Colon Cancer
Surgical Standard of Care and Operative Techniques

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How much colon should be resected?
• Classic teaching 5 cm margin on either side of tumor
• Concern regarding microscopic intramural spread
• Shrinkage of margins 45%
  o Immediate contraction 29%
  o Shrinkage in formalin 24%

Which lymph nodes should be removed?
• Lymphatic drainage of colon follows mesenteric blood supply
• Drainage: epicolic, paracolic, intermediate, principal and retroperitoneal LN
• Drainage affected by location of tumor
  o Between primary blood vessels
  o Blockage of lymphatics
• Prognosis affected by resection of unaffected LN but not affected LN

Lymph node metastasis

Sternberg A J Surg Onc 2008
How many lymph nodes should be removed?

- LN retrieved is considered a quality measure
- 1996-1997 15% hospitals compliant with 12 LN retrieval measure
- 2004-2005 compliance only 38%
- Most compliant were NCI designated cancer centers (78%) compared to academic (52%), VA (53%) or community (33%)
- Many patient-level studies suggest that retrieval of 12 LN confers survival advantage
- However, use of national database for a hospital-level study suggests that hospitals with higher LN retrieval rates after colectomy for colon cancer do not have better survival rates

Does LN harvest affect stage and prognosis?

SEER Database 1998-2008
86,3094 patients with colon cancer
Evaluate LN number with positivity and hazard of death

Parsons JAMA 2011

What about radial margins?

Guideline for Optimization of Colorectal Cancer Surgery and Pathology

Systematic Review of colorectal resection margins and lymph nodes
107 articles
Majority of poor quality
What about laparoscopic resections?

- Localization critical
- Colonoscopy for cecum with landmarks or verification by CT
- Tattoo at time of colonoscopy or even repeat procedure to tattoo may be indicated
- Distant disease
  - Can assess peritoneal and liver surfaces
  - Cannot palpate for deeper parenchymal tumors
  - Always need preoperative CT Scan
  - Laparoscopic ultrasound/guided biopsy

Published Trials

- NIH sponsored COST trial
  - Prospective Randomized Controlled Trial
  - Multicenter- 48 institutions
  - 872 patients
  - Early follow up reported (NEJM 2004)
  - 5 yr follow up reported (Ann Surg 2007)
  - Planned follow-up 8 years
- Six other international trials
  - COLOR (RCT)
  - LCSSG (Prospective cohort)
  - CLASSIC

Does laparoscopy affect resections?

<table>
<thead>
<tr>
<th></th>
<th>Laparoscopic</th>
<th>Open</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowel Length (cm)</td>
<td>26</td>
<td>27</td>
</tr>
<tr>
<td>Proximal Margin (cm)</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>Distal Margin (cm)</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Mesenteric length (cm)</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td># of Lymph Nodes</td>
<td>12</td>
<td>13</td>
</tr>
</tbody>
</table>
Wound / Port Site Recurrences

<table>
<thead>
<tr>
<th>Author</th>
<th>Yr</th>
<th>N</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berends</td>
<td>94</td>
<td>14</td>
<td>21.0</td>
</tr>
<tr>
<td>Drouard</td>
<td>95</td>
<td>507</td>
<td>2.4</td>
</tr>
<tr>
<td>Boulez</td>
<td>96</td>
<td>117</td>
<td>2.5</td>
</tr>
<tr>
<td>Franklin</td>
<td>96</td>
<td>191</td>
<td>0</td>
</tr>
<tr>
<td>Melotti</td>
<td>99</td>
<td>163</td>
<td>1.2</td>
</tr>
<tr>
<td>Schiedeck</td>
<td>00</td>
<td>399</td>
<td>0.2</td>
</tr>
<tr>
<td>Lujan</td>
<td>02</td>
<td>102</td>
<td>2</td>
</tr>
<tr>
<td>Lacy</td>
<td>02</td>
<td>111</td>
<td>0.9</td>
</tr>
<tr>
<td>COST</td>
<td>04</td>
<td>408</td>
<td>0.5</td>
</tr>
<tr>
<td>CLASSICC</td>
<td>07</td>
<td>526</td>
<td>2.5</td>
</tr>
</tbody>
</table>

COST Trial Cumulative Recurrence Rate

- Nelson NEJM 2004
- Fleshman Ann Surg 2007

COST Trial Overall Survival

- Nelson NEJM 2004
- Fleshman Ann Surg 2007

COLOR Trial

- Overall Survival
  - 3 yr Follow Up
  - 5 yr Follow Up

540 pts each arm

Bonjer et al. Lancet 2009
CLASSICC Trial

Table 3. 3-Year Local and Distant Recurrence Rates and Differences in Rates Between the Two Groups for Patients With Curative Colon Cancer Surgery

<table>
<thead>
<tr>
<th></th>
<th>Open (%)</th>
<th>Laparoscopic (%)</th>
<th>% Difference</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local recurrence rate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>7.9</td>
<td>8.6</td>
<td>-8.8</td>
<td>0.7 to 2.8</td>
<td>0.56</td>
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<tr>
<td>Patients with colon cancer</td>
<td>6.0</td>
<td>7.3</td>
<td>-1.3</td>
<td>0.7 to 3.7</td>
<td>0.40</td>
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<tr>
<td>Patients with rectal cancer, AR and APR</td>
<td>8.1</td>
<td>9.7</td>
<td>8.3</td>
<td>7.3 to 9.3</td>
<td>0.09</td>
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<tr>
<td>Distant recurrence rate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>14.3</td>
<td>18.2</td>
<td>-8.8</td>
<td>3.4 to 8.8</td>
<td>0.04</td>
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<tr>
<td>Patients with colon cancer</td>
<td>12.9</td>
<td>15.5</td>
<td>-1.6</td>
<td>0.0 to 6.0</td>
<td>0.01</td>
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<tr>
<td>Patients with rectal cancer, AR and APR</td>
<td>14.6</td>
<td>16.2</td>
<td>8.2</td>
<td>13.0 to 7.9</td>
<td>0.08</td>
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</tbody>
</table>

Abbreviations: AR, anterior resection; APR, abdominopelvic resection.


CLASSICC Trial Overall Survival

Colon Cancer: Open 67% vs Lap 68%

Meta-analysis of RCTs

All Included Studies

Table 1. Summary of Included Randomized Controlled Trials and Oncologic Outcomes Reported

<table>
<thead>
<tr>
<th>First author or study name</th>
<th>Year</th>
<th>n</th>
<th>Follow-up &gt;10 mo</th>
<th>Cancer-related survival</th>
<th>Cancer recurrence</th>
<th>Lymph node status</th>
<th>Margin status</th>
<th>Wound infection</th>
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<tbody>
<tr>
<td>Lap et al.**</td>
<td>2002</td>
<td>95</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>CLASSICC**</td>
<td>2005</td>
<td>798</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
No Difference in LN retrieval

No Difference in Recurrence Rate

No difference in Cancer-related Death

Meta-analysis of Largest RCTs

- Databases of Barcelona, COST, COLOR and CLASICC
- All patients at least 3 years of FU
- 44 institutions in North America
- 48 institutions in Europe
- Primary outcome: overall and disease free survival

Bonjer et al Arch Surg 2007
Assessment of LN harvest and resection

- COST trial analyzed the effect of LN, length of resection, mesenteric length and survival in setting of many surgeons who were credentialed and video audited for adherence to technical standards.
- No difference in survival based on LN retrieval or other anatomic factors.
- There was variability in the surgeons in terms of case volume but no effect on overall survival.
- Technical credentialing can help to standardize oncologic resection regardless of case volume.

Mathis et al Ann Surg 2013
Quality of Life Measures

- Part of NIH trial
- 449 patients with colon cancer
  - Inclusion criteria
    - Adenocarcinoma of only a single colon segment
    - >18 yo
  - Exclusion criteria
    - Transverse colon or rectal cancer
    - Obstructed/perforated colon cancer
    - Metastatic disease
    - Scars/adhesions that would prevent laparoscopic surgery
    - Concurrent or previous malignant tumor
    - ASA physical status classification of IV or V
    - Unable to speak English, cognitive impairment, no telephone (for QOL)

Quality of Life Measures

- Scores on the Symptoms Distress Scale (SDS)
  - 13-item scale
  - Nausea, appetite, insomnia, pain, fatigue, bowel, concentration, appearance, breathing, outlook, and cough
- Quality of Life Index
  - 5-item scale
  - Activity, daily living, health, support, and outlook
- Single-item Global Rating Scale
  - “On a scale of 0-100, with 0 being death, and 100 being excellent health, which number would you say best describes your state of health over the past 2 weeks?”

Symptom Distress Score

No significant difference in distress scores at 2 days, weeks or months

Single-Item Global Rating Scale
Mean scale at two weeks for Lap vs Open: 76.9 vs 74.4 (P=0.009)
All other parameters were equivalent
### Summary

- Surgery for colon cancer has advanced technologically but oncologic principles are paramount to achieving good outcomes.
- More attention is being paid to the specimen as opposed to how it was removed.
- Difficulties with laparoscopy for colon surgery have diminished with new equipment and experience.
- Newer technologies such as Robotics, single site laparoscopy and NOTES continue to be tested but have not yet achieved widespread use.