Early detection and risk stratification of gastric cancer are likely to be refined with biopsies targeted through high-resolution-enhanced imaging

We thank Dr Ghisa[1] and colleagues for their kind interest in our recently published BSG guidelines on the diagnosis and management of patients at risk of gastric adenocarcinoma.[2]

The introduction of advanced endoscopic imaging technologies has led to a re-appreciation of the fact that the progression of mucosal atrophy in the chronically inflamed stomach over time occurs in a patch-wise fashion.[3 4] In particular, gastric intestinal metaplasia arises as well delineated islands within the gastric mucosa.[5] These islands can be visualised using high-definition endoscopy and there is now good evidence that endoscopy-lead risk stratification correlates well with histology and operative link on gastric intestinal metaplasia (OLGIM) stages.[6–8] These studies have provided important impetus for us to advance endoscopy-lead risk stratification in our recently published guidelines.[2]

Ghisa writes that we have not sufficiently acknowledged the available evidence with regard to the clinical efficacy of random biopsy staging of chronic gastritis. Recent work by these authors has evaluated outcome in over 7000 unselected patients undergoing upper endoscopy and random biopsy operative link on gastric atrophy (OLGA) staging. Over 90% of these patients showed OLGA stages that would not have necessitated follow-up (OLGA 0 and OLGA I). At the end of follow-up (median 6.6 years), 28 incident neoplasias had been detected and these were strongly enriched in patients at higher OLGA stages (III and IV), although a minority (11%) of neoplasias were also recorded in patients with lower OLGA stages. The issue in evaluating the real-world impact of these data is that they suffer from ascertainment bias because patients with higher OLGA stages were offered endoscopic follow-up, whereas patients with lower OLGA stages were not. The predictive potential of OLGA staging may be overestimated due to this bias.[6] In addition, over half of all patients re-evaluated at second endoscopy moved between OLGA categories.[7] This could be due to either disease regression, between-pathologist variation, or, more likely, random sampling variation.[8]

The mosaic mucosal changes in chronic gastritis thus confound the interpretation of random biopsies. The OLGA staging protocol was developed on the back of the Sydney staging protocol and borrows from the hepatitis grading model.[9] However, chronic hepatitis affects the organ diffusively and homogeneously, in stark contrast to the focal nature of disease progression in chronic gastritis. Chronic inflammation likely accelerates the premalignant clonal selection and expansion of precursor lineages in the Helicobacter-infected stomach. Random biopsy sampling will capture some of this heterogeneity in patients with extensive mucosal changes.

The question, however, is whether random biopsies will bring us closer to patient-tailored risk assessment going forward? We feel that with the emergence of advanced endoscopic-enhanced imaging modalities, we have arrived at a fork in the road with regard the use of risk stratification strategies based on random biopsies in chronic gastritis. Designing an efficacious, cost-effective and patient-tailored gastric cancer screening strategy for use in low incidence countries will likely depend on a rational tiered implementation of non-invasive markers, invasive diagnostics and molecular studies.[10] There is now an urgent unmet need for markers that intelligently sample the evolutionary process driving progression to cancer in the chronically inflamed stomach. Recent studies have revealed that as many as 7% of gastric cancers in the UK are missed on routine endoscopy, clearly highlighting that much remains to be won with regard to upper gastrointestinal endoscopy quality control standards.[11] We anticipate that targeted biopsies, in combination with molecular studies, will increase interest in quality control, in turn refining early detection efforts for gastric cancer. Effectively, we may move to a situation wherein biopsies are only required in high-risk patients for confirmation of endoscopy staging.

Marnix Jansen [1], **Matthew Banks** [2]

[1]Department of Pathology, UCL Cancer Institute, London, UK
[2]Division of Gastroenterology, University College London Hospitals NHS Foundation Trust, London, UK

Correspondence to Dr Matthew Banks, University College London Hospitals NHS Foundation Trust, London NW12PG, UK; matthew.banks2@nhs.net

Twitter Marnix Jansen @jansen_marnix

Contributors MB and MJ contributed equally to the letter.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; internally peer reviewed.

To cite Jansen M, Banks M. *Gut* 2020;**69**:1710–1711.

Received 21 September 2019
Accepted 23 September 2019
Published Online First 14 October 2019

► http://dx.doi.org/10.1136/gutjnl-2019-319649

Gut 2020;**69**:1710–1711. doi:10.1136/gutjnl-2019-319921

ORCID iDs
Marnix Jansen http://orcid.org/0000-0003-0645-564X
Matthew Banks http://orcid.org/0000-0002-9137-2779

REFERENCES

1. Ghisa M, Rugge M, Fassan M, *et al*. There is much more to rely on histology than the sole endoscopy tells us. *Gut* 2020;69:1710–1.
2. Banks M, Graham D, Jansen M, *et al*. British Society of gastroenterology guidelines on the diagnosis and management of patients at risk of gastric adenocarcinoma. *Gut* 2019;68:1545–75.
3. Morson BC. Intestinal metaplasia of the gastric mucosa. *Br J Cancer* 1955;9:365–76.
4. Pimentel-Nunes P, Libânio D, Marcos-Pinto R, *et al*. Management of epithelial precancerous conditions and lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter and Microbiota Study Group (EHMSG), European Society of Pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019. *Endoscopy* 2019;51:365–88.
5. Muto M, Yao K, Kaise M, *et al*. Magnifying endoscopy simple diagnostic algorithm for early gastric cancer (MESDA-G). *Digestive Endoscopy* 2016;28:379–93.
6. Zakko L, Visrodia K, Wang KK, *et al*. Editorial: the effect of bias on estimation of improved survival after diagnosis of Barrett's esophagus. *Am J Gastroenterol* 2017;112:1265–6.
7. Rugge M, Meggio A, Pravadelli C, *et al*. Gastritis staging in the endoscopic follow-up for the secondary prevention of gastric cancer: a 5-year prospective study of 1755 patients. *Gut* 2019;68:11–17.
8. Kuipers EJ, Peña AS, Festen HPM, *et al*. Long-term sequelae of Helicobacter pylori gastritis. *The Lancet* 1995;345:1525–8.
9. Rugge M, Genta RM. Staging and grading of chronic gastritis. *Hum Pathol* 2005;36:228–33.
10. Yeh JM, Hur C, Ward Z, *et al*. Gastric adenocarcinoma screening and prevention in the era of new biomarker and endoscopic technologies: a cost-effectiveness analysis. *Gut* 2016;65:563–74.
11. Cheung D, Menon S, Hoare J, *et al*. Factors associated with upper gastrointestinal cancer occurrence after endoscopy that did not diagnose cancer. *Dig Dis Sci* 2016;61:2674–84.