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Effect of *Helicobacter pylori* and *Porphyromonas gingivalis* on the Correa cascade progression

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We thank Kountouras and colleagues for their interest in our review [1] and for highlighting additional mechanisms that may influence gastric carcinogenesis [2].

We agree that intestinal metaplasia (IM) is a heterogeneous lesion and that only a minority of patients progress to gastric cancer (GC). Risk assessment should therefore consider not only the presence of IM, but also its extent, histological subtype, severity of atrophy, topographic distribution, family history, and the underlying etiology of gastritis.

As the authors note, incomplete IM is more strongly associated with GC than complete IM. Similarly, extensive atrophy, identifies patients at increased risk. Our review focused on the distinct biological pathways of *Helicobacter pylori* (*H. pylori*)-associated and autoimmune atrophic gastritis. The former follows the classical Correa cascade leading predominantly to intestinal-type adenocarcinoma, whereas the latter is characterized by corpus-restricted oxyntic atrophy, hypochlorhydria, hypergastrinemia, and an increased risk of type I gastric neuroendocrine neoplasms.

We also agree that alterations in epithelial proliferation, apoptosis, p53 signaling, and bacterial virulence factors, including *CagA* and *VacA*, contribute to carcinogenesis. However, these biomarkers have not been sufficiently validated for routine clinical risk stratification. At present, histological staging using the Operative Link on Gastritis Assessment (OLGA) and the Operative Link on Gastric Intestinal Metaplasia Assessment (OLGIM) systems, together with assessment of the extent and subtype of IM, remains the most reliable approach.

The possible contribution of *Porphyromonas gingivalis* and other non-*H. pylori* microorganisms is an important area of investigation. However, current evidence is mainly experimental or observational, and these findings should be regarded as hypothesis-generating rather than ready for clinical implementation.

Finally, *H. pylori* eradication remains the cornerstone of GC prevention. Although eradication reduces cancer risk, patients with advanced atrophy, extensive or incomplete IM, or dysplasia remain at increased risk and should undergo surveillance according to current guideline recommendations.

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References

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