GI Screening/Surveillance in Lynch Syndrome

M Appleyard

Royal Brisbane and Women’s Hospital
Brisbane, Australia
GI Disease and Lynch Syndrome

- What are risks of GI disease in Lynch?
- Who do we screen for Lynch?
- Who do we put on endoscopy surveillance programs?
- National guidelines
  - Evi-Q/NHMRC
- Why do we get interval cancers in Lynch patients
- Quality in colonoscopy
Why is Lynch Syndrome Important to Gastroenterologists

- Individuals have a genetic mutation in one of the DNA repair genes MLH1, PMS2, MSH2, or MSH6, and a lifetime risk for development of colorectal cancer of 25-75%

- Increase risk of stomach and small bowel cancers, but much lower incidence
<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>MLH1 to age 70 yrs</th>
<th>MSH2 to age 70 yrs</th>
<th>MSH6 to age 70 yrs</th>
<th>PMS2 to age 70 yrs</th>
<th>Lynch syndrome to age 70 yrs*</th>
<th>General population to age 85 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal (male)</td>
<td>34%</td>
<td>47%</td>
<td>22%</td>
<td>20%</td>
<td>38%</td>
<td>10%**</td>
</tr>
<tr>
<td>Colorectal (female)</td>
<td>36%</td>
<td>37%</td>
<td>10%</td>
<td>15%</td>
<td>31%</td>
<td>6.6%**</td>
</tr>
<tr>
<td>Endometrial</td>
<td>18%</td>
<td>30%</td>
<td>25%</td>
<td>15%</td>
<td>33%</td>
<td>2 - 3%</td>
</tr>
<tr>
<td>Gastric</td>
<td>6%</td>
<td>0.2%</td>
<td>0</td>
<td>-</td>
<td>6%</td>
<td>1%</td>
</tr>
<tr>
<td>Ovarian</td>
<td>8-15%</td>
<td>8-15%</td>
<td>Low</td>
<td>-</td>
<td>9%</td>
<td>1 - 2%</td>
</tr>
<tr>
<td>Urothelial</td>
<td>0.2%</td>
<td>2.2%</td>
<td>0.7%</td>
<td>-</td>
<td>&lt;3%</td>
<td>1%</td>
</tr>
<tr>
<td>Small Bowel</td>
<td>0.4%</td>
<td>1.1%</td>
<td>0</td>
<td>-</td>
<td>&lt;3%</td>
<td>0.01%</td>
</tr>
</tbody>
</table>

*This data does not take into account the impact of surveillance.

Data Source: NSW Central Cancer Registry 2008 final dataset and NSW Health Outcomes Information Statistical Toolkit (HOIST).
So clearly the diagnosis of Lynch Syndrome comes with a significant GI cancer risk.

It is clearly important to recognise when patients might have Lynch Syndrome that might require referral for genetic testing.

When does a gastroenterologist worry about a new diagnosis of Lynch in a referred patient. In clinic or after colonoscopy?
Amsterdam II Criteria

- At least 3 relatives with Lynch cancers (colo-rectal cancer [CRC], endometrial, etc) one of whom is a first degree relative of the other 2
- At least 2 successive generations affected
- At least one relative affected under the age of 50 years
Updated Bethesda Criteria

- CRC under 50 years
- Synchronous or metachronous CRC (or other Lynch-associated cancer) regardless of age
- CRC with MSI-H histology under age 60
- CRC with one first degree relative with CRC or other Lynch-associated cancer with one of the cancers being diagnosed under 50 years
- CRC with two or more first or second degree relatives with CRC or other Lynch-associated cancers regardless of age
Histology
To Summarise

- Refer to clinical genetics
  - Amsterdam II criteria
  - CRC with updated Bethesda criteria and appropriate histology

- Gastrointestinal Endoscopy Surveillance
  - Patients with documented mutation in DNA repair genes
  - Some patients in whom we are very suspicious of Lynch Syndrome, but cannot confirm/find the genetic mutation
Endoscopy Procedures

- Colonoscopy
  - Bowel prep
  - Colonoscopy
- Gastroscopy
  - Overnight fast
  - Gastroscopy
- Capsule endoscopy
EVI-Q Guidelines

- Annual colonoscopy from age 25-30 (depending on mutation) or 5 years younger than youngest affected relative
- Biennial upper GI endoscopy from 30 for those with gastric cancer family history or with added ethnic risk
- No evidence for capsule endoscopy
NHMRC Guidelines

- Annual colonoscopy starting at 25 or 5 years prior than youngest affected relative
- Consider biennial upper GI endoscopy if family history
- No recommendation re capsule endoscopy
Quality of Colonoscopy is Important

- KPIs validated
  - Caecal intubation > 90%
  - Adenoma detection rate (<20% associated with increased interval cancer)
  - Withdrawal time < 6 minutes associated with lower adenoma detection
  - High volume colonoscopists
  - Good bowel prep

- Australia is about to recertify colonoscopists using these KPIs
Interval Cancer and Lynch Syndrome

- Colonoscopy can reduce the development of CRC by 63% in Lynch patients.
- Interval cancer (cancer found in the colon within 2 years of a colonoscopy) is reported in Lynch Syndrome.
Why do we get interval Ca in surveillance patients?

- Right colon
- Polyps
  - Flat
  - Small adenomas with advanced histology
  - Short duration of polyp-CRC sequence
- Synchronous
- Younger patients less tolerant of multiple colonoscopy
Flat Depressed Lesion, 7mm
Flat Depressed Lesion, 10mm
Where is a flat adenoma?
Colonoscopy in Lynch Patients

- Careful colonoscopists
  - Complete colonoscopy
  - Meticulous colonoscopy
    - Slow withdrawal
    - Careful inspection
    - High resolution white light
RBWH Endoscopy Surveillance Protocol

- Annual colonoscopy from 25 or 5 years younger than youngest affected relative
- Biennial upper GI endoscopy
- Consider capsule endoscopy to visualise the small bowel in patients with a personal/strong family history of small bowel cancer
In LS patients and individuals fulfilling the Amsterdam II criteria, surveillance colonoscopy should be performed using modern high resolution technology by experienced endoscopists every year, starting at age 25 years, or 5 years younger than the age of first diagnosis in the family (whichever is first).
Colonoscopy in LS patients should include meticulous inspection and precise removal of all polyps, with special attention to the right colon, alertness to flat lesions and using high resolution endoscopes.
Get pictures of gastroscopy/colonoscopy/GI tract