

Mean number of lymph nodes in colonic cancer specimen: possible quality control index for surgical performance

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Rezumat

Media numărului de ganglioni limfatici în speci­menele de cancer colonic: posibil index de calitate al performanței chirurgicale

Invazia limfatică în cancerul de colon explică necesitatea unei limfadenectomii extensive asociată rezecțiilor cu viză curativă. Acuratețea tehnicii chirurgicale poate influența extensia disecției limfatice și, indirect, numărul de ganglioni recoltați din piesa operatorie.

Material și metodă: Am analizat o serie de 329 pacienți consecutivi operați pentru cancer de colon, la care s-au practicat proceduri oncologice ce includ limfadenectomii standard. S-a evaluat în principal supraviețuirea, numărul de ganglioni pe procedură, precum și media numărului de ganglioni recoltați pe fiecare procedură și pe chirurg, având ca scop evaluarea acurateții gestului chirurgical.

Rezultate: S-au găsit diferențe în curbele de supraviețuire Kaplan-Meyer între grupele identificate ca performanță superioară și medie. Diferențele sunt majore pentru hemicolectomia dreaptă atât în stadiul II (85,7% vs 64,7%) cât și în stadiul III (71,4% vs 56,5%), dar și în stadiul II pentru colectomiile segmentare (85,7% vs 78,9%) putându-se

evidenția un beneficiu în supraviețuirea la 5 ani în cazul pacienților operați de chirurghi cu o medie mai mare a numărului de ganglioni recoltați.

Concluzii: studiul nostru sugerează că media numărului de ganglioni recoltați din piesele de colectomie pentru cancer colorectal ar putea fi folosită ca metodă de evaluare a performanței în chirurgia cancerului de colon, iar diferențele se pot reflecta în supraviețuirea postoperatorie. Extrapolarea rezultatelor trebuie făcută cu grijă, deoarece datele pot fi semnificativ influențate de factori independenți de chirurg, cum ar fi protocoalele de recoltare a ganglionilor, care pot diferi în alte instituții.

Cuvinte cheie: cancer colonic, colectomie, ganglioni limfatici, performanță, control al calității, supraviețuire

Abstract

Lymphatic involvement in colonic cancer explains the need for extensive lymphadenectomy for intended curative operations. Surgical skills may determine the actual extent of the procedure and indirectly the number of lymphnodes (LN) removed from each specimen.

Material and methods: We looked on a series of 329 consecutive patients with colonic cancer who underwent a standardized procedure including extensive lymphadenectomy. The main endpoints were survival as well as the number of LN and the mean number of

Results: Differences in Kaplan-Meyer survival curves between average and high performance colectomies have been identi-

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fied for right colectomies both in stage II (85.7% vs 64.7%) as well in stage III (71.4% vs 56.5% 5-year survival), and also in stage II for segmental colectomies (85.7% vs 78.9%), showing a definitive advantage in survival for patients operated by surgeons with a mean LN retrieval above cutoff values.

Conclusions: our study suggests that the mean number of LN retrieved from the surgical specimen can be used to evaluate surgical performance in colonic cancer, and may reflect in postoperative survival. However care should be taken when extrapolating these data as surgeon-independent factors such as protocols for LN harvesting may be different in other institutions and will influence results.

Key words: colonic cancer, colectomy, lymph nodes, performance, quality control, survival

Introduction

Colonic cancer remains a major health problem all around the world, being the second most common cancer and the second leading cause of cancer related mortality (1). Surgery alone will cure a large proportion of stage I and II patients, as well as a group of stage III patients, signaling that a good quality surgical procedure may effectively deal with regional metastatic disease. From a series analyzing independent prognostic factors, lymphatic invasion is prominent and for associated with differences in survival (2). Detailed studies demonstrated the independent significance of the number of invaded lymph nodes - LN (N1 vs N2), metastatic LN distribution, invasion of the apical node and proportion of invaded LN (3,4). Meanwhile there are controversies related to the significance of the number of LN harvested in the specimen (4,5). All these studies advocate extensive surgical procedures that will remove en bloc the entire region which is prone to lymphatic spreading.

Our problem was that we had to confront a significant lack of homogeneity in quality of surgery for colonic surgery, mostly regarding the accuracy and extent of the lymphadenectomy. Limiting the extent of LN bearing area diminishes the number of harvested nodes in surgical specimens. We undertook a retrospective study that looks into the average number of LN for individual surgeons and its association with survival as a potential tool for quality control for the surgical procedure.

Materials and Methods

The study included all cases of resectable colonic cancer operated in our department between January 2004 and December 2007. Inclusion and exclusion criteria are presented in Table 1. For all patients data were collected from the medical files, operating room records and pathological reports. Operating surgeons were allocated codes to ensure confidentiality of the study.

The main endpoint was survival, determined in a

Table 1. Inclusion and exclusion criteria

Inclusion criteria	
1.	Pathologically confirmed colonic cancer
2.	Standard colectomy with regional lymphadenectomy (right, left or segmental colectomy)
3.	Personal identification number could be located in the national electronic database
4.	Synchronous or metachronous colonic lesions, if dealt with separately
Exclusion criteria	
1.	Rectal or rectosigmoid cancer
2.	Non resectional treatment or operations that did not include a standard lymphadenectomy (palliative surgery) – including polyps resected endoscopically
3.	Recurrent colonic tumor or metastatic tumor that did not require a standard colectomy
4.	Multiple colonic tumors that required total or subtotal colectomy

transversal study. Personal identification numbers for all patients were run in the national electronic database. This identified patients as alive or with the recorded date of their death. Using this system we could not distinguish between cancer-related death and non cancer-related death. Survival was computed in all cases from the date of the operation.

All specimens were shipped en bloc to our pathology unit and pathologists with a major interest in digestive oncology analyzed LN harvesting. Almost 90% of all LN dissections were performed by two senior pathologists.

Statistical analysis

Collected data were coded as categorical or numerical variables and entered into a MS Access Office XP database and statistically analysed using SPSS ver. 15.0 for Windows (Statistical Package for the Social Sciences, Chicago, Illinois, USA). Survival was computed as censored Kaplan - Meyer curves.

Results

The study group included a series of 329 consecutive patients. Twenty were excluded from the database due to insufficient data, regarding either pathological staging or survival status at the time of the study. Male patients were dominant, with a male to female ratio of 1.19. The mean age was 63.8 years. Age distribution followed a Gaussian curve, with a peak incidence between 50 and 80 years and a significant shift to the right (data not shown).

Survival curves were computed according to stage at the time of diagnosis. As shown in Fig. 1, there is a significant difference in survival between stages. We set our focus on differences between stages II and III. In our hypothesis these survival differences may be due to distant spread of tumors, not diagnosed at the time of surgical procedure, but also to inadequate en bloc lymphadenectomy, in stage III patients.

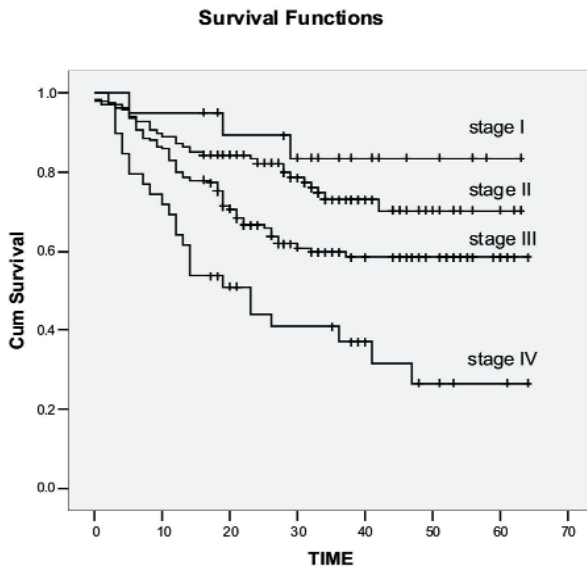


Figure 1. Overall survival in colonic cancer stratified according to postoperative stage

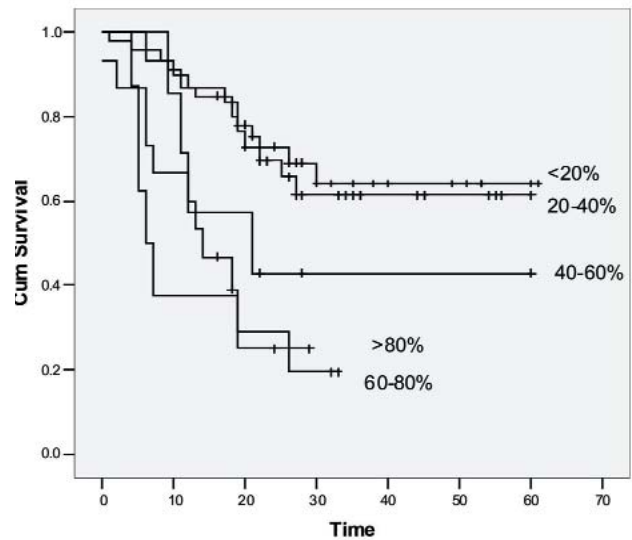


Figure 2. Survival according to percentage of LN with metastasis in resected specimens from patients with stage III colonic cancer

Patients in stages II and III were statistically analyzed for a relationship between survival and percentage of invaded LN in each specimen. Survival curves in Fig. 2 confirm the theory of step-wise LN metastatic process. As such patients with a higher proportion of non-invaded LN have a better prognosis. In other words a specimen extending apically more in healthy tissue may insure a negative margin regarding regional LN metastasis. These data support our working hypothesis: more extensive surgery might be associated with better survival.

As survival for individual surgeons is difficult to evaluate due to small individual series, we decided to group surgeons according to average number of LN retrieved in specimens for each procedure. To classify surgeons we looked at the distribution of number of LN in specimen for each procedure (Fig. 3). Based on this distribution we have chosen an arbitrary cutoff value that may distinguish between surgeons with average performance and surgeons with possible above average performance. Cutoff values were set to 20 LN, 16 LN and 10 LN for right colectomy, left colectomy and segmental colectomy respectively. In all cases values were higher than those recommended for adequate TNM classification, and should reflect the relative difference in the size of lymphadenectomy areas. For further analysis only surgeons with more than 25 procedures in the studied period were evaluated for mean and range of LN in retrieved specimens. Surgeons were pooled in 2 groups (A and B) for each procedure. Table 2 presents the composition of each group, with average number of LN and range for each surgeon. It is striking that some surgeons are constantly allocated to group A while others are more frequently in group B, suggesting that surgeons with better performance tend to behave similarly in all procedures.

To evaluate potential benefit of more extensive lymphadenectomies we computed Kaplan-Meier survival curves for

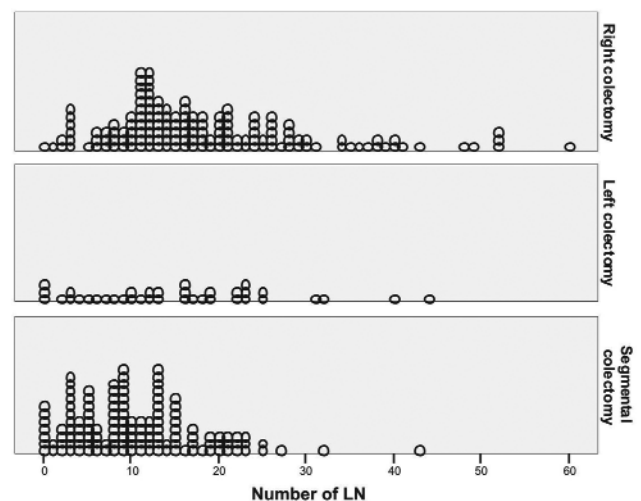


Figure 3. Distribution of number of LN retrieved from surgical specimen for each procedure

each procedure, using the stratification of surgeons in groups. Fig. 4 presents survival curves in a parallel between stage II and stage III. For right colectomy the 5 years survival difference is obvious both for stage II (85.7% vs 64.7%) as well as for stage III (71.4% vs 56.5%) in favor of group A (average > 20 LN). This suggests that a less aggressive lymphadenectomy can be responsible for under-staging (in stage II) and diminished long term survival in stage III. Both curves tend to become parallel after 30 months suggesting that the benefit of more radical operations will be reflected in a significant decrease of mortality in the first two years. Data for left colectomy are difficult to evaluate mostly because limited number of procedures. It looks as though both stage II and III group A (average

Table 2. Surgeons with significant number of procedures stratified according to average number of LN in specimen according to type of operation

	Right colectomy		Left colectomy		Segmental colectomy	
	Cut off value =20 LN		Cut off value =16 LN		Cut off value = 10 LN	
	Operator code	Number of LN	Operator code	Number of LN	Operator code	Number of LN
Group A	1	23 (11-60)	1	23 (12-44)	1	12.57 (4-21)
	2	21.36 (2-52)	7	18.67 (10-32)	2	11.91 (2-22)
	7	20.9 (9-41)	9	16.67 (3-40)	10	12.58 (2-25)
	9	21.63 (3-49)				
Group B	3	16.88 (2-43)	2	13.83 (0-25)	3	8.35 (0-22)
	10	13.18(1-26)	3	9.38 (0-31)	7	6.36 (0-17)
			10	10.67 (4-19)	9	7.89 (0-27)

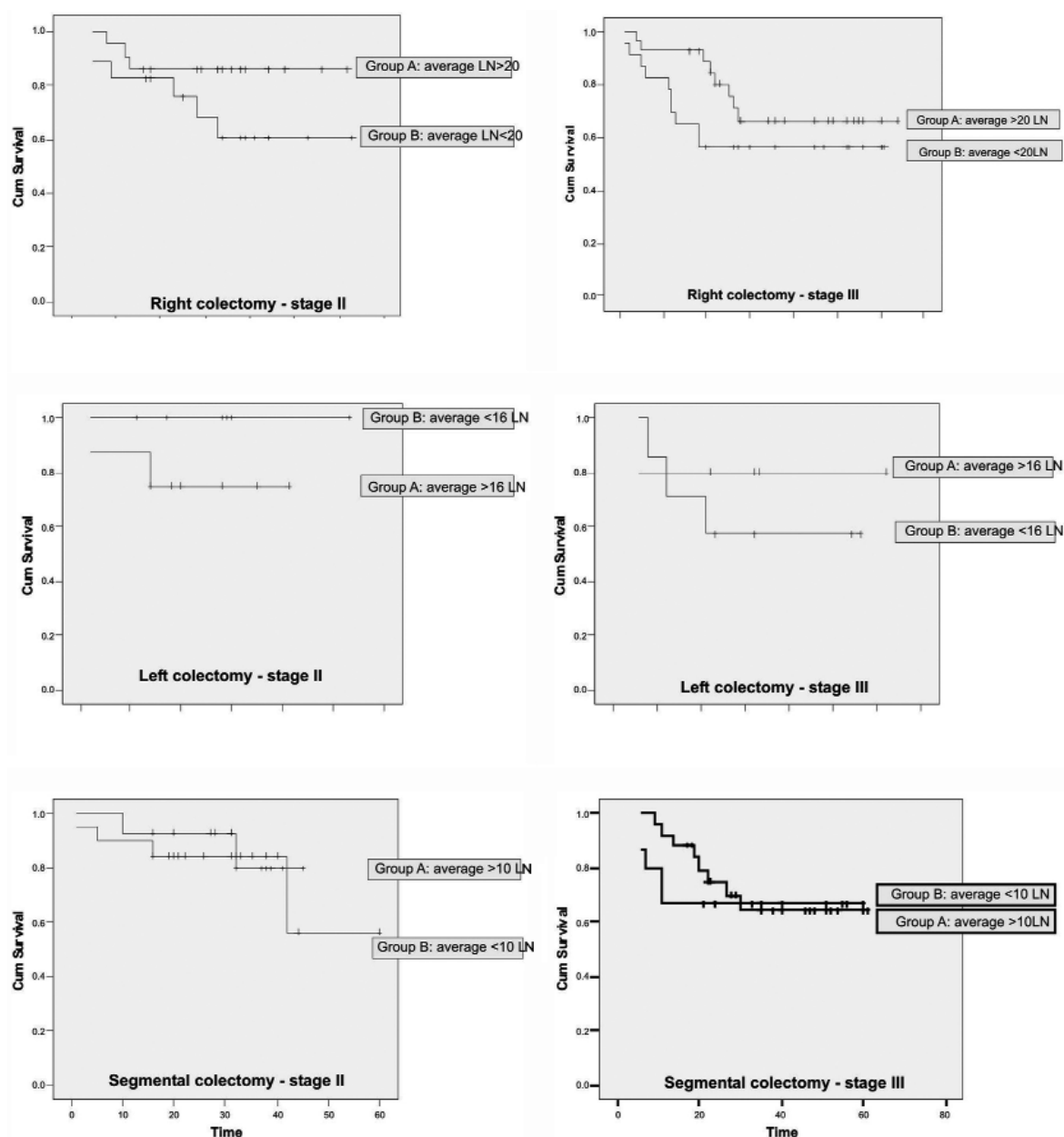


Figure 4. Survival curves for each surgical procedure with surgeons grouped on the basis of average number of LN retrieved in specimen

>16 LN) are associated with early postoperative mortality, while group B survival in stage III decreases stepwise for 20 months before flattening. Segmental colectomy data demonstrate again the obvious benefit of more radical group A surgeons (average > 10 LN) but only in 5-year-survival for stage II (85.7% vs 78.9%), with no significant difference in stage III (66.7% vs 68.0%). These data suggest that local control is achieved in most cases and probably the only drawback of more limited resections might be under-staging.

Discussion

There are controversies regarding a correlation between number of LN in resected specimen of colonic cancer and survival, but other studies looked for direct correlation between actual number of LN and survival (6,7). One study showed that in T3N0 cases a larger number of resected LN is associated with better survival, probably due to a more correct staging (8). We think that lower numbers of retrieved LN could be responsible for under-staging and may represent non-radical procedures, as the metastatic pathways do not follow strict step-wise rules (9). Instead of looking at the actual number of retrieved LN in each case, we assessed the average number of LN in specimens for an individual surgeon, for each procedure, as a possible predictor of the quality and completeness of surgery. We assumed that consistently more extensive lymphadenectomies with implicit larger number of retrieved LN might characterize a pattern of a better-performing surgeon, providing a better survival to the patient.

The cutoff value chosen by us differs from other studies (6) as it is highly unlikely that a segmental colectomy will retrieve similar numbers of LN as a standardized right or left colectomy. Considering the extent of lymphatic territories resected in each procedure and distribution data in our series we used different cutoff values for each procedure, with the intent of separating surgeons with average and above average performance. Choosing these cutoff values is arbitrary and may be a subject for discussion, but that is the case with any value, including that used for adequate TNM staging. The wide distribution of LN numbers in specimens can not be attributed to harvesting errors and some specimens have obviously inadequate number of LN. The unacceptable situation with less than four LN in a specimen is relatively rare, but demonstrates that non radical surgery was performed in some situations, mostly for polyps with malignant foci. That is more often in sigmoid cancer.

Our data suggest that surgeons with a consistently larger number of LN in resected specimens might have better survival both in stage II for right colectomy and segmental colectomy as well as stage III for right and left colectomy, with no benefit in stage III for segmental colectomy. Supporting an operator-dependent factor, the structure of each group shows that surgeons with larger number of LN for one procedure tend to maintain this in all procedures.

An interesting aspect can be suggested by the shape of survival curves in segmental colectomy. As there are no

significant differences in stage III one would expect that the procedure is well standardized and all surgeons perform in a similar manner. Nevertheless surgeons in group A have better results in stage II which can only be explained by an inappropriate reduction of the extent of lymphadenectomy, which may be responsible for under-staging. More so, 5-year survival rate for segmental colectomy is worse in stage II than in stage III for group B surgeons which also suggest under-staging.

We accept that only the number of LN, even if evaluated as averages for individual surgeons, might not completely reflect the surgeon's performance. LN sampling is not done by surgeons but by pathologists and operator dependent variations may occur at this level, although there are no significant differences between the two senior pathologists regarding LN sampling. Other factors might influence these figures but we believe, with support from our data, that a surgeon who constantly resects larger lymphatic territories may obtain better long term survival rates.

Conclusions

Analysis of performance in surgical practice is very difficult and not welcomed either by surgeons or by institutions. Simply looking at survival functions can produce misleading results due to low number of cases in each category of procedures. Based on our results we believe that averaging the number of LN for a specific procedure will give an estimate of the quality of surgery performed by individual surgeons. However data can not be directly extrapolated to other institutions or series, as the internal protocol regarding LN retrieval from specimens may vary.

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