

24 Hour ambulatory oesophageal pH monitoring in uncomplicated Barrett's oesophagus

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Abstract

The aim of this study was to compare acid reflux in 16 patients with uncomplicated Barrett's oesophagus with 37 patients with reflux oesophagitis and 10 control subjects of comparable age. All patients had 24 hour ambulatory pH monitoring within one week of endoscopy. The controls differed significantly from the other groups in all indices of reflux but there was no difference between the Barrett's oesophagus patients and the reflux oesophagitis patients in any index of reflux over the total 24 hour period. Barrett's oesophagus patients differed significantly, however, with respect to the percentage time pH <4 and the number of reflux episodes of >five minutes during the supine period when compared with patients with grade I reflux oesophagitis, but not when compared with patients with grade II and III reflux oesophagitis. Barrett's oesophagus patients with associated grade II reflux oesophagitis had more reflux than those with no oesophagitis or grade I reflux oesophagitis. Within each disease group patients ≥ 50 years had more acid reflux than patients <50 years. The severity of acid reflux in patients with uncomplicated Barrett's oesophagus was no greater than in patients with reflux oesophagitis of comparable age. It seems probable that other factors must be important in the development of Barrett's oesophagus.

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In Barrett's oesophagus, metaplastic columnar epithelium replaces the normal stratified epithelium of the distal oesophagus.¹ The condition is common and about 10% of patients with gastro-oesophageal reflux disease who undergo endoscopic examination are found to have Barrett's oesophagus.² It is also thought that Barrett's epithelium has malignant potential and adenocarcinoma may develop in as many as 8-15% of patients with Barrett's oesophagus.²

Although it is accepted that Barrett's oesophagus is acquired and related to gastro-oesophageal reflux, it is not clear why some patients with gastro-oesophageal reflux develop Barrett's oesophagus and why some only develop reflux oesophagitis. A widely held view is that acid reflux is greater in patients with Barrett's oesophagus than in patients with reflux oesophagitis,³ and this may be a factor in the development of Barrett's oesophagus. To date there have been six published studies comparing the amount of acid reflux in Barrett's oesophagus with that in reflux oesophagitis⁴⁻⁹; five of the six studies showed excessive acid reflux in patients with Barrett's oesophagus.⁴⁻⁷ Three of six studies, however included Barrett's oesophagus patients with complications of gastro-oesophageal reflux such as oesophageal ulcers or oesophageal strictures,⁴⁻⁶ or both. In four of six studies, the ages of the patients investigated were recorded⁵⁻⁸ but in three of four studies that recorded the age, patients with Barrett's oesophagus were older than those with reflux oesophagitis.⁵⁻⁷ Moreover, there may have been a referral bias in that five of six studies came from surgical units⁴⁻⁶ and therefore may have included Barrett's oesophagus patients with more severe symptoms. Therefore the purpose of our study was to measure intraoesophageal acid exposure by 24 hour ambulatory pH monitoring in age comparable patients with uncomplicated Barrett's oesophagus and with reflux oesophagitis, attending a medical gastroenterology clinic.

Patient and methods

Fifty three white patients underwent 24 hour ambulatory pH monitoring. Sixteen patients had Barrett's oesophagus and 37 had reflux oesophagitis of whom 21 had mild reflux oesophagitis (revised Savary Miller grade I)¹⁰ and 16 had more severe reflux oesophagitis (revised Savary Miller grade II and III). Of these 16, 12 had grade II and four had grade III reflux oesophagitis. Barrett's oesophagus was diagnosed when the columnar epithelium extended 3 cm or more above the gastro-oesophageal junction at endoscopy.² It was confirmed by histological examination of oesophageal biopsy specimens. None of the patients with Barrett's oesophagus had stricture, oesophageal ulcer, dysplasia or adenocarcinoma, but three had associated grade I reflux oesophagitis and eight had grade II reflux oesophagitis. Five patients with Barrett's oesophagus had no evidence of reflux oesophagitis at the time of pH monitoring. Ten

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TABLE 1 Patient and controls according to sex and age

	Sex M : F	Range	Age Mean	Median
Oesophagitis Grade I	7:14	26-83	50	50
Oesophagitis Grade II and III	9:7	26-75	53	54
Barrett's oesophagus	6:10	36-78	58	57
Controls	4:6	40-66	57	59

TABLE II Results of 24 hour ambulatory pH monitoring over a 24 hour period – controls, patients with reflux oesophagitis, and patients with Barrett's oesophagus

Total period	Percentage time pH<4 median (range)	Number of reflux episodes median (range)	Number of reflux episodes <5 minutes median (range)	Longest reflux episode median (range)
Controls (n=10)	2.15* (0.1–4.9)	28.0† (2–49)	0.5‡ (0–4)	6† (1–13)
Oesophagitis Grade I (n=21)	11.90 (NS) (1.5–57.4)	72.0 (NS) (21–356)	6.0 (NS) (0–17)	25 (NS) (1–155)
Oesophagitis Grade II and III (n=16)	14.10 (NS) (1.3–44)	91.5 (NS) (17–679)	8.5 (NS) (0–25)	32 (NS) (4–90)
Barrett's oesophagus (n=16)	16.00 (1.1–70.7)	66.0 (12–567)	9.5 (0–28)	36 (1–327)

Barrett's group *v* other groups: *p=0.005, †p=0.05, ‡p=0.002, NS p=not significant.

patients with atypical chest pain and normal endoscopy and oesophageal biopsy served as controls. The groups were comparable in sex and age (Table 1).

pH Monitoring was carried out using the Synectics solid state Digitrapper with an antimony electrode, which was calibrated according to manufacturer's recommendation. Patients were fasted for six hours. The electrode was passed through the nose and positioned 5 cm above the gastro-oesophageal junction, which was identified endoscopically and by the pH step up technique. Continuous recording was performed for 24 hours on an outpatient basis within one week of endoscopy. The diet was unrestricted, except for acid foods and drinks, and H₂ receptor antagonists or proton pump inhibitors were not permitted for seven days before or during the test. DeMeester's criteria¹¹ for acid reflux was used and a reflux episode was defined as a drop of pH below 4. The indices of reflux measured were the percentage time pH was less than 4, number of reflux episodes, number of episodes lasting more than five minutes and duration of the longest reflux episode and each was recorded for total, upright, and supine time.

Statistical analysis of the data was carried out on the Elonex PC 386B/25 computer using the OXSTAT Scientific and Statistical Data Analysis System. Fisher's exact test was used to compare the sex between the groups and the Mann-Whitney U test for non-parametric data was used to compare age and acid reflux of the different groups.

Results

Table II shows the results of the 24 hour pH monitoring. Over the total 24 hour period controls differed significantly in all indices of reflux from the reflux oesophagitis

patients as well as from patients with Barrett's oesophagus, but there were no significant differences between the reflux oesophagitis patients and the Barrett's oesophagus patients.

During the supine period controls again differed significantly in all indices of reflux from the reflux oesophagitis patients and the Barrett's oesophagus patients. When the Barrett's oesophagus patients were compared with the reflux oesophagitis patients, however, significant differences were found between the grade I oesophagitis patients and the Barrett's oesophagus patients with respect to the percentage time pH<4 (p=0.03) and the number of reflux episodes lasting >5 minutes (p=0.03). There were no differences between the grade II and III reflux oesophagitis patients and the Barrett's oesophagus patients (Table III).

To find out if within the Barrett's oesophagus group there was any correlation between acid reflux and the presence of reflux oesophagitis, the eight Barrett's oesophagus patients with grade II reflux oesophagitis were compared with the eight Barrett's oesophagus patients with no reflux oesophagitis or with grade I reflux oesophagitis. There were significant differences between the two Barrett's oesophagus group with respect to the total and the supine percentage time pH<4 (p<0.05) (Table IV).

It was also considered that age might be an important factor in gastro-oesophageal reflux. Each group was divided into patients <50 years and patients ≥50 years (Figure). In each group, subjects ≥50 years had more acid reflux than patients <50 years.

Discussion

Our results show that acid reflux over 24 hours in patients with uncomplicated Barrett's

TABLE III Results of 24 hour ambulatory pH monitoring during the supine period – controls, patients with reflux oesophagitis, and patients with Barrett's oesophagus

Supine period	Percentage time pH<4 mean/median (range)	Number of reflux episodes median (range)	Number of reflux episodes <5 minutes median (range)	Longest reflux episode median (range)
Controls (n=10)	0.2/0.0* (0.9)	0.5† (0–20)	0‡ (0–0)	0§ (0–3)
Oesophagitis Grade I (n=21)	7.2/4.5¶ (0.1–56.2)	6 (NS) (1–126)	1¶ (0–8)	11.5 (NS) (0–145)
Oesophagitis Grade II and III (n=16)	14.7/4.2 (NS) (0–64.7)	8 (NS) (0–89)	2 (NS) (0–9)	7 (NS) (0–90)
Barrett's oesophagus (n=16)	19.8/12.9 (0.1–89.6)	9 (1–98)	3 (0–8)	28 (0–307)

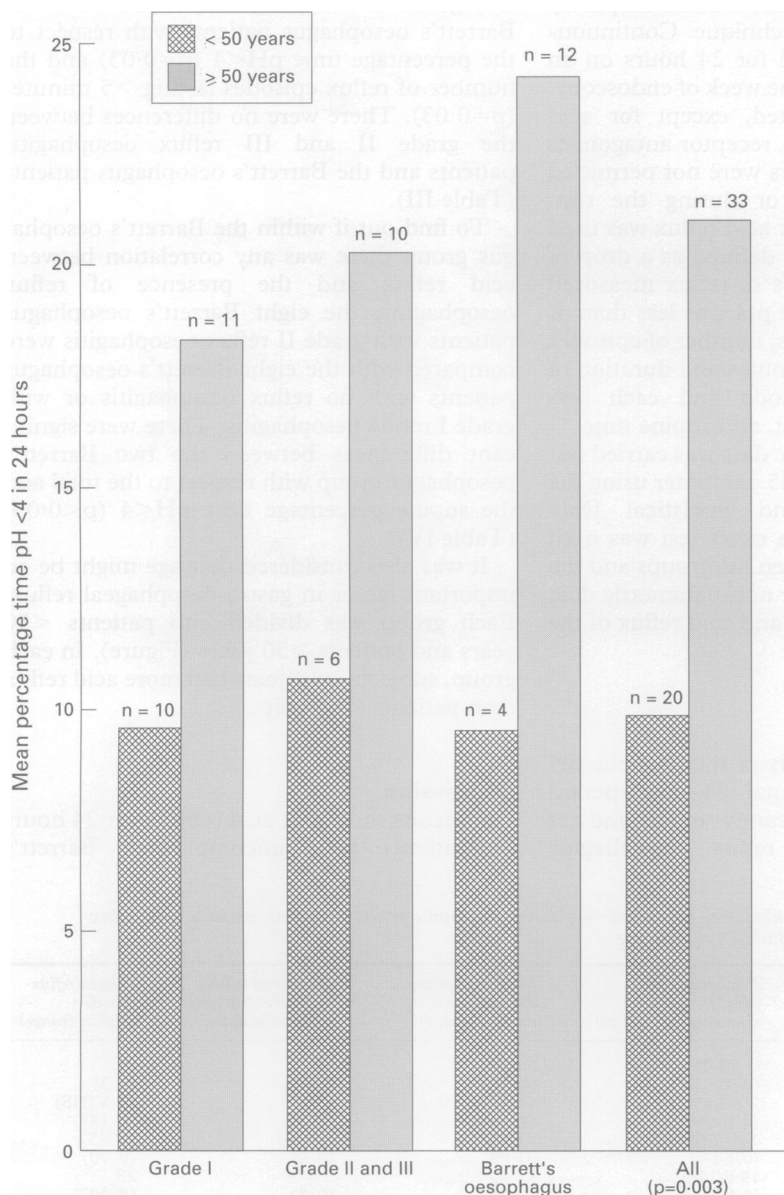
Barrett's group *v* other groups: *p<0.001, †p<0.05, ‡p=0.01, §p<0.03, ¶p<0.03, NS p=not significant.

TABLE IV Results of 24 hour ambulatory pH monitoring – patients with Barrett's oesophagus and Grade 0 or Grade I oesophagitis and patients with Barrett's oesophagus and Grade II oesophagitis

	Total percentage time pH<4 median (range)	Supine percentage time pH<4 median (range)
Barrett's oesophagus with Grade 0 or Grade I oesophagitis (n=8)	6.55* (1.1–70.7)	3.7* (0.1–89.6)
Barretts oesophagus with Grade II oesophagitis (n=8)	22.8 (12.9–40.6)	26.1 (1.9–38.1)

*p=0.05.

oesophagus was not significantly different from that in patients with reflux oesophagitis. Our results differ from five of six previously published studies on acid reflux in Barrett's oesophagus, which suggested that acid reflux in patients with Barrett's oesophagus was greater than in patients with reflux oesophagitis.^{4–7,9} Our study agreed with that of Parrilla *et al*,⁸ who showed no differences in acid reflux over 24 hours between patients with severe reflux oesophagitis and with Barrett's oesophagus. Unlike these authors, however,



24 Hour ambulatory pH monitoring in patients with reflux oesophagitis and Barrett's oesophagus, comparing patients <50 years of age and patients ≥50 years of age.

we showed no significant differences in acid reflux over 24 hours between patients with mild reflux oesophagitis and with Barrett's oesophagus. Parrilla *et al* did not compare their Barrett's oesophagus patients with and without associated reflux oesophagitis, but we showed greater acid reflux in patients with Barrett's oesophagus associated with grade II reflux oesophagitis than with the remaining patients with Barrett's oesophagus who either had mild reflux oesophagitis or no evidence of oesophagitis at all. Parrilla *et al* did not report the result of acid reflux during the supine period but our study showed that supine reflux was greater in patients with Barrett's oesophagus than in those with mild reflux oesophagitis. This raises the possibility that supine reflux may participate in the development of Barrett's oesophagus and there is some evidence that supine (nocturnal) reflux may be important in the development of severe oesophageal damage.¹² We could not show, however, a statistically significant difference between severe reflux oesophagitis and Barrett's oesophagus and between mild and more severe reflux oesophagitis with respect to supine reflux. This failure to show significant differences is possibly related to the small number of patients with grade III reflux oesophagitis available for study. It has been suggested in a study using twin channel recording that acid reflux in Barrett's oesophagus occurs to a higher level in the oesophagus than in patients with reflux oesophagitis.¹³ We could not obtain, however, any information in our study that used single channel recordings only.

Of the six studies on acid reflux in Barrett's oesophagus published to date, the ages of the patients who were studied was recorded in only four. In three of these studies the patients with Barrett's oesophagus were older than those with reflux oesophagitis^{5–7} and each study showed greater acid reflux in Barrett's oesophagus compared with reflux oesophagitis patients. In contrast, our study and that of Parrilla *et al*⁸ included patients of comparable age and there was no evidence of excessive reflux in Barrett's oesophagus. There is some evidence from published reports that acid reflux becomes greater with age^{14,15} and we found that for each patient group, those patients aged 50 years or more had greater reflux than those less than 50 years of age. Therefore it seems probable that the greater reflux in Barrett's oesophagus seen in some of the previous studies was related to the age of the patients rather than to the Barrett's oesophagus itself. Three of the previous studies included patients with Barrett's oesophagus who had severe complications of gastro-oesophageal reflux^{4–6} such as ulcer or stricture, which suggests the possibility that these patients had more severe reflux leading to these complications and the Barrett's oesophagus was coincidental. Neither our study or the study of Parrilla *et al* included such patients.

Therefore all but one of the published studies that showed excessive gastric acid

reflux in Barrett's oesophagus may have been flawed either because the patients with Barrett's oesophagus were older than the patients with reflux oesophagitis or the patients with Barrett's oesophagus often had severe complications of gastro-oesophageal reflux. The remaining study was only published in abstract and no clinical details were apparent.⁹ We conclude, that patients with uncomplicated Barrett's oesophagus do not have worse reflux than patients with reflux oesophagitis although there is evidence suggesting the possibility of greater supine reflux in patients with Barrett's oesophagus. It seems probable that other factors must be important in the development of Barrett's oesophagus. Such factors are unknown but may include the number of years the oesophagus is exposed to excessive acid reflux, alkaline reflux, genetic susceptibility or exposure to environmental agents.

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