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Mixed-etiology atrophic gastritis: from overlap label to practical risk assessment

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We thank Dr. Perets for his thoughtful comments on our review [1] and for highlighting the clinical importance of mixed-etiology atrophic gastritis [2]. We agree that this phenotype is more than a simple overlap of diagnoses, as it likely reflects the coexistence of *Helicobacter pylori* (*H. pylori*)-related mucosal injury and autoimmune oxyntic gastritis, with variable contributions from chronic inflammation, immune-mediated gland loss, endocrine alterations, and changes in the gastric microbiome.

A standardized definition would facilitate both clinical practice and research. Evaluation should include documentation of current or previous *H. pylori* infection, the topographic distribution of atrophy, autoimmune serology, serum gastrin, pepsinogen I and pepsinogen I/II ratio, enterochromaffin-like cell hyperplasia, vitamin B12 deficiency or pernicious anemia, and histological staging using the Operative Link on Gastritis Assessment (OLGA) and the Operative Link on Gastric Intestinal Metaplasia Assessment (OLGIM) systems after high-quality endoscopy with systematic biopsies according to the updated Sydney protocol.

However, we deliberately avoided proposing formal diagnostic criteria or surveillance intervals because current evidence remains insufficient. Prospective studies are limited, definitions vary across published cohorts, and no validated model has established whether mixed-etiology gastritis carries additive or synergistic malignant risk compared with isolated *H. pylori*-associated or autoimmune atrophic gastritis.

At present, surveillance should be guided by the highest validated risk factor, including extensive or incomplete intestinal metaplasia, advanced OLGA or OLGIM stage, dysplasia, family history of gastric cancer, severe corpus atrophy, marked hypergastrinemia, enterochromaffin-like cell hyperplasia, or previous type I gastric neuroendocrine neoplasia. This approach is consistent with current international recommendations while avoiding both under- and over-surveillance.

Future prospective studies integrating molecular biomarkers, microbiome profiling, and artificial intelligence-assisted endoscopy may allow more precise risk stratification. Until then, careful endoscopic assessment, systematic biopsy sampling, accurate histopathological staging, and correct etiological classification remain the cornerstone of management.

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References

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