

The New Era and Challenges after Endoscopic Submucosal Dissection of Superficial Gastric Cancers

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Novos tempos, novos desafios após a disseção endoscópica pela submucosa de lesões gástricas superficiais

Palavras Chave

Neoplasias gástricas · Neoplasias primárias múltiplas · Segundas neoplasias primárias · Disseção endoscópica pela submucosa

Gastric adenocarcinoma remains a public health problem representing the fifth most common malignancy worldwide, with the highest incidence rates in Eastern Asia [1]. In Portugal, a country with a moderate/high incidence of gastric cancer [2], incidence rates are almost twice as high compared with the Europe region, approaching Eastern Asia numbers [1], along with the high

prevalence of *Helicobacter pylori* infection rates [2]. Although gastric cancer mortality has been decreasing, it still represents the third leading cause of cancer death worldwide and in our country [1], mainly a consequence of the advanced stages at diagnosis [2].

However, with the increasing availability of diagnostic endoscopic exams and associated technologies, early diagnosis of gastric cancer is easier than ever, turning minimally invasive endoscopic techniques, such as endoscopic submucosal dissection (ESD), not only possible, but also the recommended treatment for gastric superficial neoplasms in selected patients [3], with high rates of curative resection and a good safety profile [4]. It should be noted, though, that after this stomach-preserving endoscopic treatment (as opposed to surgical treatment that removes the organ), new challenges arrive, since patients remain at risk for developing synchronous or metachronous gastric neoplastic lesions (SGLs or MGLs), demanding endoscopic surveillance thereafter. How to identify the risk factors and the magnitude of the risk for the development of multiple gastric lesions are still unanswered questions in the management of these patients.

According to the current European guidelines on endoscopic submucosal dissection [3], a high-quality endoscopy with contrast or digital chromoendoscopy, by an experienced endoscopist, is recommended before ESD to establish the feasibility of resection; after curative endoscopic resection, follow-up endoscopy should start within 3–6 months and then annually. Surprisingly, these recommendations are based mostly upon Eastern population studies. Whether they are representative of the Western reality is arguable, since there are significant differences in the epidemiology and biological characteristics of gastric cancers between the East and the West, as well as different management approaches with regard to screening and treatment strategies [5].

In this issue of *GE – Portuguese Journal of Gastroenterology*, Brito-Gonçalves et al. [6] assess clinicopathological characteristics of patients with early gastric neoplasms submitted to endoscopic submucosal resection in a tertiary oncologic center, in Portugal. Most importantly, risk factors for multiple gastric lesions, including SGLs, MGLs or both, were all evaluated for the first time in a Western cohort.

In this retrospective, single-center cohort, 230 patients were included during a 6-year period from January 2012 until December of 2017, with a median follow-up time of 33 months. The study has several strengths such as the high number of patients, the long-term follow-up, the use of OLGA and OLGIM pathologic staging systems as well as the recently described endoscopic grading of gastric intestinal metaplasia (EGGIM) staging.

Regarding the baseline characteristics of the patients, two major discrepancies were found compared to Eastern data. First, *H. pylori* infection was found only in 27.2% of the patients at the time of gastric neoplasia diagnosis, a lower frequency than previously reported [2]. Some pitfalls may explain these results since (1) previous *H. pylori* eradication was not assessed; (2) *H. pylori* status was evaluated by Giemsa stain at histopathologic specimens; and (3) most patients presented extensive atrophy which limits this evaluation [7, 8]. Second, this study population had no gender preponderance, unlike Eastern countries, where male gender prevails. Also interesting, a significant proportion of the patients had only mild gastric atrophy or focal intestinal metaplasia (32.6% OLGA I/II, 44.1% OLGIM I/II, and 29.6% EGGIM 1–4). These results suggest that early gastric lesions in the Western population may appear equally in both sexes and in all stages of gastritis, supporting the recent European guideline on the management of epithelial precancerous conditions and lesions in the stomach [9] that recommends surveillance of some patients with only focal metaplasia, given they

present an additional risk factor for gastric cancer (e.g., family history of gastric cancer, incomplete IM or persistent *H. pylori* gastritis).

SGLs were detected in 14.3% of the patients, not only previously to the ESD procedure (63.6%) but also at the first follow-up endoscopy (33.3%). Although the authors do not mention the type of gastroscopes used in this evaluation, these results highlight, firstly, the importance of a high-quality endoscopy at both the diagnostic and therapeutic endoscopies for superficial lesions and, secondly, the rationale for an early first endoscopic follow-up (at 3–6 months) [3]. Also, the authors suggest that this evaluation should be even more careful in patients over 60 years, current/former smokers or with advanced stages of gastritis (OLGIM III/IV), since all these were identified as independent risk factors for SGLs.

During the follow-up period, 8.6% of patients developed MGLs (3 of them adenocarcinomas) with a mean annual incidence of 3.1 per 100 patient-year. Despite a relatively short follow-up, this finding supports the European recommendations of long-term annual endoscopic follow-up [3].

Also EGGIM, which takes advantage of high-resolution endoscopy with narrow-band imaging to evaluate the extent of intestinal metaplasia across the stomach, was shown for the first time to correlate with the risk of having multiple neoplastic lesions, with a more significant association than histologic staging. In the future, this validated method [10] will probably fit in all endoscopic reports since, as it attempts to quantify metaplasia in all gastric mucosa and not only in small biopsy fragments, it may be a more reliable indicator of gastritis stage in experts' hands. We should note, though, that in this study EGGIM score started to be assessed only from 2014 onwards [11], thus, the first patients in this cohort had the EGGIM calculated only at follow-up endoscopies, which may have limited the conclusions regarding this finding.

In conclusion, despite a few differences in the baseline population (i.e., gender, *H. pylori* infection), this study reports similar results to those in Eastern countries regarding primary gastric lesion characteristics, as well as similar SGL and MGL identification rates, characteristics and associated risk factors. These data approach the East and the West and reinforce the current European recommendations on the diagnosis and follow-up of superficial gastric lesions.

Disclosure Statement

The authors have no conflicts of interest to declare.

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