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Prevalence, risk factors and clinical consequences of chronic atrophic gastritis

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Chronic atrophic gastritis (CAG) is an important precursor lesion in the development of intestinal gastric cancer, the most common type of gastric cancer, which continues to be the second leading cause of cancer deaths worldwide. Given that the process of gastric carcinogenesis usually takes decades, there might be good perspectives for early detection of precancerous lesions and intervention. However, since the majority of individuals carrying CAG do not suffer from any symptoms, CAG and early stage gastric cancer remain unrecognized in most cases and only little is known about the epidemiology of CAG (partly also caused by existing difficulties and heterogeneity in the diagnosis of CAG). It is widely accepted that infection with the gastric bacterium *Helicobacter pylori* is a key risk factor for both CAG and noncardia gastric cancer, but estimates of the strength of the association between *H. pylori* infection and CAG have varied widely.

The objectives of this project were to assess the prevalence of CAG in different parts of the world (by means of a systematic literature review) and to analyse the epidemiology of CAG in a large population-based study among elderly persons in Germany. Additionally, the impact of different diagnostic methods of CAG on estimates for epidemiological parameters was assessed both within the population-based study and by means of second systematic literature review.

The MEDLINE database was searched for articles containing data on the prevalence of CAG published until November 2005 and for articles on the association between *H. pylori* infection and CAG published until July 2007. Concerning the latter, separate meta-analyses were carried out for studies defining CAG based on gastroscopy with biopsy, serum pepsinogen

(PG) I only, the PG I / PG II ratio only, or a combination of PG I and the PG I / PG II ratio. In the baseline examination of ESTHER, a population-based cohort study conducted in Saarland/Germany, concentrations of serum PG I and II and antibodies against *H. pylori* were measured by ELISA in 9,444 women and men aged 50–74 years. Information on potential risk factors and medical history were obtained by questionnaire.

The systematic literature search identified 41 studies providing data on the prevalence of CAG, determined by gastroscopy in 15 studies and by serum PG levels in 26 studies. Although results are difficult to compare due to the various definitions of CAG used, a strong increase of CAG prevalence with age, the lack of major gender differences, and strong variations between populations and population groups were observed quite consistently. In the ESTHER study, likewise no association with gender was observed. The prevalence of CAG increased from 2.7% in age group 50–54 to 9.1% in age group 70–74 when CAG was defined by PG I < 70 ng/ml & PG I / PG II ratio < 3. With this definition, the odds ratios (OR) for the association between any or CagA-positive *H. pylori* infection and CAG were 2.9 and 4.1, respectively, when all cases were included. They ranged from 10.7 and 16.1 for the quintile of cases with highest PG I (least severe cases) to 1.0 and 0.9 for the quintile of cases with lowest PG I (most severe cases). Application of the various pepsinogen based definitions of CAG to the ESTHER study population resulted in a wide range of estimates of CAG prevalence (2.1% – 8.2%, with an outlier of 18.8%) and its associations with age and *H. pylori* infection (age adjusted ORs for CagA positive *H. pylori* infection: 0.98–4.48). Definitions of CAG based on the PG I / PG II ratio (alone or in combination with PG I) revealed much stronger associations with both age and *H. pylori* infection than definitions of CAG based on PG I only. These findings are consistent with the results from the meta-analyses, where numbers of identified studies and summary ORs (95% confidence intervals) were as follows: gastroscopy with biopsy: n=34, OR=6.4 (4.0–10.1); PG I only: n=13, OR=0.9 (0.7–1.2); PG I / PG II ratio: n=8, OR=7.2 (3.1–16.8); combination of PG I and the PG I / PG II ratio: n=20, OR=5.7 (4.4–7.5).

In conclusion, CAG is relatively common among older adults in different parts of the world, but large variations exist. According to the ESTHER study, overall prevalence is rather low among older adults in Germany, but it strongly increases with age and *H. pylori* infection. There are strong indications for clearance of the infection in advanced stages of CAG to a major extent, and the *H. pylori* – CAG association is probably much stronger than estimated by most epidemiological studies to date. Furthermore, the association of *H. pylori* infection with CAG seems to be strongly underestimated when CAG is defined by PG I only. While the

association is missed entirely in studies relying on PG I only, studies with definitions based on gastroscopy with biopsy or the PG I / PG II ratio (alone or in combination with PG I) yield similarly strong associations. Large scale international comparative studies with standardized methodology to determine CAG are needed to provide a coherent picture of the epidemiology of CAG in various populations.