PERGAMON

European Journal of Cancer 38 (2002) 911–918

European Journal of Cancer

www.ejconline.com

Patterns of lymphatic spread in rectal cancer. A topographical analysis on lymph node metastases

W.H. Steup[a,*], Y. Moriya[b], C.J.H. van de Velde[c]

[a]*Department of Surgery, Leyenburg Hospital, PO Box 40551, 2504 LN The Hague, The Netherlands*
[b]*Department of Colorectal Surgery, National Cancer Center Hospital, Tokyo, Japan*
[c]*Department of Surgery, Leiden University Medical Center, Leiden, The Netherlands*

Received 18 December 2001; accepted 4 February 2002

Abstract

The presence of lymph node (LN) metastases is the most important prognostic factor in rectal cancer. The exact LN status can only be known when an extended lymph node dissection (LND) has been performed, a process not routinely performed. If the likelihood of LN metastases can be more accurately assessed preoperatively, then an optimal multimodality treatment plan can be established. 605 patients with primary rectal cancer operated upon with wide LND (D3 level) were analysed for LN metastases combining topographical localisation and morphological features of the tumour. More distal rectal tumours tend to more LN metastases and more lateral lymphatic spread. Tumours $\geqslant 3$ cm show more LN metastases compared with those smaller than 3 cm. Depth of bowel wall invasion is strongly related to the presence of LN metastases. The peritoneal reflection has no discriminating role in the mode of spread. Intra-operative assessment by the surgeon for presence of LN metastases is not reliable. When localisation, depth of bowel wall invasion and diameter of a rectal tumour are known, a likelihood of LN metastases can be assessed pre-operatively, not intra-operatively.

Keywords: Rectal Cancer; LN; Topography; Lymphadenectomy

1. Introduction

The most important prognostic factor at present for survival after surgery for rectal cancer is both distant metastases and lymph node (LN) involvement. Since the basic publication of Grinnell [1] on the pattern of lymphatic spread of rectal cancer, various studies have been published on this subject. The early investigations focused on central spread of lymphatic metastases; later reports also emphasised local and lateral spread and the need for LN clearance [2–4]. The need for extended lymph node dissection (LND) is not accepted worldwide. There is no proof of a better locoregional control or survival and morbidity appears to be higher [5]. In the National Cancer Center Hospital, Tokyo, Japan, extended LND, upward and lateral, and *en-bloc* resection with the primary tumour is performed for invasive adenocarcinoma (i.e. beyond the proper muscle layer) of the rectum as a standard procedure. The surgical team meticulously manually dissects every fresh specimen and the LNs are mapped according to number and topography. This very comprehensive method enabled us to update and analyse the topographical anatomy of metastatic LNs in relation to those aspects of the primary tumour, which can be documented before surgery. This can be of help to predict more accurately for each individual patient the possibility, location and extent of lymph node metastases.

2. Patients and methods

In order to investigate the incidence, level and mode of spread of lymph node metastases, 837 patients with extended LND for primary adenocarcinoma of the rectum between 1974 and 1990 at the National Cancer Center Hospital, were reviewed retrospectively. Patients with distant metastases were included in this study only when a maximum effort had been made to remove the primary lesion together with regional or more distant LNs in case these metastases were considered resectable and the primary operation, therefore, was carried out with curative intent. Cancers confined to the mucosa were

* Corresponding author. Tel.: +31-70-359-2740; fax: +31-70-359-2477.

E-mail address: w.steup@leyenburg-ziekenhuis.nl (W.H. Steup).

0959-8049/02/$ - see front matter
PII: S0959-8049(02)00046-1

excluded because of the total lack of lymph node involvement in this series. Also excluded were patients with synchronous double cancers of the colon and/or rectum. In total, 605 patients were eligible for the analysis. In Japan, codes for the extramesenteric LN of the rectum are based on their localisation in relation to the internal and external iliac arteries as described in the rules of the Japanese Research Society for Cancer of the Colon and Rectum [6]. The same applies for the intramesenteric nodes, along the superior rectal arteries and inferior mesenteric artery. The LN are grouped into four levels, ranging from N1 (nearest) to N4 (most distant) according to their localisation and distance from the primary tumour; the approach is similar to that applied for the epirectal and pararectal, distal intermediate, proximal intermediate and central LN. The extent of LND is divided into four grades (D0–D3) according to the level of LN dissected, whereby D0 is incomplete dissection of N1 level LN, D1 complete dissection of N1 level nodes, D2 complete dissection of N1 and N2 level nodes and D3 complete dissection of N1, N2 and N3 level nodes. A D3 resection therefore implies para-aortic and paracaval stripping performed up to the level of the inferior margin of the transverse duodenum. Complete dissection of N4 nodes is not considered resection aimed for cure, although sometimes these LN are biopsied for intra-operative confirmation of metastatic spread. Extensive LND (D3 resections) implies removal of all fatty tissue containing lymphatics and LNs around the major abdominal and pelvic arteries (i.e. aorta below the level of the inferior margin of the transverse duodenum, inferior mesenteric artery (IMA), superior rectal artery (SRA), common iliac arteries and internal iliac arteries and their branches). The LNs of the external iliac and inguinal region are dissected only when LN metastases were suspected. The rectum was defined as lying below the upper edge of the second sacral vertebra, as can be observed on the barium-enema films, and was divided into three regions for analysis depending on the localisation of the tumour (as determined during surgery): when the tumour was located above the peritoneal reflection (PR) the region was called Ra ($n=133$), when located below the PR it was called Rb ($n=373$) and when located at the level of the PR (meaning 1 cm above and below), the region was called Rpr ($n=99$) (Figs. 1 and 2).

After surgery, all LNs were dissected from the fresh specimen and their localisation and number mapped. This approach yields an exact topographical representation of the LN combined with their number. All dissected LNs were evaluated by the surgeons for suspicion of metastases. Finally, all specimens and LN were examined histopathologically. Sensitivity, specificity, positive and negative predictive value and accuracy could be calculated. An analysis was performed of the localisation of the main tumour load in relation to bowel circumference, mesenteric (anterior), anti-mesenteric (pos-

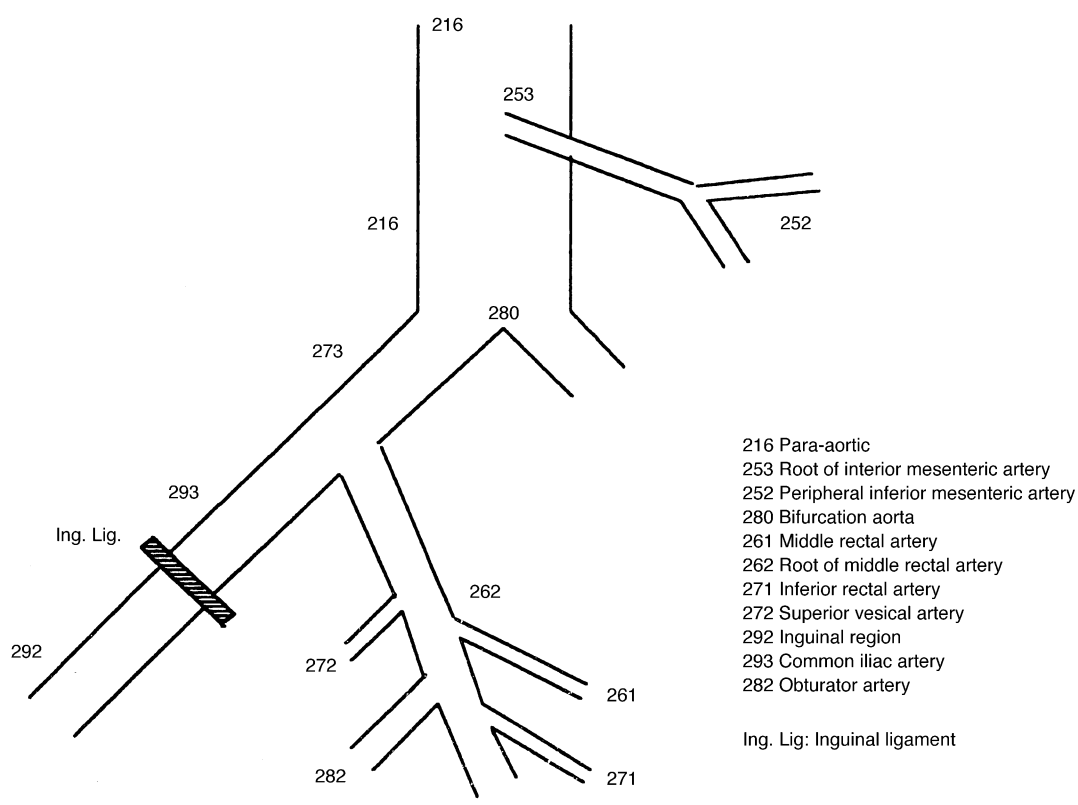

Fig. 1. Coding of the lymph nodes of the rectum (extramesentric) (Japanese Research Society for Cancer of the Colon, Rectum and Anus).

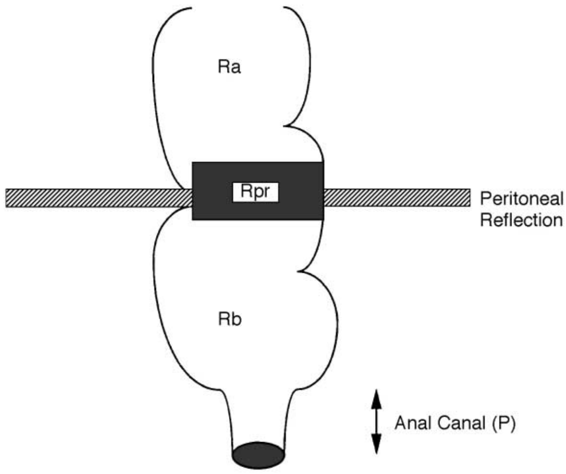

Fig. 2. Regions of the rectum (according to the Japanese Research Society for Cancer of the Colon, Rectum and Anus). Ra, rectum above peritoneal reflection; Rpr, rectum at peritoneal reflection; Rb, rectum below peritoneal reflection.

terior), lateral (left or right) or circular as well as diameter of the tumour (<3 cm, between 3 and 6 cm and >6 cm). As far as tumour histopathology is concerned analyses of depth of penetration (submucosal = sm, proper muscle layer = pm, subserosal = ss (called a1 below the PR because of lack of serosa), serosal = s (a2 below PR) and invading surrounding structures = si (ai below the PR)) were performed. In relation to localisation in segment and site in circumference of the primary tumour, the mode and level of spread were analysed (upward, lateral (unilateral or bilateral) or combined upward and lateral). Upward spread was defined as spread in the para-rectal direction, i.e. along the superior rectal and inferior mesenteric arteries. Lateral spread follows the middle rectal, obturator, external and internal iliac arteries. Furthermore, a separate group of those patients with massive metastases was distinguished ($n = 8$). Differences between the various groups were tested for statistical significance using the Chi-square test.

3. Results

Staging according to Turnbull's modification of Dukes' classification yielded stage A in 133 patients, B in 178, C in 226 and D (operated with extended LND with curative intent) in 69 patients. 3 patients had inguinal metastases, all with the primary localisation at the anus; and they were not included in further analyses, because they represent a separate route of lymph node metastatic spread (downward, extramesenteric). Of the 69 patients with distant metastasis, 62 had positive nodes, thus leaving in total 288 patients with lymph node metastases (47.6%) eligible for this study.

In total, 19 854 LN from 605 patients (average 32.8 per patient) were examined revealing 1510 (7.6%) with metastatic involvement in 288 patients (average 5.2 per patient). Of all the LN examined, therefore, 18 344 (92.4%) were tumour-free.

For the separate regions of the rectum, 56 patients out of 133 (42.1%) with nodes in the Ra region had metastasis in an average of 3.1 (range 13–1) nodes. For the Rpr region, 54 patients out of 99 (54.5%) had an average of 6.4 (range 44–1) nodes and for the Rb region 178 patients out of 373 (47.7%) had an average of 5.5 (range 84–1) metastatic LN (Table 1).

The incidence of LN metastasis along the inferior mesenteric artery (IMA) was 14.2% for the whole rectum, only 0.3% of which were at the root of the IMA. In contrast, the incidence of metastatic nodes along the MRA was 11.1%, the majority of which (9.6%) were located at its origin from the internal iliac artery. Surprising was the relatively large number of positive LN at the level of the obturator artery (6.0%, overall), the majority being attributable to tumours located below

Table 1
Incidence of lymph node (LN) metastases

	Para-rectal	r-IMA	p-IMA + SRA	Para-aortic	Ao.bif.	CIA	EIA	IIA	Inguin.	r-IMA	p-MRA	OA	IRA
Ra ($n = 133$)													
n	56	–	16	–	–	–	–	–	–	2	–	–	–
%	42.1	–	12.0	–	–	–	–	–	–	1.5	–	–	–
Rpr ($n = 99$)													
n	54	1	20	–	–	3	8	–	–	6	–	3	1
%	54.5	1.0	20.0	–	–	3.0	8.1	–	–	6.1	–	3.0	1.0
Rb ($n = 373$)													
n	162	1	48	19	2	13	17	28	3	50	9	33	1
%	43.4	0.3	12.9	5.1	0.5	3.5	4.6	7.5	0.8	13.4	2.4	8.9	0.3

r-IMA, root of inferior mesenteric artery; p-IMA, peripheral inferior mesenteric artery; Ao.bif., aortic bifurcation; CIA, common iliac artery; external iliac artery; IIA, internal iliac artery; Inguin., inguinal region; r-MRA, root of middle rectal artery; p-MRA, peripheral middle rectal artery; OA, obturator artery; IRA, inferior rectal artery; Ra, rectum above peritoneal reflection; Rpr, rectum at peritoneal reflection; Rb, rectum below peritoneal reflection.

Table 2
Incidence of lymph node (LN) metastases according to mode of spread ($n = 285$)

	Only pararectal	SRA + p-IMA	r-IMA/para-aortic	Lat. and upw.	Lateral alone	Massive
Ra ($n = 56$)	41	12	1	2	–	–
Rpr ($n = 54$)	30	14	2	4	1	3
Rb ($n = 175$)	82	16	4	55	13	5
Total	153	42	7	61	14	8
%	53.7	14.7	2.5	21.4	4.9	2.8

SRA, superior rectal artery; p-IMA, peripheral of inferior mesenteric artery; r-IMA, root of inferior mesenteric artery; Lat., lateral spread; Upw., upward spread; Ra, rectum above peritoneal reflection; Rpr, rectum at peritoneal reflection; Rb, rectum below peritoneal reflection.

the peritoneal reflection (5.4%, overall; 8.9% in the Rb region).

For Ra tumours, node metastasis was found in 54.1% of cases in the pararectal and IMA regions (upward spread), but there were only two (1.5%) occurrences of LN exhibiting a different mode of spread: both were at the root of the middle rectal artery (lateral spread). Pararectal and IMA metastases were found in 75.8 and 56.6% for the Rpr and Rb regions, respectively. It is, however, noted that the incidence of positive nodes representing the lateral spread was high in the Rpr and Rb regions: 21.2 and 41.8%, respectively.

The distribution according to the route of metastatic dissemination (Table 2), reveals that the incidence of only pararectal metastatic spread was 53.7%, 14.7% along the SRA and peripheral IMA, and 2.4% at the root of the IMA/para-aortic. Combined lateral and upward spread was found in 21.4%, only lateral in 4.9% and massive metastases in 2.8% of cases. For each region separately, the percentage of patients with only upward spread decreased as the distance of the tumour from the anal verge increased, meaning that other routes of spread became important. Lateral spread alone did not occur in the Ra region. Only 2 cases out of 56 (3.6%) exhibited combined lateral and upward spread; both were unilateral metastases and both tumours were located low in the Ra region. In contrast, for the Rb region, the tumours showed a higher incidence of lateral spread alone (13 out of 175, 7.4%) and combined mode of spread (55 out of 175, 31.4%). The 68 tumours in the Rb region exhibiting lateral spread caused 60.6% unilateral and 39.4% bilateral metastases.

Smaller tumours (< 3 cm) are associated with a lower incidence of lymph node metastases (22.7%) compared with tumours 3 cm and over (53.2%, $P < 0.001$). In the three separate regions, higher incidences of metastasis along the SRA, only lateral spread and combined upward and lateral spread were found for tumours $\geqslant 3$ cm (Table 3). For upward spread, no relationship could be demonstrated between the incidence of central LN (root IMA/para-aortic) and tumour size.

Lateral spread occurred only in antimesenteric or circular tumours in the Ra region, although the figures are too small to be conclusive. As for the sites of lymph node metastasis, mesenteric localisation seemed less common (25.9%) compared with the antimesenteric (48.8%), lateral (37.5%) and circular (56.0%) locations. For Rb tumours, a preference for unilateral versus bilateral could be demonstrated for the antimesenteric and mesenteric locations, but not for the lateral and circular tumours (Table 4).

A more specific look at this relationship reveals the large number of nodes representing combined and lateral spread both in the whole group and in the group of lower rectal cancers, in particular; in the latter, no real

Table 3
Incidence and way of spread of lymph node (LN) metastases in relation to tumour diameter ($n = 602$)

	< 3 cm	3–6 cm	> 6 cm
Ra ($n = 133$)			
Positive/total (%)	8/35 (22.9)	34/71 (47.9)	14/27 (51.9)[a]
Only pararectal	8	24	11
SRA/p-IMA	–	7	6
r-IMA/para-aortic	–	1	–
Upw./lat.	–	2	–
Lateral alone	–	–	–
Massive	–	–	–
Rpr ($n = 99$)			
Positive/total (%)	0/1	32/56 (57.1)	22/42 (52.4)
Only pararectal	–	17	15
SRA/p-IMA	–	11	5
r-IMA/para-aortic	–	1	1
Upw./lat.	–	2	3
Lateral alone	–	1	–
Massive	–	–	3
Rb ($n = 373$)			
Positive/total (%)	19/84 (22.6)	89/195 (45.6)	76/94 (71.3)[a]
Only pararectal	13	43	26
SRA/p-IMA	1	10	5
r-IMA/para-aortic	1	1	2
Upw./lat.	2	27	26
Lateral alone	2	6	5
Massive	–	2	3

r-IMA, root of inferior mesenteric artery; p-IMA, peripheral inferior mesenteric artery; SRA, superior rectal artery; Upw., upward spread; Lat., leteral spread; Ra, rectum above peritoneal reflection; Rpr, rectum at peritoneal reflection; Rb, rectum below peritoneal reflection.
[a] Chi-square: $P < 0.001$ between tumours smaller or $\geqslant 3$ cm.

Table 4
Incidence of lymph node (LN) metastases and mode of lateral spread in relation to tumour site ($n = 602$)

	Mesenteric	Antimesenteric	Lateral	Circular
Ra ($n = 56$)				
Pos/total	7/27	20/41	15/40	14/25
%	25.9	48.8	37.5	56.0
Unilateral	–	1	–	1
Bilateral	–	–	–	–
Rpr ($n = 54$)				
Pos/total	7/13	11/23	11/22	25/41
%	53.8	47.8	50.0	70.0
Unilateral	2	–	2	3
Bilateral	–	–	–	1
Rb ($n = 175$)				
Pos/total	44/88	51/105	57/129	23/48
%	50.0	48.6	44.2	47.9
Unilateral	12	14	10	7
Bilateral	4	8	10	6

Ra, rectum above peritoneal reflection; Rpr, rectum at peritoneal reflection; Rb, rectum below peritoneal reflection; pos, positive.

preference for mode of spread according to tumour site could be distinguished (Table 5).

Table 6 shows the incidence of lymph node metastasis in relation to the depth of bowel wall penetration. Of interest is the observation that there seems to be a tendency toward more LN metastases as the depth of penetration increases; it becomes statistically significant when the proper muscle layer is reached. This confirms once again that the incidence of LN metastasis is directly related to the depth of bowel wall invasion.

No correlation could be found between the mode of spread and level of spread, except for the fact that Rpr and Rb tumours spread to a higher N level (Table 7).

Of the 288 node-positive patients, the surgeon correctly staged 251 macroscopically. Understaging occurred in 37 cases. When no metastatic LN could be found ($n = 317$), 199 patients were correctly staged and 118 patients overstaged by the surgeon. As far as the macroscopic assessment by the surgeon as to whether the nodes were tumour-bearing is concerned, the final

Table 5
Level of spread of lymph node (LN) metastases in relation to tumour circumferential site ($n = 285$)

	Mesenteric	Antimesenteric	Lateral	Circular
Ra ($n = 56$)				
Only pararectal	3	16	13	9
SRA/p-IMA	4	3	2	3
r-IMA/para-aortic	–	–	–	1
Upw./lat.	–	1	–	1
Lateral alone	–	–	–	–
Massive	–	–	–	–
0.5				
Rpr ($n = 54$)				
Only pararectal	4	7	5	14
SRA/p-IMA	1	4	4	5
r-IMA/para-aortic	1	–	–	1
Upw./lat.	–	–	2	2
Lateral alone	1	–	–	–
Massive	–	–	–	3
Rb ($n = 178$)				
Only pararectal	199	25	29	9
SRA/p-IMA	6	3	5	3
r-IMA/para-aortic	1	–	2	1
Upw./lat.	14	16	17	8
Lateral alone	4	5	3	1
Massive	–	2	1	2

SRA, superior rectal artery; r-IMA, root of inferior mesenteric artery; p-IMA, peripheral inferior mesenteric artery; Lat., lateral; Upw., upward; Ra, rectum above peritoneal reflection; Rpr, rectum at peritoneal reflection; Rb, rectum below peritoneal reflection.

microscopic pathological evaluation revealed an accuracy of 74.3%, with a sensitivity of 87.1% and a specificity of 62.7%. The negative predictive value (NPV) was calculated 84.3%, whereas the positive predictive value (PPV) was 68.0%.

4. Discussion

There is still considerable controversy about the amount of tissue to be resected, i.e. the extent of resection with respect to the regional lymphatics and LNs. It has been demonstrated, in both clinical [7] and animal

Table 6
Incidence of lymph node (LN) metastases in relation to depth of invasion ($n = 605$)

	Ra			Rpr			Rb			Total % pos LN
	n	Pos LN	%	*n*	Pos LN	%	*n*	Pos LN	%	
sm	12	0	0	–	–	–	32	3	9.4	6.8
pm	30	6	20.0	9	3	33.3	93	32	34.4	31.1
ss/a1	34	18	52.9	26	13	50.0	88	38	43.2	46.6
s/a2	55	32	58.2	56	34	60.7	134	87	64.9	62.4
Invasive	2	0	–	8	4	50.0	26	18	69.2	61.1
Total *n*	133	56		99	54		373	178		

sm, submucosal; pm, proper muscle layer; ss, subserosal; al, rectum 'subserosal'; s, serosal; a2, rectum subserosal'; Ra, rectum above peritoneal reflection; Rpr, rectum at peritoneal reflection; Rb, rectum below peritoneal reflection.

Table 7
Level of spread according to mode of spread ($n=605$)

	Rectum	Ra	Rpr	Rb
Upward				
n1	153	40	30	83
n2	83	15	15	53
n3	15	1	5	9
n4	23	–	3	20
Lateral				
n1	2	–	–	2
n2	45	2	1	42
n3	16	–	5	11
n4	19	–	3	16
Combined upward and lateral	–			
n1	–	2	–	
n2	40	–	1	37
n3	13	–	4	9
n4	19	–	3	16

Ra, rectum; rectum above peritoneal reflection; Rpr, rectum at peritoneal reflection; Rb, rectum below peritoneal.

studies [8], that inadequate removal of tumour cells in lymph vessels and/or LNs can contribute to the development of recurrent colorectal cancer growth. The basic question remains, however, whether LN metastasis represents distant spread of disease or is still locoregional. If one accepts the latter theory, LND appears to be logical and should be done as radically as possible. In this way, one might prevent this secondary spread of cancerous cells by removing the LN and lymphatics. Although no circumstantial evidence is available that LND in solid cancer surgery has a beneficial impact on survival, it has been demonstrated to increase local tumour control [9]. Reports on local recurrence in rectal cancer remain conflicting, varying between 3 and 50%, but the cause of these differences is probably related to different interpretations of the definition of local recurrence and the use of different surgical techniques and definitions [10]. Concerning technique, this has already been demonstrated by Heald and colleagues [11]. Reports on the pattern of recurrence after LND show less local and pelvic recurrence [12], which supports the conclusion that some of the 'recurrent disease' after minimal resection might very well be residual disease rather than true recurrence.

An exact analysis of the topography and mode of spread is difficult, because such an analysis should include all LNs in the drainage area of the tumour. Grinnell's analysis of lymphatic metastases is still considered to be the standard work and his average number of 45 LN harvested per specimen (using the fat clearance technique, explaining his higher average number of LN per specimen) is evidence of his meticulous methods [1]. However, his specimens were surgical resection specimens which were, for his time, extensive but with relatively little lateral tissue in the pelvis. He himself already recognised this as a handicap, making it therefore not comparable to the extended LNDs performed in this study.

Any analysis regarding the number of involved LN, as already stated, is dependent on many different techniques, which might account for the large variations in the data available. Durkin and colleagues [13] showed that the use of fat clearance for pathological examination of cancer of the breast was superior to manual dissection, for both the number and the diameter of the LN. Later, more authors showed the superiority of the fat clearance technique also for colorectal cancer [14–17]. It was even suggested that when less than 13 LN are detected after manual dissection and the tumour is staged node-negative (Dukes' B), fat clearance should be performed as well [18]. Hermanek and colleagues [19] reviewed gross dissection and clearing techniques and noticed that the mean number of LN obtained by gross dissection of the rectum varied between 3.1 and 31.9. With clearance techniques, the number was higher, as was to be expected, and varied between 16.4 and 68. They proposed two programmes for pathological examination, one minimal and one extended, depending on the interest and funding possibilities of the institution. The main advantage of the fat clearance technique is that it yields a large number of LN, even nodes only 1 mm in diameter which have been shown to harbour cancerous deposits [20]. Arguments against this technique are that it is time-consuming (and therefore not practical in the clinical setting) and expensive. In this respect, it remains important to realise that there is still not really a standardised method for lymph node salvage from surgical specimens and this can be held responsible for the differences in staging, which makes comparison between different institutes hazardous, if not impossible [21].

Our finding of a 47.6% incidence of LN metastases is comparable to previous reports from the NCCH [5]; for the three separate regions of the rectum, too, there seems to be little difference in incidence. Distal tumours have a greater tendency toward lateral spread. The tumour location in relation to the peritoneal reflection for identification of different types of rectal tumours is not very specific as far as LN metastasis is concerned. Tumours located at the level of the peritoneal reflection already have an increasing tendency towards lateral spread. Our findings, however, as supported by Morikawa and colleagues [22], clearly show the relationship between the level of the rectum (low or high) and LN metastasis.

Our results also confirm earlier findings that the incidence of metastatic LNs at the base of the IMA is relatively low for all regions of rectal cancer. This had already been reported by Rosi and colleagues [23]. These findings undermine the rationale of a high ligation of the IMA.

Intra-operative staging by the operating surgeon is claimed to be unreliable [24] and confirmed by our findings that the sensitivity of a surgeon for prediction of LN involvement was only 87.1%, with a specificity of 62.7%. If macroscopic intra-operative assessment of LN were considered a tool in deciding to perform a LND, 37% of patients would undergo a LND unnecessarily and 12.8% of patients would be denied the procedure.

Intra-operative lymphatic mapping appears to be feasible in colorectal cancer, although the sentinel node concept, which has proven to be of value in breast carcinoma and melanoma, cannot yet be validated for rectal cancer [25].

A strong argument against pelvic LND is the very high rate of bladder and sexual dysfunction compared with conventional resections, directly related to damage to the pelvic autonomic nerves. The technique of nerve-sparing LND might decrease these complications, but it requires a meticulous surgical technique and accurate knowledge of the anatomy of the pelvic autonomic nervous system and prolongs operation time significantly [26].

Although, in the early years, endo-ultrasound staging seemed a very promising method, recently its value has been questioned—especially its ability to detect metastatic LN [27]. However, the accuracy of endorectal ultrasonography for estimation of the depth of invasion should make it possible to choose the surgical procedure suitable for each individual patient, taking into account the possibility of metastatic LNs. The risk for LN metastases in clinically estimated small tumours, however, can easily be underestimated by 15% [28].

This analysis again raises some questions about which surgical technique is to be used in the treatment of rectal cancer, depending on the preoperative assessment of whether LN metastases are present or not. Is total mesorectal excision sufficient in those tumours which are at a high risk for LN metastases or should radiotherapy and/or chemotherapy be added? Is total mesorectal excision warranted in rectal tumours located in the upper third of the rectum, or should these tumours be treated with either wider LND or in a multimodality (neo-)adjuvant scheme?

The importance of reliable preoperative staging of rectal tumours becomes more and more important since advances have been made in local treatment [29] and (neo-)adjuvant treatment [30]. Furthermore, new molecular biology techniques can detect micrometastases in LNs, previously pathologically examined and staged as N0 [31].

5. Conclusions

Tumour size, location and depth of bowel wall invasion can help in the prediction of whether LN metastases are present or absent in rectal cancer. Intra-operative judgement on the presence or absence of LN metastases by the surgeon is unreliable. At present time, however, our diagnostic preoperative methods cannot predict the true behaviour of a malignant rectal tumour concerning lymphatic spread. In the near future, more accurate preoperative staging techniques, in combination with molecular biology techniques, might designate whether patients with rectal cancer will need a local excision or wide resection, alone or in combination with (neo-)adjuvant treatment modalities, depending on the pre-treatment estimation of LN metastases.

Acknowledgements

This present study was supported in part by the Japanese Foundation for Promotion of Cancer Research (FPCR).

References

1. Grinnell RS. Lymphatic metastases of carcinoma of the colon and rectum. *Ann Surg* **131**, 1950, 494–507. Rectal cancer. *Cancer* **69**, 1992, 322–326.
2. Huddy SPJ, Husband EM, Cook MG, *et al*. Lymph node metastases in early rectal cancer. *Brit J Surg* 1993, **80**, 1457–1458.
3. Moriya Y, Hojo K, Sawada T, *et al*. Significance of lateral node dissection for advanced rectal carcinoma at or below the peritoneal reflection. *Dis Colon Rectum* 1989, **32**, 307–315.
4. Sanchez-Maldonado W, Rodriguez-Bigas MA, Weber TK, Penetrante RB, Petrelli NJ. Utility of mapping LN cleared from rectal adenocarcinoma specimens. *Surg Oncol* 1996, **5**, 123–126.
5. Hojo K, Koyama Y. The effectiveness of wide anatomical resection and radical lymphadenectomy for patients with rectal cancer. *Jap J Surg* 1982, **34**, 532–540.
6. Jinnai D. General rules for clinical and pathological studies on cancer of the colon, rectum and anus. Part I. Clinical classification. Japanese Research Society for Cancer of the Colon and Rectum. *Jap J Surg* 1983, **13**, 557–573.
7. Rao AR, Kagan AR, Chan PM, *et al*. Patterns of recurrence following curative resection alone for adenocarcinoma of the rectum and sigmoid colon. *Cancer* 1981, **48**, 1492–1495.
8. Schackert HK, Fidler IJ. Development of an animal model to study the biology of recurrent colorectal cancer originating from mesenteric lymph system metastases. *Int J Cancer* 1989, **44**, 177–181.
9. Heys SD. The relevance of tumour draining LN in cancer. *Surg Gynecol Obstet* 1992, **174**, 533–540.
10. Marsh PJ, James RD, Schofield PF. Definition of local recurrence after surgery for rectal carcinoma. *Br J Surg* 1995, **82**, 465–468.
11. Heald RJ, Husband EM, Ryall RHD. The mesorectum in rectal cancer: clue to pelvic recurrence? *Br J Surg* 1982, **69**, 613–616.
12. Philipshen SJ, Heilweil M, Quan SHQ, *et al*. Patterns of pelvic recurrence following definitive resections of rectal cancer. *Cancer* 1984, **53**, 1354–1362.
13. Durkin K, Haagensen CD. An improved technique for the study of LN in surgical specimens. *Ann Surg* 1980, **191**, 419–429.
14. Cawthorn SJ, Gibbs NM, Marks CG. Clearance technique for the detection of LN in colorectal cancer. *Br J Surg* 1986, **73**, 58–60.
15. Crucitti F, Doglietto GB, Bellantone R, *et al*. Accurate specimen preparation and examination is mandatory to detect LN and

avoid understaging in colorectal cancer. *J Surg Oncol* 1992, **51**, 153–157.
16. Herrera L, Villarreal JR. Incidence of metastases from rectal adenocarcinoma in small LN detected by a clearing technique. *Dis Colon Rectum* 1992, **35**, 783–788.
17. Hyder JW, T.M.T, Maycroft TC. A critical review of chemical lymph node clearance and staging of colon and rectal cancer at Ferguson Hospital, 1977 to 1982. *Dis Colon Rectum* 1990, **33**, 923–925.
18. Scott KWM, Grace RH. Detection of lymph node metastases in colorectal carcinoma before and after fat clearance. *Brit J Surg* 1989, **76**, 1165–1167.
19. Hermanek P, Giedl J, Dworak O. Two programmes for examination of regional LN in colorectal carcinoma with regard to the new pN classification. *Pathol Res Pract* 1989, **185**, 867–873.
20. Dworak O. Number and size of LN and node metastases in rectal carcinomas. *Surg Endosc* 1989, **3**, 96–99.
21. Morschel M, Heintz A, Dutkowski P, Bottger T, Junginger T. Influence of the number of dissected LN on local recurrence of rectal carcinomas. A staging effect. *Chirurgia* 1997, **68**, 1023–1028.
22. Morikawa E, Yasutumi M, Shindou K, *et al*. Distribution of metastatic LN in colorectal cancer by the modified clearing method. *Dis Colon Rectum* 1994, **37**, 219–223.
23. Rosi PA, Cahill WJ, Carey J. Ten year study of hemicolectomy in the treatment of carcinoma of the left half of the colon. *Surg Gynecol Obstet* 1962, **114**, 15–24.
24. Gall FP, Hermanek P. Die erweiterte lymphknotendissektion beim Magen-und Kolorektalen Karzinom. *Nutzen und Risken Chirurg* 1988, **59**, 202–210.
25. Joosten JJ, Strobbe LJ, Wauters CA, Pruszczynski M, Wobbes T, Ruers TJ. Intraoperative lymphatic mapping and the sentinel node concept in colorectal carcinoma. *Br J Surg* 1999, **86**, 482–486.
26. Hojo K, Vernava III AM, Sugihara K, *et al*. Preservation of urine voiding and sexual function after rectal cancer surgery. *Dis Colon Rectum* 1991, **34**, 532–534.
27. Detry RJ, Kartheuser AH, Lagneaux G, Rahier J. Preoperative lymph node staging in rectal cancer: a difficult challenge. *Int J Colorectal Dis* 1996, **11**, 217–221.
28. Blumberg D, Paty PB, Guillem JG, *et al*. All patients with small intramural rectal cancers are at risk for lymph node metastasis. *Dis Colon Rectum* 1999, **42**, 881–885.
29. Demartines N, von Flue MO, Harder FH. Transanal endoscopic microsurgical excision of rectal tumors: indications and results. *World J Surg* 2001, **25**, 870–875.
30. Saltz LB, Kemeny NE. Adjuvant chemotherapy for colorectal cancer. *Oncologist* 1996, **1**, 22–29.
31. Liefers GJ, Cleton-Jansen AM, van de Velde CJ, *et al*. Micrometastases and survival in stage II colorectal cancer. *N Engl J Med* 1998, **339**, 223–228.