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Original Article

Rectal cancer lateral lymph nodes: multicentre study of the impact of obturator and internal iliac nodes on oncological outcomes

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Abstract

Background: In patients with rectal cancer, enlarged lateral lymph nodes (LLNs) result in increased lateral local recurrence (LLR) and lower cancer-specific survival (CSS) rates, which can be improved with (chemo)radiotherapy ((C)RT) and LLN dissection (LLND). This study investigated whether different LLN locations affect oncological outcomes.

Methods: Patients with low cT3–4 rectal cancer without synchronous distant metastases were included in this multicentre retrospective cohort study. All MRI was re-evaluated, with special attention to LLN involvement and response.

Results: More advanced cT and cN category were associated with the occurrence of enlarged obturator nodes. Multivariable analyses showed that a node in the internal iliac compartment with a short-axis (SA) size of at least 7 mm on baseline MRI and over 4 mm after (C)RT was predictive of LLR, compared with a post-(C)RT SA of 4 mm or less (hazard ratio (HR) 5.74, 95 per cent c.i. 2.98 to 11.05 *vs* HR 1.40, 0.19 to 10.20; $P < 0.001$). Obturator LLNs with a SA larger than 6 mm after (C)RT were associated with a higher 5-year distant metastasis rate and lowered CSS in patients who did not undergo LLND. The survival difference was not present after LLND. Multivariable analyses found that only cT category (HR 2.22, 1.07 to 4.64; $P = 0.033$) and margin involvement (HR 2.95, 1.18 to 7.37; $P = 0.021$) independently predicted the development of metastatic disease.

Conclusion: Internal iliac LLN enlargement is associated with an increased LLR rate, whereas obturator nodes are associated with more advanced disease with increased distant metastasis and reduced CSS rates. LLND improves local control in persistent internal iliac nodes, and might have a role in controlling systemic spread in persistent obturator nodes.

Members of the Lateral Node Study Consortium are co-authors of this study and are listed under the heading Collaborators.

Introduction

The 5-year local recurrence (LR) rate in patients with advanced rectal cancer remains between 5 and 10 per cent, despite advances in preoperative planning with MRI, the introduction of neoadjuvant (chemo)radiotherapy ((C)RT) and standardized surgery with total mesorectal excision (TME)[1–7]. Accumulating evidence suggests that malignant lateral lymph nodes (LLNs) are a cause of LR after surgery with clear resection margins (R0)[8].

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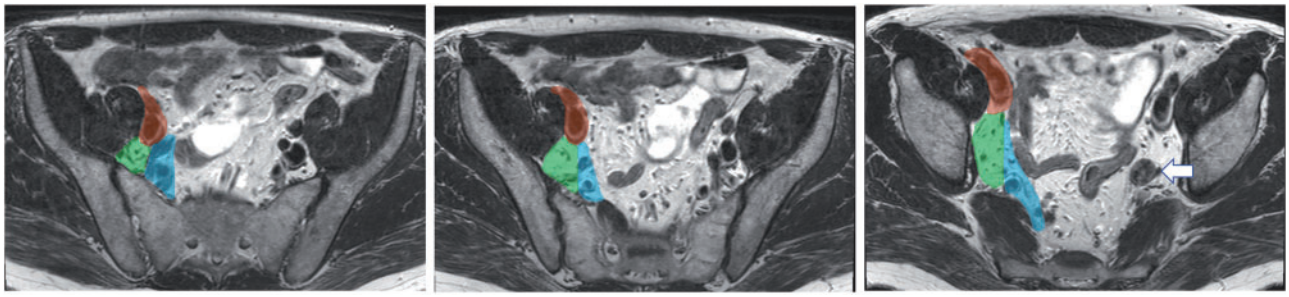

Fig. 1 MRI of lateral lymph nodes

Transverse MRI images demonstrating an enlarged lymph node with a short-axis size of 16 mm located in the internal iliac compartment (arrow), and topographical annotation of the external iliac compartment (red), obturator compartment (green), and internal iliac compartment (blue) at different levels.

Japanese studies[9,10] have shown that these lateral nodes occur mainly in low cT3–4 rectal tumours. Previous research[11] has found that the involvement of LLNs located in the external iliac compartment is predictive of metastatic disease, but not LR. Surgeons in the East, predominantly in Japan, have treated lateral nodes with a primarily surgical approach, combining TME with LLN dissection (LLND); some centres also add neoadjuvant (C)RT[12]. Conversely, standard Western surgical treatment for clinical stage II and III rectal cancer has been TME (without LLND), which relies on neoadjuvant treatment to eradicate lateral nodal disease[13].

A retrospective multicentre study[14] of 1216 patients with low cT3–4 rectal cancer from the East and the West found that an enlarged node with a short-axis (SA) size of at least 7 mm on pretreatment imaging in patients treated with (C)RT and TME led to a lateral local recurrence (LLR) rate of 19.5 per cent, which was lowered if LLND was performed (LLR rate 5.7 per cent; $P = 0.042$). In a further study[15] of 741 patients who underwent neoadjuvant (C)RT, the 3-year LLR was zero if a LLN with a pretreatment SA length of 7 mm or more had a SA size of 4 mm or less in the internal iliac compartment, or no more than 6 mm in the obturator compartment, on the restaging MRI.

The aim of this study was to determine whether enlarged LLNs in the internal iliac or obturator compartment occur differently, and are associated with dissimilar oncological outcomes thereby potentially requiring separate treatment strategies.

Methods

Each of the 12 participating centres received local ethical approval for the study. All patients who underwent surgery for cT3–4 rectal cancer located within 8 cm from the anal verge were identified in the participating centres[14,15]. Exclusion criteria were the absence of good-quality primary MRI, the presence of distant metastases (DM) at the time of initial staging, or a non-curative (R2) resection. Analyses of baseline characteristics, and LLN size and features on the primary MRI involved all included patients. For analyses of LLN size and response on the restaging MRI, only data from patients who had received neoadjuvant (C)RT and underwent restaging MRI were included. Data regarding staging, (neoadjuvant) treatment, and oncological follow-up were obtained.

Radiological assessment

Primary and, if available, restaging MRI was re-evaluated by an experienced local radiologist who was blinded to the patient outcomes. T2-weighted images, with a maximum slice thickness of 5 mm, were acquired in sagittal and transversal planes. Besides height and length of the tumour, cTNM stage, mesorectal fascia involvement, and LLN involvement were assessed using a specific guideline with a colour atlas of the pelvis that has been published previously[14]. A LLN was scored as visible when it was detectable on MRI, both with and without malignant features. LLN status assessment was based on the largest node on baseline MRI. The largest LLN SA (pre-SA) and long-axis size, and the presence of malignant features such as internal heterogeneity or border irregularity, were evaluated. Furthermore, the location of the LLN was divided into the internal iliac, external iliac, and obturator compartments as described previously (*Fig. 1*)[11]. The division between the internal iliac and obturator compartment was defined as the lateral border of the main trunk of the internal iliac vessels. The benign, long-stretched lymph nodes, located just behind the external iliac vein were not included in the assessment.

For all patients who received neoadjuvant (C)RT followed by restaging MRI, potential changes in SA (post-SA) and long-axis size, and the presence of malignant features of the same lateral node were evaluated.

Based on results published previously by the Lateral Node Study Consortium[15], the LLN response was defined as sufficient when a LLN with a pre-SA of at least 7 mm was downstaged to a post-SA of 4 mm or less in the internal iliac compartment, or 6 mm or under in the obturator compartment, as none of these patients had developed LR by 3 years.

(Surgical) treatment strategies and follow-up

All patients were discussed in a local multidisciplinary team meeting to determine individual treatment strategies. In general, both the internal iliac and obturator nodes were located in the standard irradiation field in each centre. However, specific information about irradiation fields could not be retrieved. There was no consensus on the surgical treatment of lateral nodal disease among the hospitals. LLND was defined as resection of the entire lymphatic tissue from the internal iliac and obturator compartments. Patient follow-up was undertaken according to local protocols. When a LR occurred, the MRI was further reviewed to determine the location according to the following, previously described division: anterior, presacral, anastomotic site, perineal or lateral[16,17].

Statistical analysis

Individual variables were compared using the *t* test and χ^2 tests. LR, LLR, DM, cancer-specific survival (CSS) and overall survival curves were calculated using the Kaplan–Meier method, and compared by means of the log rank test. Univariable logistic and Cox regression models were used to analyse the effects of covariables and thereby determine risk factors. Subsequently,

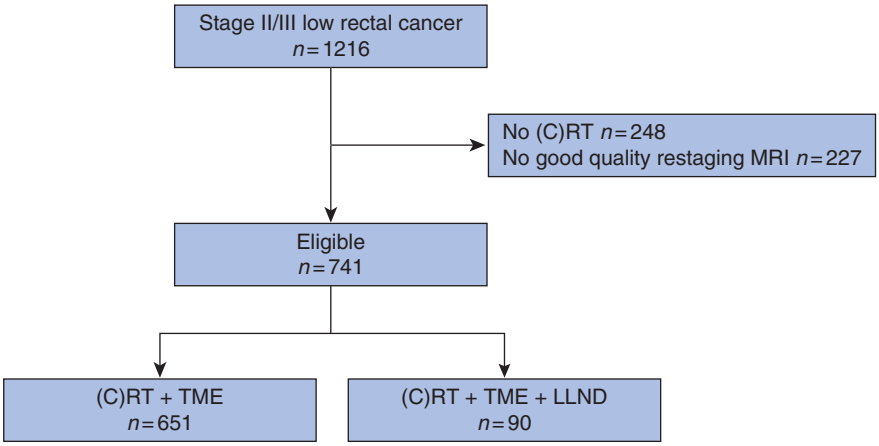

Fig. 2 Study flow diagram

(C)RT, (chemo)radiotherapy; TME, total mesorectal excision; LLND, lateral lymph node dissection.

multivariable analysis was performed using co-variables with a significant effect ($P < 0.100$) in univariable analyses. $P < 0.050$ was considered significant. Statistical analyses were done using SPSS® version 24 (IBM, Armonk, New York, USA).

Results

A total of 1216 patients were included in the study (*Fig. 2*), 192 (15.8 per cent) of whom had a LLN with a pre-SA of at least 7 mm. Of these 192 patients, 74 (38.5 per cent) had a LLN with a pre-SA of at least 7 mm in the internal iliac compartment and 103 (53.6 per cent) in the obturator compartment, resulting in a prevalence of 6.1 and 8.5 per cent respectively. *Table 1* shows general, tumour, and treatment characteristics of patients with a LLN with a pre-SA of at least 7 mm in the internal iliac or obturator compartment compared with those in patients without an enlarged LLN or a LLN with a pre-SA smaller than 7 mm in that specific compartment. Interestingly, advanced disease, cT4 and cN2 category were not associated with a LLN with a pre-SA of at least 7 mm located in the internal iliac compartment; however, they were associated with a LLN with a pre-SA of at least 7 mm in the obturator compartment. In 12 patients, only a selected resection of specific suspected lymph nodes was performed, which was not regarded as a formal LLND.

Among 53 patients with an enlarged LLN (pre-SA at least 7 mm) who underwent formal LLND, 27 (51 per cent) had at least one pathologically positive LLN. For patients with a LLN with a pre-SA of at least 7 mm and post-SA larger than 4 mm in the internal iliac or obturator compartment, respective rates were 17 of 23 and 5 of 11 patients[14,15].

Predictors of LLNs with a pre-SA of at least 7 mm in internal iliac and obturator compartments on baseline MRI

Table 2 shows the multivariable analyses for predictive factors for a LLN with a pre-SA of at least 7 mm in the internal iliac and obturator compartments; all factors from *Table 1* were tested in univariable analyses. This multivariable analysis demonstrated that there were no predictive factors for the occurrence of a LLN with a pre-SA of at least 7 mm in the internal iliac compartment. In contrast, a higher cT category (hazard ratio (HR) 2.57, 95 per cent c.i. 1.68 to 3.94; $P < 0.001$) and cN category (HR 2.57, 1.49 to 4.43; $P = 0.001$) were associated with LLNs with a pre-SA of at least 7 mm in the obturator compartment.

Response to neoadjuvant therapy of nodes in the internal iliac and obturator compartments

In the 741 patients who received (C)RT and restaging MRI (*Fig. 2*), univariable and multivariable analyses revealed that an increased SA size on baseline imaging was predictive of an insufficient response of LLNs in the internal iliac (HR 1.46, 95 per cent c.i. 1.09 to 1.97; $P = 0.012$) and obturator (HR 1.19, 1.03 to 1.38; $P = 0.017$) compartments, with a post-SA of more than 4 mm and over 6 mm respectively; no other factor influenced the response rate. Looking at the association between the primary tumour response and LLN response, among patients with an internal iliac node with a pre-SA of at least 7 mm, 17 per cent of those with a post-SA of 4 mm or less had a complete response of the primary tumour, compared with 4 per cent of patients with a post-SA exceeding 4 mm ($P = 0.120$). In patients with an obturator node with a pre-SA of at least 7 mm, 23 per cent of those with a post-SA of 6 mm or less had a complete response of the primary tumour, compared with 11 per cent of those with was a post-SA larger than 6 mm ($P = 0.219$).

Association between internal iliac nodes and oncological outcomes

Tables 3 and *S1* show the univariable and multivariable analyses of oncological outcomes and survival. Independent of a higher cT category or the type of surgery, the occurrence of an unresponsive LLN in the internal iliac compartment, with a pre-SA of at least 7 mm and post-SA larger than 4 mm, was associated with LLR (HR 5.74, 95 per cent c.i. 2.98 to 11.05; $P < 0.001$). In univariable Cox regression analyses, the occurrence of unresponsive LLNs in the internal iliac compartment did not influence DM (HR 0.69, 0.34 to 1.40; $P = 0.298$), CSS (HR 1.53, 0.94 to 2.57; $P = 0.116$) or overall survival (HR 1.17, 0.64 to 2.14; $P = 0.790$). Response of a LLN with a pre-SA of at least 7 mm in the internal iliac compartment to a post-SA of 4 mm or less did not influence the 5-year DM rate (13 *versus* 18 per cent respectively; $P = 0.517$) or CSS (87 *versus* 84 per cent respectively; $P = 0.793$), and results were similar in separate analyses of patients who underwent surgery with or without LLND (*Figs 3,b* and *4a,b* respectively).

Association between obturator nodes and oncological outcomes

In multivariable analysis, cT category (HR 2.22, 95 per cent c.i. 1.07 to 4.64; $P = 0.033$) and margin involvement (HR 2.95, 1.18 to

Table 1 Baseline characteristics according to presence of a lateral lymph node with a short axis length of at least 7 mm in the internal iliac or obturator compartment on initial MRI (1216 patients)

	Node with SA length ≥ 7 mm in internal iliac compartment on baseline MRI			Node with SA length ≥ 7 mm in obturator compartment on baseline MRI		
	No ($n = 1142$)	Yes ($n = 74$)	$P^{\dagger}$	No ($n = 1113$)	Yes ($n = 103$)	$P^{\dagger}$
Age (years)*	63 (54–71)	63 (54–70)	0.284‡	63 (54–71)	60 (51–69)	0.104‡
Sex ratio (M : F)	736 : 406	38 : 36	0.023	707 : 406	67 : 36	0.758
cT category			0.147			< 0.001
cT3	872 (76.4)	51 (69)		867 (77.9)	56 (54.4)	
cT4	270 (23.6)	23 (31)		246 (22.1)	47 (45.6)	
cN category			0.074			< 0.001
cN0	377 (33.0)	17 (23)		377 (33.9)	17 (16.5)	
cN+	765 (67.0)	57 (77)		736 (66.1)	86 (83.5)	
Distance from anorectal junction on MRI (cm)			0.055			0.018
≤ 4	563 (49.3)	45 (61)		545 (49)	63 (61.2)	
> 4	579 (50.7)	29 (39)		568 (51)	40 (38.8)	
Neoadjuvant therapy			< 0.001			0.046
None	243 (21.3)	5 (7)		236 (21.2)	12 (11.7)	
Short course radiotherapy	166 (14.5)	5 (7)		158 (14.2)	13 (12.6)	
CRT	733 (64.2)	64 (86)		719 (64.6)	78 (75.7)	
Type of surgery			0.242			< 0.001
Low anterior/ Hartmann's resection	574 (50.3)	32 (43)		573 (51.5)	33 (32.0)	
(Extended) abdominoperineal resection	568 (49.7)	42 (57)		540 (48.5)	70 (68.0)	
Lateral lymph node dissection			< 0.001			< 0.001
No	1038 (90.9)	36 (49)		994 (89.3)	80 (77.7)	
Yes	104 (9.1)	38 (51)		119 (10.7)	23 (22.3)	
Adjuvant chemotherapy			0.283			0.295
No	620 (59.7)	31 (53)		604 (59.8)	51 (54.3)	
Yes	418 (40.3)	27 (47)		406 (40.2)	43 (45.7)	
Missing	4	16		3	9	
ypT category			0.083			0.566
ypT0	158 (13.8)	5 (7)		146 (13.1)	17 (16.5)	
ypT1	56 (4.9)	6 (8)		56 (5.0)	6 (5.8)	
ypT2	302 (26.4)	15 (20)		288 (25.9)	29 (28.2)	
ypT3	560 (49.0)	40 (54)		557 (50.0)	43 (41.7)	
ypT4	66 (5.8)	8 (11)		66 (5.9)	8 (7.8)	
ypN category			< 0.001			0.467
ypN0	786 (68.8)	36 (49)		755 (67.8)	67 (65.0)	
ypN1	240 (21.0)	21 (28)		240 (21.6)	21 (20.4)	
ypN2	116 (10.2)	17 (23)		118 (10.6)	15 (14.6)	
Completeness of resection			0.079			0.753
R0	1076 (94.2)	66 (89)		1046 (94.0)	96 (93.2)	
R1	66 (5.8)	8 (11)		67 (6.0)	7 (6.8)	

Values in parentheses are percentages unless indicated otherwise:
*values are median (i.q.r.). SA, short axis; (C)RT, (chemo)radiotherapy.
† χ^2 test, except
‡ t test.

7.37; $P = 0.021$) were independent risk factors for DM, whereas unresponsiveness of obturator nodes to (C)RT was not an independent risk factor for metastatic disease (*Tables 3* and S1). The 5-year DM rate was significantly higher in patients with a node with a post-SA larger than 6 mm in the obturator compartment than in patients with a node with a post-SA of 6 mm or less (37 *versus* 15 per cent respectively; $P = 0.031$). Among patients who underwent surgical LLND, the 5-year DM rate in these subgroups did not differ (17 *versus* 22 per cent respectively; $P = 0.866$). However, in patients who had surgery but did not undergo LLND, the 5-year DM rate was significantly higher in patients with a post-SA exceeding 6 mm (43 *versus* 14 per cent; $P = 0.015$) (*Fig. 3c,d*). Furthermore, a LLN with a post-SA larger than 6 mm in the obturator compartment was associated with a lower 5-year CSS rate than a post-SA of 6 mm or less (79 *versus* 96 per cent respectively; $P = 0.005$). The 5-year CSS rate did not differ according to post-SA among patients who underwent LLND (83 *versus* 100 per cent respectively; $P = 0.221$);

Table 2 Multivariable regression analyses of predictive factors for a lateral lymph node with a a short-axis length of at least 7 mm in the internal iliac or obturator compartment (1216 patients)

	Node with SA length ≥ 7 mm in internal iliac compartment (*n* = 74)		Node with SA length ≥ 7 mm in obturator compartment (*n* = 103)	
	Hazard ratio	***P***	**Hazard ratio**	***P***
cT category		0.391		< 0.001
cT3	1.00 (reference)		1.00 (reference)	
cT4	1.26 (0.74, 2.13)		2.57 (1.68, 3.94)	
cN category		0.057		
cN0	1.00 (reference)		1.00 (reference)	0.001
cN+	1.73 (0.98, 3.03)		2.57 (1.49, 4.43)	
Distance from anorectal junction on MRI (cm)		0.057		0.067
≤ 4	1.00 (reference)		1.00 (reference)	
> 4	1.62 (0.99, 2.66)		1.50 (0.97, 2.31)	

Values in parentheses are 95 per cent confidence intervals. SA, short axis.

Table 3 Multivariable regression analyses of risk factors for lateral local recurrence, distant metastasis, cancer-specific survival and overall survival (741 patients)

	Lateral local recurrence		Distant metastasis		Cancer-specific survival		Overall survival	
	Hazard ratio	***P***	**Hazard ratio**	***P***	**Hazard ratio**	***P***	**Hazard ratio**	***P***
Age (per year)							1.05 (1.01, 1.08)	0.010
cT category		0.358		0.033		0.019		0.508
cT3	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
cT4	1.29 (0.73, 2.29)		2.22 (1.07, 4.64)		1.37 (1.03, 1.77)		0.76 (0.33, 1.73)	
cN category				0.594		0.001		
cN0			1.00 (reference)		1.00 (reference			
cN+			1.30 (0.50, 3.40)		1.61 (1.22, 2.12)			
SA length of LLNs in internal iliac compartment on baseline MRI (mm)		< 0.001						
< 7	1.00 (reference)							
≥ 7, unresponsive	5.74 (2.98, 11.05)							
≥ 7, responsive	1.40 (0.19, 10.20)							
Type of surgery		0.009		0.830		0.019		0.456
Low anterior/ Hartmann's resection	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
(Extended) abdominoperineal resection	2.22 (1.22, 4.03)		0.92 (0.44, 1.92)		1.35 (1.02, 1.72)		0.75 (0.35, 1.61)	
LLN dissection				0.562		0.067		0.137
No			1.00 (reference)		1.00 (reference)		1.00 (reference)	
Yes			0.79 (0.36, 1.73)		0.66 (0.43, 1.03)		0.53 (0.23, 1.23)	
Adjuvant chemotherapy								0.192
No							1.00 (reference)	
Yes							0.57 (0.24, 1.33)	
Margin involvement		0.059		0.021		< 0.001		0.003
R0	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
R1	2.12 (0.97, 4.64)		2.95 (1.18, 7.37)		3.51 (2.46, 5.01)		3.96 (1.58, 9.93)	

Values in parentheses are 95 per cent confidence intervals. SA, short axis; LLN, lateral lymph node.

however, for patients who did not undergo LLND, the 5-year CSS rate was 58 per cent in those with a post-SA larger than 6 mm and 87 per cent in those with a smaller post-SA ($P = 0.002$) (*Fig. 4c,d*).

Discussion

This study demonstrated that unresponsive LLNs located in the internal iliac compartment resulted in an increased 5-year LLR rate. In contrast, the occurrence of unresponsive obturator LLNs

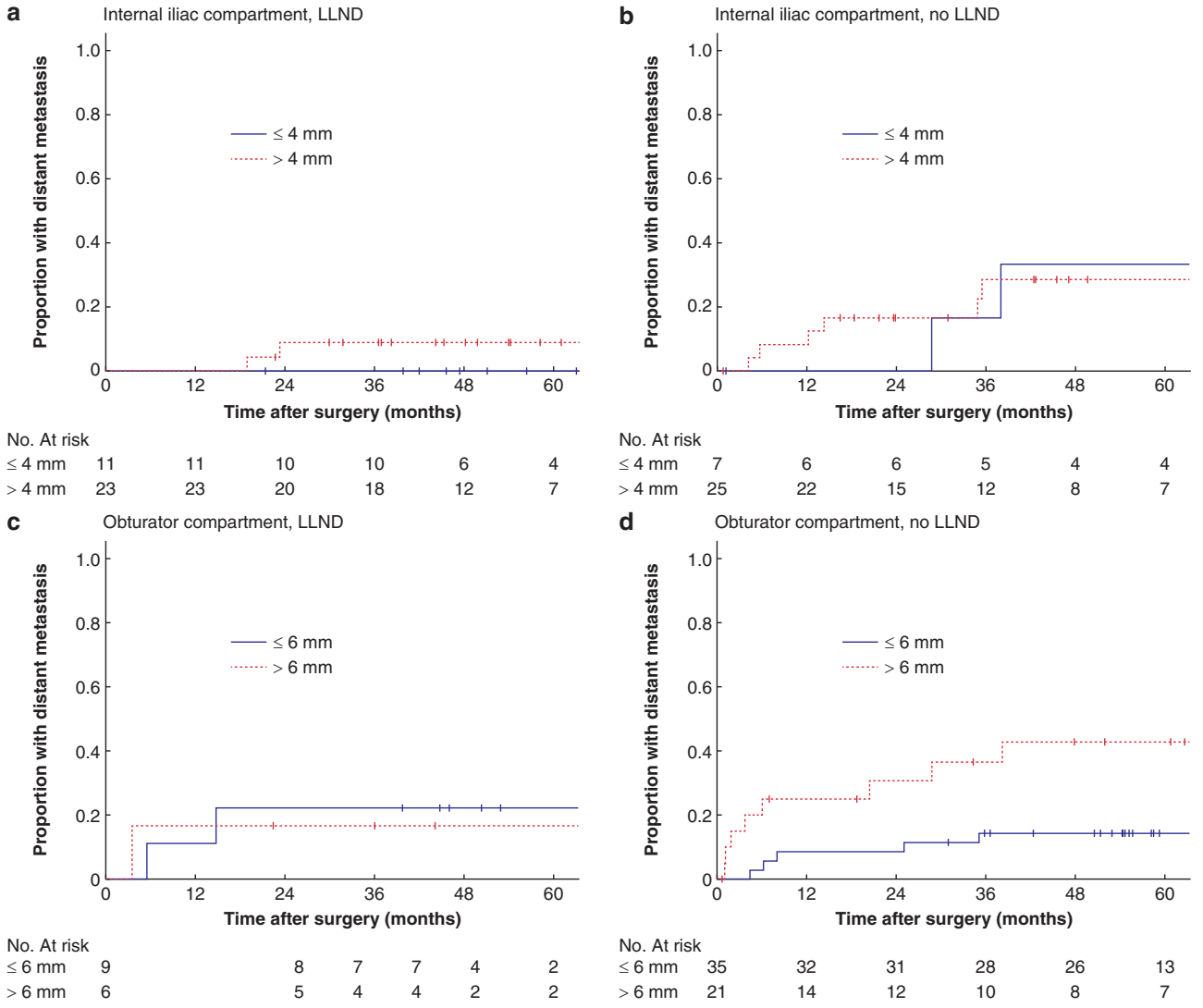

Fig. 3 Kaplan–Meier analyses of distant metastasis

a,b According to the short-axis (SA) length after (chemo)radiotherapy (post-SA) in patients with a lateral lymph node (LLN) with a SA length on baseline MRI (pre-SA) of 7 mm or more in the internal iliac compartment who **a** did or **b** did not undergo LLN dissection (LLND); **c,d** according to post-SA in patients with a LLN with a pre-SA of 7 mm or more in the obturator compartment who **c** did or **d** did not undergo LLND. **a** P = 0.329, **b** P = 0.976, **c** P = 0.866, **d** P = 0.015 (log rank test).

was related to more advanced tumour stage, and resulted in worse 5-year DM and CSS rates.

It has been shown previously that an enlarged node with a SA size of 7 mm or more on pretreatment imaging results in a high LLR rate[14]. In a subsequent study[15] it was found that, although the obturator compartment commonly contained the largest node, such nodes were less often enlarged and led to less LLR than when the internal iliac compartment contained the largest node. This study also identified different cut-off values on the restaging MRI for obturator and internal iliac nodes; the risk of LLR at 3 years was zero when obturator nodes had a SA size of 6 mm or less after neoadjuvant (C)RT, whereas this was 4 mm or less in internal iliac nodes. Internal iliac nodes also behaved more aggressively, with persistently enlarged nodes with a post-SA over 4 mm resulting in a 5-year LLR of 52.3 per cent, compared with 17.8 per cent in patients with obturator nodes with a post-SA exceeding 6 mm. The present study demonstrated that internal iliac nodes are less likely to respond to neoadjuvant therapy than obturator nodes (22 and 63 per cent respectively). These findings suggest that enlarged obturator nodes (pre-SA at least 7 mm) are more likely to be reactive.

The aim of the present study was to evaluate which factors are associated with the occurrence of enlarged lymph nodes in the internal iliac or obturator compartment, and the different behaviour patterns of these nodes. It was found that internal iliac node enlargement occurred independently of primary tumour stage, whereas higher cT and cN categories were associated with the presence of an enlarged node in the obturator compartment. In addition, the presence of unresponsive internal iliac nodes was associated with an increased 5-year LLR rate; in unresponsive obturator nodes 5-year LLR rate is also increased compared to small or responsive obturator nodes, but not significantly. These findings suggest that, although internal iliac nodal enlargement may be considered a locoregional ‘sentinel node’ without the tendency to metastasize, obturator nodes seem to behave more reactively and unresponsiveness in these nodes is an indicator of advanced disease that is likely to metastasize to distant sites. These findings support the work of Akiyoshi and colleagues[18], who showed

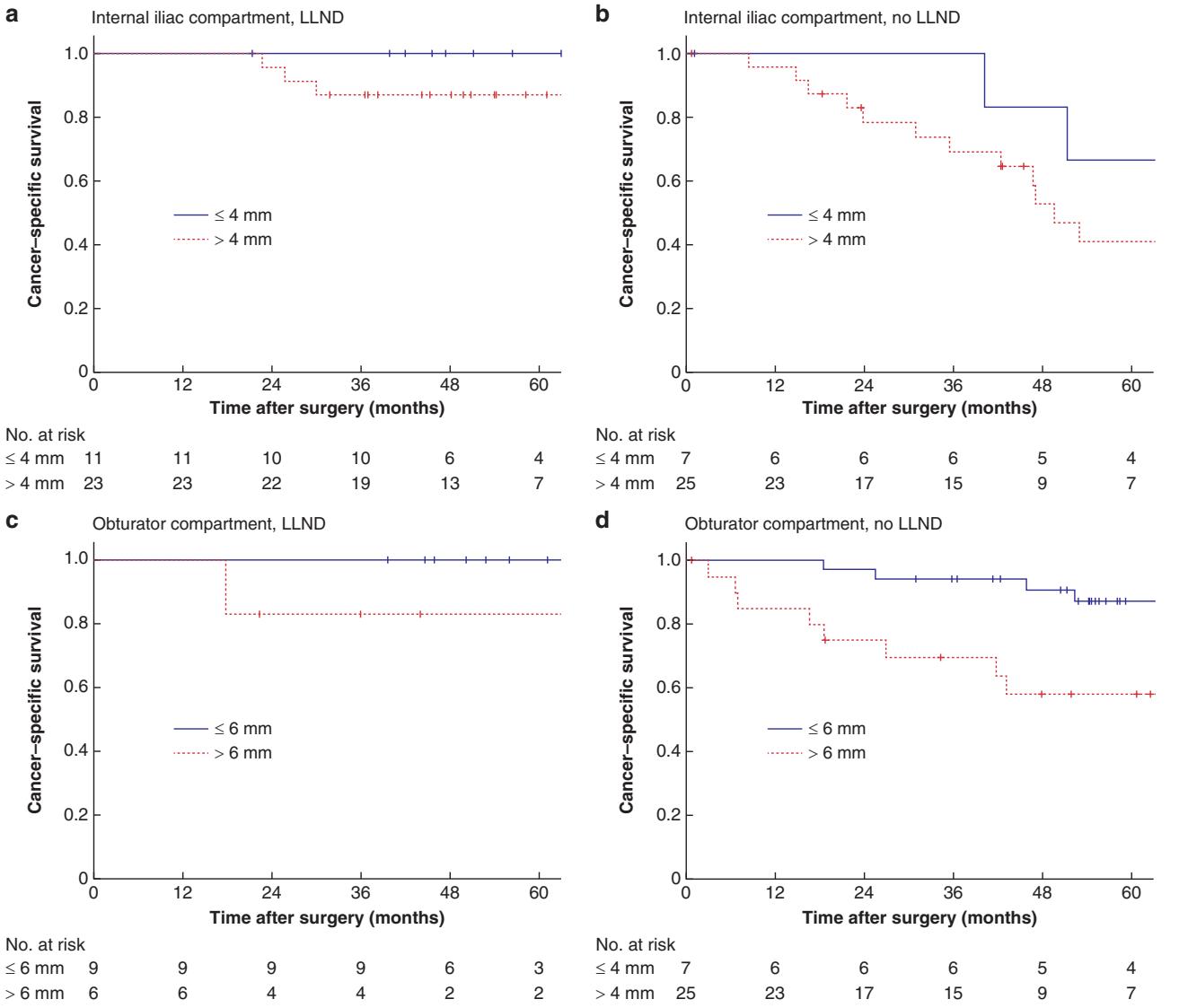

Fig. 4 Kaplan-Meier analyses of cancer-specific survival

a,b According to the short-axis (SA) length after (chemo)radiotherapy (post-SA) in patients with a lateral lymph node (LLN) with a SA length on baseline MRI (pre-SA) of 7 mm or more in the internal iliac compartment who **a** did or **b** did not undergo LLN dissection (LLND); **c,d** according to post-SA in patients with a LLN with a pre-SA of 7 mm or more in the obturator compartment who **c** did or **d** did not undergo LLND. **a** P = 0.243, **b** P = 0.213, **c** P = 0.221, **d** P = 0.002 (log rank test).

that the survival rate of patients with lateral node involvement confined to the internal iliac compartment was comparable to that of patients with N2a disease, and was significantly better than that of patients with LLN metastases beyond the internal iliac compartment.

In the present study, all MRI was re-evaluated by experienced radiologists, using a specially developed colour atlas to ensure uniformity. The atlas topographically displayed the locations of the internal and external iliac and obturator compartment based on easily recognizable landmarks in different planes. In this atlas, the medial border of the compartments is formed by the mesorectal fascia, and the internal iliac and obturator compartments are divided by the lateral border of the main trunk of the internal iliac vessels. Everything caudally of the infra–piriformis foramen was considered to comprise the obturator compartment as the main trunk of the internal iliac compartment leaves the pelvis as the internal pudendal artery at this point. This subdivision of compartments is clinically applicable as the landmarks are in accordance with the dissection planes during LLND; the obturator compartment resection is usually carried out first to facilitate clearance of the internal iliac compartment.

Routine LLND for all patients would be inappropriate[19] but appears to be beneficial in specific subgroups of patients. Patients with an unresponsive internal iliac node with a post-SA larger than 4 mm had a five-fold higher risk of developing of a LLR. In patients with unresponsive internal iliac nodes, the 5-year LLR rate was lowered from 52.3 to 8.7 per cent with LLND, stressing the importance of LLND in this specific subgroup. However, enlarged obturator nodes tend to be more responsive to neoadjuvant therapy and so might behave more reactively. Failure of an enlarged obturator node to respond to neoadjuvant therapy is a surrogate marker of more advanced disease, with a significantly increased 5-year DM rate and lower CSS compared with when obturator nodes are responsive. Although firm conclusions from this study are limited by the small sample size, it is noteworthy that patients with unresponsive obturator nodes did not develop

more local or distant recurrence or have decreased CSS after LLND, whereas those who did not undergo LLND had worse outcomes. The LaNoReC study (Lateral Nodal Recurrence in Rectal Cancer) may help clarify whether LLND can improve distant disease control.

Besides the limited number of participants, the retrospective multicentre nature of this study has intrinsic limitations, including the heterogeneity of patients and treatments. For example, most of the LLNDs were done in patients from Eastern centres, and subgroup analyses resulted in relatively small patient numbers making interpretation of these results difficult. Furthermore, the study design is associated with variability in the treatment and assessment of the included patients. It was possible to make radiological evaluation as uniform as possible by use of a colour atlas, but this was impossible for local treatment regimens. In addition, it is unclear what the response rates in the lateral compartment will be in the era of newer total neoadjuvant therapy and induction chemotherapy protocols[20], and whether the impact of lateral compartment disease will be reduced in this context.

The results of this study suggest that internal iliac nodal enlargement, which occurs independently of tumour stage, has a specifically high risk of LLR without the tendency to metastasize. Obturator nodes are more likely to respond to neoadjuvant therapy and more frequently behave reactively, and lack of response of these nodes is a marker of advanced disease that is likely to metastasize. LLND improves local control in persistent internal iliac nodes and there might be a role for this procedure in controlling systemic spread in patients with persistent obturator nodes.

Collaborators

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Supplementary material

Supplementary material is available at *BJS* online.

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