Lymph Node Examination Rates in Colorectal Cancer: More=Better

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PGY-1
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Colorectal Carcinoma Importance

- Most common GI malignancy in US
- Second most common cause of CA death
- Surgery is the only curative option
- Adjuvant chemo based on staging
- Lymph node analysis important in staging
Colorectal Carcinoma (CRC): Staging Systems

- TNM staging system preferred by ACS
- Stage of resected tumor is the most important prognostic factor
Important Distinction

• N1 typically offered adjuvant chemotherapy, N0 typically not

• Chemo is toxic, expensive, time consuming, and emotionally difficult

• We want to treat all who need it and none who do not
Accuracy of Determining Nodal Status

- Secondary Analysis of INT0089 (prospective multicenter trial of 1585 pts to evaluate effects of chemo)

A mathematical model was used to estimate the true underlying number of involved mesenteric lymph nodes in patients undergoing right or left hemicolecction. This model relies on two quantities:

1. The probability of having $M$ involved nodes, $q(M)$, where $q(M) = \frac{\text{number of patients with } M \text{ involved nodes}}{\text{total number of patients in group}}$.

2. The probability of $m$ nodes observed positive in a sample size of $n$ resected, $P(n,m,N,M)$. $N$ represents the total number of lymph nodes with $M$ nodes positive. $P(n,m,N,M)$ is obtained from the hypergeometric distribution, where

$$P(n,m,N,M) = \frac{M!}{m!(M-m)!(n-m)!(N-M) - n + m!} \cdot \left(\frac{N!}{n!(N-n)!}\right)$$
# Accuracy of Determining Nodal Status

**TABLE 3.** Number of nodes to accurately predict nodal negativity

<table>
<thead>
<tr>
<th>Tumor stage</th>
<th>Probability 85%</th>
<th>Probability 50%</th>
<th>Probability 25%</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1/T2 right colon</td>
<td>42</td>
<td>36</td>
<td>25</td>
</tr>
<tr>
<td>T1/T2 left colon</td>
<td>44</td>
<td>39</td>
<td>30</td>
</tr>
<tr>
<td>T3 right colon</td>
<td>40</td>
<td>29</td>
<td>13</td>
</tr>
<tr>
<td>T3 left colon</td>
<td>40</td>
<td>23</td>
<td>&lt;10</td>
</tr>
<tr>
<td>T4 right colon</td>
<td>31</td>
<td>&lt;10</td>
<td>&lt;10</td>
</tr>
<tr>
<td>T4 left colon</td>
<td>29</td>
<td>&lt;10</td>
<td>&lt;10</td>
</tr>
</tbody>
</table>
Accuracy of Determining Nodal Status

- Overall Survival in Node Negative Patients

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Recommended

- **Recommended Minimum Number of Lymph Nodes in Colorectal Specimens**

<table>
<thead>
<tr>
<th>Authors</th>
<th>No. of Nodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fielding et al(^1)</td>
<td>12</td>
</tr>
<tr>
<td>Goldstein et al(^4)</td>
<td>17-20</td>
</tr>
<tr>
<td>Wong et al(^5)</td>
<td>14</td>
</tr>
<tr>
<td>Ratto et al(^6)</td>
<td>13</td>
</tr>
<tr>
<td>Compton(^7)</td>
<td>12</td>
</tr>
<tr>
<td>Tepper et al(^8)</td>
<td>14</td>
</tr>
<tr>
<td>Prandi et al(^9)</td>
<td>&gt;7</td>
</tr>
<tr>
<td>LeVoyer et al(^10)</td>
<td>20</td>
</tr>
<tr>
<td>Swanson et al(^11)</td>
<td>13</td>
</tr>
</tbody>
</table>

- **Current consensus: 12 LN per specimen**
Probability of Finding Positive Lymph Nodes

Turner, John and Robin T.
Probability of Metastases

Prospective Multicenter Trial of Staging Adequacy in Colon Cancer

• “Intuitively, the more nodes that are recovered the greater the likelihood of discovering an occult metastasis”

• Approximately 25-30% of node-negative CRC patients have fatal recurrence

• *Why*? Understaging
  – Aberrant drainage pathways
  – Missed micrometastases
  – Skipped Nodes

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Prospective Multicenter Trial of Staging Adequacy in Colon Cancer

• Methods
  – 132 Pts with Stage I and II CRC at 5 centers
  – Laparotomy or Laparoscopy
  – Lymphatic Mapping
  – En Bloc Resection
  – H&E Staining, CK-IHC Stains
  – Analysis
Prospective Multicenter Trial of Staging Adequacy in Colon Cancer

• Preliminary Conclusions
  – Micromets and/or isolated tumor cells in 24% of pts who otherwise may have been considered node negative
  – Current techniques not adequate
    • IHC and PCR not cost effective and unproven
  – Need better techniques so chemo can be given to all and only all who need it.
Aberrant Lymph Nodes

• Nodes identified by SNL mapping as outside the limits of the initially planned resection

• Includes nodes at the base of the mesentery

• Understaged…
Why Understaging is Bad

\textbf{Figure 4} Shown are 5-year survival rates for cases of colon cancer diagnosed in 1,735 U.S. hospitals in 1995 and 1996.
Why Understaging is Bad

Figure 6  Shown are 5-year survival rates for cases of stage III colon cancer diagnosed between 1987 and 1993, stratified according to stage III subgroups established by 6th edition of AJCC Staging Manual. 38

Brenner, Bruce and David Ota.
ACS: Surgery Principles and Practice, 2005
The Prognosis of T3N0 Colon Cancer

• 5 year, 35,787 pt prospective study to evaluate whether the number of examined lymph nodes is prognostic.

• Analyzed NCDB using AJCC staging scheme, 5-year relative survival rate
The Prognosis of T3N0 Colon Cancer

FIG. 1. Proportion of T3N0 colon cancer cases with at least one positive regional lymph node, by the number of regional lymph nodes examined.

The Prognosis of T3N0 Colon Cancer

The Prognosis of T3N0 Colon Cancer

FIG. 4. Kaplan-Meier 5-year survival curves of surgically resected T3N0 colon cancers, by the number of regional lymph nodes pathologically examined.
What to do

• More nodes = more accurate
• More nodes = more cure
• More extensive nodal harvest is easy
• What about Grandma?
References