Has the issue of the "point of no return" in gastric carcinogenesis already been resolved?

To the Editor:

We have read the article focusing on the timing of *Helicobacter pylori* eradication on the risk of development of metachronous gastric cancer (MGC) after treatment of early gastric cancer (EGC) by Kim et al.[1] The authors showed that the timing of *H pylori* eradication within 1 year after treatment was better to reduce the risk of development of MGC than the late timing based on a large-scale national insurance database. They described that this finding was supported by a randomized controlled study by Choi et al[2] showing that *H pylori* eradication after endoscopic resection (ER) of EGC improved atrophy and intestinal metaplasia during the 3-year follow-up. Consequently, they concluded that the "point of no return" may no longer be an issue.

Recently, Kato et al[3] extended the follow-up period of a previous study and showed that *H pylori* eradication after ER of EGC had a preventive effect on the development of MGC in patients with mild to moderate atrophic gastritis, but this was not observed in severe atrophy.[4] They compared patients with *H pylori* eradication within 1 year after ER to those without or with failed eradication. This finding can mean that atrophic severity can have interaction effects, a predictive factor of MGC, but not confounding factors as a prognostic value. Therefore, it is suggested that the "point of no return" may not be resolved in patients with severe gastric atrophy. A recent meta-analysis revealed that a preventive effect was more significant in patients with extended follow-up (≥5 years) (OR, 0.32; 95% CI, 0.24-0.43) than in those with short follow-up (<5 years) (OR, 0.55; 95% CI, 0.41-0.72).[5] Therefore, we may need more additional observation times in patients with severe gastric atrophy to conclude whether the issue of the "point of no return" is resolved.

DISCLOSURE

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Response:

We wish to thank Dr Nishida and his colleagues[1] for their interest in our article.[2] In the past, the benefit of *Helicobacter pylori* eradication was less evident if intestinal metaplasia occurred.[3] This "point of no return" concept raised questions about the preventative effect of *H pylori* eradication therapy against metachronous gastric cancer in patients who underwent endoscopic resection for gastric cancer because they usually present with advanced precancerous lesions, including metaplasia, on histologic evaluation.[4,5] However, the point-of-no-return concept has been challenged by recent studies showing the beneficial effect of *H pylori* eradication for the prevention of metachronous gastric cancer.[5-7] The severity of atrophic gastritis and intestinal metaplasia improved and the risk of metachronous gastric cancer decreased after *H pylori* eradication in patients with early gastric cancer.[5]

Nevertheless, we agree with the opinions of Nishida et al[1] that we need more observations of patients with severe atrophic gastritis. As they mentioned, Kato et al[8,9] successfully identified the preventative effect of *H pylori* eradication against metachronous gastric cancer in patients with mild-to-moderate atrophic gastritis by extending the observation period in their cohort. Although early atrophic gastritis and intestinal metaplasia are precancerous lesions that may be controllable by *H pylori* eradication, advanced grades of atrophic gastritis and intestinal metaplasia may be a concern. Our study also demonstrated that *H pylori* eradication does not completely eliminate the risk of metachronous lesions.[2] The risk of metachronous lesions increases when *H pylori* is eradicated late. These findings imply that the preventative effect of *H pylori* eradication may decrease if atrophic gastritis and intestinal