Upper GI cancer - suspected

1 Care map information

Quick info:
Scope:
• presentation, diagnosis and management of upper gastrointestinal (oesophageal and gastric) tumours, including:
  • squamous cell cancer of the thoracic oesophagus
  • adenocarcinoma of the oesophagus and stomach
  • diagnosis and management of pre-malignant Barrett’s oesophagus
  • non-surgical and surgical therapy, including neoadjuvant/adjuvant therapy and newer therapy modalities (not yet established)
Out of scope:
• squamous cell cancer of the cervical oesophagus
• other rare tumours (eg lymphoma, small cell cancer or gastrointestinal stromal tumours)
Incidence, prevalence, and prognosis:
• gastric cancer is the second leading cause of cancer-related deaths worldwide [1]
• about 900,000 cases (700,000 deaths) reported each year [1]
• affects approximately:
  • 1 per 100,000 in people under the age of 40 [2]
  • 155 per 100,000 in people age 55 years or older [2]
• 5-year survival rates:
  • 16% for gastric cancer [5]
  • 12% for oesophageal cancer [5]
Risk factors include:
• age:
  • 92% of patients are 55 years old or more [2]
  • median age of presentation is 72 years [3]
  • rarely diagnosed in patients under 40 years old [3]
• male gender (incidence is approximately twice as high in males than in females)
• Barrett’s oesophagus [3]:
  • 2-3 fold increased risk of developing oesophageal adenocarcinoma
  • about 15% of oesophageal adenocarcinoma cases have preceding history of Barrett’s oesophagus
• reflux:
  • gastro-oesophageal reflux disease (GORD) is a major risk factor for developing oesophageal adenocarcinoma
  • the more frequent, more severe, and longer-lasting the symptoms of reflux, the greater the risk
  • the risk of oesophageal squamous-cell carcinoma is not associated with reflux
• obesity:
  • strongly associated with oesophageal adenocarcinoma
  • also associated with site-specific gastric cancer (risk is greatest in non-Asians)
• *Helicobacter pylori* (*H. pylori*) infection:
  • classified as a group I carcinogen by the World Health Organization
  • associated with a 2-3 fold increased risk of gastric cancer [3]
  • conversely, has been associated with a reduced risk of developing oesophageal adenocarcinoma – may reduce acid production in stomach and weaken effects of reflux on oesophageal tissue
• achalasia:
  • 16-fold increased risk of developing squamous cell carcinoma of the oesophagus [4]
  • malignancy commonly identified in first year following diagnosis
• family history:
  • established link between heredity and development of oesophageal cancers
  • additional increased risk of squamous cell carcinoma of the oesophagus with rare inherited diseases such as tylosis
  • heredity may also play role in development of gastric cancer:
  • 2-3 fold elevated cancer risk in first degree relatives [4]
  • the only proven genetic defect associated with familial gastric cancer is an E-cadherin mutation (CDH-1)
• previous peptic ulcer and gastric surgery
• smoking – increases the risk of:
  • squamous cell carcinoma of the oesophagus (by about 9-fold) [3]
  • oesophagogastric junction and gastric cancers
• alcohol consumption:
  • increases risk of gastric cancers and squamous cell carcinoma of the oesophagus
  • unclear whether increases risk of oesophageal adenocarcinoma or oesophagogastric junction cancer
  • heavy smoking and drinking together dramatically increase the risk of oesophageal cancer
• diet – a high intake of:
  • animal-based food increases risk
  • salted and smoked foods may increase risk (of gastric cancer specifically)
  • fruit, vegetables, fibre and antioxidant-rich foods reduces risk
  • low socioeconomic status
  • pernicious anaemia
  • coeliac disease

References:
[5] Contributors representing the National Cancer Action Team (NCAT); 2011.

NB: This information appears on each page of this care map.

2 Information resources for patients and carers

Quick info:
Patients and carers in England can access this care map through NHS Choices at http://healthguides.mapofmedicine.com/choices/map/upper_gastrointestinal_gi_cancer1.html

The following resources have been produced by organisations certified by The Information Standard:
  • 'Gastroscopy' (URL) from Bupa at http://www.bupa.co.uk/
  • 'Barrett's oesophagus' (URL) from Bupa at http://www.bupa.co.uk/
  • 'Oesophageal cancer' (URL) from Bupa at http://www.bupa.co.uk/
  • 'Removal of part of the oesophagus and stomach (oesophago-gastrectomy)' (URL) from Bupa at http://www.bupa.co.uk/
  • 'Understanding NICE guidance: Treating Barrett's oesophagus with a radiofrequency energy coil' (PDF) from National Institute for Health and Clinical Excellence (NICE) at http://www.nice.org.uk
  • 'Understanding NICE guidance: Photodynamic therapy for high-grade dysplasia in Barrett’s oesophagus' (PDF) from National Institute for Health and Clinical Excellence (NICE) at http://www.nice.org.uk
  • 'Should I see an oesophageal cancer specialist' (URL) from Cancer Research UK at http://www.cancerresearchuk.org/
  • 'What is Barrett's oesophagus' (URL) from Cancer Research UK at http://www.cancerresearchuk.org/
  • 'Stomach (gastric) cancer' (URL) from Cancer Research UK at http://www.cancerresearchuk.org/
  • 'Cancer of the gullet' (URL) from Macmillan Cancer Support at http://www.macmillan.org.uk/Home.aspx

Information for carers and people with disabilities is available at:
  • 'Caring for someone' (URL) from Directgov at http://www.direct.gov.uk
  • 'Disabled people' (URL) from Directgov at http://www.direct.gov.uk

Explanations of clinical laboratory tests used in diagnosis and treatment are available at 'Understanding Your Tests' (URL) from Lab Tests Online-UK at http://www.labtestsonline.org.uk

The Map of Medicine is committed to providing high quality health and social care information for patients and carers. For details on how these resources are identified, please see 'Map of Medicine Patient and Carer information'.

NB: This information appears on each page of this care map.

3 Updates to this care map

Quick info:
Date of publication: 31-Oct-2011
Interim update:

Published: 13-Oct-2011    Valid until: 30-Nov-2012 © Map of Medicine Ltd   All rights reserved
This care map was published by International. A printed version of this document is not controlled so may not be up-to-date with the latest clinical information.
Upper GI cancer - suspected

The clinical content of this care map has been accredited by the National Cancer Action Team (NCAT).

Date of publication: 29-Jul-2011

Interim update:

Additional practice-based contributions have been added to the care map from contributors representing the National Cancer Action Team (NCAT).

Date of publication: 29-Apr-2011

This care map was updated in line with the following guidelines:

- [41] The Royal College of Physicians (RCP), the Academy of Medical Royal Colleges (AMRC). A clinician’s guide to record standards – Part 2: Standards for the structure and content of medical records and communications when patients are admitted to hospital. London: Digital and Health Information Policy Directorate; 2008.

Further information was provided by the following references: [1,5-7,12,14-29,31,33,35-39,43]. For further information, please see the care map's Provenance.

NB: This information appears on each page of this care map.

4 Upper gastrointestinal (GI) cancer - clinical presentation

Quick info:

Alarm symptoms:

- require urgent referral to a medical or surgical gastroenterologist (seen within 2 weeks) [3,4]
- include [3,4]:
  - dysphagia
  - persistent vomiting
  - anorexia/cachexia
  - progressive unintentional weight loss
  - chronic gastrointestinal bleeding
  - palpable epigastric mass
  - sudden onset dyspepsia in patients age 55 years or older
  - worsening dyspepsia with past history of Barrett’s oesophagus, dysplasia, atrophic gastritis, or intestinal metaplasia
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• the majority of patients with alarm symptoms are found not to have cancer [3]
• however, for those that do, the disease is invariably relatively advanced [3]

Non-alarm symptoms include:
• gastro-oesophageal reflux (GOR) [3]:
  * characterised by recurrent/persistent heartburn – may be indicative of gastro-oesophageal reflux disease (GORD)
  * extremely common in the general population – occurs in about 50% of adults on a monthly basis and 20% of adults on a weekly basis
  * does not warrant further investigation (eg endoscopy) unless:
    • alarm symptom/s are also present
    • GOR is of recent onset, and patient is age 55 years or older
    • GOR is persistent despite treatment
    • symptoms have progressed since previous examination
    • patient history of Barrett's oesophagus/dysplasia
    • strong family history of Barrett's oesophagus/dysplasia/upper gastrointestinal cancer

• dyspepsia:
  • approximately 70% of patients with early gastric cancer present with dyspepsia (either alone or with presence of alarm symptom/s) at time of initial consultation [4]
  • characterised by recurrent pain in upper abdomen and problematic digestion [3]
  • uncomplicated dyspepsia does not usually warrant referral for endoscopy [3]
  • however, dyspepsia warrants urgent referral for investigation (eg endoscopy) under the following circumstances:
    • alarm symptoms are also present [3]
    • onset is sudden and patient is age 55 years or older [4]
    • symptoms are persistent despite treatment [4]
    • dyspepsia is worsening and history of Barrett's oesophagus, dysplasia, atrophic gastritis, or intestinal metaplasia [3]

References:

5 History and examination

Quick info:
Discuss and document presence of the following symptoms and signs (including details regarding time of onset, rate of progression and current severity).

History:
• dysphagia
• nausea/vomiting
• anorexia/weight loss
• gastro-oesophageal reflux (GOR)
• dyspepsia
• heartburn
• indigestion
• acid reflux
• acid or water brash
• odynophagia
• gastrointestinal bleeding
• altered bowel habit/other gastrointestinal symptoms
• holistic psychological assessment to determine suitability for interventions

Examination:
• signs of anaemia/pallor/jaundice/liver signs
• body mass index (BMI)
• lymphadenopathy
• cachexia
• abdominal scars
• abdominal masses
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- organomegaly
- per rectum examination
- nutritional assessment

Awareness of ‘at risk’ individuals is essential to facilitate early referral for assessment.

Discuss and document presence of the following risk factors (including appropriate detail):

- Barrett’s oesophagus
- gastro-oesophageal reflux disease (GORD)
- obesity
- previous peptic ulcer and gastric surgery
- *Helicobacter pylori* (*H. pylori*) infection
- family history
- smoking
- alcohol consumption
- diet
- pernicious anaemia
- achalasia
- coeliac disease

This information was drawn from the following references:


[5] Contributors representing the National Cancer Action Team (NCAT); 2011.


6 Alarm symptoms

Quick info:

**Alarm symptoms:**

- require urgent referral to gastroenterologist (seen within 2 weeks) [3,4]
- include [3,4]:
  - dysphagia
  - persistent vomiting
  - anorexia/cachexia
  - progressive unintentional weight loss
  - chronic gastrointestinal bleeding
  - palpable epigastric mass
  - sudden onset dyspepsia in patients age 55 years or older
  - worsening dyspepsia with past history of Barrett’s oesophagus, dysplasia, atrophic gastritis, or intestinal metaplasia

- the majority of patients with alarm symptoms are found not to have cancer [3]
- however, for those that do, the disease is invariably relatively advanced [3]

At time of referral, consider the following:

- blood tests:
  - to include full blood count, urea and electrolytes, liver function tests, bone biochemistry, and tumour markers [5]
  - may assist specialist assessment in the outpatient clinic [8]
- discontinuing acid suppression therapy for a period of at least 2 weeks prior to endoscopy – may increase the detection rate for early cancer [3,4]

However, be aware that the priority of patients with alarm symptoms is rapid specialist assessment, and referral for endoscopy should not be delayed (eg due to pending blood test results) [2].

References:


7 Non-alarm symptoms

Quick info:
Non-alarm symptoms include:
- gastro-oesophageal reflux (GOR):
  - characterised by recurrent/persistent heartburn [3]
  - may be indicative of gastro-oesophageal reflux disease (GORD) [3]
  - extremely common in the general population [3]
- occurs in about 50% of adults on a monthly basis, and 20% of adults on a weekly basis [3]
- does not warrant further investigation (eg endoscopy) unless:
  - alarm symptom/s are also present [3]
  - GOR is of recent onset, and patient is age 55 years or older [5]
  - GOR is persistent despite treatment [5]
  - symptoms have progressed since previous examination [5]
- patient history of Barrett's oesophagus/dysplasia [5]
- strong family history of Barrett's oesophagus/dysplasia/upper gastrointestinal cancer [5]
- dyspepsia:
  - approximately 70% of patients with early gastric cancer present with dyspepsia (either alone or with presence of alarm symptom) at time of initial consultation [4]
  - characterised by recurrent pain in upper abdomen and problematic digestion [3]
  - uncomplicated dyspepsia does not usually warrant referral for endoscopy [3]
- however, dyspepsia warrants urgent referral for investigation (eg endoscopy) under the following circumstances:
  - onset is sudden and patient is age 55 years or older [3]
  - symptoms are persistent despite treatment [4]
  - dyspepsia is worsening and history of Barrett's oesophagus, dysplasia, atrophic gastritis, or intestinal metaplasia [3]

References:
[5] Contributors representing the National Cancer Action Team (NCAT); 2011.

9 Further investigations

Quick info:
Consider the following investigations:
- taking a full blood count – may show iron deficiency anaemia [3]
- treating suspected gastro-oesophageal reflux with acid suppression therapy (eg proton pump inhibitors) [3]
- testing and treating for Helicobacter pylori (H.pylori) infection [9]:
  - recommended for all patients with uncomplicated dyspepsia
  - test is either a carbon-13 breath test or a stool antigen test
  - treat with a 7-day eradication course
  - all patients should be reviewed following H.pylori eradication treatment
- patients with recurrent/persistent symptoms should be further investigated with endoscopy to enable detection of early cancers

References:

10 Consider differential diagnosis
Upper GI cancer - suspected

Quick info:
Review alternative possible causes of dyspepsia, such as [9]:
• bisphosphonates
• corticosteroids
• non-steroidal anti-inflammatory drugs (NSAIDs)
• calcium antagonists
• nitrates
• theophyllines
Consider the following differential diagnoses [9]:
• gastro-oesophageal reflux disease (GORD)
• peptic ulcer disease
• non-ulcer dyspepsia – see 'Non-ulcer dyspepsia' care map
• cardiac or biliary disease
• rarer conditions such as Zollinger-Ellison syndrome or Crohn's disease
Reference:

11 History and examination

Quick info:
Careful evaluation of the patient's pretreatment health should be made, with particular attention paid to the cardiovascular and respiratory systems, and performance status.
Discuss and document presence of the following symptoms and signs (including details regarding time of onset, rate of progression and current severity).
History:
• dysphagia
• nausea/vomiting
• anorexia/weight loss
• gastro-oesophageal reflux (GOR)
• dyspepsia
• heartburn
• indigestion
• acid reflux
• acid or water brash
• odynophagia
• gastrointestinal bleeding
• altered bowel habit/other gastrointestinal symptoms
• holistic psychological assessment to determine suitability for interventions
Examination:
• signs of anaemia/pallor/jaundice/liver signs
• body mass index (BMI)
• lymphadenopathy
• cachexia
• abdominal scars
• abdominal masses
• organomegaly
• per rectum examination
• nutritional assessment
For formal discharge planning at the point of admission use your local discharge form based on the HIU Discharge Summary developed by the Health Informatics Unit of the Royal College of Physicians (RCP), London, UK [40,41].
Awareness of 'at risk' individuals is essential to facilitate early referral for assessment.
Discuss and document presence of the following risk factors (including appropriate detail):
• Barrett's oesophagus
• gastro-oesophageal reflux disease (GORD)
• obesity
• previous peptic ulcer and gastric surgery
• Helicobacter pylori (H. pylori) infection
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- family history
- smoking
- alcohol consumption
- diet
- pernicious anaemia
- achalasia
- coeliac disease

This information was drawn from the following references:


[5] Contributors representing the National Cancer Action Team (NCAT); 2011.


[41] The Royal College of Physicians (RCP), the Academy of Medical Royal Colleges (AMRC). A clinician’s guide to record standards – Part 2: Standards for the structure and content of medical records and communications when patients are admitted to hospital. London: Digital and Health Information Policy Directorate; 2008.

12 Upper gastrointestinal (GI) endoscopy

Quick info:

Preprocedural considerations:
- ideally, patients should be free of acid suppression therapy for a period of 2 weeks prior to endoscopy [3]
- antisecretory therapy should be withheld until after endoscopy [4]

Upper gastrointestinal (GI) endoscopy [3]:
- recommended as the diagnostic procedure of choice in all patients with suspected oesophageal or gastric cancer
- does not require intravenous sedation
- allows accurate localisation and mapping of tumours
- frequently identifies presence of dysplasia (both high grade and low grade)
- is preferable to barium radiology studies as:
  - barium studies cannot reliably diagnose premalignant lesions
  - endoscopy avoids the use of ionising radiation
  - endoscopy allows biopsy
- chromoendoscopy:
  - not routinely recommended for upper GI cancer
  - may be of value for selected patients at high risk of oesophageal or gastric cancers
  - involves spraying stains (eg methylene blue) onto the mucosa during endoscopy to enhance the detection of small, subtle lesions and/or dysplasia
  - stain used depends on mucosa being examined

Biopsy protocol:
- a minimum of eight biopsies should be taken during endoscopy to diagnose oesophageal malignancy [3]
- vitally important that precise sites of biopsies are recorded by endoscopist in terms of distance from incisor teeth and in relation to the oesophago-gastric junction [10]
- a more comprehensive biopsy protocol should be applied to ‘at risk’ individuals (eg patients already diagnosed with Barrett’s oesophagus) – see ‘Background information’ point for more information on risk factors [3]:
  - multiple four quadrant biopsies of oesophagus should be taken at 2cm intervals
  - biopsy should be taken of any visible lesion

Potential complications:
- incidence of minor complications (eg sore throat) is approximately 10% [3]
- incidence of major (mostly sedation related) complications is approximately 0.1% [3]
- in the UK, mortality rates associated with upper GI endoscopy are estimated at 1 in 2000 [9]

References:

13 Follow-up and advise

Quick info:
Reviewing patient care:
• all patients should be subsequently followed up, regardless of age [3]
• an annual review should be offered to patients with dyspepsia – dyspepsia is a remitting and relapsing disease with symptoms recurring in about half of all patients [9]
• refractory, recurrent or worsening symptoms should be further investigated with endoscopy to enable detection of early cancers [3]

For managing dyspepsia/gastro-oesophageal reflux, consider the following recommendations [9]:
• raising the head of the bed
• having a main meal several hours before going to bed
• advising a return to self-treatment with antacid and/or alginate therapy (either prescribed or purchased)
• avoiding fatty foods – may delay gastric emptying
• avoiding smoking, alcohol, coffee and chocolate – may cause transient lower oesophageal sphincter relaxations

Advise patient on the following measures for reducing cancer risk:
• theoretical risk of developing oesophageal cancer may be reduced by limiting duration and severity of GOR [4]
• risk of developing gastric cancer may be reduced by eradication of H. pylori [4]
• risk of developing all upper GI cancers may be reduced by [3]:
  • improving diet
  • reduction in obesity
  • cessation of smoking
  • reduction in alcohol consumption

References:

14 Diagnosis

Quick info:
Diagnosis:
• diagnosis of malignancy should be confirmed pathologically from endoscopic biopsies [3]
• dysplasia and malignancy should be reviewed urgently by a specialist GI pathologist at an appropriate multidisciplinary meeting [3]
• pathologists should use the Vienna classification for reporting dysplasia [3]
• most common histological types of oesophageal cancer are [11]:
  • adenocarcinoma
  • squamous cell carcinoma
• oesophagogastric junctional cancers can be classified clinically using the Siewert system [4]:
  • type I (distal oesophageal)
  • type II (cardia)
  • type III (proximal stomach)

References:
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15 Malignancy found

Quick info:
In general:
- patients should be referred urgently (seen within 2 weeks) to a specialist Oesophago-gastric Cancer Multidisciplinary Team (MDT) [2,3,4,5,8]
- there should be honest, open, sensitive, early, and ongoing communication between the patient and the MDT to ensure that the patient is fully involved in all decisions, and that their views and preferences are clearly understood [3]
- the MDT is the most useful forum to discuss entry into clinical trials of interventions and treatments [5]
- a named contact person (key worker) from the MDT should be appointed to each patient and given responsibility for guiding them throughout the management care map [3]
- the key worker is usually a clinical nurse specialist [5]
- patients should be offered written information, detailing the possible sequence of events and providing them with the name of their appointed MDT contact [3]
- GP should have access to the key worker, who can offer specific advice and guidance on dealing with the patient [2]

In a small minority of patients [2]:
- referral may be inappropriate when patient is very frail, or has aggressive metastatic disease or other serious illness
- instead palliative care may be provided locally by Local Upper GI Cancer Care Teams, working closely with the specialist teams to which patients are normally referred
- many regional MDTs collect important clinical data for the cancer network to assess outcomes, and referral for 'rubber stamping' of treatment may be appropriate

References:
[5] Contributors representing the National Cancer Action Team (NCAT); 2011.

16 Dysplasia and/or Barrett's oesophagus

Quick info:

Dysplasia:
- characterised by a lack of normal maturation and differentiation as one ascends the crypt [10]
- note that sampling (ie biopsy) and pathological reporting errors can under-stage disease [5]
- where macroscopic appearance is contrary to histological report, urgent re-assessment and biopsy are advised [5]
- low grade dysplasia (LGD) [10]:
  - represents a more stable phenotype than high grade dysplasia (HGD)
  - some studies have shown no evidence of malignant transformation for up to 84 months
  - other studies have shown progression to invasive cancer after 52-56 months (without apparent areas of HGD)
- high grade dysplasia (HGD):
  - approximately 40% of patients with biopsy-proven oesophageal HGD will already have an underlying cancer [4]
  - this proportion increases significantly when there is a visible lesion [12]
  - assessment and management of patients with HGD should be centralised to units with the appropriate endoscopic facilities and expertise [4]
  - diagnosis should be confirmed by a second pathologist with specialist experience (non-specialist pathologists may under or overdiagnose dysplasia) [3]
  - a diagnosis of 'indefinite for dysplasia' is most often made where there are changes suggestive of dysplasia but inflammatory changes make the distinction impossible [10]
Barrett's oesophagus (or columnar-lined oesophagus):

- develops as a consequence of acid and bile reflux [36]
- defined as an oesophagus in which any portion of the normal squamous lining has been replaced by a metastatic columnar epithelium, which is visible macroscopically [10]
- for a positive diagnosis, a segment of columnar metaplasia must be visible endoscopically above the oesophago-gastric junction and confirmed histologically [10]
- patients with Barrett's oesophagus may have few/none of the symptoms typical to gastro-oesophageal reflux disease (GORD) (eg heartburn) as columnar mucosa is relatively insensitive to acid [10]
- precursor lesion of oesophageal adenocarcinoma [10]:
  - in a minority of patients, Barrett's oesophagus may progress through a series of increasingly severe stages (dysplasia) to cancer [13]
  - patients with Barrett's oesophagus have a 2-3 fold increased risk of developing oesophageal adenocarcinoma [3]
  - approximately 15% of oesophageal adenocarcinoma cases have preceding history of Barrett's oesophagus [3]
  - most cases of oesophageal adenocarcinoma are associated with underlying (and unknown) Barrett's oesophagus [5]
- incidence has increased 3-fold in the last 3 years [10]

References:
[5] Contributors representing the National Cancer Action Team (NCAT); 2011.

19 Acid suppression and/or further biopsies

Quick info:
Low grade dysplasia (LGD) [10]:
- initially managed with intensive acid suppression therapy (proton pump inhibitors prescribed for 8-12 weeks)
- followed by extensive re-biopsy and re-evaluation

High grade dysplasia (HGD):
- further biopsies should be taken immediately (ie prior to acid suppression therapy) using a more comprehensive biopsy protocol [10]:
  - multiple four quadrant biopsies of oesophagus should be taken at 2cm intervals throughout entire length of oesophagus
  - biopsy taken of any visible lesion
  - sampling can also be improved by taking 'jumbo' biopsies of oesophageal mucosa
  - biopsies should be evaluated with knowledge of the clinical and endoscopic background [10]
  - refer patient urgently (seen within 2 weeks) to a specialist Oesophago-gastric Cancer Multidisciplinary Team (MDT) if:
    - HGD is confirmed [3]
    - malignancy is found [3]
    - doubt persists over the diagnosis (eg indefinite for dysplasia or macroscopic findings contrary to histological diagnosis) [5]
  - true HGD should be managed with intensive acid suppression therapy (proton pump inhibitors prescribed for 8-12 weeks), followed by extensive re-biopsy and re-evaluation [5,10]
  - if this fails to reveal definite evidence of dysplasia, a subsequent surveillance endoscopy with multiple biopsies should occur after 6 months [10]
  - if both initial and surveillance endoscopies fail to reveal dysplasia, patient may return to routine surveillance (performed every 2 years) [10]

Non-dysplastic Barrett's oesophagus (or columnar-lined oesophagus) [10]:
- managed with intensive acid suppression therapy
- normalisation of acid exposure may not be achieved, even with doses of up to 4 times the prescribed standard
- in the absence of a satisfactory response, consider increasing dose to the maximum recommended by manufacturer
- be aware that the improvement of symptoms does not necessarily signify normalisation of acid exposure as columnar mucosa is less sensitive to acid
- if considered appropriate, normalisation of acid may be monitored using pH manometry
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References:
[5] Contributors representing the National Cancer Action Team (NCAT); 2011.

20  Consider differential diagnosis

Quick info:
Review alternative possible causes of dyspepsia, such as [9]:
• bisphosphonates
• corticosteroids
• non-steroidal anti-inflammatory drugs (NSAIDs)
• calcium antagonists
• nitrates
• theophyllines
Consider the following differential diagnoses [9]:
• gastro-oesophageal reflux disease (GORD)
• peptic ulcer disease
• non-ulcer dyspepsia – see non-ulcer dyspepsia care map
• cardiac or biliary disease
• rarer conditions such as Zollinger-Ellison syndrome or Crohn's disease

Reference:

21  Further investigations and tumour staging

Quick info:
Tumour staging [3]:
• tumours should be accurately staged before considering any intervention
• staging investigations are complementary rather than mutually-exclusive procedures
• most commonly-used staging investigations are:
  • endoscopic assessment
  • contrast-enhanced computer tomography (CT) scan
  • endoscopic ultrasound (EUS)
• the following staging investigations may be considered, depending on the type, size and location of the cancer (often ascertained from initial CT/EUS scans):
  • laparoscopy
  • bone scan
  • magnetic resonance imaging (MRI)
  • neck or abdominal ultrasound (USS)
  • thoracoscopy
  • bronchoscopy
  • positron emission tomography (PET) scan (usually as a combined PET-CT)
  • bronchial endoscopic ultrasound (EBUS)
  • mediastinoscopy

Staging investigations:
• CT scan:
  • indicated in all patients with upper gastrointestinal (GI) cancer [3]
  • most accurate, widely-used and non-invasive method for detecting metastases (predicts mediastinal invasion in over 80% of patients) [3,4]
  • identifies patients with advanced metastatic disease who may not require further staging investigations [3]
  • routinely includes chest, abdomen and pelvis (may also include neck) [3]
  • gastric distension achieved immediately prior to procedure with oral water and intravenous (IV) buscopan [5]
  • used in combination with other investigations for accurate staging [14]
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- CT-PET scan [5]:
  - increasing role in staging, but future prospects unclear due to false negative rates
  - less sensitive and specific for gastric cancer than oesophageal cancer
  - may have a role in identification of responders to neoadjuvant therapy
- EUS:
  - indicated in all patients with oesophageal/oesophagogastric junction cancers who are eligible for potentially-curative therapy [3]:
    - highly accurate for locoregional staging of oesophageal cancers
    - less accurate for oesophagogastric junction tumours (but still indicated)
    - may also be useful in some gastric cancers (more accurate for advanced cancers than for early cancers) [5]
    - safe and relatively non-invasive complication rate of just 0.5-2.3% [14]
    - echoendoscope passed directly into the oesophagus, allowing visualisation of the individual layers of the oesophagus/gastric mucosa [14,15]
    - EUS-guided fine needle aspiration may be helpful for investigating suspicious lymph nodes, which will generally have some/all of the following features [3]:
      - greater than 1cm in diameter
      - rounded
      - hypoechoic
  - stenotic oesophageal/oesophago-gastric cancer may require the use of an oesophagoprobe EUS placed over a radiological guidewire [5]
    - can detect low volume ascites (poor prognostic indicator in gastric cancer) [16]
- USS [17]:
  - may be used to characterise liver lesions and assess cervical lymph nodes
  - can be combined with fine needle aspiration cytology or biopsy
- Laparoscopy [3]:
  - with or without peritoneal washing [5]
  - most specific investigation for detecting peritoneal metastases (via peritoneal washing cytology)
  - should be considered for patients with:
    - oesophageal tumours with proximal gastric component
    - gastric tumours, who are being considered for surgery with suspected full thickness gastric wall involvement
    - suspicion of peritoneal spread on CT/EUS
- MRI [3]:
  - still in development phase for the staging of upper GI cancer
  - may be as accurate as CT for locoregional staging of tumours and nodes
  - currently reserved for patients:
    - who cannot undergo CT
    - with specific indications (eg suspicious bony or liver lesions) that need further characterisation
- Thoracoscopy – possibly the most accurate method for detecting mediastinal lymph nodes in oesophageal cancer, but highly invasive and not routinely used [3]
- Bronchoscopy [3]:
  - recommended for patients with features suspicious of tracheobronchial invasion
  - may be used in combination with EBUS and/or biopsy
- Bone scan – bone is frequently the first site of identifiable distant metastatic spread, and bone scintigraphy is recommended to exclude metastatic disease before radical treatment of advanced oesophageal carcinoma (unless a PET/PET-CT has been performed) [5]

References:
[5] Contributors representing the National Cancer Action Team (NCAT); 2011.
Upper GI cancer - suspected

23 Co-existing malignancy

Quick info:
In general:
• patients should be referred urgently (seen within 2 weeks) to a specialist Oesophago-gastric Cancer Multidisciplinary Team (MDT) [2,3,4,5,8]
• there should be honest, open, sensitive, early, and ongoing communication between the patient and the MDT to ensure that the patient is fully involved in all decisions, and that their views and preferences are clearly understood [3]
• the MDT is the most useful forum to discuss entry into clinical trials of interventions and treatments [5]
• a named contact person (key worker) from the MDT should be appointed to each patient and given responsibility for guiding them throughout the management care map [3]
• the key worker is usually a clinical nurse specialist [5]
• patients should be offered written information, detailing the possible sequence of events and providing them with the name of their appointed MDT contact [3]
• GP should have access to the key worker, who can offer specific advice and guidance on dealing with the patient [2]
In a small minority of patients [2]:
• referral may be inappropriate when patient is very frail, or has aggressive metastatic disease or other serious illness
• instead palliative care may be provided locally by Local Upper GI Cancer Care Teams, working closely with the specialist teams to which patients are normally referred
• many regional MDTs collect important clinical data for the cancer network to assess outcomes, and referral for ‘rubber stamping’ of treatment may be appropriate

References:
[5] Contributors representing the National Cancer Action Team (NCAT); 2011.

25 Follow-up and advise

Quick info:
Reviewing patient care:
• all patients should be subsequently followed up, regardless of age [3]
• an annual review should be offered to patients with dyspepsia – dyspepsia is a remitting and relapsing disease with symptoms recurring in about half of all patients [9]
• refractory, recurrent or worsening symptoms should be further investigated with endoscopy to enable detection of early cancers [3]

For managing dyspepsia/gastro-oesophageal reflux disease (GORD), consider the following recommendations [9]:
• raising the head of the bed
• having a main meal several hours before going to bed
• advising a return to self-treatment with antacid and/or alginate therapy (either prescribed or purchased)
• avoiding fatty foods – may delay gastric emptying
• avoiding smoking, alcohol, coffee and chocolate – may cause transient lower oesophageal sphincter relaxations

Advise patient on the following measures for reducing cancer risk:
• theoretical risk of developing oesophageal cancer may be reduced by limiting duration and severity of GORD [4]
• risk of developing gastric cancer may be reduced by eradication of H. pylori [4]
• risk of developing all upper GI cancers may be reduced by [3]:
  • improving diet
  • reduction in obesity
  • cessation of smoking
  • reduction in alcohol consumption

References:
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26 Incurable cancers

Quick info:
Incurable cancers:
• are generally referred to as stage IV cancers [3]
• 75-80% of oesophageal and gastric cancer patients have inoperable disease at diagnosis [5]
• includes cancers with [3];
  • presence of distant metastases
  • tumour invasion of adjacent structures (spleen, colon, liver, diaphragm, pancreas, abdominal wall, adrenal gland, kidney, small intestine or retroperitoneum) that would not be suitable for en bloc resection with the tumour
  • multiple regional lymph node involvement (although there is no strong evidence on the number of nodes that render a tumour incurable)
  • metastases in lymph nodes in the following three compartments:
    • neck
    • mediastinum
    • abdomen
  • metastatic lymph nodes distant to the primary tumour (eg cervical nodes with oesophago-gastric cancer)

Consider palliative treatment to [3]:
• control dysphagia and other symptoms
• improve quality of life (eg number of hospital-free days)
• potentially improve length of survival

References:
[5] Contributors representing the National Cancer Action Team (NCAT); 2011.

27 Potentially-curable cancers

Quick info:
Potentially-curable cancers [3];
• any localised cancers
• generally referred to as stage I cancers
• locally-advanced cancers:
  • generally referred to as stage II/III cancers
  • tumour invasion of adventitia or subserosa, with or without nodal involvement
• may be suitable for potentially curative treatments, such as:
  • surgical resection
  • chemoradiotherapy
  • radical radiotherapy
  • endoscopic resection and/or ablation
  • multimodality therapy (eg neoadjuvant chemotherapy plus surgical resection)

Reference:

28 High grade dysplasia (HGD)

Quick info:
High grade dysplasia (HGD):

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- approximately 40% of patients with biopsy proven oesophageal HGD will already have an underlying cancer [4] – this proportion increases significantly when there is a visible lesion [12]
- the average time for progression to malignancy for true HGD is estimated at 24 months [5]
- however, HGD may remain as a stable phenotype for several years and there have even been reports of regression to no dysplasia or low grade dysplasia [10]

Refer patient to a specialist oesophago-gastric cancer Multidisciplinary Team (MDT) [18]:
- there should be honest, open, sensitive, early and ongoing communication between the patient and the MDT to ensure that the patient is fully involved in all decisions, and that their views and preferences are clearly understood [3]
- a named contact person from the MDT (key worker) should be appointed to each patient and given responsibility for guiding them throughout the management pathway [3]
- patients should be offered written information, detailing the possible sequence of events and providing them with the name of their key worker [3]
- GP should have access to the key worker, who can offer specific advice and guidance on dealing with the patient [2]

Treatment options:
- all patients should undergo intensive acid suppression therapy (proton pump inhibitors prescribed for 8-12 weeks) followed by extensive re-biopsy and re-evaluation [10] – HGD is diagnosed by two separate and concordant biopsy specimens reviewed by two independent specialist histopathologists [5]
- patients with persistent, multifocal HGD [10]:
  - should be considered for oesophagectomy
    - if unfit for surgery, should be considered for radiofrequency ablation (RFA) – requires lifelong endoscopic surveillance using comprehensive biopsy protocol at 6-monthly intervals
- patients with a persistent focal area of HGD:
  - should be considered for surgery if other risk factors for adenocarcinoma are present and operative risk is low [10]
  - if high operative risk and absence of other risk factors for adenocarcinoma, should be treated with endotherapy [10]
  - if high operative risk and presence of other risk, should be examined closely by the MDT when determining treatment choice [10]
- endoscopic mucosal resection (EMR) is increasingly considered as first-line option for biopsy treatment [5]

NB: The National Institute for Health and Clinical Excellence (NICE) is currently examining epithelial RFA for Barrett's oesophagus and will publish guidance on its safety and efficacy in May 2010 [5].

References:
[5] Contributors representing the National Cancer Action Team (NCAT); 2011.
[5] Contributors representing the National Cancer Action Team (NCAT); 2011.

29 No dysplasia or low grade dysplasia (LGD)

Quick info:
No dysplasia or low grade dysplasia (LGD) with/without Barrett’s oesophagus [10]:
- further treatment (ie resection/ablation) is not generally required
- surveillance endoscopy should be performed where appropriate

Reference:

31 Surveillance endoscopy
Quick info:

When considering surveillance endoscopy, clinician should [10]:

- discuss the potential benefits of early detection of tumours with the patient
- explain that the efficacy of surveillance is unproven
- make it clear that, for most patients with Barrett's oesophagus, the actual risk of death from oesophageal cancer is small
- explain the physical and psychological morbidity associated with surveillance
- ensure that the patient understands that surveillance cannot guarantee detection of every tumour that may develop

Surveillance endoscopy protocol [10]:

- surveillance biopsies should occur at 6-monthly intervals
- if apparent regression occurs on 2 consecutive examinations, surveillance intervals may be increased to once every 2-3 years
- patient should remain on proton pump inhibitors throughout surveillance

Consideration should be given to entry into the Barrett's Oesophagus Surveillance Study (BOSS) study, which aims to determine whether endoscopic surveillance is preferable to endoscopic surveillance for the prevention of early mortality in patients diagnosed with Barrett's oesophagus [5].

References:

[5] Contributors representing the National Cancer Action Team (NCAT); 2011.

32 Consider endotherapies (if LGD is persistent)

Quick info:

For persistent LGD:

- consider endoscopic ablation techniques, such as epithelial radiofrequency ablation (RFA):
  - in patients with dysplastic Barrett's oesophagus, RFA has been associated with a high rate of complete eradication of both dysplasia and intestinal metaplasia, and a reduced risk of disease progression [24]
  - however, current evidence on the efficacy and safety of epithelial RFA in patients with Barrett's oesophagus with either low-grade dysplasia (LGD) or no dysplasia is inadequate in quality and quantity, and the balance of risks and benefits is not clear [42]
  - should be used only with special arrangements for clinical governance, consent and audit, or research [42]
- consider entry into a UK trial [3]
- alternative diagnoses should be considered to account for presence of alarm symptoms (see 'Consider differential diagnosis' care point for more information) [3]

References:

[5] Contributors representing the National Cancer Action Team (NCAT); 2011.

33 Oesophagectomy

Quick info:

Overview of oesophagectomy for high grade dysplasia (HGD):

- should be performed by an experienced surgeon at a specialist centre [3]
- a full fitness assessment is required when planning treatment [5]
- removes the risk of an occult cancer or the risk of progression to a new cancer [13]
- most radical treatment option for HGD [13]
- an oesophagectomy is a major operation with the potential for morbidity and mortality [13]
- most specialist centres are now reporting very low complication and mortality rates for tailored oesophagectomy for HGD [19]
- long-term outcomes suggest complete cure for those who survive the perioperative period [20]
- minimally-invasive approach to part of all of the surgical resection may reduce morbidity [21]
- controlled trials of open versus minimally invasive approach are required [5]

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Quick info:

Endotherapies:
- includes endoscopic mucosal ablation (EMA), endoscopic mucosal resection (EMR), and endoscopic mucosal submucosal dissection (ESD) techniques [5]
- offers alternative to surgery for management of high grade dysplasia (HGD) [3]
- most commonly-used techniques are EMR and radiofrequency ablation (RFA) [5]
- a full fitness assessment is required when planning therapy [5]
- have been associated with:
  - a reduction in cancer incidence [22]
  - cancer-free survival rates equivalent to those achieved from surgical resection [3]
  - however, very little evidence is available to compare endotherapies with surgical resection and comparisons with surgical results will need to be done when the long-term results of these procedures become available [5]
  - resectional techniques (EMR and ESD) obtain a histological specimen but are generally only suitable for visible and focal disease [23]
  - EMR of early carcinoma in Barrett's oesophagus [5]:
    - associated with promisingly low morbidity and mortality rates
    - useful diagnostic adjunct, as the larger and more complete nature of specimens obtained may make histological examination easier
    - allows informed decision making on management choices [5]
    - ablative techniques are limited by the fact that no histological specimen is obtained [5]
    - the most important consideration is the depth of destruction that allows both destruction of metaplastic mucosa and neoplastic tissue, and safe healing [3]
- Photodynamic therapy (PDT):
  - shown in a recent review to be successful at eradicating Barrett's oesophagus and dysplasia [36]
  - there are concerns that PDT may 'bury' the pre-malignant tissue under neo-squamous epithelium [5]
  - associated with a relatively high rate of complications (eg strictures, photosensitisation) [5]
  - remains an experimental technique and should not be used outside of clinical trials [5]
- Argon photocoagulation (APC):
  - shown in a recent review to be successful at eradicating Barrett's oesophagus and dysplasia [36]
  - allows localised ablation of tissue, but may 'bury' dysplastic tissue [5]
  - limited by the lack of a histological specimen [5]
- Radiofrequency ablation (RFA):
  - recent data suggests that RFA is promising for the treatment of Barrett's oesophagus (with and without dysplasia) [24]
  - associated with fewer side effects than PDT and APC [36]
  - overall, RFA is a useful therapeutic option in patients with HGD in Barrett's oesophagus and appears to be the most successful endotherapy, but has significant limitations and the balance of risks and benefits is unclear [5]
  - long-term follow-up data are still needed before radiofrequency ablation can be used in routine clinical care without the need for very careful post-treatment surveillance [36]
  - consider entry into a UK trial [5]

References:

[5] Contributors representing the National Cancer Action Team (NCAT); 2011.
Upper GI cancer - suspected

[5] Contributors representing the National Cancer Action Team (NCAT); 2011.

35 Follow-up

Quick info:
To ensure the patient's discharge record has been adequately updated, to ensure proper documentation and appropriate continuity of care, use your local discharge form based on the HIU Discharge Summary developed by the Health Informatics Unit of the Royal College of Physicians (RCP), London, UK [40,41].

Reviewing patient care:
- all patients should be subsequently followed up, regardless of age [3]
- following endotherapy, intensive endoscopic surveillance may be required [3]
  * an annual review should be offered to patients with dyspepsia – dyspepsia is a remitting and relapsing disease with symptoms recurring in about half of all patients [9]
  * refractory, recurrent or worsening symptoms should be further investigated with endoscopy to enable detection of early cancers [3]

For managing dyspepsia/gastro-oesophageal reflux disease (GORD), consider the following recommendations [9]:
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  * avoiding fatty foods – may delay gastric emptying
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- risk of developing all upper GI cancers may be reduced by [3]:
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  * reduction in obesity
  * cessation of smoking
  * reduction in alcohol consumption

References:
[41] The Royal College of Physicians (RCP), the Academy of Medical Royal Colleges (AMRC). A clinician’s guide to record standards – Part 2: Standards for the structure and content of medical records and communications when patients are admitted to hospital. London: Digital and Health Information Policy Directorate; 2008.
Evidence summary for Upper GI cancer - suspected

This care map has been developed according to the Map of Medicine editorial methodology (http://mapofmedicine.com/whatisthemap/editorialmethodology). The content of this care map is based on high-quality guidelines [2-4,8-11,13,30,32,34,40-42,44,45], and critically appraised meta-analyses and systematic reviews [1,6,14-16,25,26,31,36,37,43]. Practice-based knowledge has been added by the Map of Medicine's Clinical Editorial team and Fellows [29] and contributors with front-line clinical experience [5,38], including any literature endorsed by the contributor group [7,12,17-24,27,28,33,35,39]. The evidence-based, practice-informed care map has been peer-reviewed by central committees within stakeholder groups.

Search date: Dec-2010

References

This is a list of all the references that have passed critical appraisal for use in the care map Upper gastrointestinal (GI) cancer

<table>
<thead>
<tr>
<th>ID</th>
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<tr>
<td>5</td>
<td>Contributors representing the National Cancer Action Team (NCAT). 2011.</td>
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ID Reference
38 Contributors invited by the Map of Medicine (MoM). London: MoM; 2011.

Disclaimers

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It is not the function of the National Cancer Action Team to substitute for the role of the clinician, but to support the clinician in enabling access to know-how and knowledge. Users of the Map of Medicine are therefore urged to use their own professional judgement to ensure that the patient receives the best possible care. Whilst reasonable efforts have been made to ensure the accuracy of the information on this online clinical knowledge resource, we cannot guarantee its correctness or completeness. The information on the Map of Medicine is subject to change and we cannot guarantee that it is up-to-date.

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