The significance of heartburn

Heartburn is a common symptom which 10% of the general population experience on a weekly basis.\textsuperscript{1,2} Along with other symptoms of dyspepsia, it accounts for 1 in 20 GP consultations, with prescriptions for proton-pump inhibitors consuming more than 6% of the primary-care drugs budget.\textsuperscript{3,4} Recent studies into the long-term effects of reflux symptoms have shown that gastro-oesophageal reflux disease (GORD) causes both a profound and prolonged reduction in quality of life.\textsuperscript{5–7}

Despite this, there remains uncertainty whether heartburn should be treated as a nuisance or as an indicator of pathology. Some studies have shown a correlation between the severity of symptoms and the degree of acid reflux;\textsuperscript{8,9} others found no relationship between symptom severity and the grade of oesophagitis.\textsuperscript{10,11}

A recent publication has settled the debate, effectively demonstrating that heartburn is indeed a significant indicator of pathological damage. In a case-controlled study, researchers in Sweden found that reflux symptoms were a risk factor for oesophageal adenocarcinoma (OAC) and to a lesser extent adenocarcinoma of the gastric cardia.\textsuperscript{12} They interviewed 189 patients with OAC, and 262 with adenocarcinoma of the gastric cardia, and compared them with 820 control subjects. Patients with weekly reflux symptoms were nearly eight times as likely to develop OAC, compared to those without symptoms. This association became progressively stronger the more frequent and severe the symptoms and the greater their duration. For those with longstanding, severe symptoms, the odds ratio for OAC rose to as high as 43.5 (18.3–103.5).

The importance of this paper is accentuated by the increasing incidence of OAC. In the last 20 years, its incidence has risen 400–800% in Caucasian populations, rising faster than any other cancer.\textsuperscript{13,14}

What should be our response to the message of this paper? In the accompanying editorial, Cohen and Parkman recommend that patients with significant reflux symptoms ought to undergo endoscopy and biopsy with a view to having sufficient treatment to maintain healing of oesophagitis and in addition possibly undergo ablation therapy for Barrett’s mucosa.\textsuperscript{15} These suggestions do little to address the majority of refluxers who have symptoms alone (in the absence of Barrett’s oesophagus or oesophagitis). Ought they too to be aggressively managed with surveillance endoscopy and long-term proton-pump inhibitors?

Addressing the question of surveillance, Lagergren et al. calculated that endoscopic screening of males over 40 years of age with severe symptoms (representing a 20-fold increased risk of carcinoma) would detect only one OAC per 1400 patient-years. They suggest that this is impractical. The question of treating heartburn symptomatically is more complex. In their study, short courses of therapy were associated with a threefold increase in risk of OAC. However, the authors are careful to point out that the benefit of long-term acid suppression in these patients has not been assessed.

The issues of body weight and Helicobacter pylori were not addressed in this paper. In a publication by the same authors using the same patient database, a strong relationship was demonstrated between body mass index (BMI) and OAC.\textsuperscript{16} The odds ratio for those in the highest BMI quartile, compared to persons in the lowest quartile, was 7.6 (3.8–15.2). The authors suggest that the striking increase in OAC can be explained in part by increasing obesity in Western society. This finding has been supported by others.\textsuperscript{17} There is good justification for urging patients with heartburn not to put on weight.

The role of H. pylori in GORD is controversial. Various strands of evidence support the hypothesis that H. pylori is actually protective against GORD and its complications. Firstly, the declining rates of infection with H. pylori can be linked epidemiologically to the increasing incidence of GORD and OAC.\textsuperscript{18} Secondly, 25% of patients developed oesophagitis over a three-year period after H. pylori eradication.\textsuperscript{19} Thirdly, infection with H. pylori (especially the cagA+ strains) is associated with a significantly decreased risk of oesophagitis, Barrett’s oesophagus and OAC.\textsuperscript{20–22} Although there are dissenting voices,\textsuperscript{23} it would seem prudent at present to avoid eradication of H. pylori in the management of reflux symptoms.
In conclusion, the strong association between reflux symptoms and oesophageal adenocarcinoma emphasizes that heartburn is more than just a nuisance. In some cases, it is a precursor to malignancy. The possible protective effects of *H. pylori* and a low BMI need to be considered. The benefit of curing heartburn by long-term acid suppression is undetermined.

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References