Silent gastroesophageal disease: Clinical implications of an unknown disease

Khean-Lee Goh and Shiaw-Hooi Ho

Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia


Gastroesophageal reflux disease (GERD) is usually associated with the classical symptoms of heartburn and acid regurgitation, which have, in clinical practice, defined the disease. However it has long been known that extra-esophageal GERD and Barrett’s esophagus occur in patients without typical reflux symptoms. In recent years, several studies have uncovered a significant proportion of patients with reflux esophagitis but with no symptoms. In the well conducted, population-based, Kalixanda study from Sweden, for example, up to 36.8% of patients with erosive esophagitis had no symptoms. Other studies from the Asian Pacific region have shown a prevalence of asymptomatic reflux esophagitis ranging from 26.4% to 35.0% (Table 1). In this issue of the Journal of Gastroenterology and Hepatology, Cho and colleagues from Korea, in a survey of over 5000 patients undergoing health-screening gastroscopy, found that 145 of 320 (45.3%) patients with erosive esophagitis were asymptomatic. This is indeed a large proportion of patients who have “silent GERD”.

In another endoscopy-based study, Ho et al. found that 33.9% of 186 patients with erosive esophagitis had no typical symptoms of heartburn and acid regurgitation. Instead these patients had predominant complaints of “wind” and abdominal distension. Clearly, the problem could be one of interpretation of symptoms. It has long been known that many Asian patients do not exactly understand the meaning of heartburn and acid regurgitation and there is a large overlap between reflux and dyspeptic symptoms. Furthermore, non-cardiac chest pains, for example, have often been considered in the Asia–Pacific region to be a manifestation of GERD and many patients with non-cardiac chest pains have been shown to have underlying GERD.

This notwithstanding, silent GERD is now a well-recognized entity. Fass and Dickman have defined silent GERD as the presence of esophageal mucosal injury that is typical of GERD (erosions, peptic ulceration and Barrett’s esophagus) during upper gastrointestinal endoscopy in individuals who lack typical or atypical extra-esophageal manifestations of GERD. The ramifications of such a “disease” are huge. The list of reflux-related diseases caused by silent disease include: refractory asthma, persistent laryngopharyngitis, poor sleep, dental caries, Barrett’s esophagus and, particularly in children, unexplained asthma and recurrent pneumonia. Of practical concern is the screening for Barrett’s esophagus. Currently, only patients with symptomatic GERD are screened for Barrett’s esophagus. How do you screen for a disease without symptoms? The whole adult population would require evaluation and this is clearly a monumental if not impossible task. Although Barrett’s esophagus and Barrett’s associated adenocarcinoma are still uncommon in the Asia–Pacific region, this may change with the rapid emergence of GERD in the region.

What factors determine or predict silent reflux disease? In this study, Cho et al. identified older age and male sex as predictive factors. Nozu and Komiyama and Wang et al. also identified male sex as a predictive factor for silent esophagitis. In the Japanese study, smoking and lower body mass index (BMI) were also identified as predictive factors. In contrast Wang et al. found that a higher BMI predicted absence of symptoms. Men and older patients have been thought to have a higher pain threshold but clearly we need to understand the pathogenesis of symptoms in better. The classical explanation of evocation of heartburn is that it is caused by the contact of acid on the nerve endings in the lower esophagus. Patients with erosive reflux esophagitis would then intuitively experience more pain than those with non-erosive reflux disease (NERD). This, however, has not been the case and NERD patients may in fact experience more severe symptoms than those with erosive disease. It is clear therefore that apart from the degree of acid exposure, various other putative mechanisms are plausible. Esophageal mucosal sensitivity, prolonged or abnormal esophageal contraction and psychological factors have all been shown to play a role. The role of esophageal sensitivity in the pathogenesis of symptoms is intriguing. In a recent study from our group, we identified a group of patients with asymptomatic esophagitis who did not report “heartburn” with acid perfusion, which we labeled as having a “hyposensitive” esophagus.

What are the clinical implications of silent GERD? The highest prevalence of asymptomatic GERD is in patients with extra-esophageal manifestations of GERD. In patients with refractory asthma and chronic cough associated with GERD, it has been noted that 25–75% do not have classical symptoms of GERD. For these groups of patients, the presence of underlying GERD should be suspected and investigated. Proton-pump inhibitors could be empirically prescribed and this is a common clinical practice. Similarly, asymptomatic GERD is also common in children, with unexplained pneumonia and recurrent asthma. These children should also be investigated and treated for GERD where appropriate.

We do not understand yet the natural history of silent esophagitis. While the majority of cases are of milder grades, do we know whether they will evolve to more severe grades and Barrett’s esophagus without treatment? If so, this would be a cause for concern, given that 25% of Barrett’s esophagus and 40% of all esophageal adenocarcinomas occur in patients without, or with only minimal, prior reflux symptoms.

This group of patients with silent GERD and erosive esophagitis clearly needs further, in-depth study and long-term follow up.
Table 1  Summary on studies with silent or asymptomatic esophagitis

<table>
<thead>
<tr>
<th>Study</th>
<th>Location</th>
<th>Asymptomatic/total esophagitis (%)</th>
<th>Predictive factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ronkainen et al. 2004²</td>
<td>Sweden</td>
<td>57/155 (36.8%)</td>
<td>—</td>
</tr>
<tr>
<td>Ohara et al. 2005⁵</td>
<td>Japan</td>
<td>210/600 (35%)</td>
<td>Male sex, smoking and lower body mass index</td>
</tr>
<tr>
<td>Nozu and Komiyama 2008⁶</td>
<td>Japan</td>
<td>23/87 (26.4%)</td>
<td>Male sex, high body mass index</td>
</tr>
<tr>
<td>Wang et al. 2010⁷</td>
<td>Taiwan</td>
<td>70/203 (34.5%)</td>
<td>Male sex, older age</td>
</tr>
<tr>
<td>Present study, Cho et al. 2011⁷</td>
<td>Korea</td>
<td>145/320 (45.3%)</td>
<td>—</td>
</tr>
</tbody>
</table>

References
