Managing Oesophagogastric (O-G) Cancer in General Practice

Wednesday 18th October 2018
Presenters: Prof Jon Emery
            Prof Alex Boussioutas

The education has been developed in partnership with Cancer Council Victoria, the University of Melbourne and supported by the Victorian Government.

Acknowledgement of Country

We recognise the traditional custodians of the land and sea on which we live and work.

We pay our respects to Elders past and present.
Where is my control panel?

Look in the top right of your screen for a small red arrow. Click on it to open the rest of the control panel.

Listen only mode

You have been placed on “mute” to optimise the learning experience for you and your peers.

Use the question box function to talk to us.
Learning Outcomes

By the end of this online QI & CPD activity you should be able to:

1. Describe the current evidence related to prevention, early detection, presentation, initial investigations and referral for oesophagogastric (O-G) cancer
2. Describe the current evidence about surveillance for Barrett’s oesophagus
3. Use evidence-based tools and resources to determine patients risk of O-G cancer and to help the assessment of common symptoms associated with O-G cancer
4. Identify how to access local referral pathways for diagnostic imaging and specialist appointment for patients presenting with signs and symptoms of oesophagogastric cancers
Polling question

How would you rate your current awareness of the Optimal Care Pathways?

- Excellent
- Very good
- Good
- Fair
- Poor
- None

Optimal Care Pathways

- Facilitate consistent care based on best evidence and practice
- Guides to optimal care across 15 tumour types for health professionals, including quick reference guides for GPs
- Have become recognised as a “standard of care”
- Encourage concept of an integrated pathway of care
- Emphasises the importance of communication across care sectors and at transition points for patients and carers
- Inform quality improvement projects by identifying gaps
Oesophageal and Gastric Cancer

Gastric cancer statistics

Estimated number of new cases in 2018

\[
2,332 = 1,517 \text{ \male} + 815 \text{ \female}
\]

15\textsuperscript{th} commonest cancer in Australia

Estimated number of deaths in 2018

\[
1,078 = 677 \text{ \male} + 401 \text{ \female}
\]

29\% 5-year survival
Gastric cancer statistics

Risk factors: age

Source: Australian Institute of Health and Welfare
**Risk factors**

- Age – risk increases from 55 years
- Male
- Family history
- H pylori infection
- Smoking
- Race – Asian descent
- Pernicious anaemia
- Partial gastrectomy for ulcer disease

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**Oesophageal cancer statistics**

Estimated number of new cases in 2018

\[1,685 = 1,182 + 504\]

19th commonest cancer in Australia
12th commonest cause of cancer death

Estimated number of deaths in 2018

\[1,447 = 1,045 + 403\]

21% 5-year survival

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Oesophageal cancer statistics

Incidence of adeno-carcinoma increasing while squamous cell carcinoma is decreasing

Risk factors: age
Risk factors

- Age – risk increases from >55 years
- Male
- Smoking
- Obesity
- Gastro-oesophageal reflux
- Alcohol
- Achalasia
- Barrett’s oesophagus

Polling question

Barrett’s oesophagus can progress into:

Options:
- Squamous cell carcinoma of the oesophagus
- Adenocarcinoma of the oesophagus
- Either type of oesophageal cancer
Defining Barrett’s Oesophagus

Replacement of Stratified squamous epithelium with intestinal metaplasia (columnar epithelium)

Importance of Barrett’s Oesophagus
- Premalignant condition
  - Risk of Oesophageal adenocarcinoma
- Increasing incidence
  - Australian detection rates for patients having endoscopy
    - 0.3% in 1990 to 1.9% 2002

(Falk, Gastro, 2002)

Changing definitions of Barrett’s

Combined Endoscopic and Pathological
- Endoscopy
  - proximal migration of Z-line
- Pathology
  - Intestinal metaplasia (goblet cells)
  - Columnar epithelium

(Sharma, Gastro, 2004)
(Playford, Gut, 2006)
(Spechler, Gastro, 2011)
Barrett’s a premalignant condition - progression to adenocarcinoma

Model of Barrett’s progression

- Normal squamous mucosa
- GORD
- Glandular epithelium
- Low grade dysplasia (0.25% over 5yrs)
- High grade dysplasia (0.5-28% over 5yrs)
- Adenocarcinoma (16-59% over 5yrs)

Risk of cancer
- 0.25% over 1yr
- 16-59% over 5yrs

Clonal evolution theory of progression

- Neoplastic Progression in Barrett Esophagus
- Risk of cancer (Schnell, Gastro, 2001)
- Reid, Am J Gastro, 2000
- Skacel, Am J Gastro, 2000
- (Amano, Gastrointestinal Endo, 2005)

Challenges in diagnosis

Endoscopic landmarks
- Where does oesophagus end and stomach begin?
  - Gastric folds best landmark to begin measure
Challenges in diagnosis

How long is my Barrett’s?
- Measurement from GOJ
- Prague criteria
  - Measure maximal extent of IM
  - Measure circumferential IM
- Length is one factor that determines risk for OA

Defining Barrett’s - summary

- Barrett’s defined - endoscopy and pathology
- Barrett’s oesophagus increasing prevalence
- Oesophageal adenocarcinoma increasing prevalence exponentially
- Barrett’s is a premalignant condition
- Risk of progression associated with:
  - Length of Barrett’s oesophagus
  - Presence and degree of dysplasia
  - Degree of molecular changes
Endoscopic surveillance for Barrett’s oesophagus

BSG guidelines for Barrett’s surveillance

- No dysplasia on two endoscopies
- Endoscopy every 2-3 years (segments >3cm)
- Endoscopy every 3-5 years (segments <3cm)
- Dysplasia
  - Indefinite dysplasia
  - Low grade dysplasia
  - High grade dysplasia
  - Carcinoma
  - Confirmed by expert path
  - 6/12 PPI and rescope
  - Low grade dysplasia
  - High grade dysplasia
  - Endoscopy every 6 mths
  - MDT discussion
  - Therapeutic intervention

Developments in detection

Technology used to detect BE

- Chromoendoscopy
  - Use of vital stains to visualise metaplasia/dysplasia
    - Methylene Blue; Toluidine Blue
    - Indigo carmine
    - Lugols Iodine
  - Narrow Band Imaging
    - Use of blue bandwidth of light to illuminate oesophagus
    - Blue light allows visualisation of mucosal vasculature
  - Confocal Endomicroscopy
  - Optical Coherence Tomography

Therapeutic technologies

- Thermal and Photothermal
  - Electrocoagulation (MPEC)
  - APC (Argon Plasma Coagulation)
  - Nd-YAG laser
  - Photodynamic therapy (PDT)
    - Use oral photosensitizer (5-ALA)
    - 530nm light

- Radiofrequency Ablation

- Mucosal resection
  - EMR (Endoscopic mucosal resection)
  - ESD (Endoscopic Submucosal Dissection)

(Sharma, Gut, 2006)
Complications of Ablation

- Stricture: 10-50%
- Chest pain: 30-50%
- Dysphagia: <20%
- Odynophagia: 30-60%
- Photosensitivity in PDT
- Subsquamous Barrett’s
  - 5-90%
  - Progression rate to OA unknown

HALO\textsuperscript{360} Ablation Catheter
Endoscopic Appearance-
post ablation

Baseline, 4 cm IM

Immediate Slough
Complete Response after ablation

127 patients dysplastic BE
Randomised sham control
  – PPI therapy/Sham vs PPI/HALO ablation
Endpoints
  – Primary: Eradication of dysplasia; Eradication of Metaplasia
  – Secondary: Progression of disease
High rates of dysplasia eradication at 12m

(Shaheen et al, NEJM, 2009)

Durability of response to ablation

(Cotton et al, Gastro, 2018)
Endoscopic resection

Take homes

• Barrett’s oesophagus is a premalignant condition
• Screening to find Barrett’s oesophagus not cost effective but perhaps in select populations
• Surveillance programs have altered to reflect local incidence rates
• Active research into endoscopic imaging to target bx
• Ablation and resection technologies have improved but not yet advocated for non-dysplastic Barrett’s oesophagus*
Polling question

Collin is a 59 year old man with a history of reflux controlled with intermittent PPIs. He sees you for a repeat prescription and says that he has started feeling food sticking in his chest. He has no other symptoms. What is the probability that he has oesophageal cancer?

2%
5%
15%
33%

Symptoms of O-G cancer in primary care
Symptoms of O-G cancer in primary care

Dysphagia
43% of patients with O-G cancer had at least 3 visits to GP before referral

Research

Presentations to general practice before a cancer diagnosis in Victoria: a cross-sectional survey

Karen Lacey, James F Becho, Hannah L Cross, Patty Chondros, Georgios Lyntzopoulos, Jon D Emery

Symptoms of OG cancer in primary care

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<table>
<thead>
<tr>
<th>Symptom</th>
<th>PPV (%)</th>
<th>Probability of cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raedated platelets</td>
<td>4.1</td>
<td>4.1%</td>
</tr>
<tr>
<td>Constipation</td>
<td>4.2</td>
<td>2.5%</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>4.5</td>
<td>2.5%</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>4.8</td>
<td>2.5%</td>
</tr>
<tr>
<td>Dyspepsis</td>
<td>9.6</td>
<td>1%</td>
</tr>
<tr>
<td>Epigastric pain</td>
<td>9.2</td>
<td>1%</td>
</tr>
<tr>
<td>Reflux</td>
<td>3.2</td>
<td>1%</td>
</tr>
</tbody>
</table>

Figure 1 shows the probability of oesophageal or gastric cancer for individual symptoms and pairs of symptoms, including second presentation of same symptom in people over 55 years.

# Upper gastrointestinal endoscopy categorisation guidelines for adults 2018

<table>
<thead>
<tr>
<th>Category 1 (20 days)</th>
<th>Category 2 (40 days)</th>
<th>Category 3 (180 days)</th>
<th>Comments/Not Indicated</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indication &amp; Symptoms and Investigations</strong></td>
<td><strong>Dysphagia occurs in an automatic Category 1</strong></td>
<td><strong>Abdominal symptoms, dyspepsia, NASH, upper abdominal pain, persistent nausea/vomiting, early satiety in unexplained loss of appetite</strong></td>
<td><strong>Abdominal blood test (&lt;100) or X-ray, ultrasound, endoscopy, histology, raised patients</strong></td>
</tr>
<tr>
<td>1. Dysphagia &amp; any age</td>
<td>Any age with symptoms</td>
<td>Any age with symptoms</td>
<td>Any age with symptoms</td>
</tr>
<tr>
<td>2. Haematemesis/Vomiting &amp; any age (see Comments)</td>
<td>Any age with symptoms</td>
<td>Any age with symptoms</td>
<td>Any age with symptoms</td>
</tr>
<tr>
<td>3. Anaemia and/or iron deficiency &amp; any age (&lt;25 years)</td>
<td>Any age with symptoms</td>
<td>Any age with symptoms</td>
<td>Any age with symptoms</td>
</tr>
<tr>
<td>4. Abnormal imaging, e.g. abnormal results of gastric cancer &amp; any age</td>
<td>Any age with symptoms</td>
<td>Any age with symptoms</td>
<td>Any age with symptoms</td>
</tr>
<tr>
<td>5. Weight loss, unexplained, and any age with additional symptoms</td>
<td>Any age with symptoms</td>
<td>Any age with symptoms</td>
<td>Any age with symptoms</td>
</tr>
<tr>
<td>6. Dyspepsia and any age with additional symptoms &amp; any age with abnormal test results and raised patients</td>
<td>Any age with symptoms</td>
<td>Any age with symptoms</td>
<td>Any age with symptoms</td>
</tr>
</tbody>
</table>

**Combinations of symptoms, age and abnormal test results**

**Urgent upper GI endoscopy**

- Dysphagia at any age
- Haematemesis or melaena at any age
  - Assume delayed presentation and haemodynamically stable
  - Not requiring immediate admission

**Polling question**

Mary is a 57 year old woman who came to see you after being found to be anaemic when she went to donate blood. She has no relevant symptoms. Her last period was 5 years ago. She is a non-smoker, drinks 10 units per week and is vegetarian. Her Hb is 111 g/l and MCV 78. Her serum ferritin is low and total iron binding capacity increased. What will you do next?

Refer for colonoscopy
Refer for colonoscopy and gastroscopy
Order immunochemical FOBT and coeliac screen
Prescribe 3 months of iron supplements and repeat FBC and iron studies
Anaemia or iron deficiency

Gastro-oesophageal reflux (GORD)

<table>
<thead>
<tr>
<th>CATEGORY 1 (&lt;30 days)</th>
<th>CATEGORY 2 (&lt;60 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GORD, recent onset, and:</strong></td>
<td><strong>GORD, recent onset, and:</strong></td>
</tr>
<tr>
<td>age ≥ 55 years, with</td>
<td>age &lt; 55 years, with</td>
</tr>
<tr>
<td>any additional symptom</td>
<td>any additional symptom</td>
</tr>
<tr>
<td>or</td>
<td>or</td>
</tr>
<tr>
<td>abnormal blood test or imaging</td>
<td>abnormal blood test or imaging</td>
</tr>
</tbody>
</table>

Additional symptom: dyspepsia, upper abdominal pain, persistent nausea/vomiting, weight loss
Abnormal blood test: low Hb, low ferritin, raised platelets
How useful is thrombocytosis in predicting an underlying cancer in primary care? a systematic review

Sarah E R Bailey**, Obi C Ukoumunne*, Elizabeth Shephard* and Willie Hamilton*

<table>
<thead>
<tr>
<th>Ref</th>
<th>Cancer site</th>
<th>Cases</th>
<th>Controls</th>
<th>LR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n</td>
<td>Total</td>
<td>n</td>
</tr>
<tr>
<td>[5]</td>
<td>Lung</td>
<td>34</td>
<td>247</td>
<td>19</td>
</tr>
<tr>
<td>[7]</td>
<td>Oesophago-gastric</td>
<td>767</td>
<td>7657</td>
<td>588</td>
</tr>
<tr>
<td>[8]</td>
<td>Uterine</td>
<td>110</td>
<td>3166</td>
<td>207</td>
</tr>
<tr>
<td>[34]</td>
<td>Breast</td>
<td>91</td>
<td>4407</td>
<td>359</td>
</tr>
<tr>
<td>[33]</td>
<td>Bladder</td>
<td>156</td>
<td>4935</td>
<td>247</td>
</tr>
<tr>
<td>[10]</td>
<td>Pancreatic</td>
<td>214</td>
<td>3635</td>
<td>222</td>
</tr>
<tr>
<td>[31]</td>
<td>Ovarian</td>
<td>26</td>
<td>212</td>
<td>9</td>
</tr>
<tr>
<td>[11]</td>
<td>Colorectal</td>
<td>48</td>
<td>349</td>
<td>42</td>
</tr>
</tbody>
</table>

Dyspepsia, and:
- age ≥ 55 years, with
  - any additional symptom
  or
  - abnormal blood test or imaging

Dyspepsia and:
- age ≥ 55 years, non-responsive to PPI and/or H. pylori therapy or H. pylori-negative

Dyspepsia and:
- age < 55 years, non-responsive to PPI and/or H. pylori therapy or H. pylori-negative

Dyspepsia and:
- age < 55 years, with
  - any additional symptom
  or
  - abnormal blood test or imaging
**Helicobacter pylori**

GI Disease association
- Peptic Ulcer Disease
- Gastric Cancer
- Gastric MALT lymphoma

Extragastric associations
- Iron deficiency anaemia
- Idiopathic Thrombocytopenic Purpura (ITP)

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**Who to eradicate H. pylori?**

H. pylori infected persons with
- Peptic ulcer disease
- Early Gastric Cancer treated curatively
- Gastric Intestinal Metaplasia
  - Although only ~50% regress (atrophic gastritis)
- Unexplained iron deficiency anaemia
- ITP
- Vitamin B12 deficiency
- MALToma
- Dyspepsia (with no alarm symptoms)
  - test and treat strategy
- chronic NSAID or aspirin use
  - Particularly if previous peptic ulceration

(Malfertheiner et al, Gut, 2017)
What test to use?

Non-invasive testing
- Urea Breath Test – C13
  - Sensitivity 88-85%; Specificity 95-100%
- Stool antigen test
  - Sensitivity 94%; Specificity 97%
- Serology
  - Sensitivity ~85%; Specificity ~79%
    (Loy et al, Am J Gastro, 1996)

Invasive testing
- Rapid Urease Test
- Histology
- Culture

Initial therapy for H. pylori infection
Second line therapy for H. Pylori

Persisted H. pylori infection?

Clarithromycin based triple therapy

Yes

No

Is a penicillin allergy present?

Bismuth quadruple therapy

Yes

No

Clarithromycin based quadruple therapy

Treat with any one of the following salvage regimens:
- Loxofloxacin triple therapy
- Bismuth quadruple therapy
- High dose dual therapy

Clarithromycin based concomitant therapy

Confirm eradication of H. pylori

- In patients with persistent H. pylori infection perform H. pylori culture and susceptibility testing to guide antibiotic treatment
- If testing unavailable, treat with rifabutin triple therapy, or alternate salvage regimen
- Refer to UpToDate topic on treatment of H. pylori

Prevalence of Antibiotic Resistance in Helicobacter pylori: A Systematic Review and Meta-Analysis in World Health Organization Regions

Alarming rates of resistance
How to eradicate H. pylori?

1st line therapy
- PPI + amoxicillin + clarithromycin for 7 days
- Beware global resistance to clarithromycin and metronidazole

2nd line therapy
  - Dependent on region and rates of clarithromycin and metronidazole resistance
  - Bismuth containing Quadruple therapy
    - (Bismuth + PPI + metronidazole + tetracycline (14 days)
    - Or
    - Levofloxacin triple therapy
      - Levofloxacin + PPI + amoxicillin (10-14 days)

3rd line therapy
- Endoscopy and culture for sensitivities

Thank you
Supportive care resources

- Cancer Council
  - Phone 13 11 20
- OCP - quick reference guide & full version
- What to expect: only if a positive diagnosis
- LiveLighter program
  - www.livelighter.com.au
  - Resources for HPs and Patients
- Quitline
  - www.quit.org.au for HP referral
  - GP software link
  - 13 78 48

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