Lymph Node Harvest in Resected Colon Cancer Specimens

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Background: The number of lymph nodes evaluated may be a measure of quality in colon cancer care and appears to be inadequate in most patients treated for colon cancer. We performed a systematic review of the evidence for the association between lymph node evaluation and oncologic outcomes in patients with colon cancer.
Aim: The adequate lymph node evaluation for cancer involvement, prognosis and adequate treatment of patients with colon cancer.
Method: It 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. We analyzed data from the cancer registry of 1st Surgical Clinic of Sibiu including 287 patients with colon cancer. This registry includes follow-up information from 1998 to 2009. Identification of ≥12 LN (lymph nodes) in resected colon cancer specimens has been considered as a quality indicator. In patients with resected colorectal cancer, LN the involvement has particular importance for patient prognosis and adjuvant therapy.
Results: The average number of LN identified increased 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. No significant change in the proportion of patients diagnosed with just one positive LN (10% versus 10.6%) was observed.
Conclusion: The results suggest a relationship between the survival and identification of 12+ LN for stage I or II, considering the disease.

Keywords: colon cancer, lymph nodes (LN), adjuvant therapy

Introduction

Regarding the colon cancer a 5 year survivability in 1st stage is between 85-95%, for 2nd stage 60-80% and for 3rd stage (with lymph nodes metastasis) 33%.

Nevertheless, 25% of 1st and 2nd stage cancers can recidivate. This can be attributed to either vascular dissemination or incorrect lymph node evaluation.

The lymph node study was made using multi-series examination with hematoxilin-eozyn, using imunohistochemistry techniques and chain polymerization reactions, all together for maximizing the rate of neoplazic deposits identification.

Materials and methods

We performed a retrospective, observational study on 287 patients who underwent surgery for colon cancer, we looked for variables including 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).

Data set for analysis

Patients with rectal cancer were excluded. Only patients with colon cancer as the main disease were included in this study. All statistical measures of probability were two-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 increased 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 number of LN identified in colon cancer specimens by surgeons ranged from 12 to 19, the proportion 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 ship in colorectal surgery had the higher average number of LN found in his resections.

Anatomic location within the colon

The probability of identifying 12 or more LN varied with the anatomic site of the resected colon cancer (the results are shown in table I).

Table I. Numbers of LN identified in resected colon cancers

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

Different among all sites in percentage with 12 or more nodes was 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 was 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 was more likely 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. The difference among identified sites in percentage with < 12 nodes by general stage was significant (p = 0.004).

Discussion

Our study confirms that the number of LN identified in resected colon cancer specimens, can be greatly increased by changes in pathology department procedures [1,2]. It also shows there is evident variation in the number of LN by anatomic region, age and stage of disease [3,4,5] .

Identification of ≥12 LN in resected colon cancer specimens was predictive for results in stage I and II [6].

Table II. Number of LN identified in resected colon cancer with fewer than 12 LN identified

Anatomic location	No of cases	Average no of nodes	Median no of nodes	% with 12 or more nodes identified
Local (T1 or T2)	120	14±5	12	58%
Local extension (T3, T4)	163	17±5	16	72%
Positive nodes (N+)	182	16±2	15	71%
Distant metastasis (M+)	104	15±2	13	60%

Our study confirms that the numbers of LN identified in colon cancer resection can be increased with intra-operative lymphography with in-vivo and ex-vivo determination, with a standard protocol implying the removal of the mesentery, fixing it in 10% formalin and identifying LN by visual inspection, and manual palpation [7,8,9].

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

The extent of LN dissection is determined by bloc-resection of the lymphatics with the blood supply to the origin of the primary arterial vessel feeding the tumoral bowel segment [10,11,12].

The right side of the colon, transverse colon and splenic flexure all drain to lymph node 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 [13,14]. Hepatic flexure tumors require an extended right hemicolectomy with ligation of the middle colic artery [15,16]. Transverse colon and splenic flexure tumors require a subtotal colectomy with ligation of the left colic artery [17]. Descending and sigmoid cancers are treated by left hemicolectomy with ligation of the inferior mesenteric artery [18,19].

Based on the volume of arterial distribution, we expect to find the highest number of LN for cancers on the splenic flexure, followed by the transverse colon and hepatic flexure, than ascending colon and cecum, and ultimately on the sigmoid and descending colon [20,21].

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 [22,23]. Folowing right hemicolectomy, more LN were identified with lesions of the ascending colon (median = 19) than the cecum (median = 14) [24].

Patients younger than 65 years 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 [12].

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 [25].

In our study the 12 LN was predictive for survival to 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 [26,27].

In a cohort study with 60.000 colon cancer patients identification of higher number of LN was associated with an increased survival in stage II colon cancer in 16 of 17 studies, and for patients with stage III in 4 of 6 studies [12,27,22,9,1].

Conclusions

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

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