LETTER

Oesophageal cancer incidence in 20-year follow-up in a population-based sample of 12 000 middle-age men with or without *Helicobacter pylori* infection in Finland

Two consensus reports on *Helicobacter pylori* (Hp), published recently in *Gut*, summarise the role of Hp gastritis in upper GI diseases, including gastric cancer (GCA). Although Hp gastritis definitely increases the risk of GCA as suggested in both reports, Hp is, on the other hand, also associated with a notable low incidence of oesophageal cancer (EC), of both adenomatous and squamous type.

In our earlier 15-year follow-up of a large population-based sample of males aged 50–65 years (n = 12 016) from two Finnish cities, with or without Hp, diagnosed in 1994–1996 by serological (IgG) Hp test (Biohit HealthCare, Helsinki, Finland), 57 GCA cases were recorded in the study population by the nationwide Cancer Registry during the follow-up. Of these cancers, 50 were in men and seven in those with and without Hp, respectively. The relative standardised incidence ratio (RR) of GCA incidence in Hp positive compared with that in Hp-negative men, calculated with the Altman’s procedure, was 6.0 (95% CI 2.3 to 19.0).

In a 20-year follow-up of the same population sample, 39 ECs appeared during the follow-up. Of these, 29 were in the Hp-negative subgroup (6625 men) and 10 in the Hp-positive subgroup (5391 men) (table 1). Of the cancers in Hp-negative and in Hp-positive subgroups, 11 and three were ECs of adenocarcinoma type and 14 and six of squamous cell type, respectively. In five cases, the histological type was unknown. All estimates of RR of EC in the Hp-positive men compared with EC in the Hp-negative men were very low, as shown in table 1, indicating that the Hp gastritis associates strongly with reduced EC risk. In addition to ECs of adenocarcinoma type also, the RR of squamous cell EC was notably low (table 1). Serum level of pepsinogen I did not markedly alter any of the RR estimates.

The prevented fraction of EC due to Hp positivity was very high, 78%. In comparison, the corresponding attributable percentage of GCA in Hp-positive men was 84%. Thus, relatively, the Hp gastritis reduces EC incidence roughly similarly as it increases GCA incidence. However, the incidence rate of GCA in the present study population was nearly twice as high as the incidence of EC. Therefore, the numbers of GCA caused by Hp positivity were nearly twice the numbers of EC prevented by Hp positivity.

Lower than the expected risk of oesophageal cancer in men with Hp gastritis has been presented in several other studies (see, eg, Nie et al, Rokkas et al, Islami and Kamangar, Xie et al, Ye et al, de Martel et al, Whiteman et al). The reason of this low risk is unknown. So far, the most plausible explanation is the intragastric acidity that tends to be lower in patients with Hp gastritis than in those without it. In people with ‘healthy’ stomach, a highly acid gastro-oesophageal refluxate, in persons prone and liable to GERD, may promote cascades that result in acid-related erosive and finally cancerous lesions in the oesophageal epithelium. In this context, in contrast to alkaline reflux, the acid reflux into the oesophagus is likely the key factor that associates with the increased risk and incidence of EC.

Table 1 Numbers and relative standardised incidence ratios (RR and 95% CI) of oesophageal cancer in *Helicobacter pylori* (Hp) antibody (HpAb) positive and negative middle-age men from two cities followed up by National Cancer Registry in Finland from 1994 to 1996 to 2014

| Hp status | Hp positive (≥30 HpAb [IgG] enzyme immunoassay unit) | Hp negative (<30 HpAb [IgG] enzyme immunoassay unit) | Risk ratio (RR) | 95% CI of RR |
|-----------|------------------------------------------------------|-----------------------------------------------------|----------------|--------------|
| Number of men | 6625 (6178) * | 5391 (5232)* | 0.22 | 0.05 to 0.95 |
| Number of person years | 107 714 (100 810)* | 89 961 (87 461)* | 0.35 | 0.12 to 1.01 |
| Number of cancers in follow-up by type of cancer | | | | |
| Adenomatous | 3 | 11 | 0.28 | 0.13 to 0.60 |
| Squamous | 6 | 4 | – | – |
| Other or unknown | 1 | 4 | – | – |
| Total | 10 (7)* | 29 (28)* | 0.28 | 0.05 to 0.95 |

* Numbers in brackets give the respective number of cases after excluding the men with atrophic gastritis (serum pepsinogen I <25 µg/L).
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REFERENCES
1 Malfertheiner P, Megraud F, O’Morain CA, et al. Management of Helicobacter pylori infection—the Maastricht V/Florence Consensus Report. Gut 2017;66:6–30.
2 Sugano K, Tack J, Kuipers EJ, et al. Kyoto global consensus report on Helicobacter pylori gastritis. Gut 2015;64:1353–67.
3 Vohlonen I, Pukkala E, Malila N, et al. Risk of gastric cancer in Helicobacter pylori infection in a 15-year follow-up. Scand J Gastroenterol 2016;51:1159–64.
4 Nie S, Chen T, Yang X, et al. Association of Helicobacter pylori infection with esophageal adenocarcinoma and squamous cell carcinoma: a meta-analysis. Dis Esophagus 2014;27:645–53.
5 Rokkas T, Pistiolas D, Sechopoulos P, et al. Relationship between Helicobacter pylori infection and esophageal neoplasia: a meta-analysis. Clin Gastroenterol Hepatol 2007;5:1413–7.
6 Islami F, Kamangar F. Helicobacter pylori and esophageal cancer risk: a meta-analysis. Cancer Prev Res 2008;1:329–38.
7 Xie F, Zhang YP, Zheng QQ, et al. Helicobacter pylori infection and esophageal cancer risk: an updated meta-analysis. World J Gastroenterol 2013;19:6098–107.
8 Ye W, Held M, Lagergren J, et al. Helicobacter pylori infection and gastric atrophy: risk of adenocarcinoma and squamous-cell carcinoma of the esophagus and adenocarcinoma of the gastric cardia. J Natl Cancer Inst 2004;96:388–96.
9 de Martel C, Llosa AE, Farr SM, et al. Helicobacter pylori infection and the risk of development of esophageal adenocarcinoma. J Infect Dis 2005;191:761–7.
10 Whiteman DC, Parmar P, Fahey P, et al. Association of Helicobacter pylori infection with reduced risk for esophageal pylori infection is independent of environmental and genetic modifiers. Gastroenterology 2010;139:73–83.