Epidemiology and Quality of Life Concerns in Gastroesophageal Reflux Disease

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1. The prevalence of heartburn and acid regurgitation in the community has not changed in three decades.
2. GERD is a relapsing, symptomatic problem for the majority of patients.
3. Widespread use of proton pump inhibitors is reducing the incidence of complications.
4. The disease-modifying nature of proton pump inhibitors does not seem to hold true for Barrett’s Esophagus.
5. Quality of life is reduced with GERD and this is a longstanding outcome.

INTRODUCTION

The recently published “burden of digestive diseases” report documented that gastroesophageal reflux disease (GERD) was the third most common gastrointestinal disorder, following only infectious diarrheas and gallstones. The economic burden of GERD was greater than for any other gastrointestinal disease, affecting 19 million individuals in the United States with an estimated cost of $9.3 billion dollars annually (in 1998 dollars) (1). Yet the epidemiology and natural history of this disease has been poorly understood for many years. Increasingly, it is being appreciated that GERD is a spectrum of diseases rather than a single entity. In particular, patients with erosive esophagitis have a different response to treatment and outcome compared with patients with typical symptoms, such as heartburn and acid regurgitation, but no abnormality on endoscopy (2).

This article will review the epidemiology of three types of GERD patient: (i) patients with symptoms alone, (ii) patients with symptoms and excessive acid reflux on esophageal pH monitoring and (iii) patients with erosive esophagitis. Two other important issues will be addressed. First, the impact proton pump inhibitors (PPIs) are having on the epidemiology of GERD and second, the influence of GERD on quality of life (QoL).

PREVALENCE DATA

The prevalence of reflux symptoms has been remarkably consistent over the last 30 years throughout North America and Europe, with approximately 20% of the

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population experiencing symptoms at least once per week (Table 1). The majority of these individuals never consult their family doctor, with up to 75% preferring to self-medicate (3). Symptoms are persistent, being present for more than five years in 60% of patients and more than 10 years in 40%. The proportion of the population experiencing reflux symptoms does not increase with age (4). If anything, the specific symptom of heartburn may decrease with age. By contrast, complications of GERD do increase with age (5) (Figure 1).

Compared with prevalence data, less is known about the incidence of GERD, i.e. how many new cases occur. Brunnen, et al reported an incidence of 4.5/100,000 for new presentation with esophageal strictures or ulcers over the period 1951–67 (6). From these data, they estimated that the incidence of simple esophagitis would be 86/100,000. A more recent study from Sweden demonstrated remarkably similar incidences: esophagitis 120/100,000, complications (esophageal ulcer/stricture) 5.6/100,000 (7). In both studies the incidence of complicated GERD increased with advancing age.

THE CURRENT EPIDEMIOLOGY OF GERD

As mentioned in the prevalence section, the vast majority of GERD sufferers self-medicate. Of those who do present to their family doctor, most are managed without referral to secondary or tertiary care and without the need for further investigation. This has been described as the part of the GERD iceberg that lies below the surface. Although it comprises the bulk of GERD patients, little research has been done in this area. By contrast, we have a much greater knowledge of the natural history of patients whose reflux symptoms have been severe enough to merit referral to hospital. In such cases there is evidence of progression from simple GERD to complicated GERD with strictures, hemorrhage and Barrett’s Esophagus occurring at an older age and after a longer duration of symptoms (8). Of possibly greater significance is the apparent relationship between the frequency and duration of reflux symptoms and the development of esophageal adenocarcinoma (Figure 2) (9). Evidence of a genetic component in GERD is increasing with familial clustering or genetic linkage being demonstrated for both simple GERD (10) and Barrett’s Esophagus (11). This emphasizes that environmental issues are not the sole determinants of disease manifestation.

GERD patients can be divided into three groups: those with erosive esophagitis, those without esophagitis but with increased esophageal acid exposure on pH monitoring and those with typical symptoms but normal endoscopy and pH monitoring. Studies of consecutive patients referred to hospital suggest a breakdown of 40%–50% esophagitis, 20%–30% positive pH monitoring and 30%–40% symptoms only (12,13).
Symptoms Alone

Of 32 symptom-only patients followed-up for 3–5 years, 10 (31%) progressed to either erosive esophagitis or increased esophageal acid exposure on pH monitoring (Figure 3) (14). Follow-up over 4–6 years demonstrated that the requirement for daily acid suppression among symptom-only patients and patients who have abnormal levels of acid reflux was the same (52% vs 56%) as was the persistence of symptoms (87% vs 79%) (15). One study, based in primary care, demonstrated a relapse rate of 75% after six months off therapy among 123 symptom-only patients (16). This compared with a relapse rate of 90% in 145 patients with esophagitis. Although relapse is higher among patients with erosive esophagitis, many symptom-only patients also demonstrate an ongoing need for acid suppression. This is especially true if their symptoms are not completely relieved on initial therapy (17).

Increased Esophageal Acid Exposure

Approximately one quarter of patients presenting to secondary care with reflux symptoms will have raised levels of esophageal acid exposure on pH monitoring despite a normal endoscopy. Sixteen (94%) of 17 such patients continued to have frequent symptoms or require daily acid suppression therapy or both after 3–5 years (Figure 4) (14). Four (24%) progressed to develop esophagitis. Yet esophageal pH results were unchanged over that period of time (% time pH <4, 9.5% (7.4%–17.1%) vs 8.7% (4.9%–12.6%)). Pace, et al showed similar progression to esophagitis in 5/33 (15%) patients over a six month period (18).

Esophagitis

Patients who have required a PPI to heal their erosive esophagitis will almost universally relapse within 12 months of stopping therapy (19). In a 10 year follow-up study, 71% continued to have frequent symptoms or require daily acid suppression (20).

COMPLICATIONS

Historically 10% of esophagitis patients progressed to strictureing (21). More recent studies suggest that strictures develop in only 1%–2% in patients with esophagitis (20). Stricture patients are older than control subjects with simple GERD and have a longer duration of... (continued on page 68)
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Figure 4. Percentage of patients with ongoing frequent symptoms (S) or taking daily medication (M) or both 4 years after initial presentation. Adapted from McDougall et al (14).

heartburn (8). When assessed manometrically, their lower esophageal sphincter (LES) pressure is lower and they have a higher likelihood of esophageal body dysmotility. Approximately half require no further dilatation after the initial restoration of normal swallowing. The other half require repeat dilatations at a median rate of one per year (22). Hemorrhage and anemia from complicated esophagitis were significant problems with older series quoting rates of 5%–7% (21). A recent study confirms that these remain significant problems in patients with severe esophagitis (23).

Barrett’s Esophagus has been reported as developing in 8%–11% of esophagitis patients over a 3–6 year follow-up (14,24,25). By contrast, a Finnish study noted a 40% progression from esophagitis to Barrett’s Esophagus over 17–22 years (26). Factors associated with its development include a longer duration of symptoms and the presence of complicated esophagitis (stricture, ulcer and hematemesis).

THE FUTURE EPIDEMIOLOGY OF GERD

The widespread use of PPIs has altered the severity of GERD and the frequency of its complications. Proton pump inhibitors have the ability to heal esophagitis and esophageal ulcers refractory to other forms of therapy (19). They prevent the recurrence of esophageal strictures (25,27). It is likely that fewer patients will progress to stricturing or ulceration and that the number of admissions to hospital with these complications will also decline (5). The one area in which PPIs do not appear to modify disease relates to progression of Barrett’s Esophagus. There is little or no regression of Barrett’s Esophagus on PPIs, albeit with some development of squamous islands (28). Ten percent of esophagitis patients developed Barrett’s Esophagus over a 6.5 year period despite being on PPIs (25). To summarize the future of GERD, it would appear that we will be able to eliminate the benign complications. However, we are not yet able to modify Barrett’s Esophagus and its premalignant potential.

QUALITY OF LIFE

Quality of life in GERD has largely been assessed in tertiary referral centres treating esophagitis. It demonstrates an impairment in QoL comparable to that reported by patients with chronic heart failure(29). The impact of GERD on QoL is persistent, being present at least ten years after initial diagnosis (20) (Figure 5). Interestingly, patients with symptom-only GERD have an equal reduction in QoL compared to patients who have erosive esophagitis (30,31). Proton pump inhibitors restore QoL levels to those of the normal population (30). Data are also emerging of economic and productivity issues in a work force in whom reflux symptoms have failed to be treated (32).

Much of the data referred to in this paper comes from studies conducted in the secondary and tertiary care setting. It portrays a disease process which appears progressive, which carries the potential of serious complications and markedly impairs QoL. However, there are minimal data on the long term outcome of refluxers.
in the primary care setting. Even less is known of the prognosis of those who self-medicate without ever consulting their family doctor. These individuals comprise the bulk of GERD sufferers. It is likely that the epidemiology of their GERD is much more benign.

References