Total Proctocolectomy for Rectal Cancer in Lynch Syndrome

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Our patient
What surgery do you recommend?

Primary Rectal Cancer
Rectal Cancer in Lynch Syndrome

- 15-17% of LS patients present with cancer in the rectum\(^1,2,3\)
- Family history of rectal cancer is predictive\(^4\)
  - 62% of rectal cancer patients have a FDR with rectal cancer

\(^1\)Lee, American Journal of Surgery, 2001
\(^2\)Moslein, 1998
\(^3\)Lindor, JAMA, 2006
\(^4\)Cirillo, Annals of Surgery, 2013
Rectal Tumor

TPC with IPAA

LAR
What are the reported rates of metachronous colon cancer?

<table>
<thead>
<tr>
<th>Author</th>
<th>Observed Rate</th>
<th>N</th>
<th>Interval (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Moslein et al</td>
<td>54%</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>2 Lee et al</td>
<td>17%</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td>3 Kalady et al</td>
<td>15% **</td>
<td>33</td>
<td>6</td>
</tr>
<tr>
<td>4 Cirillo et al</td>
<td>22%</td>
<td>18</td>
<td>15</td>
</tr>
<tr>
<td>5 Win et al</td>
<td>27%</td>
<td>79</td>
<td>9</td>
</tr>
</tbody>
</table>

**Additional 36% of patients developed high risk adenomas during screening**

1 Moslein, Langenbecks Archiv, 1998
2 Lee, American Journal of Surgery, 2001
3 Kalady, Annals of Surgery, 2012
4 Cirillo, Annals of Surgery, 2013
5 Win, Annals of Surgical Oncology, 2013
Why not opt for the more extensive surgical strategy?

<table>
<thead>
<tr>
<th>QoL Concern</th>
<th>TPC with IPAA(^1)*</th>
<th>LAR(^2,3,4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avg # Bowel Movements/Day</td>
<td>6</td>
<td>2-4(^2,3)</td>
</tr>
<tr>
<td>% Incontinent</td>
<td>29%</td>
<td>3-10(^4)</td>
</tr>
<tr>
<td>% Urgent</td>
<td>48%</td>
<td>15-28(^4)</td>
</tr>
<tr>
<td>Pad Usage</td>
<td>16-22%</td>
<td>6-7(^2)</td>
</tr>
</tbody>
</table>

\(^1\)IPAA Assessed 5 years PO, LAR assessed at a range of 1.3-12.3 Years PO, median 4.3 yrs
\(^2\)Lin, Surgery Today, 2002
\(^3\)Paty, American Journal of Surgery, 1994
\(^4\)Breghendahl, Colorectal Disease, 2013

**Lynch Syndrome**
Factors mitigating surgical approach

- Stage of Primary Rectal Cancer
  - Need for RT/Chemo?
- Location of Rectal Cancer
  - Sphincter involvement?
- Preoperative Sphincter function
  - Strong or poor?
- Prior Small Bowel Resection
  - Adequate bowel length?
- Patient Age?
- Patient Compliance?
Incidence of metachronous colon cancer following proctectomy for rectal cancer

<table>
<thead>
<tr>
<th>MMR Mutation</th>
<th>N</th>
<th># Metachronous Colon Cancer (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MLH1</td>
<td>18</td>
<td>5 (28%)</td>
</tr>
<tr>
<td>MSH2</td>
<td>55</td>
<td>16 (29%)</td>
</tr>
<tr>
<td>MSH6</td>
<td>4</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>PMS2</td>
<td>2</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

¹Win, Annals of Surgical Oncology, 2013
Pros and Cons of LAR and Surveillance Colonoscopy

- Surveillance reduced risk of CRC by 62%\(^1\)
- Missed adenomas reported as high as 55%\(^2\)
- Interval cancers, 20-35%\(^3\)
- High likelihood of metachronous cancer to be at an early stage, 72% TNM stage\(^1\)\(^4\)

\(^1\)Jarvenin, Gastroenterology, 2000
\(^2\)Stoffel, Cancer Prevention Research, 2008
\(^3\)Mecklin, Gastroenterology, 2007
\(^4\)Win, Annals of Surgical Oncology, 2013
Decision Analysis in the Surgery of CRC due to MMR Gene Defect

- Life Expectancy (LE) for surgical options by age

<table>
<thead>
<tr>
<th>Surgical Treatment</th>
<th>LE for dx at age 27 (yrs)</th>
<th>LE for dx at age 47 (yrs)</th>
<th>LE for dx at age 67 (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemicolecotomy/segmental resection</td>
<td>31.6</td>
<td>20.6</td>
<td>10.5</td>
</tr>
<tr>
<td>Subtotal colectomy</td>
<td>33.9</td>
<td>21.6</td>
<td>10.8</td>
</tr>
<tr>
<td>TPC</td>
<td>34.8</td>
<td>21.9</td>
<td>10.8</td>
</tr>
</tbody>
</table>

More extensive surgery provides larger benefit for earlier ages of onset and lesser stages of disease

¹De Vos tot Nederveen Cappel, Gut, 2003
# Surgical guidelines for Lynch Syndrome

<table>
<thead>
<tr>
<th>Source</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCRS, Practice Parameters, 2003</td>
<td>Offer LAR or TPC with IPAA to patients presenting with Rectal Ca</td>
</tr>
<tr>
<td>Mallorca Group, Gut, 2013</td>
<td>Subtotal over partial colectomy recommended, no mention of Rectal Ca</td>
</tr>
<tr>
<td>NCCN Guidelines, 2015</td>
<td>“Update in Progress”</td>
</tr>
<tr>
<td>Multi-Society Task Force, Diseases of the Colon and Rectum, 2014</td>
<td>Discuss TPC + IPAA with patient, consider less extensive resection for older patients</td>
</tr>
</tbody>
</table>
Summary

- Rectal CA not uncommon as a first cancer for patients with Lynch Syndrome or Amsterdam Criteria
- Surgical options include local resection alone (LAR) or LAR plus prophylactic resection of the whole colon (TPC with IPAA)
  - In lieu of reliable predictive factors for development of metachronous cancer in the remaining colon, surgical decisions must occur on a case-by-case basis
- Rectal Cancer Stage, location, preoperative sphincter function, prior resections, patient age, compliance, etc need to be considered.
What factors need to be present to tip the balance in favor of a Total Proctocolectomy and IPAA?
What surgery do you recommend?

Rectal Cancer + Lynch Syndrome

Gradations of Metachronous Colon Cancer Risk

Low risk = LAR

High risk = TPC-IPAA
What surgery do you recommend?

Rectal Cancer

+ Lynch Syndrome

+ Synchronous Colonic Adenomas
What surgery do you recommend?

Rectal Cancer
+
MSI
What surgery do you recommend?

Rectal Cancer
+
Lack of MMR on IHC