Number of Nodes Examined and Staging Accuracy in Colorectal Carcinoma

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**Purpose:** The objective of this study was to determine the number of nodes that need to be examined to accurately reflect the histology of the regional lymphatics in colorectal carcinoma.

**Patients and Methods:** Patients undergoing curative resection for T2 and T3 colorectal cancer between 1992 and 1996 were reviewed. Pathologic data from these patients were entered into a computerized database for storage, retrieval, and analysis. The major outcome measured was the number of nodes that need to be examined to achieve a node-positive rate consistent with that reported in the National Cancer Data Base (NCDB) report.

**Results:** The number of nodes examined ranged from 0 to 78 (mean, 17 nodes). Node-negative patients had fewer nodes examined (mean, 14 nodes) than node-positive patients (mean, 20 nodes; \( P = .003 \)). The entire sample had a node-positive rate of 38.8% (95% confidence interval [CI], 32% to 45.5%), not statistically different from that in the NCDB report. When at least 14 nodes were examined, the percent of patients with at least one positive node was 33.3% (95% CI, 24.6% to 42.3%), not statistically different from the NCDB report.

**Conclusion:** In a sample of patients statistically similar to the sample in the NCDB report, the examination of at least 14 nodes after resection of T2 or T3 carcinoma of the colon and rectum will accurately stage the lymphatic basin.

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Since 1992, the Department of Pathology at the Queen’s Medical Center (Honolulu, HI) has used a computerized synoptic reporting method to summarize the histologic characteristics of all cancer.
resections. In addition to the histologic type and grade, the size of the tumor, depth of invasion, the presence or absence of invasion into contiguous structures, and the total number of lymph nodes, along with the number of lymph nodes involved with metastatic disease, are routinely recorded. This database allows for easy and accurate retrieval of patients based on tumor-node-metastasis staging criteria.

Because the presence of either locally advanced disease or a notably superficial tumor (T1) might have led to a surgical approach that differed from standard recommendations, only patients with T2 or T3 tumors of the colon or rectum during the period between January 1992 and September 1996 were retrieved from the computerized database of the Department of Pathology at the Queen’s Medical Center and reviewed. Two hundred forty-two patients were initially identified. To exclude the possibility that the presence of metastatic disease might have resulted in more limited surgical resections, tumor-node-metastasis stage was reviewed at the time of diagnosis, and patients with M1 disease were subsequently excluded from this analysis. A total of 196 patients, who presumably underwent resections with curative intent, were retrospectively analyzed to determine the number of nodes removed.

Pathology
Specimens were delivered to the Department of Pathology in the fresh state. The location of the primary tumor was recorded based on the surgeon’s description of the primary site, and the specimen was grossly examined before overnight fixation in formaldehyde. After overnight fixation, the specimen was cut. Lymph nodes were obtained as follows: The peritoneum overlying the mesentery was incised and examined by careful palpation for the presence of lymph nodes. Any firm tissue remaining after gentle pressure on the mesenteric fat was isolated from the surrounding mesenteric fat and sent as a lymph node specimen for histologic examination by routine hematoxylin and eosin staining. A single section of the lymph node was examined routinely.

Specimens were categorized by site of primary tumor, length of bowel removed, number of nodes removed, and number of positive nodes in the specimen. All lymph nodes were measured and the length of the node was used to determine the size of the lymph node.

Statistical Analysis
The data were analyzed using independent sample t tests, the Mann-Whitney test (a nonparametric test), the binomial test for proportions, and 95% confidence intervals for proportions. The level of significance (alpha) was set to 0.05 for all tests and confidence intervals. SPSS 7.5 for Windows (SPSS, Inc, Chicago, IL) was the statistical software used.

RESULTS
Table 1 summarizes the anatomic distribution of the primary lesions. The majority of primary tumors were located in the right colon and sigmoid colon, with decreasing numbers occurring in the transverse and descending colon and rectum. Because the length of the segment of bowel removed might reflect the extent of mesenteric lymphadenectomy, the length of specimen at the time of gross examination before overnight fixation was examined. There was substantial variation in the specimen length received. The length of the specimen received varied from 10 cm to 114 cm, with a mean length of bowel removed of 23 cm.

There was wide variability in the number of lymph nodes recovered from each specimen. The number of lymph nodes recovered from these specimens ranged from zero to 78 (mean, 17 nodes). Two percent of specimens had no identifiable lymph nodes, whereas 24% had fewer than 10 lymph nodes recovered from the specimen (Fig 1). The number of lymph nodes recovered varied with the anatomic site of the primary tumor (Table 1). The mean number of nodes recovered was highest in the ascending and descending colon (mean, 20 nodes) and lowest in the rectum (mean, 11 nodes).

Those patients who were found to be node-negative had fewer nodes examined on average (mean, 14 nodes) than patients who were node-positive (mean, 20 nodes; P = .003). In patients who were node-positive, 25% had 10 or fewer nodes removed, 50% had 17 or fewer nodes removed, and 90% had 35 nodes or fewer nodes removed (Fig 2). In contrast, of patients who were found to be node-negative, 25% had seven or fewer nodes removed, 50% had 13 or fewer nodes removed, and 90% had 30 or fewer nodes removed.
fewer nodes removed, and 90% had 28 or fewer nodes removed, which suggests that the more nodes removed the more accurate the staging. However, the number of node-negative patients who are false-negative, if any, is unknown.

Because the size of the lymph nodes might have led to some nodes being more easily identifiable than others, we examined the difference in size between specimens that were node-positive and specimens that were node-negative. The average size of the nodes removed in node-negative specimens was 3.6 mm (SD, ± 2.4 mm), whereas the average size of nodes in node-positive specimens was 4.0 mm (SD, ± 3.0 mm).

To determine the minimal number of nodes that need to be examined to accurately characterize the histology of the regional lymphatic basin, we compared our study population with that reported by the National Cancer Data Base (NCDB),16 in which we estimated that approximately one third of patients with T1, T2, and T3 tumors were found to be node-positive. In our study sample, 76 (38.8%) of the 196 patients had at least one positive node (95% confidence interval [CI], 32% to 45.5%), which does not represent a statistically significant difference from the estimated node-positive rate of the NCDB report (P = .954).

We then determined the minimal number of nodes that would need to be examined to approximate the estimated node-positive rate observed in the NCDB report. We defined groups of patients based on the number of nodes removed and estimated the proportion of patients with at least one positive node in the group. Each succeeding group included patients from the previous group. Table 2 summarizes the percent of node-positive cases by number of nodes examined along with the 95% CI. As an increasing number of nodes were removed, we observed an increase in the percent of node-positive cases, with a narrowing of the 95% CI. The data show that, after removal of 14 nodes, the proportion of node-positive patients was 33.3% (95% CI, 24.6% to 42.3%), which is consistent with the NCDB observations. This proportion did not improve substantially when the number of nodes examined was increased beyond 14.

**DISCUSSION**

The single most powerful prognostic factor in apparently localized carcinoma of the colon and rectum is the presence or absence of nodal metastases at the time of surgical resection of the primary tumor.3-5 In addition to the prognostic significance of nodal metastases, the presence of tumor in the regional node basin is an important criterion for a recommendation for adjuvant systemic therapy.2 This study examined patients who underwent resection of T2 and T3 carcinoma of the colon and rectum with curative intent to determine the number of nodes that need to be examined to obtain a node-positive rate consistent with that observed in the NCDB report. Our analysis suggests that the minimum number of nodes that need to be examined is 14 and that the examination of fewer nodes could lead to a potentially substantial, lower node-positive rate that would not be consistent with that identified in the NCDB report.

The comparison with the NCDB report warrants special comment. Although not without its detractors, the NCDB report does represent a mechanism to standardize data for major cancer sites, including that of the colon and rectum, and comprises 52% of the estimated new cancer cases in the United States. Because of the number of cases analyzed and the number of hospitals involved, the majority of which represent nonacademic referral centers, it is reasonable to presume that the NCDB is representative of the surgical care and pathologic analysis and reporting most commonly performed in community hospital settings. For this reason, the NCDB report represents a particularly useful benchmark.

The present study demonstrates that the greater the number of nodes examined yields a greater number of node-positive patients. Node-negative specimens had fewer nodes examined than node-positive specimens (P = .003). As the number of nodes examined increased, the percent of patients identified as harboring metastatic disease increased.

<table>
<thead>
<tr>
<th>No. of Nodes Examined</th>
<th>Node-Positive Patients (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 8</td>
<td>26.0</td>
<td>15.1-38.0</td>
</tr>
<tr>
<td>≤ 10</td>
<td>27.4</td>
<td>17.9-38.0</td>
</tr>
<tr>
<td>≤ 12</td>
<td>28.9</td>
<td>19.7-38.9</td>
</tr>
<tr>
<td>≤ 14</td>
<td>33.3</td>
<td>24.6-42.3</td>
</tr>
<tr>
<td>≤ 16</td>
<td>32.2</td>
<td>24.1-40.7</td>
</tr>
<tr>
<td>≤ 18</td>
<td>30.2</td>
<td>22.6-38.3</td>
</tr>
<tr>
<td>≤ 20</td>
<td>33.3</td>
<td>25.7-41.2</td>
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This might result from the fact that node-positive specimens are more likely to have larger nodes, which, therefore, leads to an increased yield, whereas node-negative specimens have smaller nodes, which are more difficult to recover. However, although node-positive specimens had larger nodes, on average, than node-negative specimens, the difference was not statistically significant. This suggests that factors other than the presence of nodal metastases alone contribute to the identification of regional lymph nodes.

The observation that an increased number of nodes examined yields an increased number of node-positive specimens confirms the conclusions of Goldstein et al. Their results demonstrated that, in patients who were node-positive, the percent of individuals identified as node-positive continued to increase until 17 to 20 lymph nodes were examined, which led to their recommendation that at least 17 nodes need to be examined and the examination of more than 17 nodes would be preferred. Scott and Grace used clearing techniques for lymph node dissection and found that the examination of a minimum of 13 lymph nodes would detect 90% of patients with nodal metastases. However, to make recommendations regarding the number of nodes that need to be examined in colorectal carcinoma based solely on those specimens in which lymph node metastases were present would overestimate the number of nodes required, because it fails to take into account those individuals who were truly node-negative despite the limited number of nodes that may have been removed.

To address this issue, we assumed that our study sample included patients who were truly without nodal metastases. Furthermore, because our study sample size of 196 patients with colorectal carcinoma is a sufficient size to detect a 10% or greater deviation from the NCDB data, we were able to demonstrate that our sample was similar to the national population with respect to the node-positive rate. Although our node-positive rate was slightly higher than that observed in the NCDB study, our 95% CI for the node-positive rate indicated no statistically significant difference between the two groups of patients.

After demonstrating that a proportionally equivalent number of patients with nodal metastases were in our study sample as in the NCDB, we proceeded to analyze our sample based on an increasing number of nodes removed, estimating the proportion of patients with at least one positive node and computing a 95% CI for this proportion. In this fashion, we identified the first group in which the proportion of node-positive patients was close to the expected (NCDB) proportion and for which the 95% CI had a reasonable range. On the basis of this analysis, we can expect that, in a group of patients whose nodal involvement is unknown, the minimum number of nodes that need to be examined to detect a number of patients with nodal metastases that approximates the nodal metastases proportion of the NCDB data is 14.

The Working Party Report to the World Congress of Gastroenterology recommended that a minimum of 12 nodes be recovered and examined before the lymphatic basin is considered free of metastases. The estimates of our report and the report by Scott and Grace are consistent with the Working Party Report but somewhat lower than that of Goldstein et al. Scott and Grace used clearing techniques for the lymph node dissection, which resulted in higher node recovery and, therefore, a more thorough examination of the available pathologic material. As a result, their data would be anticipated to have fewer false-negative results. This is supported by the observation that the mean number of nodes recovered in the Scott and Grace report was 18.5 in comparison with only 9.8 recovered in the Goldstein et al report. The mean number of nodes removed in our study was 17, a number nearly identical to that reported by Scott and Grace, which suggests that careful gross pathologic examination in the fashion described in Patients and Methods is adequate to identify nodes.

Our results were derived from an analysis of surgical outcomes from a large number of surgeons practicing in a private teaching hospital setting. Therefore, our study is particularly relevant because the surgical approaches and techniques used and the variations among surgeons are presumably representative of most large community hospitals and the pathologic evaluation the hospitals use. In any case, surgeons should use techniques that obtain the maximum number of nodes, and pathologists should strive to recover a minimum of 14 nodes to accurately stage the regional lymphatic basin in carcinoma of the colon and rectum.

REFERENCES

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