Gastric tumours

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Abstract

Gastric tumours are subdivided into those of epithelial or stromal origin. Malignant tumours are far more common than benign, with adenocarcinomas being the most common type of malignancy. Rarer gastric malignancies include gastrointestinal stromal tumours (GIST), lymphomas and neuroendocrine tumours. Gastric cancer is the sixth most common cancer in Europe and the fourth most common cause of cancer death. Multi-disciplinary treatment planning is an essential part of management of these cancers. The only curative treatment option is surgical resection although this is usually accompanied by perioperative chemotherapy or adjuvant chemoradiotherapy. GISTs are most commonly due to a mutation in the *KIT* gene. They are the most common mesenchymal malignancies of the gastrointestinal tract and are most commonly found in the stomach. Intestinal lymphomas are also most commonly found in the stomach and the majority arise from the mucosa-associated lymphoid tissue.

Keywords Gastric adenocarcinoma; gastric lymphoma; GIST

Introduction

Gastric tumours are classified histologically according to their tissue of origin (Table 1). Adenocarcinomas, gastrointestinal stromal tumours (GISTs) lymphomas and neuroendocrine tumours are the most clinically important of these tumours and will be discussed in detail.

Gastric adenocarcinoma

Epidemiology

Gastric cancer is the sixth most common cancer in Europe with approximately 140,000 cases diagnosed each year, and it accounts for 107,000 deaths annually.[1] It is twice as common in males as in females and shows marked geographical variation, with the highest prevalence in East Asia, South America and Eastern Europe. Over the last 20 years there has been a decline in gastric non-cardiac cancers (GNCC) with an increase in more proximal or cardiac cancers (GCC) (Figure 1). The aetiological factors are shown in Table 2.

Pathology

Early gastric cancer is defined as adenocarcinoma that is limited to the mucosa or submucosa, and takes no account of the size of the lesion.[2] If an adenocarcinoma has infiltrated into or through the muscularis propria it is defined as advanced gastric cancer. This distinction is independent of the presence of lymph node metastasis. The growth pattern of advanced gastric cancers may be polypoidal, ulcerative, or locally or diffusely infiltrating (linitis plastica).

Gastric adenocarcinoma is classified histologically using the Lauren classification system[3] into intestinal (53%), diffuse (33%) and mixed types (14%), with each type thought to have different underlying molecular mechanisms. Intestinal type cancers are typically located in the antrum, cause hepatic metastasis and are more common in males. Diffuse type cancers are typically found in the body and cardia of the stomach, cause transperitoneal metastasis and are more common in young females.

Metastatic spread includes direct infiltration, via lymphatics to regional and distant lymph nodes, haematogenous and transcoelomic, spreading through body cavities. Tumour staging is based on the TMN system.[2]

Diagnosis

In the UK, the National Institute for Health and Care Excellence has introduced guidelines for symptomatic referral (Table 3), which are intended to expedite referral from primary care to endoscopy and improve early diagnosis. In particular, recent onset or persistence of dyspepsia over the age of 55 years should prompt early referral for endoscopy rather than empirical treatment. In 2013, 56% of newly diagnosed gastric cancers were referred from primary care, with emergency presentations accounting for 25% of cases.[4] Endoscopy should be performed in patients with suspected gastric cancer; it provides detailed information on tumour characteristics, including morphology and position, and allows a tissue diagnosis to be made (Figure 2).

Population-based screening in high incidence areas such as the Far East diagnoses early gastric cancer (EGC) in 60% of new cases. Fifty per cent of these have dyspeptic symptoms. However, early detection based on this experience in low-incidence areas would not be resource efficient as dyspepsia is such a non-specific symptom.[5]

Staging

Once a diagnosis has been made the initial imaging investigation should be multidetector computed tomography (MDCT) of the thorax, abdomen and pelvis. Although MDCT has an accuracy of 85% in detecting lung and liver metastases,[6] sensitivity is low for characterizing lesions <1 cm in diameter, and for distinguishing metastatic lymph nodes from reactive lymph node hyperplasia. MDCT is also of limited value for assessing small volume ascites and peritoneal disease; these require laparoscopy and peritoneal biopsy.

Once metastatic disease has been excluded additional modalities can provide further detail on T and N stage. Endoscopic ultrasound (EUS) can assess depth of penetration, and increases accuracy of local T staging and evaluation of local perigastric nodal involvement. It can be limited by the presence of ulceration, as inflammatory thickening can be difficult to distinguish from tumour infiltration.

Positron emission tomography combined with CT (PET-CT) may also improve staging accuracy, detecting increased labelled glucose uptake in malignant tissue. However, it can be limited, particularly in patients with diffuse type cancers, which demonstrate significantly less glucose uptake.[7]

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Histological classification of gastric tumours

Benign	Epithelial	Squamous papilloma
		Adenoma
	Stromal	Benign GIST
		Haemangioma
		Granular cell tumour
Malignant	Epithelial	Squamous cell carcinoma
		Adenocarcinoma
		Small cell carcinoma
		Carcinoid
		Undifferentiated carcinoma
	Stromal	Malignant GIST
	Other	Malignant melanoma
		Lymphoma
	Secondary tumours	

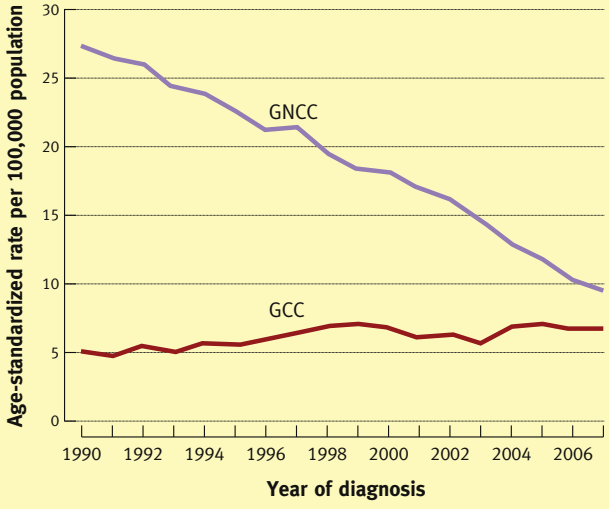
GIST, gastrointestinal stromal tumour.

Table 1

Preoperative assessment

In view of the physiological stress associated with treatment of gastric cancer, a thorough assessment of the patient's pre-operative fitness is vital in determining which treatment options are appropriate. A detailed clinical history should be sought, with a focus on pre-existing cardiopulmonary and renal disease. In addition to standard haematological and biochemical investigations, patients should undergo pulmonary function tests and cardiopulmonary exercise testing (CPX). Poor exercise tolerance has been shown to correlate with an increased risk in postoperative complications, independent of other patient factors.[8]

UK incidence rates of gastric antrum and cardiac cancers



Data from the Office for National Statistics.
GCC, gastric cardiac cancer; GNCC, gastric non-cardiac cancer.

Figure 1

Complications of treatment relate to poor nutritional status — a body mass index <18 kg/m^2 or weight loss >20% should prompt the need for dietetic review and consideration of supplemental feeding.

Treatment

In the UK, multidisciplinary treatment planning is mandatory and should involve surgeons, medical and clinical oncologists, gastroenterologists, radiologists, pathologists, dieticians and specialist nurses.[9] Although the proportion of patients suitable for radical intervention in the UK has increased in recent years, it remains low at approximately 30% of patients,[4] reflecting the advanced stage of disease at presentation.

Surgery: early gastric cancers can be excised endoscopically, either by endoscopic mucosal resection (EMR) or (perhaps more completely) by endoscopic submucosal dissection (ESD). The meticulous and vast experience of the Japanese has shown that, for mucosal-only disease, the risk of lymph node metastasis is 3%, whereas for submucosal disease this rises to 20%. It is thus oncologically safe to use endoscopic techniques for mucosal EGC.[9]

Surgical resection is the only potentially curative treatment modality although, due to high rates of relapse, multimodal treatments are now standard. In established T2 and T3 disease,[2] radical gastrectomy is indicated, the extent of the resection being dependent on the distance between the proximal tumour margin and the oesophagogastric junction. Sub-total gastrectomy may be performed if a proximal margin of 5 cm may be achieved in intestinal type cancers and 8 cm in diffuse type cancers.[9] If this is unachievable, total gastrectomy should be performed.

Either procedure should be accompanied by a lymph node dissection. The lymphatic drainage of the stomach is divided anatomically into three tiers, with the first being perigastric nodes (N1), the second being related to the principal arterial supply to the stomach (N2) and the third being more distant (N3). Current practice is to remove the first two tiers and is known as a D2 lymphadenectomy.[9] This is based on two large randomized trials completed in the UK and Holland.[10,11] Although early results failed to show any advantage of local node dissection over extended approaches, longer-term follow-up in the Dutch trial has shown an advantage for the D2 operation. Furthermore, with increasing experience more Western centres are reporting similar results to the Japanese and the consensus is that, where appropriate, a D2 lymph node dissection should be performed.

Minimally invasive surgery is currently investigational but may offer potential benefits in terms of decreased operative morbidity and reduced recovery times. However, this may be at the cost of reduced nodal harvests and poorer long term outcomes.[12,13] Further evidence to support a role for laparoscopic or robotic surgery may be provided by ongoing trials in Japan and South Korea.

Chemotherapy and chemoradiotherapy with curative intent: gastric cancer has been confirmed by studies in advanced disease to be chemosensitive. The role of adjuvant chemotherapy has been investigated by many groups. In a comprehensive meta-analysis of over 6300 patients there was confirmatory evidence of an advantage to postoperative treatment.[14] However, peri-operative chemotherapy is now the standard of care that has