Stomach cancer

What is stomach cancer?
Stomach cancer, also known as gastric cancer, can form in the tissues of the main stomach body or the gastroesophageal junction (where the stomach joins the oesophagus). Early stage stomach cancer refers to cancer that is confined to the stomach tissue. However, it can spread to other parts of the body, referred to as metastatic stomach cancer.
Prevalence

Stomach cancer is the second most common cause of cancer-related death in the world – it leads to around 800,000 deaths each year, yet it is only the fourth most commonly diagnosed cancer, with around one million people diagnosed each year.

The incidence of stomach cancer varies hugely geographically, with a much bigger prevalence in Asian countries (such as Korea) than in the West, with men more prone to stomach cancer than women.

Figure 1: International variation in age-standardized stomach cancer incidence rates among males

Figure 2: International variation in age-standardized stomach cancer incidence rates among females
Worldwide, approximately half the cases of stomach cancer are diagnosed in the early stages and half in the advanced setting. Extensive screening programmes are in place in Eastern countries, where screening for early stomach cancer is effective. Typical symptoms in later stages of the disease include: indigestion, acidity, burping, feeling full, weight loss and loss of appetite, pain, nausea, difficulty swallowing, anaemia and blood in the stools.

Risk factors
Factors increasing the risk of stomach cancer include:

• Gender. Men are more likely to develop stomach cancer
• Age. Incidence of stomach cancer increases with age
• About 59% of cases in developing countries and 63% of cases in developed countries are attributable to a bacterial infection with *Helicobacter pylori*
• Medical conditions such as Barrett’s oesophagus, pernicious anaemia and blood group A
• High intake of salty foods and preserved meat
• Smoking
• Obesity
• Environment / socio-economic deprivation
• Genetic and familial risk factors

A diet high in fresh fruit and vegetables, and vitamin C in particular, may help to prevent damage to the stomach lining which can promote stomach cancer.

Diagnosis of stomach cancer
Several types of tests are used in the diagnosis of stomach cancer. The main methods are:

- Endoscopy – this is where a long tube with a tiny light and camera is swallowed so that it can enter the stomach and small bowel to allow the clinician to investigate any abnormalities
- Barium swallow or barium meal – this is where a white liquid (barium meal) is given to the patient to be swallowed. This liquid shows up on X-ray, so once swallowed, the doctor can watch the barium on the X-ray screen as it passes through the stomach

Management of stomach cancer
Treatment of stomach cancer depends on several factors including the size, location and extent of the tumour, the stage of disease, the patient’s age and overall health. Current treatment options include surgery,
chemotherapy and palliative care. Surgery is the only curative therapy for stomach cancer.\textsuperscript{vii} In advanced stages, chemotherapy is, in most cases, the only treatment option associated with a poor average survival of around 7-10 months.\textsuperscript{xviii}

**HER2-positive stomach cancer**

Human epidermal growth receptor 2 (HER2) is a protein found on the surface of a cell which, when present in more than the usual amounts (called HER2 overexpression) triggers aggressive and abnormal tumour growth, as well as rapid development of metastases. Studies have found that 16-22\% of stomach tumours show high levels of HER2 (termed HER2-positive stomach cancer).\textsuperscript{ix,x}

**HER2 testing in stomach cancer**

HER2 testing at first diagnosis is crucial to ensure appropriate stomach cancer treatment. Validated methods and scoring systems to ascertain HER2 status in breast cancer are well established and recent evidence has shown that these same techniques, with some minor modifications (i.e. scoring and staining), allow reliable identification of patients who can derive life-prolonging benefits from Herceptin.\textsuperscript{xii}

There are two main methodologies used for determining HER2 status:

1. Immunohistochemistry (IHC) can show how much of the HER2 protein is present in the tumour sample
2. In-situ hybridization methods (FISH, CISH, SISH) measures the amount of the HER2 gene in tumour cells

IHC should be used as primary testing modality. Cases with very high levels of HER2-overexpression (IHC 3+ or IHC2+/FISH+) are eligible for Herceptin treatment. All other cases with lower HER2-overexpression levels should be re-tested with ISH (preferably SISH or CISH). Patients with ISH positive results are eligible for Herceptin therapy.
References

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12 Van Cutsem, E. Efficacy results from the ToGA trial: a Phase III study of trastuzumab added to standard chemotherapy (CT) in first-line human epidermal growth factor receptor 2 (HER2)-positive advanced gastric cancer (GC) Abstract # LBA4509 Presented at ASCO 2009