ARTICLE

Influence of Obesity on Lymph Node Recovery from Rectal Resection Specimens

Dénes GÖRÖG,[1] Péter NAGY,[2] Antal PÉTER,[1] Ferenc PERNER[1]

[1]Department of Transplantation and Surgery, [2]I. Department of Pathology and Experimental Cancer Research, Faculty of Medicine, Semmelweis University, Budapest, Hungary

Careful lymph node dissection from colorectal resection specimens is important procedure for cancer staging. Present study intended to assess the impact of surgical technique and patient's obesity on this process. Number of lymph nodes harvested by manual dissection from resection specimens of 141 patients with rectal cancer and the rate of nodal metastases were analyzed and compared in different groups of patients selected by length of resection specimen and body mass index. The median and mean number of lymph nodes found per patient were 6 and 6,7. The shorter resection specimens (≤16 cm after formalin fixation) yielded significantly lower number of nodes than those with length > 16 cm (5.7 versus 7.9). Most significant reduction in mean number of lymph nodes was observed in obese patients with short specimens (4.8). This subset of patients presented the lowest rate of nodal metastases (38%). The surgical technique seems to be an important factor for lymph node recovery from rectal resections specimens. The patient's obesity had an unfavourable impact on this procedure. Standardized surgery and histopathological examination are needed even in non-specialized centers to harvest adequate number of lymph nodes. (Pathology Oncology Research Vol 9, No 3, 180–183)

Keywords: rectal resection, lymph node, obesity

Introduction

Histological examination of colorectal tumor resection specimens and accurate detection of all lymph node metastases are most important in order to stage the tumor, predict the outcome and to select the subsets of patients for adjuvant therapy.[4,8,15,17] Wide variations in number of lymph nodes harvested from colorectal resection specimens exist according to the patient's anatomy, the biological aggressiveness of the tumor, the surgical techniques and the procedures used by pathologists to search for lymph nodes.[3,11,14,16] In an effort to reduce this variation, techniques that aid in the macroscopic identification of lymph nodes were suggested.[5] The superiority of these techniques, such as fat clearance which is time-consuming, labor-intensive method, to the traditional dissection is still being debated.[13,17] On the other hand harvesting inadequate number of lymph nodes may be critical in determining therapy resulting in detrimental impact on outcome of colorectal cancer.[15,17] It has been well established that fatty tissue makes the lymph node recovery difficult,[5] especially in patients with rectal cancer[17] but less data are available whether the patient's obesity has indeed unfavourable influence on this procedure using manual dissection. The aim of this study was to test this hypothesis evaluating the results of lymph node retrieval from resection specimens of rectal tumors and the impact of surgical technique and patient's obesity on this process.

Materials and methods

181 patients underwent elective resection for carcinoma located in the rectum and rectosigmoid (up to 20 cm from anal verge) in the Transplantation and Surgical Department of Semmelweis University between January 1994 and December 2002. Thirty nine cases with known distant

metastases at the time of surgery and 1 patient with unknown number of lymph nodes examined were excluded and data of 141 patients were studied. There were 63 females and 78 males, ranging in age from 24 to 91 years (median age: 67 years). According to the length of resection speciemens measured by pathologist after fixation, patients were divided into two groups. (Group I: length of specimens median length of 16 cm, group II: length of specimens > 16 cm). The clinical features of the study population and the pathological characteristics of tumors are summarized in *Table 1*. The study groups were well matched for age, sex and body mass index (BMI) but significant differences were found between them concerning the median height of tumors above the anal margin, the type of surgery, and furthermore the rate of $_pT_{1p}T_2$ and $_pT_{3-p}T_4$ tumors.

The surgical procedures were performed by 20 surgeons. Total or partial mesorectal excision was done according to location of tumor, 12 cm or 12 cm from anal verge. Preoperative chemotherapy was not given and only four patients had preoperative radiotherapy. The surgical specimens were fixed in 10% formalin solution and were dissected by 5 pathologists. Lymph nodes were identified by sight and palpation using parallel sections of the node containing fat and recovered by manual dissection. All lymph nodes harvested from the mesorectum were submitted for routine histopathological examination using hematoxylin and eosin staining and only representative sections of nodes were used. Special stains were not used unless any doubt existed regarding the presence of tumor cells. The histopathology reports based on the recommendation of UICC TNM Supplement 1993,[9] were retrospectively reviewed. Number of lymph nodes identified and examined per specimen was recorded in both groups. The results of lymph node recovery was evaluated in further subgroups of patients who were subdivided according to their body mass index (BMI), < 25 kg/m² or 25 kg/m² - a threshold ascertained from reports in the literature.[2] Because the depth of tumor infiltration was significantly different between the in study groups (*Table 1*), the rate of nodal metastases was compared for T_3T_4 tumors only. The node-positive specimens were not specified according to the number of metastatic nodes.

Students *t* test was applied to compare continuous variables (two independent average) and chi-square test was used for categorical variables. p 0,05 was considered significant.

Results

947 lymph nodes were examined in 141 specimens ranging 0-30 with an average of 6.7 ± 3.6 lymph nodes per patient. The median number of nodes per specimen was 6. No lymph nodes were found in 7% of cases. The mean number of nodes harvested from shorter resection specimens (≤16 cm) was significantly less than that recovered from longer specimens, 5.7 versus 7.9 (*Table 2*). This significant difference was observed in patients with obesity, 4.8 versus 7.5 but not in normal weighted patients. Distribution of median and mean number of nodes per specimen is shown for study groups separately in *Table 3*. and *Table 4*. The mean number of lymph nodes did not vary significantly with age, gender or type of surgery in either groups (*Table 3* and *4*) but it was significantly lower when short surgical specimens (≤16 cm) from obese patients were examined comparing with those from normal weighted patients (*Table 3*). In case of longer specimens (> 16 cm) the lymph node recovery resulted in similar mean number of lymph nodes in both obese and non-obese patients (*Table 4*). Thirty five percent of all patients and forty five percent of patients with T_3T_4 tumors had detectable nodal metastases. The rate of metastatic lymph nodes for T_3T_4 tumors was higher in longer resection specimens than that in shorter ones, especially in obese patients but the difference did not reach significance (*Table 5*). In normal weighted patients the incidence of nodal metastases was similar in both groups.

Discussion

As regards the lymph node harvesting from colorectal tumor resection specimens there are some arguments in the literature that the metastatic disease can be underesti-

Table 1. **Clinical features of patients and pathological characteristics of tumors in two groups of study population selected by length of resection specimens.**

	I ≤ 16 cm	*II > 16 cm*	*p value*
No. of patients	76	65	
Age median/mean (years)	68/65,8	64/64,1	0,18
Male/female	40/36	38/27	> 0,25
BMI* median (kg/m²)	25,9	25,5	0,26
Height of tumor† (cm)	12	7	< 0,0001
Type of operation AR‡	68	31	< 0,001
APR§	8	34	
Depth of infiltration			
$_pT_1 - _pT_2$	38	19	< 0,025
$_pT_3 - _pT_4$	38	46	
Grade of malignancy 1	27	23	0,25
2	42	36	
3	7	6	

* body mass index, †median height of tumor from anal verge, ‡anterior resection, §abdominoperineal resection

mated when inadequate number of nodes is examined.[5,17] The aim of some recently reported studies has been to establish the adequate number of lymph nodes above which there is no risk of understaging.[3,6,14] The fact that minimum number of nodes varied in wide range in the literature[6-17] indicates the lack of agreement in determining a universally accepted number.[1,3,6,7,10,14,16] Numerous factors are considered to influence results of lymph node the

Table 2. **Distribution of number of lymph nodes harvested per specimen according to body mass index in two groups of patients**

	I ≤ 16 cm	*II > 16 cm*	*p value*
	Median (mean)	*Median (mean)*	
All patients	5 (5,7 ± 3,0)	6 (7,9 ± 4,3)	0,004
BMI * < 25 kg/m²	7 (7 ± 3,5)	7 (8,5 ± 5,1)	0,15
BMI ≥ 25 kg/m²	5 (4,8 ± 2,5)	6 (7,5 ± 3,7)	0,004

• body mass index

Table 3. **Distribution of number of lymph nodes recovered per specimen in group I (≤16 cm)**

	n	*Median*	*Mean*	*p value*
Male	40	6	6,0 ± 2,8	0,24
Female	36	5	5,4 ± 3,1	
Age ≤ 68 years	39	5	5,7 ± 3,0	0,44
> 68 years	37	5	5,6 ± 3,0	
Type of operation				0,33
AR*	68	5	5,8 ± 3,0	
APR†	8	5	5,1 ± 2,6	
BMI‡ < 25 kg/m²	31	7	7,0 ± 3,5	0,008
≥ 25 kg/m²	45	5	4,8 ± 2,5	

*anterior resection, †abdominoperineal resection, ‡body mass index

Table 4. **Distribution of number of lymph nodes recovered per specimen in group II (>16 cm).**

	n	*Median*	*Mean*	*p value*
Male	38	6	7,3 ± 4,0	0,15
Female	27	6	8,8 ± 4,7	
Age ≤ 64 years	33	6	8,1 ± 4,7	0,39
> 64 years	32	6	7,7 ± 3,9	
Type of operation				0,36
AR*	31	7	8,2 ± 4,1	
APR†	34	8	7,7 ± 4,5	
BMI‡ < 25 kg/m²	28	7	8,5 ± 5,1	0,25
≥ 25 kg/m²	37	6	7,5 ± 3,7	

* anterior resection; †abdominoperineal resection; ‡body mass index

Table 5. **Distribution of rate of nodal metastases for T_3–T_4 tumors according to body mass index (kg/m²) in two groups of patients selected by length of resection specimens.**

	≤16 cm		*> 16 cm*		
	*n/N₁**	*%*	*n/N₁*	*%*	*p value*
Total	38/15	39	46/23	50	> 0,1
< 25 kg/m²	17/7	41	20/8	40	> 0,25
≥ 25 kg/m²	21/8	38	26/14	54	> 0,1

* n/N_1: total number of patients / number of node-positive specimens

recovery, or to make difficult the manual dissection of resection specimens. Some of them, with a focus on surgical technique and patients' obesity were evaluated in the present series. The study population included patients with rectal cancer only to avoid the impact of tumor location on the number of nodes recovered.[3,10] A further characteristic of our study is that data were collected from a non-specialized center where both operations and histopathological examinations were routinely performed by numerous surgeons and pathologists. This fact probably explains that our results including the mean number of lymph nodes harvested per specimen and the proportion of specimens in which no lymph nodes were found, were similar to those of a multicenter population-based study.[14] An average of 6.7 nodes per specimen is comparable to that previously reported by Scott and Grace[16] when traditional dissection was used and the median number of 6 nodes per patient is consistent with the results of low volume hospitals in rectal cancer surgery.[12] On the other hand many authors found and examined higher number of lymph nodes than we have recorded and their results suggest that an appropriate lymph node harvest could be achieved by careful thorough manual dissection.[3,6,7,10]

Difficulties in lymph node recovery from rectal resection specimens are well known from the report of Cawthorn et al[5] who found that lymph node metastases in the supralevator part of the mesorectum may be difficult to identify by manual dissection. Furthermore using fat clearance, metastases were frequently found in small lymph nodes (< 5 mm) located in the pararectal area.

The number of lymph nodes examined pathologically is a common result of the surgical and pathological procedures.[17] In our study the length of resection specimens measured by the pathologist represented the degree of surgical lymphadenectomy. For assessment of the skill and energy of pathologist in making careful manual dissection, the impact of patients' obesity on results of lymph node recovery was studied. From our findings the hypothesis that an appropriate number of lymph nodes could be more difficult to harvest by manual dissection in obese patients

than in those without obesity seems to be proven in case of short resection specimens (≤16 cm) first of all. Our observation that dissection of longer (>16 cm) specimens resulted in significantly higher number of lymph nodes than those with shorter length corresponds to that found Hernanz et al[10] comparing resection specimens from the right side and left side of colon.

The relatively low proportion of nodal metasases in our patients may be due to the low number of lymph nodes harvested per specimen. It is consistent with the well known positive relationship that was found between the total number of lymph nodes harvested per specimen and the percentage of node-positive cases.[7,8,14] In contrast to normally weighted patients, examination of short resection specimens in obese counterparts yielded not only significantly less lymph nodes but a moderately lower rate of nodal metastases also than that of longer specimens.

In conclusion our results confirmed the clinical significance of surgical technique for lymph node recovery and indicated that obesity had an unfavorable influence on this process when short rectal resection specimens were examined. Using manual dissection first of all this subset of patients can be at risk of understaging. Because the heterogenieity of surgical and pathological practice were thought to be the main explanation for variation in the number of lymph nodes examined,[14] standardized surgical technique and histopathological examination is needed even in non-specialized centers to harvest adequate numbers of lymph nodes.

References

1. *Blenkinsopp WK, Stewart-Brown S, Blesovsky L, et al:* Histopathology reporting in large bowel cancer. J Clin Pathol 34: 509-513, 1981
2. *Calle EE, Thun MJ, Petrelli JM, et al:* Body mass index and mortality in a prospective cohort of US adults. N Eng J Med 341: 1097-1105, 1999
3. *Caplin S, Cerottini J-P, Bosman FT, et al:* For patients with Dukes'B (TNM stage II) colorectal carcinoma, examination of six or fewer lymph nodes is related to poor prognosis. Cancer 83: 666-672, 1998
4. *Casillas S, Pelley RJ, Milsom JW:* Adjuvant therapy for colorectal cancer with lymph node metastases. Cancer 73: 2076-2082, 1994
5. *Cawthorn SJ, Gibbs NM, Marks CG:* Clearance technique for the detection of lymph nodes in colorectal cancer. Br J Surg 73: 58-60, 1986
6. *Cianchi F, Palomba A, Boddi V et al:* Lymph node recovery from colorectal tumor specimens: recommendation for a minimum number of lymph nodes to be examined. World J Surg 26: 384-389, 2002
7. *Goldstein NS, Sanford W Coffey M, et al:* Lymph node recovery from colorectal resection specimens removed for adenocarcinoma: Trends over time and a recommendation for a minimum number of lymph nodes to be recovered. Am J Clin Pathol 106: 209-216, 1996
8. *Hermanek P:* pTNM and residual tumor classifications: Problems of assessement and prognostic significance. World J Surg 19: 184-190, 1995
9. *Hermanek P, Henson DE, Hutter RVP, et al:* UICC TNM Supplement 1993: A commentary on uniform use. Springer-Verlag, New York, 1993.
10. *Hernanz F, Revuelta S, Redondo C, et al:* Colorectal adenocarcinoma: Quality of the assessment of lymph node metastases. Dis Colon Rectum 37: 373-377, 1994
11. *Herrera L, Villareal JR, Cert RT:* Incidence of metastases from rectal adenocarcinoma in small lymph nodes detected by clearing technique. Dis Colon Rectum 35: 783-788, 1992
12. *Hodgson DC, Zhang W Zaslavsky AM, et al:* Relation of hospital volume to colostomy rates and survival for patients with rectal cancer. J Natl Cancer Inst 95: 708-716, 2003
13. *Jass JR:* Prognostic factors in rectal cancer. Eur J Cancer 31A: 862-863, 1995
14. *Maurel J, Launoy G, Grosclaude P, et al:* Lymph node harvest reporting in patients with carcinoma of the large bowel. Cancer 82: 1482-1486, 1998
15. *Newland RC, Dent OF, Lyttle MNB, et al:* Pathologic determinants of survival associated with colorectal cancer with lymph node metastases. Cancer 73:2076-2082, 1994
16. *Scott KWM, Grace RH:* Detection of lymph node metastases in colorectal carcinoma before and after fat clearance. Br J Surg 76: 1165-1167, 1989
17. *Tepper JE, O'Connel MJ, Niedzwiecki D, et al:* Impact of number of nodes retrieved on outcome in patients with rectal cancer. J Clin Oncol 19: 157-163, 2001