PAPERS

Natural history of reflux oesophagitis: a 10 year follow up of its effect on patient symptomatology and quality of life

N I McDougall, B T Johnston, F Kee, J S A Collins, R J McFarland, A H G Love

Abstract

***Background*—Although oesophagitis is the most common diagnosis made at upper gastrointestinal endoscopy, data on the longterm outcome of affected patients are sparse.**

***Aims*—This study assessed the level of reflux symptoms, quality of life, drug consumption, and complications in patients at least 10 years after diagnosis of oesophagitis at one centre.**

***Patients*—One hundred and fifty two patients with typical reflux symptoms and a first time diagnosis by endoscopy of grade I–III oesophagitis between 1981 and 1984, were followed up using a postal questionnaire and telephone interview.**

***Results*—Eighteen of 152 patients had died, 33 failed to respond, and 101 replied (mean follow up 11 years, range 121–160 months). Over 70% of patients still had heartburn at least daily (32%) or weekly (19%) or required daily acid suppression treatment (20%). Two patients (2%) had developed oesophageal strictures and one had Barrett's oesophagus. Two of eight quality of life scores (physical function and social function) measured by the Short Form-36 were significantly lower than Northern Ireland population scores.**

***Conclusion*—Nearly three quarters of patients previously diagnosed as having oesophagitis still had significant morbidity related to gastro-oesophageal reflux disease more than 10 years after diagnosis. Some quality of life scores were significantly lower than those of the general population.**

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Gastro-oesophageal reflux disease (GORD) is an extremely common condition, causing daily heartburn in 4–10% of the general population.[1–3] It encompasses a disease spectrum ranging from troublesome reflux symptoms with normal investigations, to severe reflux oesophagitis and its complications.

Oesophagitis is found in 50–68% of patients with GORD symptoms who present to a doctor.[4–7] The prevalence of oesophagitis in the community is thought to be up to 2%,[8 9] and it can ultimately progress to oesophageal complications such as deep ulceration, stricture formation, and the development of Barrett's mucosa.[10] Despite the fact that it is so common and has known complications, studies on the longterm natural history of oesophagitis (and GORD in general) are exceedingly rare.[10–13] Short term follow up studies of oesophagitis patients have been performed,[14–19] but usually restricted follow up to a maximum of one year. These studies showed that even with the best maintenance treatments there is a tendency for 11–30% of oesophagitis patients to relapse within 6–12 months, in keeping with the general impression (as yet not supported by adequate longterm data) that oesophagitis is a chronic relapsing condition.

Even though it has been suggested that this relapsing condition may diminish quality of life,[14] to date there are no published studies of the longterm effect of GORD on quality of life. The Short Form-36 (SF36) general health survey questionnaire is widely regarded as one of the most useful tools for assessing patient quality of life. Initial reports on using the SF36 in the UK population have found it to fulfil the criteria of validity, reliability, reproducibility, and sensitivity, all of which are necessary in a tool that will detect minor changes in patient health.[20–22]

The aims of this study were twofold: firstly, to perform a longterm follow up of oesophagitis assessing morbidity and drug consumption. Secondly to assess the longterm effect that oesophagitis has on patient quality of life using the SF36.

Methods

We reviewed the records of all upper gastrointestinal endoscopies performed by the medical unit of the Ulster Hospital Dundonald during the period February 1981 to March 1984, and followed up all patients fulfilling the following criteria: aged 18 or over with reflux symptoms and a first time endoscopic diagnosis of grade II or III oesophagitis (modified Savary-Miller classification according to Little

et al[7]: grade I – mucosal erythema, with or without friability, grade II – linear mucosal erosions, grade III – confluent or circumferential erosions, and grade IV – deep ulceration, stricture or Barrett's mucosa). In addition, patients with grade I oesophagitis and biopsy confirmation of histological oesophagitis (inflammatory cell infiltrate in the lamina propria) were included. Patients were excluded if they also had active peptic ulcer disease, previous oesophageal or gastric surgery, grade IV oesophagitis, malignancy or other serious illness (for example, cardiothoracic, renal, hepatic) that would be likely to preclude long-term follow up. At the time of initial endoscopy, patients were treated with a course of the standard dose of an H_2 receptor antagonist (H_2RA) and discharged after one or two follow up appointments unless symptoms failed to settle.

Patients fulfilling these criteria were sent a symptomatic questionnaire including the English language version of the SF36. Non-responders were sent a reminder letter after six to eight weeks or contacted by phone if possible, and a repeat questionnaire after three months if necessary. Patients who had changed address were traced through the Central Services Agency for Northern Ireland (NI). Death certificates were retrieved from the Registrar General's office for deceased patients. All responders were contacted by phone to complete any missing details and confirm drug consumption data. Repeat endoscopy was offered to all patients with dysphagia weekly or daily and to those with daily heartburn.

The SF36 contains 36 questions on aspects of both physical and mental health. The scores for each question are used to compute a score between 0 and 100 for each one of eight quality of life scale. The eight scales are ordered from left to right when represented graphically (as in Fig 1) according to the extent to which they measure physical or mental health respectively. The scales are: physical function, role-physical, bodily pain, general health, vitality, social function, role-emotional, and mental health. Quality of life scores are affected by sex and age and we took account of this in our analysis as described below.

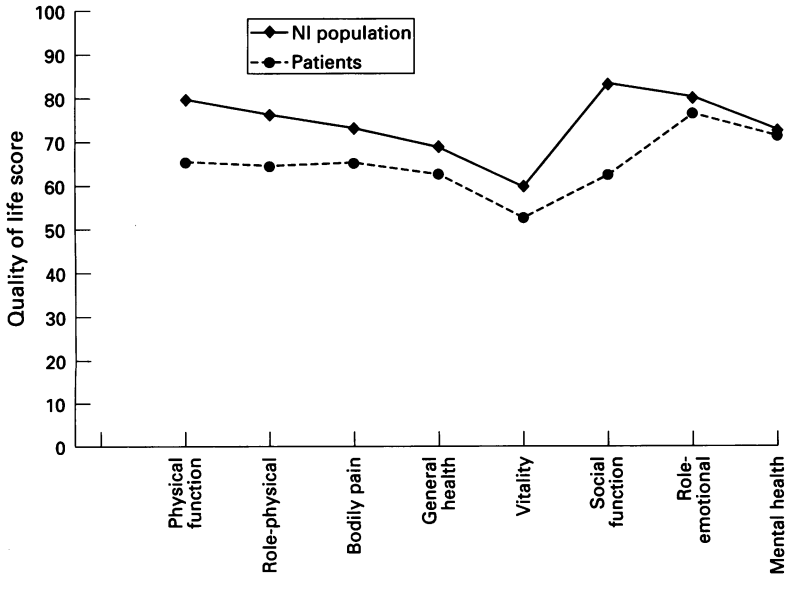

Figure 1: Quality of life results for NI population sample and study group.

For analysis purposes the drugs consumed by responders over the review period were converted to equivalent weeks of treatment. The standard doses we used were ranitidine 150 mg twice daily, cimetidine 400 mg twice daily, nizatidine 150 mg twice daily, omeprazole 20 mg in the morning, metoclopramide 10 mg thrice daily, and cisapride 10 mg four times daily.

The study was approved by the ethical committee of Queen's University of Belfast.

Statistical analysis

The role of several variables in determining outcome were analysed using the *t* test for independent samples for continuous variables (age), the χ^2 test where appropriate, and logistic regression analysis. In addition, the χ^2 test was used to determine the significance of any differences between patients with grade I oesophagitis and those with grades II–III oesophagitis.

Quality of life scores obtained with the SF36 are not normally distributed and we used the following methods to analyse the results for our study group: for each of the eight quality of life parameters measured by the SF36, we derived a prediction equation from the NI sample using linear regression analysis with age as an explanatory variable. Separate equations were obtained for men and women. Then for each study patient the 'deviation from predicted' was obtained by subtracting the NI predicted score for the relevant age and sex from the patient's score. The mean deviation in the study group was assessed to determine if it differed significantly from zero using the single sample *t* test. In addition, 95% confidence limits were calculated. Deviations were also analysed using the independent samples *t* test to compare subgroups defined by sex and oesophagitis grade to see if these variable affected quality of life.

Results

In total, 1187 endoscopy results were reviewed, with a total of 194 showing grade I–III oesophagitis. Forty two were excluded from follow up (16 were repeat endoscopies on patients who had already been included, 11 had malignancy or other serious illness, and 15 had peptic ulcer disease) leaving 152 who fulfilled the criteria.

Eighteen of 152 patients died during the follow up period, five could not be traced, 28 failed to respond, and 101 patients replied giving a response rate of 75% (101 of 134 capable of responding).

None of the 18 deceased patients (11 male, four grade I oesophagitis, 13 grades II–III) died from a disorder related to oesophageal disease. The 33 patients (21 male) who failed to reply or could not be traced had very similar demographic details to the 101 responders

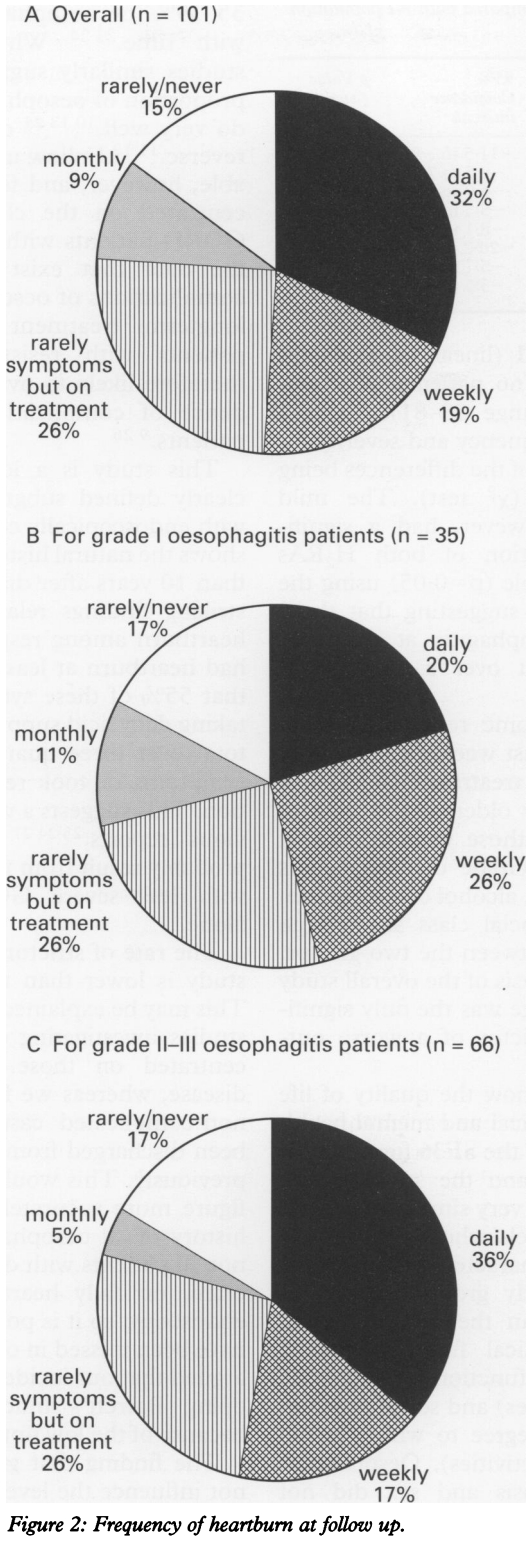

Figure 2: Frequency of heartburn at follow up.

TABLE I *Comparison of symptoms between grade I oesophagitis patients and grade II–III patients*

	Grade I patients (n=35)	*Grade II–III patients (n=66)*	*p Value*
No (%) with daily heartburn	7 (20%)	24 (36%)	NS
No (%) with weekly heartburn	9 (26%)	11 (17%)	NS
No (%) receiving daily acid suppression treatment	14 (40%)	34 (52%)	NS
No (%) whose symptoms are a moderate or severe nuisance	15 (43%)	36 (54%)	NS
Drug consumption (weeks of treatment)			
H_2RAs median (IQR)	8 (0–126)	62 (8–436)	0·02
PPIs median (IQR)	0 (0–0)	0 (0–10)	0·05

IQR=interquartile range, PPI=proton pump inhibitor.

(mean age 54·5 years (range 29–85), 10 (30%) with grade I oesophagitis, and 23 (70%) with grades II–III at initial endoscopy).

The 101 responders (47 male) had a mean age of 55·2 years (28–81) at the time of follow up, and completed their questionnaires a mean of 134 months (121–160), or 11·2 years after their initial diagnostic endoscopy.

Thirty two patients (32%) reported having heartburn at least daily, and a further 19 (19%) had heartburn at least weekly. Twenty eight (55%) of these 51 patients said they were taking daily acid suppression treatment – H_2RAs (n=14), omeprazole (n=14), a proton pump inhibitor. Figure 2 shows the frequency of heartburn in responders for the overall group (A) and for those with different grades of oesophagitis at initial diagnosis ((B) and (C)). In total, 77 patients (76%) had frequent heartburn or required frequent antireflux treatment, or both.

Five patients (5%) reported dysphagia for solids/meat at least daily (of whom two had an endoscopically confirmed benign stricture, one had grade II oesophagitis, and two refused endoscopy), and four patients (4%) had dysphagia for solids/meat at least weekly (one of whom had Barrett's oesophagus on endoscopy, one had normal endoscopy, and two refused follow up). One further patient with daily heartburn despite treatment with a proton pump inhibitor had an endoscopy that was normal. In total 26 of 32 patients who were offered repeat endoscopy refused. One patient had antireflux surgery performed during the follow up period.

When asked how they rated the severity of their symptoms (if present), three of 101 patients (3%) reported that their symptoms were unbearable, 15 (15%) said it was a major nuisance (interfering with daily activities), 32 (32%) a moderate nuisance, 32 (32%) a minor nuisance, and 19 (19%) said it was no problem at all.

Forty eight patients (47·5%) were taking daily acid suppression treatment, 24 (23·8%) were taking antacids at least several times weekly, seven (6·9%) took antacids at least monthly, and the remaining 22 (21·8%) said they rarely or never took any treatment for heartburn. The bulk of the drug treatment consumed over the review period was in the form of H_2RAs with the equivalent of 17 317 weeks of treatment with the standard doses taken (based on patient estimates), or 171·5 weeks (3·3 years) of H_2RA treatment per patient. The total consumption of other prescribed drugs for reflux symptoms was as follows: 1980 weeks of omeprazole, 27 weeks of metoclopramide, and 56 weeks of cisapride. Based on the current cost of each of these drugs, the total cost of the drugs consumed by the 101 follow up patients over the review period was approximately £137 273, which equates to a cost of £121.35 per patient per year.

There was no significant difference in the age or sex distribution of those with grade I (non-erosive) oesophagitis (35 patients, 14 male, mean age 51 years, range 30–73) and

TABLE II *Quality of life (QOL) results for the study group compared with NI population data*

QOL parameter	NI population sample (n=3015)	Study group (n=101)	Mean (SD) of patients' 'deviations from predicted'	95% Confidence intervals	p Value (Significant if <0·05*)
Physical function	79·7	65·4	−5·9 (28·4)	−11·5 to −0·3	0·038*
Role - physical	76·2	64·1	−0·6 (40·0)	−8·5 to 7·3	0·88
Bodily pain	73·1	65·2	−1·5 (27·5)	−6·9 to 3·9	0·59
General health	69·6	62·5	−0·5 (25·2)	−5·5 to 4·5	0·85
Vitality	59·6	52·3	−3·1 (25·6)	−8·1 to 2·0	0·23
Social function	83·3	62·5	−16·1 (20·7)	−20·2 to −12·0	<0·001*
Role - emotional	79·9	76·5	2·1 (39·4)	−5·7 to 9·8	0·60
Mental health	72·8	71·7	0·5 (20·0)	−3·5 to 4·4	0·82

those with grades II–III (linear or confluent erosions) oesophagitis (66 patients, 33 male, mean age 57 years, range 28–81). Table I shows the symptom frequency and severity for these two groups, none of the differences being statistically significant (χ^2 test). The mild oesophagitis group, however, had a significantly lower consumption of both H_2RAs (p=0·02) and omeprazole (p=0·05) using the Mann-Whitney U test, suggesting that those with more severe oesophagitis at diagnosis require more treatment over a 10–13 year period.

Those with troublesome reflux disease at review (heartburn at least weekly or requiring daily acid suppression treatment (n=71) or both) were significantly older at the time of initial endoscopy than those with infrequent symptoms (p=0·015). Grade of oesophagitis at initial endoscopy, sex, alcohol consumption, smoking status, and social class showed no significant difference between the two groups. Logistic regression analysis of the overall study group confirmed that age was the only significant independent predictor of a worse outcome at review.

Table II and Fig 1 show the quality of life scores in the eight physical and mental health parameters measured by the SF36 for a sample of the NI population and the study group. The NI sample data are very similar to general population data from elsewhere in the UK and USA, showing a characteristic dip in the vitality score. The study group had significantly lower scores than the NI population sample for both physical function (which measures the level of function over a wide range of physical activities) and social function (which measures the degree to which health interferes with social activities). Oesophagitis grade at initial diagnosis and sex did not significantly affect quality of life.

Thirty eight (38%) patients reported having other medical conditions at the time of follow up. Most (28) of these patients said their reflux disease was the main problem, 23 required daily acid suppression treatment, and only seven (7%) said they rarely or never had trouble with reflux disease.

Discussion

Few studies have considered the issue of the longterm natural history of GORD. Some years ago, when the mere presence of a hiatus hernia was considered sufficient evidence of reflux disease, both Rex *et al* and Palmer produced follow up studies showing that 35–39% of oesophagitis patients improved with time.[23 24] While some more recent studies similarly suggested that a significant proportion of oesophagitis or GORD patients do very well,[10 13 25] others have reported the reverse.[11 12] Follow up periods were very variable, however, and few of these studies concentrated on the clearly defined group of GORD patients with oesophagitis. Similarly, the data that exist on the prevalence of complications of oesophagitis or outcomes of longterm treatment are often based on patients with resistant disease, and are therefore likely to overestimate the true incidence of complications in all oesophagitis patients.[9 26]

This study is a longterm follow up of a clearly defined subgroup of GORD patients with endoscopically confirmed oesophagitis. It shows the natural history of the condition more than 10 years after diagnosis. One of the most striking findings relates to the frequency of heartburn among responders. More than half had heartburn at least weekly despite the fact that 55% of these symptomatic patients were taking daily acid suppression treatment, and in total over three quarters either had frequent symptoms or took regular antireflux medication. This suggests a worse prognosis than previous reports,[23 24 27] but the discrepancies probably result from their inclusion of patients with less severe GORD or hiatus hernia alone.

The rate of stricture formation (2%) in this study is lower than that quoted by others.[10] This may be explained by the fact that previous studies investigating complications have concentrated on those patients with resistant disease, whereas we followed up consecutive, non-complicated cases, most of whom had been discharged from hospital follow up years previously. This would suggest that our lower figure more accurately represents the natural history of all oesophagitis patients. However, not all patients with dysphagia weekly or more often, or daily heartburn, agreed to repeat endoscopy, so it is possible that strictures may have been missed in our study. It could also be argued that our incidence of one patient developing Barrett's mucosa is too low, again because of the low uptake of repeat endoscopy.

The finding that grade of oesophagitis did not influence the level of symptoms or quality of life scores at review is in keeping with the findings of others who have reported that oesophagitis grade is not a useful predictor of longterm outcome.[10 12] However, those with more severe oesophagitis did have significantly higher consumption of both H_2RAs and proton pump inhibitors.

Our finding that age at the time of diagnosis is the only independent predictor of outcome after diagnosis of oesophagitis has not been previously reported. Hiatus hernia and complications of oesophagitis (Barrett's mucosa and stricture) are more common over the age of 50 years,[8] which may explain why those with a worse outcome in this study were older than the comparatively asymptomatic group receiving no treatment.

This study is one of the first to use the SF36 to assess the longterm effect of oesophagitis on quality of life. It has shown that oesophagitis is significantly associated with impaired quality of life, even though most of our patients did not have complications. Our previous work using the SF36 to measure the short- term effect of treating acute oesophagitis, showed that the quality of life parameters of bodily pain and vitality both improved with treatment.[28] Surprisingly, in this study it was not bodily pain and vitality that were impaired, but general health and social function. This may be because this follow up group have a chronic condition, diagnosed over 10 years ago and still troubling them. It is not possible from this study to determine if this chronic condition has affected how patients perceive their own health or if they have adopted the 'sick role'. Further work is obviously necessary to consider these issues. It would be wrong to suggest that our patient group were generally 'less healthy' than the overall population when diagnosed 10 years ago. Our criteria specifically excluded patients with other significant health problems at the time of diagnosis, thus selecting an otherwise 'healthy' group for follow up.

If the longterm outcome of oesophagitis patients treated conservatively is poor (as our data suggests), it might be concluded that more patients should be referred at an earlier stage for antireflux surgery. Currently there is insufficient data to support this conclusion. The few studies comparing surgical and medical treatment of GORD and in particular oesophagitis, showed that surgery gave a better result on short-term follow up than antacids/lifestyle advice,[29] or H_2RAs.[30] These studies were performed before the development of proton pump inhibitors, however, which are now established as the most effective medical treatment for erosive oesophagitis.[16 19] There are very few longterm studies of the outcome of reflux patients after antireflux surgery. While some of these studies reported good longterm results with antireflux surgery,[31 32] others suggested that after 10 years or more, surgery may not give much better results than medical treatment.[33–35]

The short-term treatment of oesophagitis with potent acid suppression is now well established. There remains much uncertainty regarding the best mode of longterm maintenance treatment, something which, as this study suggests, most oesophagitis patients will require. Ever since the introduction of the proton pump inhibitor omeprazole, there has been concern about the safety of longterm proton pump inhibitor treatment. Recent data following up patients taking omeprazole for three to five years showed no serious side effects, though the significance of persistently increased serum gastrin concentrations, and increased incidence of micronodular hyperplasia and atrophic gastritis remains uncertain.[26] A prospective randomised study comparing antireflux surgery to maintenance treatment with either high dose H_2RAs or a proton pump inhibitor (including quality of life assessment) would perhaps be the best way of determining the optimal treatment for oesophagitis patients whose symptoms persist or relapse after initial medical treatment.

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