

LYMPH NODES IDENTIFICATION AFTER COLORECTAL CANCER RESECTION

Total de linfonodos identificados após a ressecção do câncer colorretal

Kátia Cibebe **CISZ**¹, André da Luz **MOREIRA**¹, Luciana de Oliveira **FIALHO**¹, Hiram José Villanueva **AGUERO**¹,
Daurita Darci de **PAIVA**², Albanita Viana de **OLIVEIRA**², Francisco Lopes **PAULO**¹

From ¹Coloproctology and ²Pathology Department of Pedro Ernesto University Hospital, State University of Rio de Janeiro, RJ, Brasil.

ABSTRACT - Background - The main base in surgical treatment of colorectal cancer is en-bloc removal of the tumor with adequate proximal and distal margins, combined with the removal of lymph nodes. **Aim** - To evaluate factors associated with the number of lymph nodes found in surgical specimens from patients with colorectal cancer. **Methods** - Analysis of a retrospective data of consecutive patients operated with a diagnosis of colorectal adenocarcinoma. Were excluded those undergoing palliative surgery. Demographic data, operative and histopathological findings were analyzed using the Fisher exact test, chi-square, Wilcoxon rank-sum and a logistic regression model. **Results** - From 2000 to 2008, were operated 298 patients with colorectal cancer. The data included in the analysis were available for 173 patients. Of these, 85 (49%) were female and median age was 65 (26-94) years. The resection was the most common left colectomy (45%), followed by right colectomy (23%). The median number of lymph nodes were isolated from eight (0-67) and 33% of patients had 12 or more lymph nodes identified in surgical specimens. Patients younger than 50 years and those who underwent right colectomy had a greater number of lymph nodes isolated. **Conclusions** - Patient age less than 50 years and the type of surgical resection are associated with higher number of lymph nodes found in surgical specimens.

HEADINGS - Colorectal cancer. Lymphnodes. Surgery. Neoplasm Staging.

Correspondence:

André da Luz Moreira,
e-mail: andreluzmoreira@yahoo.com.br

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DESCRITORES - Câncer colorretal. Linfonodos. Cirurgia. Estadiamento de Neoplasias.

RESUMO - Racional - A base cirúrgica principal no tratamento do câncer colorretal é a remoção em bloco do tumor com adequadas margens proximal e distal, associada à remoção dos linfonodos mesentéricos. **Objetivo** - Avaliar fatores associados à quantidade de linfonodos encontrados em peças cirúrgicas de pacientes com câncer colorretal. **Métodos** - Estudo retrospectivo, de pacientes consecutivos, operados com diagnóstico de adenocarcinoma colorretal. Foram excluídos aqueles submetidos ao tratamento cirúrgico paliativo. Os dados demográficos, operatórios e histopatológicos foram analisados utilizando os testes exato de Fisher, Qui-quadrado, Wilcoxon rank-sum e um modelo de regressão logística. **Resultados** - No período de 2000 a 2008, foram operados 298 pacientes com câncer colorretal. Os dados incluídos na análise estavam disponíveis para 173 pacientes. Destes, 85 (49%) eram do sexo feminino e a idade mediana era de 65 (26-94) anos. A ressecção mais comum foi a colectomia esquerda (45%), seguida pela colectomia direita (23%). O número mediano de linfonodos isolados foi oito (0-67) e 33% dos pacientes tiveram 12 ou mais linfonodos identificados na peça cirúrgica. Os pacientes com idade menor que 50 anos e aqueles submetidos à colectomia direita obtiveram maior número de linfonodos isolados. **Conclusões** - A idade do paciente menor que 50 anos e o tipo de ressecção cirúrgica estão associados ao maior número de linfonodos encontrados nas peças cirúrgicas.

INTRODUCTION

Colorectal cancer (CRC) is the second leading cause of cancer death in North America and fourth in Brazil, with an estimate of 28.11 million new cases in January 2010⁷, behind only lung cancer followed by prostate and breast. For most patients with CRC, surgery is the primary curative therapy. The base is surgical en-bloc removal of the tumor with adequate proximal and distal margins, combined with the removal of lymph nodes¹¹.

In the presentation of the disease, 40% have them positives. Currently, clinical, histopathological and molecular genetics have been linked to disease-free survival in patients. However, the presence of lymph node involvement is undoubtedly the most important prognostic factor and one of the most studied¹¹.

Current literature indicates that the accuracy of staging and overall survival increases with the number of lymph nodes examined. Get the largest number of lymph nodes in surgery, benefits the patient in assessing the extent of the disease allowing appropriate adjuvant therapy^{9,16,17,21} and can also be used as a measure of quality in oncological resections for this disease^{4,15}. Previous studies recommend the analysis of at least 12 lymph nodes in surgical specimens⁶; however, it is not always possible to achieve this minimum value in these patients.

Although controversies exist, some variables have been associated with the total number of lymph nodes found in specimens, such as patient age, time of diagnosis, tumor size, location and stage T².

The aim of this study was to identify possible factors associated with the number of lymph nodes found in surgical patients with CRC.

METHODS

This is a retrospective study of consecutive patients diagnosed with CRC who underwent surgery from January 2000 to December 2008. Patients were identified through prospective database of the Department of Pathology, University Hospital Pedro Ernesto, State University of Rio de Janeiro, RJ, Brazil. Patients with palliative surgical treatment, different histological types of adenocarcinoma and when records could not be identified or that did not contain data about the number of dissected nodes, were not used. The variables collected included age, sex, operation type, TNM stage, tumor size, lymphovascular invasion and tumor grade. Demographic data, operative and histological findings were obtained by reviewing medical records, histopathological and clinical consultations at the clinic of coloproctology. To facilitate statistical analysis, sigmoidectomies and retossigmoidectomies in rectal tumors were classified as upper left colectomy, since anatomically the inferior mesenteric artery ligation is routinely done at the origin, in these types of resection.

Data were analyzed using the Fisher exact test and chi-square test for categorical variables and the Wilcoxon rank-sum for continuous variables. Multivariate analysis was performed using

a logistic regression model using as a criterion for inclusion p value smaller than 0.1. The p value below 0.05 was considered statistically significant.

RESULTS

Of 289 patients undergoing colorectal cancer in this study, 173 met the inclusion criteria. The median age was 65 (26-94), the most common operation performed was left colectomy (45%) and six patients (3%) underwent total colectomy. Nine (5%) were operated on an emergency basis. Twenty-two (49%) with tumors of the rectum and distal underwent neoadjuvant chemotherapy and radiotherapy. Table 1 describes the clinical characteristics of patients selected.

TABLE 1 - Clinical characteristics of the population

Variables	n	(%)
Sex		
Female	85	49
Male	88	51
Age (years) *	65 (26-94)	
Type operation		
Right colectomy	39	23
Transversectomy	7	4
Left colectomy	77	45
Anterior rectal resection	19	11
Abdomino-perineal resection	25	14
Total colectomy	6	3

* Median (range)

The median tumor size was 5 (1.8 to 16) cm. Twenty-nine (17%) had a diagnosis of mucinous adenocarcinoma. The presence of lymphovascular invasion was found in 37 (17%) patients. Ninety-six (71%) had histological grade diagnosed as moderately differentiated (Figure 1). The majority (44%) was in TNM stage II disease (Figure 2).

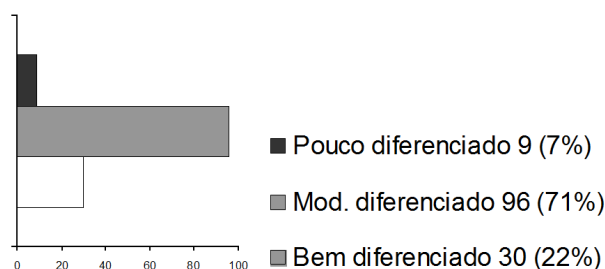


FIGURE 1 - Histological grade

The median number of lymph nodes isolated was eight (0-67) and only 54 (33%) had 12 or more lymph nodes in surgical specimen. In univariate analysis, type of resection, degree of tumor invasion in the intestinal wall (T stage) and tumor size greater than or equal to six centimeter were associated with greater

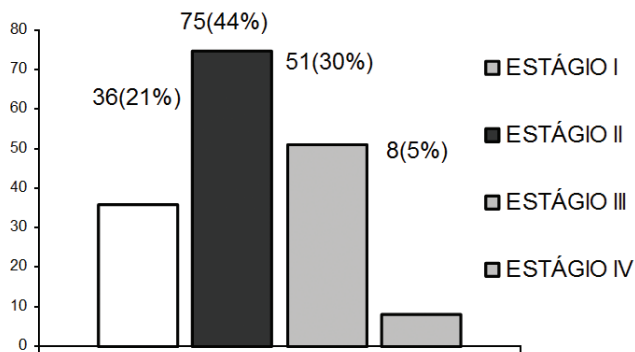


FIGURE 2 - Tumors staging

number of lymph nodes isolated from the surgical specimen. However, in multivariate analysis, only age younger than 50 years and type of operation correlated independently with the number of lymph nodes found by the pathologist. Regarding the type of operation, a greater number of lymph nodes was found in right colectomies and smaller one in resections including tumors of the medium and distal rectum (Table 2).

TABLE 2 - Correlation between the number of lymph nodes found and the demographic, surgical and pathological aspects

	LYMPH NODES ISOLATED**	P Univariate	Log-Rank P multivariable
AGE			
> 50 years	7 (0-57)		
<50 years	11 (0-67)	0,08*	0,01
SEX			
MALE	9 (0-67)		
FEMALE	7 (0-57)	0,9	
TYPE OF SURGERY			
Right colectomy	12 (0-41)		
Left colectomy	8 (0-67)		
Anterior rectal resection	4 (0-24)		
Abdomino-perineal resection	4 (1-18)	<0,0001*	0,001
SIZE (TUMOR)			
<6 cm	7 (0-57)		
> = 6 cm	11 (0-67)	0,02*	0,06
URGENCY	9 (5-14)	0,7	
WALL INVASION			
T1	3 (0-11)		
T2	5 (0-21)		
T3	8 (0-57)		
T4	13 (0-67)	<0,01*	0,3
DEGREE OF DIFFERENTIATION			
Well	7 (0-26)		
Moderate	8 (0-67)		
Small	9 (0-34)	0,7	
Mucinous	7 (0-41)	0,8	
Lymphovascular invasion	8 (0-57)	0,7	

* Variables included in logistic regression model; ** Median (range)

DISCUSSION

The CRC has a variable incidence in different countries. In Brazil, ranks among the most prevalent. Fazio et al.⁸ reported 768 cases from the Family Registry

for Colorectal Cancer in Ontario, where there were virtually no gender preference (male 49.3% and 50.7% female) and age diagnosis was more than 60 years in 60.8% of cases. Mahmut et al.¹⁰ reported a study of 179 cases of patients with CRC. Most patients were male (50.8%), mean age 57 years. According to the TNM system, 44.7% had stage II disease. In this series there was a male predominance (88 patients, 51%), with a median age of 65, and 44% was in TNM stage II, which is consistent with the data found in literature.

Histopathologic analysis of resected lymph nodes and its prognosis element of the CRC have driven a large number of studies conducted with the aim of increasing its accuracy^{5,20}. The real benefit of lymphadenectomy is the possibility to stage correctly the disease, besides its therapeutic effect, what may represent an improvement in survival.

Wong et al.¹⁹ conducted a study involving 196 patients undergoing surgical treatment for CRC, and the average number of lymph nodes recovered in each part was 17 (range 0 to 78) in which 38.6% had at least one positive lymph node, suggesting that the greater the number of lymph nodes examined, the greater the chance of finding lymph node metastases. Although there is no consensus in spite of other studies that followed this observation, it is known that the evaluation of more lymph nodes increases proportionally the chances of finding metastatic lymph node¹⁸. However, the optimal number of lymph nodes to be resected remains controversial, varying according to the literature, between 10 and 18^{5,20}.

In patients with CRC is currently recommended that 12 would be the ideal minimum number of lymph nodes to be resected. Hence, resection of lymph nodes containing numbers less than 12 could be considered inappropriate, the patient understaged^{21,23}.

The values found in this study (median of eight lymph nodes isolated) are smaller than those proposed. Only 33% (54) of patients included in this sample had 12 or more lymph nodes resected. One reason for this finding may be explained by the inclusion in this series a few cases of tumor resections of the medium and distal rectum. Forty-nine percent of these were previously irradiated, which can reduce the number of lymph nodes dissected in the surgical specimens. Another reason includes the methods used to optimize the detection of lymph node specimens, since the number of lymph nodes dissected by the surgeon does not always correspond to the number identified by the pathologist. Experience and technique employed in the recovery of pathological lymph nodes 12 are essential for accurate analysis. Some techniques have been applied to facilitate the identification of lymph nodes in the mesocolon, as the use of developing solutions to prepare the specimens¹.

Aiming better accuracy in staging, the surgical specimen containing the mesocolon or mesorectum excised en-bloc, must be carefully handled and packaged

so that the pathologist can identify the largest possible number of lymph nodes¹⁴. Recently at our institution, the specimens excised are sent promptly fresh to the pathology sector, thus avoiding inappropriate manipulation and violation of the specimen by unauthorized persons, which could hinder precise pathological study. With this, it was achieved considerable increase on number of lymph nodes examined in accordance with international recommendations.

In the analysis performed, type of resection, degree of tumor invasion in the intestinal wall and tumor size greater than or equal to six centimeters were associated with higher number of lymph nodes found in surgical specimens. Of these, only the type of resection proved to be an independent variable in multivariate analysis. Canessa et al.³ described that the number of lymph nodes varies with the target location and the tumor diameter. Also Pereira Junior et al.¹³, evaluating 185 cases CRC, noted that the number of lymph nodes isolated from surgical specimens and the presence of metastases in these lymph nodes was associated with tumor size. Possibly this is due to the amount of material assigned to the lesion, the extent of the operation or characteristics of each intestinal segment.

Age below 50 years also correlated independently with the number of lymph nodes found by the pathologist. The CRC in young patients is described as bigger, more advanced and higher degree of histopathological indicators of aggression^{12,22,23}, which may have contributed to more extensive surgical resection of the surgeon, and as a consequence, a greater number of lymph nodes identified.

This study had some limitations. First, it is a retrospective and relatively small group of cases. Second, the results were obtained from analysis of surgical procedures performed by a large number of surgeons, involving many pathologists during a period of 10 years, which may have influenced the results.

Surgeon and pathologist are both responsible and should be engaged in greater identification of lymph nodes in surgical specimens.

CONCLUSION

Patient age less than 50 years and the type of surgical resection are associated with higher number of lymph nodes found in surgical specimens.

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