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Johannes Lenglinger and Martin Riegler

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LETTERS

Novel genetic marker for dilated end stage oesophagus and oesophageal adenocarcinoma risk?

With interest we read the article by Asling et al,1 entitled “Collegen type III (COL3A1) is a gastro-oesophageal reflux disease (GORD) susceptibility gene and a male risk factor for hiatus hernia”, which has been published in a recent issue of Gut. The major findings of the study were that a single nucleotide polymorphism within the gene encoding for collagen type III (COL3A1) was associated with GORD in both sexes and hiatal hernia in males. In keeping with these findings, immunohistochemistry of oesophageal biopsies showed increased connective tissue abnormalities (ie, collagen type III-positive staining) in GORD patients compared with asymptomatic controls.1 GORD has been defined by symptoms, endoscopy and pH monitoring data.2,3 Furthermore, the study is based on the model anatomy that the stomach commences at the level of the rise of the endoscopically visible gastric type folds.4 In keeping with this assumption, hiatal hernia has been diagnosed if gastric type folds were present above the level of the diaphragmatic impression.1,2 In contrast to that, modern histopathology and anatomy based understanding shows that what has been taken for hiatal hernia may represent “dilated end stage oesophagus”.2 Briefly, loss of function and shortening of the lower oesophageal sphincter, possibly induced by repeated distension, result in gastric type folds covered by metaplastic columnar epithelium (ie, cardiac, oxyntocardiac mucosa or intestinal metaplasia equals Barrett’s oesophagus). At some point the dilated end stage oesophagus extends proximal to the level of the diaphragm inducing widening of the oesophageal hiatus. During endoscopy this dilated columnar lined distal oesophagus may be mistaken for hiatal hernia. Therefore differentiation between hiatal hernia and dilated end stage oesophagus requires histopathology of biopsies obtained at and above the level of the diaphragmatic impression.4 The data obtained by Asling et al1 strongly indicate that mutations within the COL3A1 gene favour the formation of dilated end stage oesophagus. COL3A1 associated dysfunction of the antireflux barrier may contribute to the development of columnar metaplasia, dysplasia and adenocarcinoma of the oesophagus. Thus, identification of COL3A1 gene mutations may act as a marker for increased risk of oesophageal adenocarcinoma5 and explain why gene mutation induced connective tissue alterations are linked to cancer development.6 The authors are kindly asked to comment on these considerations.

Johannes Lenglinger, Martin Riegler
Medical University Vienna, Vienna, Austria
Correspondence to: Johannes Lenglinger, Medical University Vienna, Waehringer Guertel 18–20, Vienna, 1090 Austria; johannes.lenglinger@meduniwien.ac.at

Contributors Both authors contributed equally to the letter.
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Authors’ response

We sincerely appreciate the interest in our recent paper in Gut entitled “Collagen type III (COL3A1) is a gastro-oesophageal reflux disease (GORD) susceptibility gene and a male risk factor for hiatus hernia”.1 The diagnosis of hiatal hernia requires endoscopy, a barium meal and/or manometric assessment.2 Histology is not required for confirmation. Barrett’s oesophagus, however, does need histopathological confirmation to safely separate it from oesophageal squamous epithelium.3 In fact, this has been carefully investigated in the original Kalixanda cohort where the prevalence of Barrett’s was determined to be 1.6% in the general population and 2.5% in patients with reflux symptoms.4 The cohort we have used to assess hiatal hernia association is the Kalixanda cohort with the addition of 100 GORD patients with the same demographics. The Kalixanda cohort contains 16 individuals affected with Barrett’s oesophagus. The 100 GORD patients added an additional two or three Barrett’s cases. In total, we expect 18–19 Barrett’s cases in the cohort we have used. Even if all of these have been missed, they amount to less than 10% of the 239 hiatal hernia cases. It is therefore clear that the association we report, where we show that one single nucleotide polymorphism in COL3A1 is associated with hiatus hernia, cannot be attributed to lack of differentiation between hiatal hernia and metaplastic columnar epithelium. Unfortunately, due to the low frequency of Barrett’s and hence adenocarcinoma, the present study does not allow the investigation of biomarkers for these conditions.

B Åsling, J Jirholt, P Hammond, M Knutsson, A Walentinsson, G Davidson, A Agreus, A Lehmann, M Lagerström-Fermer
1 AstraZeneca R&D, Mölndal, Sweden; 2 Women’s & Children’s Hospital, Gastronenterology Unit, North Adelaide, South Australia, Australia; 3 Center for Family and Community Medicine, Karolinska Institutet, Huddinge, Sweden
Correspondence to: Dr B Asling, AstraZeneca R&D, Pepparedsleden 1, S-431 83 Mölndal, Sweden; bengt.asling@astraZeneca.com

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Transluminal endoscopic necrosectomy: revisited from the surgeon’s perspective

In a retrospective analysis of 93 patients, Seifert et al7 investigated the role of transluminal endoscopic necrosectomy after acute pancreatitis. From the authors’ point of view, the mortality rate of only 7.5% and a good long-term outcome appear to make this relatively new approach look favourable when compared with the results of published studies on surgical debridement in necrotising pancreatitis. However, a detailed look at the characteristics of the patients in the GEPARD study shows that this is like comparing apples and oranges. Surgical series on acute pancreatitis predominantly investigate the subset of patients with infected necrosis and severe organ dysfunction. Data on the severity of the disease are regularly presented, usually as severity scores (eg, Ranson, APACHE II, SOFA), the incidence of single or multiple organ failure or the extent of pancreatic necrosis.3,8 However, severity data are missing in the GEPARD study. Importantly, the patients in the GEPARD study appear to be much healthier. Their predominant symptoms were abdominal pain and gastric obstruction/vomiting. The majority of patients with so-called sepsis.