LYMPH NODE HARVEST IN RESECTED COLON CANCER SPECIMENS (L.N)

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Keywords: colon cancer, lymph nodes (LN), pathology procedures

Abstract: Background: Identification ≥12 LN in resected colon cancer specimens has been considerate as a quality indicator. In patients with resected colorectal cancer, LN the involvement has particular importance for patient prognosis and adjuvant therapy. Methods: The I-st Surgical Clinic cancer registry was used to identify patients diagnosed with colon cancer. The proportion of colon cancer specimens which ≥12 were identified was determine by anatomic location, patients ages and stage of disease. Survival was correlated with stage and while ≥12 LN were identified. Results: Pathology procedural change in 1998 were associated with a increase in the average number of LN, identified from 6 to 14 (p<0,001). The analysis was limited to 287 patients who suffered surgical resection of colon adenocarcinoma during 1998-2009. Identification of ≥12 LN varied from 57% to 83% by 7 anatomic location (p<0,001), from 65% to 75% during 5 years (p=0,27) from 59% to 73% by 4 general stage of disease (p=0,04). Identification ≥12 LN was associated with better survival for patients with stage I (p=0,6) and stage II (p=0,21). Conclusions: Anatomical location, colorectal surgical training were strongly correlated with the number of LN identified.

INTRODUCTION

Key words: colon cancer, lymph nodes (LN), pathology procedures.

The accuracy of LN staging depends on the adequate of surgical resection and identification of LN metastases by the pathologist.

Stage III colon cancer patients with metastases to regional LN have worse survival than stage I and II patients without metastases and randomized trials prove that such patients benefit from adjuvant systemic therapy (1-5). The sentinel lymph node approach has not proved to be as useful in the staging of colon cancer as in melanoma breast cancer (6-9).

Identification and evaluation of all LN in an appropriately resected specimen is critical for accurate staging to direct therapy (10), and large randomized trials (10, 11, 12, 13, 14, 15) and single institution studies (16-25), demonstrate that the number of LN identified in resected colon cancer specimens is predictive for survival.

Various studies support examining 7(16-17), 9(18-20), 11(21) or 12(12, 15, 22, 26, 27) LN microscopically.

Many trials that emphasized lower thresholds for enumeration of LN included rectal cancer which anatomically is associated with fewer LN and which increasingly is managed with preoperative radio-chemotherapy.

In recent years, several National Institutes, Societies of Surgery, Oncology have endorsed identification of ≥12 LN from resected colon cancer specimens who represent a quality performance indicator (28).

In this analysis we search to determine the consequences of LN enumeration over time the predictive ability of the 12 LN thresholds for survival in our pathology and the association of this 12 LN thresholds with several variables including anatomical location, patient age and stage of disease.

THE AIM OF THE PAPER

Identification ≥12 LN in resected colon cancer specimens has been considerate as a quality indicator. In patients with resected colorectal cancer, LN the involvement has

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particular importance for patient prognosis and adjuvant therapy.

MATERIALS AND METHOD
We analyzed data from the cancer registry of the 1st Surgical Clinic a 287 patients with colon cancer. This registry includes follow-up in information from 1998 at 2009. Variables included information about diagnosis, patient age at diagnosis, the surgical procedure that was performed, anatomic location of the cancer, histology, tumor size, number of LN identified, number of LN positive for cancer, general stage (local, regional or to distance, TNM stage/(A7CC). Rectal cancer was excluded.

Data set for analysis
Patients with rectal cancer were excluded. Only the patients with colon cancer as the principal disease were included in this study. All statistical measures of probability had 2 tailed. The Q-square test was used for comparison of multiple proportions. Methods were compared using the ‘T’ test. Survival curves were compared using the log-rank test.

RESULTS
Between 1998-2005 we had 2 different protocols for identification of LN by pathologist. Between 2003-2005 we used the intra-operative in-vivo and ex-vivo sentinel LN identification that facilitate identification of smaller LN.

The average number of LN identified increase from 6±3 during 1998-2003, to 14±5 during 2003-2009 the proportion of patients diagnosed with positive LN increased from 31.6% during 1998-2003 to 37% during 2003-2009 (p=0,29). There was no change in the proportion of patients diagnosed with just one positive LN (10% versus 10.6%).

Surgeon performing resections
The median numbers of LN identified in colon cancer specimens by surgeons ranged from 12 to 19, the proportions of resections with 12 or more LN identified ranged from 51% to 80%. The surgeon with the highest volume of resections who completed a follow up in colorectal surgery had the higher average number of LN found in his resections.

Anatomical location within the colon
The probability of identifying 12 or more LN varied with the anatomic site of the resected colon cancer (table1).

Table no. 1. Numbers of LN identified in resected colon cancers

<table>
<thead>
<tr>
<th>Anatomic location</th>
<th>No of cases</th>
<th>Average no of nodes</th>
<th>Median no of nodes</th>
<th>% with 12 or more nodes identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cecum</td>
<td>148</td>
<td>12.5±7</td>
<td>14</td>
<td>64%</td>
</tr>
<tr>
<td>Ascending colon</td>
<td>124</td>
<td>16±4</td>
<td>17</td>
<td>80%</td>
</tr>
<tr>
<td>Hepatic flexure</td>
<td>34</td>
<td>15±7</td>
<td>15</td>
<td>73%</td>
</tr>
<tr>
<td>Transvers colon</td>
<td>45</td>
<td>14±6</td>
<td>12</td>
<td>64%</td>
</tr>
<tr>
<td>Splenic flexure</td>
<td>18</td>
<td>14±7</td>
<td>13</td>
<td>72%</td>
</tr>
<tr>
<td>Descending colon</td>
<td>30</td>
<td>14±7</td>
<td>12</td>
<td>56%</td>
</tr>
<tr>
<td>Sigmoid colon</td>
<td>169</td>
<td>12±8</td>
<td>12.8</td>
<td>56%</td>
</tr>
</tbody>
</table>

Differences among all sites in percentage with 12 or more nodes is significant p=0.0004. Right sided colon lesions treated with right hemicolectomy, extended hemicolectomy or subtotal colectomy, had a higher average number of nodes (15±7, vs 12±6) p=0.0028 and a higher percentage of resections with 12 or more LN compared to left-sided lesions treated by left hemicolectomy (258/359 vs 110/197, p=0.001).

The average and median numbers of LN were ≥12 for all anatomic sites, but the range was 57% to 84% for resections in which ≥12 LN were identified. The highest average of LN were identified in ascending colon resections, a figure that was higher than cecum (p<0.001), sigmoid colon (p<0.001), and descending colon (p=0.023) but not higher than transverse colon (p=0.11) or splenic or hepatic flexures.

The average numbers of LN identified and proportion with fewer than 12 LN identified did not differ by procedure for other cecal or ascending colon location.

Patients age
There were differences in LN identifications by age of the patients. The highest average (16.8) and median numbers of LN were identified in resections from patients younger than 50 years. In patients < 60 years of age it’s more highly to have ≥12 LN identified, but there were no differences between any other pairs of age groups.

Disease stage
There were more LN identified and higher proportion of resections, containing ≥12 LN from patients with regional disease (T3 or T4 local extension and/or LN metastasis), than cases who had other local disease (T1 or T2) or distant metastasis. Difference among identified sites in percentage with ≥12 nodes by general stage is significant (p=0.004).

Table no. 2. Number of LN identified in resected colon cancer with fewer than 12 LN identified

<table>
<thead>
<tr>
<th>General stage</th>
<th>No of cases</th>
<th>Average no of nodes</th>
<th>Median no of nodes</th>
<th>% with ≥12 LN identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local(T1orT2)</td>
<td>120</td>
<td>14±5</td>
<td>12</td>
<td>58%</td>
</tr>
<tr>
<td>Local extension (T3,T4)</td>
<td>163</td>
<td>17±5</td>
<td>16</td>
<td>72%</td>
</tr>
<tr>
<td>Positive nodes(N+)</td>
<td>182</td>
<td>16±2</td>
<td>15</td>
<td>71%</td>
</tr>
<tr>
<td>Distant metastasis(M+)</td>
<td>104</td>
<td>15±2</td>
<td>13</td>
<td>60%</td>
</tr>
</tbody>
</table>

DISCUSSIONS
Our study confirms that the numbers LN identified in resected colon cancer specimens, can be greatly increased by changes in pathology department procedures (25,27). It also shows there is evident variation in the number of LN by anatomical region, age, stage of disease.

Identification of ≥12 LN in resected colon cancer specimens was predictive for results in stage I and II (30).

Our study confirms that the numbers of LN identified in colon cancer resection can be increased with intra-operative lymphographic with in-vivo and ex-vivo determination, with a standard protocol was include removing the mesentery, fixing it in 10% formalin and identifying LN by visual inspection, manual palpation.

With this protocol the median number of LN in resected samples increased from 6-7 to 14 during 2003-2009.

The extend of LN dissection is determinate by bloc-resection of the lymphatics with the blood supply to the origin of the primary arterial vessel feeding the tumoral bowel segment (31-32).

The right side of the colon, transverse colon and splenic flexure all drain to lymph node who follow the superior mesenteric artery. The left side of the colon drains to lymph node who follow the inferior mesenteric artery. Lesions of the cecum and ascending colon ideally are treated by right hemicolectomy with ligation of the ileocolic and right colic
arteries. Hepatic flexure tumor requires an extended right hemicolecotomy with ligation of the middle colic artery. Transverse colon and splenic flexure tumors require a subtotal colectomy with ligation of the left colic artery. Descending and sigmoid cancers are treated by left hemicolecotomy with ligation of the inferior mesenteric artery.

Based on the volume of arterial distribution, we expect to find the highest number of LN for cancers of the splenic flexure, followed by the transverse colon and hepatic flexure, than ascending colon and cecum, than sigmoid and descending colon.

In this study more LN were identified from the distribution of the superior mesenteric than inferior mesenteric artery. The average number of LN was highest for tumors of the ascending colon, but not for the splenic flexure tumors and after right hemicolecotomy more LN were identified with lesions of the ascending colon (median=19) than the cecum (median=14). Patient younger than 65 year had a higher number of LN identified in their cancer specimens than older patients, and the greatest number of LN were in patients <50 years of age, because the immune status and cancer specific immune responses may stimulate reactive LN, and increasing age is associated with a decline in immune competence.

In patients with T3 or T4 stage (local extension) the identified LN number is highest, compared with local disease, LN positive disease or distant metastatic disease.

In our study the 12 LN was predictive of survival for patients with local (stage I, T1 or T2) or local extensive cancer (stage II, T3 or T4), but not for patients with LN positive (stage III) or stage IV(M1) disease.

In a cohort study with 60.000 colon cancer patients identification of higher number of LN was associated with a increased survival in stage II colon cancer in 16 of 17 studies, and for patients with stage III in 4 of 6 studies(33, 12,15,20,25).

CONCLUSION

In this study were several variables associated with the failure to identify ≥12 LN in resected colon specimens. The results suggested a relationship between survival and identification of 12 or more LN for stage I or II disease.

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