

The Pros and Cons of *Helicobacter pylori* Treatment: A Focus on Cardiovascular Mortality

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See "Effect of *Helicobacter pylori* Treatment on Long-term Mortality in Patients with Hypertension" by Young-II Kim, et al. on page 47, Vol. 14, No. 1, 2020

The eradication of *Helicobacter pylori* has reduced the incidence of gastric cancer and mortality in asymptomatic individuals.¹ *H. pylori* eradication also significantly reduced metachronous gastric cancer risk in patients with early gastric cancer treated with endoscopic resection.² Clarithromycin is the most commonly used *H. pylori* treatment regimen and has been reported to increase the risk of short-term cardiovascular mortality.³⁻⁵ In addition, the association between the use of clarithromycin and an increased risk of non-gastric cancer has been reported.^{2,6}

However, cardiovascular disease and cancer are multifactorial diseases caused by multiple etiological factors. Therefore, the relationship between the use of clarithromycin and cardiovascular mortality or cancer development requires robust evidence to support. Recent several studies also showed inconsistent results regarding the association between clarithromycin use and overall mortality.^{3-5,7,8}

In this issue of *Gut and Liver*, Kim *et al.*⁷ retrospectively analyzed 198,847 patients who treated for hypertension, based on data retrieved from the Korean National Health Insurance Service-National Sample Cohort database between 2002 and 2010. Patients in the *H. pylori* treatment cohort (5,541 patients) were matched with those in the nontreatment cohort (11,082 patients) at a ratio of 1:2. In the *H. pylori* treatment cohort, 5,342 patients (96.4%) were prescribed with a triple therapy containing clarithromycin. During a median follow-up of 4.8 years, the overall mortality rate was significantly lower in the *H. pylori* treatment cohort compared with the nontreatment cohort (4.1% vs 5.5%). In terms of cause-specific mortality, when compared with the

nontreatment cohort, the mortality risk due to cerebrovascular disease was significantly decreased in the *H. pylori* treatment cohort (adjusted hazard ratio, 0.46; 95% confidence interval, 0.26 to 0.81; $p=0.007$). On the other hand, the mortality risk due to cardiovascular disease and cancer was not significantly different between the treatment and the nontreatment cohorts. Despite the absence of any difference in mortality rate, the risk for cardiovascular disease and overall cancer incidence were significantly higher in the *H. pylori* treatment cohort than in the nontreatment cohort. The authors speculated that the increased overall cancer incidence in the *H. pylori* treatment cohort might be related to differences in health behavior between the cohorts.

Until now, several cohort studies showed inconsistent results of association between clarithromycin-containing triple therapy and overall mortality.^{3-5,7,8} Recent cohort studies from the United Kingdom and Hong Kong found higher short-term cardiovascular risks with *H. pylori* treatment containing clarithromycin.^{3,4} However, a Danish cohort study of ischemic heart disease patients found similar overall and cardiovascular mortality after *H. pylori* treatment with or without clarithromycin.⁵ These studies included patients who had cardiovascular diseases at baseline. Meanwhile, this study excluded patients with cardiovascular disease other than hypertension at baseline.⁷ There was no association between clarithromycin-containing triple therapy and overall mortality in this study. This finding indicates that *H. pylori* treatment was not related to overall mortality, consistent with previous studies.^{1,2} To date, there is little evidence that *H. pylori* treatment increases the risk of mortality in patients without cardiovascular diseases.

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Interestingly, although the mortality risk due to cardiovascular disease was not different between the *H. pylori* treatment and nontreatment cohorts, the *H. pylori* treatment cohort had significantly increased risks of cardiovascular disease incidence in this study. Although recent data pertaining to acute cardiovascular risks of clarithromycin have been mixed, clarithromycin should be used prudently in patients with cardiovascular diseases other than hypertension. Furthermore, since clarithromycin resistance has been increasing, bismuth quadruple therapy or tailored therapy may be a better treatment option in several respects, especially for patients diagnosed with cardiovascular diseases.

This study, which was performed in a large cohort of patients with hypertension, has important clinical implication because authors found that *H. pylori* treatment in patients with hypertension was not associated with an increased risk of overall mortality including cardiovascular mortality. *H. pylori* eradication reduced gastric cancer incidence and mortality in asymptomatic individuals and reduced metachronous gastric cancer risk in patients with early gastric cancer who were treated with endoscopic resection or surgery. However, serious adverse events, which may be associated with *H. pylori* treatment, should not be overlooked. Although still disputed, *H. pylori* treatment containing clarithromycin requires caution in patients with cardiovascular diseases other than hypertension.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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