Bright future for endoscopy: the new frontier of gastric cancer secondary prevention

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'Can we replace histology assessment (of gastritis) also in the West?' is the question that Marcos *et al* ask readers of their interesting study conducted at the Portuguese Oncology Institute in Porto.[1] The study further examines the clinical value of the group's promising approach to the endoscopic grading of gastric intestinal metaplasia (EGGIM) to facilitate the direct stratification of gastritis patients by their individual gastric cancer (GC) risk. The aim is to establish an endoscopy-based rationale for further endoscopic surveillance of patients at higher risk of GC. The authors conclude that endoscopy can reliably stratify GC risk. This would simplify everyday practice in terms of the GC risk assessment and management of patients with preneoplastic conditions, that is, glandular atrophy and intestinal metaplasia (IM).

Any patient-centred cancer prevention should include a set of variables that can be classified according to their invasiveness, reliability and cost. In the setting of GC prevention, there are some firmly established clinicopathological variables: (1) country-specific epidemiology and the socioeconomic setting; (2) feasibility of testing and treating *Helicobacter pylori*, the leading causative agent; (3) the use of reliable biomarkers (including the so-called 'gastric serology' or assessment of serum pepsinogens, and more sophisticated molecular markers); (4) endoscopy (as the main source of information), enhanced by high-resolution imaging and (5) histology (as its clinical consistency is supported by findings of prospective follow-up studies).

The senior author of the study by Marcos *et al* is also the first author of the recent update of the European guidelines on the 'Management of epithelial precancerous conditions and lesions in the stomach (MAPS II)'.[2] The MAPS II recommendations for assessing gastric mucosa status include both high-definition chromoendoscopy and antral-oxyntic biopsy sampling. Based on the topography of atrophy/IM, different further follow-up options are suggested, in line with the presumable cancer risk. The clinical usefulness of histological staging of lesions (as high risk vs low risk) is also considered.[3 4]

The recent guidelines of the British Society of Gastroenterology coincide with the MAPS approach (as do the recent German guidelines on GC management).[5] The British recommendations include grading of mucosal atrophy by means of both image-enhanced endoscopy and histology (the updated Sydney protocol), assessing *H. pylori* infection status, and restricting the use of atrophy biomarkers to appropriate epidemiological/clinical settings.

Focusing on endoscopy, the data presented by Marcos *et al* in this latest as well as in previous studies suggest that gastroenterologists will be able to rely on endoscopic assessments of IM to predict individual GC risk.[1 6] EGGIM is reportedly reproducible when high-resolution narrow band imaging endoscopy is applied. This would be a huge step forward in the management of preneoplastic gastric conditions at risk of progression to GC. Providing feedback to patients directly after an endoscopic procedure, without further delay, would help to improve patient satisfaction, and probably reduce the need for additional outpatient visits or consultations. There would also be a direct saving of the costs otherwise incurred for biopsy sampling and processing, as well as histopathological assessment. This would free up resources desperately needed for more sophisticated assessment of complex cases.

That said, the opportunities offered by the chance to perform direct endoscopic risk assessments would pose new challenges for the endoscopist. In addition to extending the time needed for a thorough endoscopic assessment of the gastric mucosa, investigators would need to take more care in deciding which patients should still undergo biopsy. As a system, EGGIM only addresses IM as a mucosal change, but mucosal atrophy—the elective background of non-syndromic GC—includes two variants of metaplastic transformation: IM and pseudo-pyloric metaplasia (PPM), the latter more recently defined as spasmolytic polypeptide-expressing metaplasia. While experienced endoscopists are capable of grading the extent and topography of mucosal intestinalisation, the endoscopic interobserver reproducibility of PPM assessment is less well established. The potential downgrading of a substantial metaplastic determinant of GC risk is an issue that will emerge in the next few years due to the increasing incidence of autoimmune corpus atrophy.[7 8]

There are other scenarios in which biopsy sampling should still be done in the near future. According to the Japanese Society for *Helicobacter* Research, it is 'desirable to collect biopsy tissue for histology at the same time' when performing invasive tests for *H. pylori* infection (histology, rapid urease test).[9]

The 2016 Maastricht V/Florence Consensus Report,[10] and the 2015 Kyoto global consensus conference[11] both judged that image-enhanced endoscopy is a reliable tool for assessing the atrophic/metaplastic transformation of the gastric mucosa. Both suggested tailoring endoscopic surveillance schedules based on histological staging (Operative Link on Gastritis Assessment (OLGA)/Operative Link on Intestinal Metaplasia Assessment (OLGIM), however.[12 13] This might change in the future with the availability of reliable and validated endoscopic 'tools', as presented in this study by Marcos *et al*.[1]

It is important for centres to take the same approach to this issue, and it will be crucial to validate the EGGIM system in an international multicentre cohort before promoting its widespread acceptance. Applying this method demands not only state-of-the-art endoscopic equipment, but also the availability of well-trained investigators.[14] Upper gastrointestinal endoscopy will need to be put under much greater scrutiny as regards the generally-accepted quality indicators.[15] Adopting such new strategies will naturally be easier at tertiary referral centres in industrialised countries.

While awaiting these further developments, we should still focus on 'how to combine' rather than 'how to replace' the methods used in clinical practice, and we would like to emphasise the complementary value of gross (endoscopy) and microscopic (histology) approaches

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to phenotypic profiling. Endoscopy's primary place in the assessment of GC risk is undeniable and (as in the Porto experience), it will be further improved by the increasing availability of high-definition virtual chromoendoscopy.

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