Measuring Duodeno-Gastric and Duodeno-Gastro-Esophageal Reflux in Clinical Practice: The Role of Age

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The pathological role of acid reflux to the esophagus in gastro-esophageal reflux disease (GERD) is well established: typical symptoms of heartburn are mimicked by esophageal acid perfusion [1], esophageal pH monitoring is used to quantify GERD [2] and acid-suppressive drugs are the cornerstone of medical treatment [3]. There is now an increasing body of evidence that duodeno-gastro-esophageal reflux (DGER) is also involved in the pathophysiology of GERD.

The occurrence of erosive esophagitis in patients with achlorhydria and after total gastrectomy [4, 5] argues in favor of a role for reflux of duodenal content in the pathogenesis of erosive esophagitis. The use of prolonged fiberoptic monitoring of bilirubin concentration (Bilitec®) has allowed quantifying reflux of duodenal content to the stomach and the esophagus. Bilitec® studies have shown that DGER is more common in patients with severe esophagitis and Barrett's esophagus than in patients without or with minor esophagitis [6, 7]. It is clear that duodeno-gastric reflux (DGR) is a prerequisite for DGER to occur, and a recent study has shown that DGR is a physiological phenomenon in the postprandial period and occurs sporadically in the interdigestive state [8].

In order to study the role of acid reflux, DGR and DGER in disease, knowledge of the normal range of gastric and esophageal exposure is required. Studies on the influence age on esophageal pH monitoring showed conflicting results, although there is a clear tendency for in-

creased acid exposure with age [9, 10]. In the present issue of *Digestion*, Bollschweiler et al. [11] compared normal values for DGR and DGER exposure in younger and older asymptomatic volunteers. The authors found that older volunteers (>40 years old) had higher DGER exposure compared to younger volunteers, but they reported no differences in DGR exposure.

Comparison of studies investigating DGR in the literature is hampered by the use of different positions of the probe (antrum vs. fundus), the use of different cut-offs for bilirubin absorbance, and the use of different dietary interventions to avoid food impaction artifacts [6–8]. Bollschweiler et al. [11] studied DGR exposure 10 cm distal to the LES in subjects on a white diet, and comparing DGR values at different cut-offs, they found no age-related differences.

When assessing esophageal bilirubin exposure, the authors found significantly higher DGER values in older volunteers. In the absence of a difference in gastric exposure, these findings suggest that age-related changes in esophageal motility or in competence of the esophago-gastric junction underlie the higher DGER exposure in older subjects. Peristalsis is the only clearance mechanism for DGER [12], but decreases in peristaltic function with age in asymptomatic subjects are subtle and probably of minimal impact [13]. The incidence of hiatal hernia clearly increases with age, and this is potentially an important contributor to higher levels of duodenal content

exposure with age [14]. Unfortunately, the authors did not assess the presence of small hiatal hernias with endoscopy or radiography in their group of healthy controls.

There are very few, if any, clinical applications of intragastric bilirubin monitoring, but several studies suggest usefulness of esophageal Bilitec[®] monitoring in the evaluation of difficult or refractory GERD patients [6, 7, 15]. The paper by Bollschweiler et al. [11] demonstrates that upper limits of normal may be higher in subjects >40 years, which is likely to be the majority of the patients. It is unclear whether DGER exposure would be even higher

in those older than 60 or 70 years. Furthermore, there is a major variability of normal ranges of esophageal DGER exposure across the literature, and dietary habits or restrictions have a major impact on DGER exposure values [7, 11]. Clinicians should therefore be careful when considering to take major management decisions, like referral for surgery, on the basis of Bilitec[®] studies. Based on the multiple factors that influence esophageal DGER exposure, each center will probably have to establish its own normal values, not only for younger but also for older subjects.

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