reflux oesophagitis, who were divided into five categories according to the endoscopic findings, evaluating the following parameters: (a) symptoms of gastrooesophageal reflux; (b) determination of the location of the squamous columnar junction by endoscopy, and the location of the distal and proximal end of the lower oesophageal sphincter by manometry, and (c) to determine the characteristics of the mechanical defects of the lower oesophageal sphincter in all groups.

Methods

SUBJECTS STUDIED

This prospective study was carried out between January 1985 and December 1990. Two groups were analysed:

(a) Control subjects

One hundred and nine adult asymptomatic cases without any abdominal complaints (68 women, with a mean age of 45.6 years), who agreed to participate in this study, were selected from an original group of 120 controls; 11 subjects refused to participate in the investigation. Upper gastrointestinal endoscopy was normal in all patients, and a manometric test was performed in all of them.

(b) Reflux oesophagitis patients

Seven hundred and seventy eight patients with a clear long standing history (at least three years)

TABLE I Reflux oesophagitis

Age, sex and duration of symptoms						
Oesophagitis	n	0/0	Age (years)	Relation M:F	Duration symptoms (months)	
Grade 0	332	42.6	42±12	0.5	65 (80)	
Grade I	154	19.8	41 ± 12	0.77	59 (64)	
Grade II	69	8.9	44 ± 14	0.86	65 (74)	
Grade III	93	11.9	48±13*	1.2	100 (104)	
Grade IV	130	16.7	56±15*	1.8	105 (114)	

^{*} p<0.001.

Gastrointestinal Unit, Department of Surgery, Radiology and Nuclear Medicine, University Hospital, Santiago, Chile A Csendes F Maluenda I Braghetto P Csendes A Henriquez M S Quesada

Correspondence to: Professor Attila Csendes, MD, FACS, Department of Surgery, Clinical Hospital, University of Chile, Santos Dumont # 999, Santiago, Chile.

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of gastrooesophageal reflux symptoms. This period enabled us to be sure that a single patient had a chronic and persistent history of symptoms of gastrooesophageal reflux. There were 433 women, with a mean age of 47·2 years (range 17 to 84). Eight patients with adenocarcinoma in Barrett's oesophagus were excluded as well as 22 patients with a large, fixed intrathoracic hiatal hernia and three cases with paraoesophageal hernia.

CLINICAL ANALYSIS

A careful clinical questionnaire was defined at the beginning of this study, each patient being asked about the presence of heartburn, regurgitation, and dysphagia. The severity of these symptoms was graded into four categories: absent, mild, moderate, or severe, according to De Meester *et al*'s criteria." These symptoms were assessed by three authors who had no previous knowledge of the endoscopic or manometric results.

UPPER ENDOSCOPY

Upper gastrointestinal endoscopy was performed with the Olympus fibrescopes by two of the authors who did not know the manometric findings. The severity of oesophagitis was classified into five categories according to Savary's criteria¹²: (a) Grade 0: absence of oesophageal injury; (b) Grade I: presence of few isolated erosions; (c) Grade II: presence of multiple longitudinal or confluent erosions; (d) Grade III: presence of Barrett's oesophagus or columnar lined distal oesophagus, diagnosed by endoscopy when the squamous columnar mucosal function was seen 3 cm or more proximal to the endoscopic location of the lower oesophageal sphincter. This finding was considered as an 'uncomplicated' Barrett's oesophagus. (e) Grade IV: presence of a peptic ulcer or stricture of the oesophagus, located at the level or distal to the mucosal junction, always in the presence of a Barrett's oesophagus. This latter group was considered as 'complicated' Barrett's oesophagus.

The precise location of the squamous

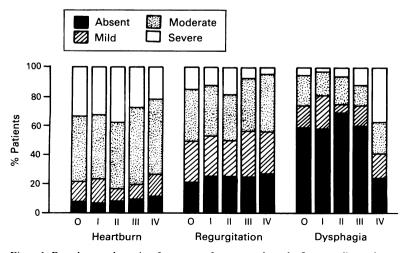


Figure 1: Prevalence and severity of symptoms of gastrooesophageal reflux according to the different degrees of endoscopic oesophagitis.

columnar mucosal junction, measured in centimetres from the incisors, was carefully defined both at the beginning and at the end of the endoscopy. In all patients with Barrett's oesophagus (Grade III and IV) serial biopsies distal to the mucosal junction (3 or 4) and proximal (1 or 2) were taken to confirm the type of epithelium lining of the distal oesophagus and to exclude adenocarcinoma. The endoscopic findings of 'erythema', 'oedema', 'friability', 'hyperaemia', 'dilated cardia', 'endoscopic reflux', which agree with Savary and Tytgat, 12 13 were not considered as evidence of oesophagitis, because they are too subjective to be evaluated and were not reproducible from one observer to another. In order to avoid any confusion, patients with small or long finger like projections of gastric mucosa or 'creeping substitution' were completely excluded from the present study and only the circumferential extension of gastric mucosa, which may be regular or irregular, was considered as Barrett's oesophagus.

OESOPHAGEAL MANOMETRY

This test was carried out after 12 hours fasting with patients in the supine position.14-16 The manometric assembly consisted of three polyvinyl tubes bounded together in such a way that the 0.8 mm side hole was 5 cm apart from each other (Arndorfer Medical Specialities, Milwaukee, USA). The tubes had an internal diameter of 1.1 mm and were constantly perfused with distilled water from a pneumohydraulic pump (Arndorfer Medical Specialities) at a rate of 0.5 ml/min. Each catheter was connected to a pressure transducer (Statham p23Dd, Hato Rey, Puerto Rico) and to a direct writer Gilson Polygraph (M4PM). Before each test, the pressure transducers and the polygraph were calibrated and the sudden occlusion of the side hole produced an increase of 200 mm Hg at one second. The recording catheter was introduced by the mouth (in order to compare results with endoscopy) after slight pharyngeal anaesthesia, into the stomach. This way, the distances from the incisors were comparable with endoscopic findings. The end expiratory fundic pressure was taken as zero reference, and all values were expressed in mm Hg. Three manometric characteristics of the lower oesophageal sphincter were determined: resting pressure, total length and abdominal length. This latter measurement was taken from the distal end of the sphincter up to the respiratory inversion point, which is the level at which the end expiratory pressure changes from a positive to a negative deflection." In each case, two rapid and two slow pull throughs were obtained. The resting pressure was taken as the mean pressure of all measurements in each of the three catheters - that is, six determinations in each patient.

STATISTICAL ANALYSIS

For statistical significance the variance analysis and the Student's t test were used and p values less than 0.05 were considered as significant. All values are expressed in mean standard deviation (SD).

TABLE II Manometric features of lower oesophageal sphincter in 109 healthy controls and 778 patients with reflux oesophagitis

Subjects	n	Resting pressure mm Hg (A)	Total length mm (B)	Abdominal length mm (C)	% cases with LOSP below 12 mm Hg
Controls	109	19.8 (7.8)	38 (10)	15 (7)	6.4
Grade 0	332	13.0 (9.6)	34 (10)	11 (6)	50-3
Grade I	154	13.0(11)	35 (9)	11 (7)	52.3
Grade II	69	11.2(10)	35 (13)	9(6)	59-4
Grade III	93	8.2 (6.3)	26 (10)	9(7)	78.5
Grade IV	130	8.8 (7.0)	25 (12)	9(5)	70.7

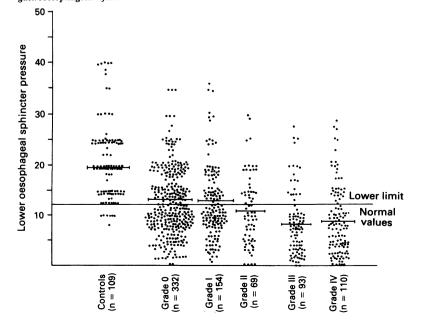
- A = controls v all oesophagitis <0.001; oesoph 0-I-II v III-IV <0.001 B = controls oesoph 0-I-II v III-IV <0.001 C = controls v all oesophagitis <0.001; oesoph 0-I v all II-III-IV <0.001

Results

The main epidemiological features of patients with reflux oesophagitis are shown in Table I. From the 778 patients, 43% showed no macroscopic evidences of endoscopic oesophagitis, while 28.6% had a Barrett's oesophagus of different degrees. The mean age increased together with the severity of the oesophageal injury. Patients with oesophagitis Grade 0, I, and II were significantly younger than patients with Barrett's oesophagus (p<0.001). Patients with uncomplicated Barrett's syndrome were also significantly younger than patients Grade IV (p<0.001) with complicated Barrett's oesophagus. The sex relationship was also different. Patients with oesophagitis Grade 0, I, and II showed a female predominance, while patients with a complicated Barrett's oesophagus (Grade IV) revealed a male predominance (p < 0.001). The duration of symptoms did not show any significant differences among the different groups, although a tendency to a shorter duration of symptoms was noted in patients with oesophagitis Grade 0, I, and II.

The prevalence of symptoms of gastrooesophageal reflux is shown in Figure 1. There were no significant differences in the prevalence of heartburn and regurgitation among the different degrees of endoscopic oesophagitis.

Figure 2: Individual values of resting lower oesophageal sphincter pressure in 109 healthy controls and 778 patients with gastrooesophageal reflux.



Only dysphagia was significantly more frequent in patients with complicated Barrett's oesophagus with ulcer or stricture (Grade IV) compared with the rest (p<0.001). Moderate and severe dysphagia, however, were significantly more frequent in patients Grade IV (p<0.001). The manometric features of the lower oesophageal sphincter are shown in Table II. Control subjects showed significantly higher resting lower oesophageal sphincter pressure compared with all degrees of oesophagitis (p<0.001). Patients with oesophagitis Grade 0, I, and II had significantly higher sphincter pressure than patients with oesophagitis Grade III and IV (p<0.001). On the contrary, patients with oesophagitis Grade 0, I, and II showed no differences as well as patients Grade III or IV. The total length of the lower oesophageal sphincter was similar in controls and in patients with oesophagitis 0, I, and II, but significantly longer than in patients with oesophagitis Grade III and IV (p<0.001). The abdominal portion of the lower oesophageal sphincter was significantly longer in controls compared with all patients (p<0.01). In patients with oesophagitis Grade 0 and I, it was significantly longer than in the other groups (p < 0.001). On the other hand, patients with oesophagitis Grade II, III, and IV had similar lengths of the abdominal portion of the distal sphincter. The percentage of cases with resting pressure below 12 mm Hg (lower limit of our normal values) is also shown in this Table. In controls, this value was 6.4% which increased to more than 50% in patients with oesophagitis Grade 0, I, and II, and to more than 70% in patients Grade III and IV. The individual values for resting sphincter pressure are shown in Figure 2. A considerable overlap of values can be seen in controls and patients with oesophagitis Grade 0 and I, as well as among all oesophagitis groups. The location of the lower oesophageal sphincter detected by manometry and the location of the squamous columnar mucosal junction seen by endoscopy are shown in Table III. No significant differences in the location of the distal limit of the lower oesophageal sphincter were shown in any group. The location of the mucosal junction, however, was significantly different in controls compared with all degrees of endoscopic oesophagitis (p<0.001). Patients with oesophagitis Grade 0 were also significantly different from all others (p<0.001) as well as oesophagitis Grade I and II compared with Grades III and IV (p<0.001). These latter groups had similar location of mucosal junction. The distances between the distal or proximal end of the lower oesophageal sphincter and the mucosal junction are observed in Table IV. In controls the mucosal junction is located in the midportion of the lower oesophageal sphincter. In patients with oesophagitis Grade 0, I, and II, this mucosal junction is very close or located at the proximal limit of the lower oesophageal sphincter. Patients with Barrett's oesophagus with oesophagitis Grade III or IV had the mucosal junction several centimetres proximal to the distal or proximal end of the lower oesophageal sphincter. The mean values for lower oesophageal sphincter pressure in patients with limited Barrett's oesophagus (mucosal junction located distal to 32 cm from

TABLE III Location of lower oesophageal sphincter and squamous columnar junction in 778 patients with reflux oesophagitis and 109 healthy controls

Subjects	n	Mucosal junction cm from incisors (A)	Distal limit LOS cm from incisors (B)
Controls	109	40.1 (2.1)	41.8 (2.7)
Grade 0	332	38.3 (2.0)	41.0 (3.0)
Grade I	154	37·2 (2.0)	41.0 (4.0)
Grade II	69	36·5 (2.1)	40 (3·4)
Grade III	93	33.2 (2.2)	41 (3.5)
Grade IV	130	32.6 (3.0)	40-4 (3-1)

p: A = controls v all oesophagitis <0·001; oesoph 0 v I-II-III-IV <0·001; oesoph I-II v III-IV <0·001 B = not significant in any group

the incisors) or extended Barrett's oesophagus (mucosal junction located proximal to 32 cm from the incisors) are shown in Figure 3. These values were taken from to the criteria proposed by Iascone et al. 11 There is a significant difference among both groups (p<0.002). The prevalence of mechanically defective cardia," defined as lower oesophageal sphincter pressure equal or below 6 mm Hg, an abdominal portion of the lower oesophageal sphincter with a length equal or shorter than 9 mm, and a total length of the distal sphincter equal or shorter than 20 mm, or a combination of these three parameters are shown in Table V. We also calculated the percentage of cases with absence of lower oesophageal sphincter pressure and the percentage of cases with absence of the abdominal portion of lower oesophageal sphincter. There is a progressive increase in the percentage of cases with defective cardia in all parameters evaluated according to the severity of endoscopic oesophagitis, which is significantly more pronounced in patients with oesophagitis Grade III and IV (p<0.001). The combination of the three parameters (sphincter pressure equal or less than 6 mm Hg, total length of lower oesophageal sphincter equal or less than 20 mm and abdominal portion of the lower

Figure 3: Mean pressure values of lower oesophageal sphincter in patients with limited (squamous columnar junction located 33 cm or more distal from incisors) or extended Barrett's oesophagus (squamous-columnar junction located 32 cm or more proximal from the incisors).

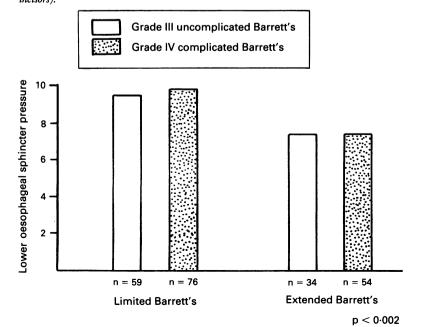


TABLE IV Mean distances between distal and proximal end of the lower oesophageal sphincter (measured by manometry) and the mucosal junction (measured by endoscopy) in 109 controls and 778 patients with reflux oesophagitis

Subjects	n	Differences distal end end LOS – mucosal junction (cm)	Differences. proximal end LOS – mucosal junction (cm)
Controls	109	+1.7	-2·1
Oesophagitis 0	332	+2.7	-0.7
Oesophagitis I	154	+3.8	+0.3
Oesophagitis II	69	+3.5	0
Oesophagitis III	93	+7.8	+5.2
Oesophagitis IV	130	+7.8	+5.3

oesophageal sphincter with a length equal or less than 9 mm) demonstrated in controls that this situation was not observed. In patients with oesophagitis Grade 0, I, and II, the percentage varies between 7 and 11%, which increased to 28% or 29% in patients with severe oesophagitis (p<0.001).

The summary of endoscopic and manometrical-findings in controls and patients with reflux oesophagitis is shown in Figure 4 where the mucosal junction seen at endoscopy is located more proximal according to the increasing severity of reflux oesophagitis. The lower oesophageal sphincter, however, remains in a similar location independent of the oesophageal damage. The abdominal portion of the lower oesophageal sphincter is shorter in patients with more severe oesophagitis.

Discussion

The present prospective study was designed to evaluate all patients with symptoms of gastrooesophageal reflux, who were submitted to a clinical assessment over a period of time. Few studies have tried to answer the question of whether clinical and demographic criteria can to distinguish patients with gastrooesophageal symptoms from patients complicated with Barrett's oesophagus. Two reports 17 18 found no differences in the mean frequency of heartburn and regurgitation, and a higher prevalence of dysphagia in the Barrett's group compared with reflux oesophagitis patients. The number of cases, however, was too small (22 v 31 cases respectively). Thus, in our opinion reflux symptoms are of no value in distinguishing Barrett's oesophagus patients from patients with reflux oesophagitis, and only the presence of a severe dysphagia may indicate Barrett's metaplasia. The age and sex distribution was also a significant finding in our study. Patients without endoscopic oesophagitis or with the presence of erosions at the distal oesophagus are younger, usually in the fourth decade and mainly women, while patients with Barrett's oesophagus (uncomplicated and complicated with ulcer and/ or stricture) are significantly older (usually in the fifth decade) and mainly men. This latter finding has been pointed out by some authors, 19-21 noting that the mean age at the time of the diagnosis of Barrett's oesophagus was about 55 years, which is the same as the value found in our study. Also male predominance was particularly significant

TABLE V Prevalence of mechanical defective cardia in 109 healthy control and 778 patients with progressive severity of endoscopic oesophagitis (expressed in %)

	Controls	Reflux oesophagitis				
Manometric features		0	I	II	III	IV
LOS pressure ≤6 mm Hg	0	17.7	18.8	31.9	42	43.0
Absence of LOSP	0	0.6	0	5.8	2.1	5.4
Total length ≤20 mm	5.5	9.9	10.4	8.7	33.3	41.5
Abdominal length ≤9 mm	6.4	18.0	24.7	36.2	51.6	55.4
Absence abdominal LOS portion LOS pressure 6 mm Hg or less	0	2.3	1.9	15.9	24.7	31.5
abdominal length ≤ 9 mm and total length ≤ 20 mm	0	7.2	7.8	11.6	28	29-2

in these cases. 19-22 What makes the difference between these reports and our study, however, is the fact that we clearly divided patients with gastrooesophageal reflux from those with endoscopic oesophagitis into different degrees or categories and in the number of patients evaluated, which is less than 50 in all these studies. The definition of a Barrett's oesophagus, although it seems very simple (distal oesophagus lined by metaplastic gastric or columnar epithelium), is subject to much controversy. Should it be an endoscopic, radiological, pathological or manometric definition? The point is to define the precise junction between the oesophagus and the stomach, which unfortunately is quite difficult. Anatomical landmarks are not clinically applicable. As it has been shown in the present study, the normal squamous columnar junction does not correspond to the distal end of the lower oesophageal sphincter, and it is located in the midportion of this sphincter, at a mean distance of 17 mm from its distal end measured by manometry. Radiological studies are not able to precisely define the muscular end of the oesophagus and when a Barrett's oesophagus is present with gastric mucosa lining the distal oesophagus, it can easily be mistaken for a hiatal hernia. Endoscopy in the diagnosis of a Barrett's oesophagus is more precise,23 but when the distal oesophagus is dilated, which is a usual finding in these cases and a hypotensive lower oesophageal sphincter is present, it is more difficult to detect the true oesophagogastric junction or cardia. In

the light of our results, we believe that the best clinical approach for an acute diagnosis of a Barrett's oesophagus is the combination of endoscopic and manometric studies; but how accurate is it to compare distances measured by manometry from distances measured by endoscopy? The tubes have a different stiffness and it is important to be able to measure distances within several millimetres. This may be a difficult question to answer, and indeed these techniques may not be comparable, unless one could simultaneously measure function and visualise the squamous columnar junction, which is very difficult. In a previous study, however, we determined the efficacy of the manometric measurements, comparing preoperative and intraoperative determinations.24 Under direct vision of the oesophagogastric junction and simultaneous manometric measurements, it is possible to observe a very similar correlation among the location of the lower oesophageal sphincter measured before operation with the values measured during surgery and under a direct observation. Besides, in six patients simultaneous endoscopy during surgery was performed in order to localise the squamous columnar junction. A very good correlation was observed with preoperative studies. The distal end of the lower oesophageal sphincter represents the true oesophagogastric junction or cardia14 19 and if the squamous columnar junction is located 3 cm or more proximal to the proximal limit of this sphincter, a true Barrett's oesophagus is present, which has been our criteria. This concept has two main difficulties: manometric studies should be performed in these patients, which is not frequently done and secondly, initial or developing Barrett's oesophagus is not considered in this group. We agree with Bremner et al25 and with Spechler and Goyal et al, 19 who stated that the established Barrett's oesophagus represents the true cases and that 'creeping substitute' or developing Barrett's oesophagus should be carefully followed up in order to determine the progression or not of these lesions.

Manometric studies in patients with Barrett's

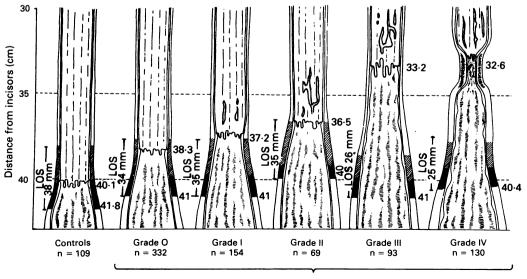


Figure 4: Summary of endoscopic and manometric findings in 109 controls and 778 patients with gastrooesophageal reflux, with different degrees of endoscopic injury.

LOS = lower oesophageal sphincter.

Oesophagitis

oesophagus are few⁶ 11 17 26 27 and the comparison with patients with gastrooesophageal reflux are less frequent. 11 17 28-30 Sarr et al 17 compared objective tests of oesophageal function in 318 patients with symptoms of gastrooesophageal reflux with 44 patients with Barrett's oesophagus undergoing endoscopy. From the reflux group, manometry was performed in only 60 cases showing a low distal oesophageal sphincter pressure in 53% of them (below 10 mm Hg), while in 11 patients with Barrett's oesophagus, this sphincter was below 10 mm Hg in all. Mann et al²⁹ compared reflux oesophagitis patients as a single group against Barrett's patients. In their study, mean lower oesophageal sphincter pressure was 19 mm Hg v 11 mm in Barrett's patients. No mention of the control group was made. Gillen et al³⁰ compared 25 patients with oesophagitis in a single group with 24 Barrett's oesophagus patients. No significant differences in sphincter pressure were noted. The best studies have been carried out by De Meester et al.112831 They compared controls, patients with oesophagitis Grade I or II and patients with Barrett's oesophagus,11 finding very similar results to those found in our study. Patients with Barrett's oesophagus had much lower oesophageal sphincter pressure, but a similar length of the sphincter exposed to the abdomen than patients with oesophagitis. Both groups had significantly lower oesophageal sphincter pressure and shorter abdominal length than controls, and cases with extended Barrett's oesophagus had lower sphincter pressure than cases with limited Barrett's oesophagus. In a further analysis,28 they determined the prevalence of the mechanically defective cardia, defined by manometric parameters. They noted an increase in these alterations according to the progression of oesophageal injury. We have found similar results in our group of reflux oesophagitis patients and Barrett's oesophagus cases. It is interesting to point out that we found in 50% of patients with gastrooesophageal reflux without oesophagitis (Grade 0), a hypotensive lower oesophageal sphincter which suggests that the decrease in sphincter pressure comes before the inflammatory or tissue damage.

Therefore, in the present study we have shown that the total length of the oesophagus, measured by the location of the distal end of the lower oesophageal sphincter is similar in all patients, but the squamous columnar junction extends more proximally parallel to the increasing severity of the endoscopic oesophagitis. This finding is closely related to the frequent problem caused by the radiological and endoscopical diagnosis of a 'small hiatal hernia'. As it can be noted in the present study, we avoided the use of this terminology. It must be clear that the squamous columnar junction does not represent the true oesophagogastric junction or cardia, as it has been previously demonstrated by simultaneous determination of potential difference change and manometric studies.32 33 This is why the distal ring noted by some authors is only a mucosal stricture, which marks only the mucosal junction and not the true muscular oesophagogastric junction as observed by Reinaldo and Gahagan,34 and Harris.35 Therefore, it may not represent a hiatal hernia as reported by Lauren³⁶ and Cauthorne,37 who showed that these mucosal rings occur near the upper margin of the lower oesophageal sphincter. We believe that the diagnosis of hiatal hernia has been over exagerated and only manometric studies combined with precise endoscopic evaluation can say whether we are dealing with a true hiatal hernia or a small initial Barrett's oesophagus.

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