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 identify was determinate 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 adeno-carcinoma 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 ≥12LN was associated with better survival for patients with stage I (p=0.6) and stage II (p=0,21) disease. Conclusions: Anatomic location, colorectal surgical training were strongly correlated with the number of LN identified.*

Cuvinte cheie: *cancer de colon, noduli limfatici (NL), procedee anatomo - patologice*

Rezumat: *Scopul lucrării: Identificarea ≥12 NL în piesele de rezecție din cancerul de colon a fost considerat ca indicator de calitate. La pacienții cu cancere rectocolice recente invazia nodulilor limfatici este în mod particular importantă pentru prognostic şi terapia adjuvantă. Metodă: Pentru identificarea pacienților diagnosticați cu cancer de colon a fost folosit registrul oncologic al Clinicii Chirurgie I. A fost identificată proporția pieselor de rezecție de colon cu ≥12 noduli limfatici şi în aceste cazuri au fost determinate topografia anatomică, vârsta pacientului, stadiul bolii. Supraviețuirea a fost corelată cu stadiul bolii, şi dacă au fost identificați ≥12 noduli limfatici. Rezultate: Modificarea procedeelor anatomo-patologice introduse în 1998 au fost asociate cu creşterea identificării nodulilor limfatici ca număr de la 6 la 14 (p<0,001). Studiul s-a limitat la 287 de pacienți care au suferit rezecție chirurgicală pentru adenocarcinom colic în intervalul 1998-2009. Identificarea a ≥12 noduli limfatici a variat între 57-83% prin 7 localizări anatomice (p<0,001), de la 65-75% în intervalul de 5 ani (p≤0,27), de la 59-73% prin cele 4 stadii ale bolii (p=0,04). Identificarea a ≥12 noduli limfatici a fost asociată cu o mai bună supraviețuire pentru pacienții din stadiul I (p=0,16) şi stadiul II (p=0,21) de boală. Concluzie: Topografia anatomică, experiența în chirurgia colorectală au fost puternic corelate cu numărul de noduli limfatici identificați.*

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 determinate 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 anatomic 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 I-st 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 analyzis

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 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 (table1).

Table no. 1. 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%

Differents 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

General stage	No of cases	Average no of nodes	Median no of nodes	% with 12 or more nodes identified
Local(T1orT2)	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%

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 anatomic 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 lymphographie 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 hemicolectomy 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 hemicolectomy 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 hemicolectomy 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 declive 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, 12,13,20,25).

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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