

Review: Pooled heterogeneous studies show an association between *Helicobacter pylori* infection and gastric cancer

Eslick GD, Lim LL, Byles JE, Xia HH, Talley NJ. Association of *Helicobacter pylori* infection with gastric carcinoma: a meta-analysis. *Am J Gastroenterol*. 1999 Sep;94:2373-9.

QUESTION

Is there an association between *Helicobacter pylori* infection and gastric cancer?

DATA SOURCES

Studies were identified by searching MEDLINE, CINAHL, CANCER CD, Biological Abstracts, and Current Contents (1983 to March 1999); scanning reference lists of selected articles; and contacting international experts in epidemiology and gastroenterology.

STUDY SELECTION

Studies in any language were selected if *H. pylori* infection was the exposure variable, gastric cancer was the disease of interest, and the publication date was after 1982.

DATA EXTRACTION

Reviewers were given only the methods section of selected articles, and they

assessed the quality of study methods by using a coding manual developed for this purpose (maximum score 13). Data were extracted on study design, country, diagnostic methods, year of publication, sex, age, stage of cancer, number of cases and control patients, and *H. pylori* status.

MAIN RESULTS

42 studies (8 cohort and 34 case-control studies) met the selection criteria. 7 of 22 studies showing a positive association had high-quality scores (scores 10 to 13) compared with 1 of the 20 negative studies. The pooled results showed an association between the presence of *H. pylori* infection and an increased risk for gastric cancer (combined odds ratio [OR] 2.04, 95% CI 1.69 to 2.45). Heterogeneity existed among the studies ($P < 0.001$). In multivariate analyses, age and intestinal-type cancers were independent effect modi-

fiers. Younger participants had a lower risk for gastric cancer than did older participants (combined OR 0.77, CI 0.68 to 0.89). The association between *H. pylori* infection and gastric cancer was stronger for intestinal cancer than for diffuse cancer (OR 1.14, CI 1.05 to 1.25).

CONCLUSION

Meta-analysis of heterogeneous studies shows an association between *Helicobacter pylori* infection and gastric cancer.

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COMMENTARY

Decreased incidence of gastric cancer in many countries is attributed at least in part to a reduced rate of *H. pylori* infection. Although *H. pylori* has been classed as a carcinogen (1), evidence that *H. pylori* infection is more common than expected in patients with gastric cancer is mixed.

Eslick and colleagues have combined data from 42 studies that were selected using appropriate inclusion criteria. They conclude that gastric cancer is twice as common in persons with evidence of *H. pylori* infection as in uninfected persons. The country of origin of the data, the type of controls (inpatients or non-inpatients), or the type of diagnostic test did not explain differences.

These results suggest that infection with *H. pylori* is an important determinant of risk for gastric cancer and that a decrease in gastric cancer incidence may indeed be attributed to decreasing rates of *H. pylori* infection. However, some oddities in the findings qualify any important clinical messages that might be taken from this review.

First, gastric cancer tends to be of 2 types. One type is proximal, diffuse in histology, more common in men than women, and probably rising in incidence in Western countries (as is esophageal adenocarcinoma) (2). The other type tends to be distal, intestinal in appearance, equally common in men and women, and decreasing in incidence. The suspicion has been that this latter type is associated with *H. pylori*; but the meta-analysis, which shows a greater, although very modest, increase in risk for intestinal cancer than for diffuse cancer, shows no relation with site.

Second, risks measured as ORs vary widely, even in studies with large numbers of patients. For instance, the OR in Finland was

1.31 (CI 0.99 to 1.74) for 243 case patients and 1408 control patients, whereas in Italy, the OR was 3.66 (CI 2.33 to 5.74) for 307 case patients and 162 control patients. Gastric cancer is a disease of poverty, and 1 possible explanation is that without matching for social class, the true risk for persons with *H. pylori* compared with those without may not be easily measured.

The third consideration is whether the particular variety of *H. pylori* matters (3). The answer is "possibly," but the results cannot tell us whether eradicating established infection will prevent gastric cancer. The risk for esophageal cancer might also increase if eradication makes patients more prone to gastro-esophageal reflux. Because esophageal and gastric cancers are about equally common now (4), the equation may be finely balanced. More evidence is needed on this matter.

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