**Proton pump inhibitors (PPIs) and the risk of gastric cancer**

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A recent study published in Gut by Cheung et al (1) has demonstrated an association between PPI use and gastric cancer in a population from Hong Kong. This has received considerable press coverage and the BSG has produced this position statement to help both clinicians and patients when considering the risks of using PPIs. NHS Choices have published a summary (2) which makes no clear recommendations.

***The study***

The study in question assessed patients who were treated for *Helicobacter pylori* for the development of gastric cancer. 153 cases were detected over 7.6 years with PPI use being associated with a 2.44 (CI 1.42-4.20) fold increased risk. No increased risk was seen with H2-receptor antagonist use and most cancers were detected in the body and antrum (i.e. non-cardia cancers).

The study initially appears of reasonable quality but there were significant differences between those patients taking PPIs and those not. Patients in the PPI group were almost 10 years older than those in the non-PPI group on average. This is important as the incidence of gastric cancer is known to increase with age. There is also some debate about how applicable these findings are to the UK population as both gastric cancer and *H. pylori* eradication (and thus subsequent PPI use) are increasingly rare.

***Gastric cancer in the UK and Hong Kong***

Gastric cancer is relatively rare in the UK and its incidence is falling – by almost 50% in the past two decades. There were 6682 cases in the UK in 2014 in a population of 65 million (10 per 100,000). Put another way the lifetime risk is 1 in 67 for men and 1 in 135 for women (cancerresearchuk.org). Most cases are found at the cardia and are thought to be due to dietary risk factors, salt intake and *H. pylori* infection. Gastric cancer associated with *H. pylori* infection is usually located in the antrum or lower body (i.e. non-cardia) and the falling prevalence of *H.pylori*  in the UK is thought to explain the falling rate of gastric cancer as a whole in the UK.

It should also be noted that PPI use in the UK has increased by 7500% in the past 2 decades (3). The falling prevalence of gastric cancer in the face of this weighs against a strong causative relationship.

Gastric cancer is seemingly more common in Hong Kong with 1167 cases in 2015 in a population of 7.3 million (16 per 100,000). Age standardised data, though suggests there is not much difference. Non-cardia cancer is more common in Hong Kong, and may develop through a different process to cancers at the gastric cardia (e.g. *H. pylori)*.

***Other studies***

A similar sized study in a Californian (USA) population looking at pantoprazole showed no increased risk of gastric cancer over a similar period in those patients taking pantoprazole compared to those not (4). However, a Swedish study published recently did show a similar increased risk of gastric cancer in PPI users although the risk was higher in younger men (5). These studies both have limitations but do look at more representative populations in both clinical setting and demography.

***Summary***

It is plausible that there is an association between PPI use and gastric cancer in some populations, although whether this is a causal relationship remains unproven. The risk may be limited to those that have had *H. pylori* eradication and may be different between different PPIs (although this would be hard to explain. The reported relative risk is around 2-fold but the absolute risk to an individual remains very low at around 1 in 2000 per year.

If acid suppression is required after *H. pylori* eradication H2-antagonists should be used first and if these are ineffective PPIs can be initiated with the above information being shared with the patient.

In other patients there is no evidence at the moment to advise against the use of PPIs first line for short term use. Prolonged use should be accompanied with an explanation of the evidence for possible risks as described above.

1. <http://gut.bmj.com/content/67/1/28>
2. <https://www.nhs.uk/news/cancer/acid-reflux-drugs-linked-increased-stomach-cancer-risk/>
3. <http://onlinelibrary.wiley.com/doi/10.1002/pds.4043/abstract>
4. <https://www.ncbi.nlm.nih.gov/pubmed/26541643>
5. http://bmjopen.bmj.com/content/7/10/e017739