Techniques in Coloproctology (2019) 23:151–159
https://doi.org/10.1007/s10151-019-01947-6

ORIGINAL ARTICLE

The clinical significance of a pathologically positive lymph node at the circumferential resection margin in rectal cancer

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Received: 14 June 2018 / Accepted: 9 February 2019 / Published online: 19 February 2019

Abstract

Background This study aimed to determine if the nature of circumferential resection margin (CRM) involvement, either by tumour or lymph nodes, had an impact upon local recurrence and survival in rectal cancer.

Methods A retrospective analysis of a prospectively collected database was performed. Consecutive patients with stage I-III rectal cancer having curative surgery were included. All specimens were analysed by a single histopathologist. Statistical analysis was performed using chi-squared test and Kaplan–Meier.

Results Of 265 patients, 29 (11%) had a positive CRM. Compared to patients with a negative CRM, a positive margin due to tumour was associated with a higher 5-year cumulative incidence of local recurrence (43.7% versus 8.8%, $p=0.001$) and distant metastases (62% versus 13.6%, $p=0.001$) with poorer 5-year cancer-specific survival (32% versus 87.8%, $p=0.001$). Although patients with margin positivity due to lymph nodes had a higher rate of distant metastases (41.3% versus 13.6%, $p=0.004$) and poorer 5-year cancer-specific survival (59.3% versus 87.8%, $p=0.038$), the rate of local recurrence was comparable to that of patients with negative margins (8.3% versus 8.8%, $p=0.694$).

Conclusions Our findings suggest that the nature of CRM involvement may be important in determining prognosis in rectal cancer. Local recurrence is higher only when there is tumour present at the margin. Lymph node involvement of the margin confers similar risk of local recurrence to patients with CRM-negative, node-positive disease. These results need further evaluation in multicentre, prospective studies.

Keywords Rectal cancer · Circumferential · Resection margin · Lymph node

Introduction

In rectal cancer surgery, the circumferential resection margin (CRM) refers to the non-peritonealised bare area of the resection specimen created by surgical dissection of the rectum from its surrounding tissue [1]. Tumour involvement of the CRM, defined as tumour within 1 mm of the CRM, is the single most important factor in predicting local recurrence after surgery [2–4]. Excision of the entire mesorectal envelope achieved through total mesorectal excision (TME) surgery significantly reduces rates of local recurrence by removing the tumour with the surrounding mesorectum which contains lymph nodes, fat and tumour deposits [5]. The use of neoadjuvant downstaging chemoradiation can result in tumour shrinkage thereby reducing the risk of tumour encroachment of the CRM [6]. Hence, both TME surgery and neoadjuvant therapy have successfully reduced rates of local recurrence for patients with rectal cancer [7]. Nevertheless, there remains a group of patients who have tumour involvement of the CRM despite these measures [8–10]. The role of CRM involvement in determining prognosis has recently been questioned [11–13] as the earlier studies which highlighted its importance included patients who had not had TME surgery. Some authors argue that CRM positivity with modern rectal cancer treatment identifies those that have an aggressive tumour which is likely to metastasize, rather than indicating insufficient surgical excision. In such cases, CRM involvement could be associated with higher distant metastasis rates, as well as with a higher likelihood of local recurrence.

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Previous studies investigating the impact of CRM involvement on local recurrence and survival have grouped together patients with tumour involving the CRM and those with involved lymph nodes at the CRM. Few have examined the role of pathological lymph nodes involving the CRM as a separate entity. Of the studies that have made this distinction, there has been no compelling evidence that positive lymph nodes involving the CRM have an adverse effect on survival. Some have argued that they are of no prognostic significance [3, 14]. The aim of this study was, therefore, to determine if positive lymph nodes involving the CRM have an impact upon local recurrence and survival following surgery for rectal cancer.

Materials and methods

Patients having surgery at our institution between April 2005 and July 2013 were included if they had stage I–III biopsy proven adenocarcinoma of the rectum where the distal edge of the tumour was up to 15 cm from the anal verge. All patients were assessed in the specialist colorectal multidisciplinary team meeting to determine a treatment pathway. Neoadjuvant and adjuvant therapy were given according to the Association of Coloproctology of Great Britain and Ireland (ACPGBI) guidelines for colorectal cancer over the study period [15]. A single histopathologist with a particular interest in rectal cancer collected histopathological data regarding these patients in a prospectively collected database and only patients whose pathological analysis was performed by this histopathologist were included. Pathological workup of the specimen was performed as previously described [16]. Additional data regarding clinical outcomes such as local recurrence, overall and disease-free survival were obtained from electronic case records.

Permission for the study was granted by the Heart of England NHS Foundation Trust Audit Department. Data were anonymised prior to analysis.

Definition of groups

An involved CRM (CRMI) was defined as the presence of tumour or a positive lymph node within 1 mm of the CRM. Patients who had a positive CRM due to extramural vascular invasion or who had pelvic exenteration were excluded from the study. Local recurrence (LR) was defined as disease in the pelvis, at the anastomosis or at the operative site, irrespective of whether there was distant recurrence. Patients with distant recurrence who also had local recurrence were included in the local recurrence group to ensure that the rate of local recurrence was not underestimated. Distant metastases (DM) included patients who only had metastatic spread to distant organs outside the pelvis with no evidence of local recurrence.

Outcomes in terms of local and distant recurrence were compared between the following groups of patients:

- CRM negative versus CRM positive.
- CRMI (T) versus CRM negative.
- CRMI (LN) versus CRM negative.
- CRMI (LN) versus CRM negative, node positive.

Statistical analysis

All data were analysed using SPSS version 21. The chi-squared test and Fisher's exact test were used to determine differences between categorical variables. The 5-year cumulative incidence of LR and DM was calculated using Kaplan–Meier analysis. The log rank test was utilised to ascertain differences in incidence of LR and DM as well as overall and cancer-specific survival. A p value of < 0.05 was considered to be statistically significant. Mean survival was calculated using Kaplan–Meier analysis. Multivariate analysis was performed to identify independent predictors of local and distant recurrence using Cox regression. Variables found to reach statistical significance (p value of < 0.05) on univariate analysis were selected for the multivariate model.

Results

In total, 265 patients were included in the study. The median lymph node yield was 38 lymph nodes (range 9–122 lymph nodes). The 5-year cumulative incidence of LR and DM was 10.5% and 16. 5% respectively, with median follow-up of 53 months (IQR 29–74 months). Patient demographics and clinical details are given in Table 1. Patients with CRM-negative tumours were more likely to have undergone an anterior resection than abdominoperineal excision and had tumours with earlier T stage which were node negative compared to patients with involved margins after surgery (see Table 2).

CRM involvement

There were 29 patients (11%) with an involved CRM; 16 patients had tumour at the CRM and 13 patients had a positive lymph node. The patient demographics and clinical details of these patients are given in Table 3. Patients with CRM involvement due to tumour were more likely to have had an abdominoperineal excision compared to those with a positive lymph node at the CRM. No preoperative neoadjuvant therapy was given to 6 patients (46.2%) with CRM involvement due to a positive lymph node, 5 (38.2%) had short course treatment and 2 (15.4%) had long course

Table 1 Demographic and clinical details of all patients that were included in the study

Variables	
Gender	
Females	83 (31%)
Males	182 (69%)
Age	
Median (IQR) years	69 (60–75)
Neoadjuvant treatment	
None	96 (36.2%)
Short course	88 (33.2%)
Long course	81 (30.6%)
Procedures	
Anterior resection	178 (67.2%)
APER	87 (32.8%)
Histology	
TME	
Muscularis propria	57 (21.5%)
Intramesorectal	72 (27.2%)
Mesorectal	136 (51.3%)
T Stage	
(y)pT0	6 (2.3%)
(y)pT1	35 (13.2%)
(y)pT2	85 (32.1%)
(y)pT3	119 (44.9%)
(y)pT4	20 (7.5%)
LN Yield - Median (IQR)	38 (29–59)
Extramural vascular invasion	
Present	78 (29%)
Absent	187 (71%)
N Stage	
(y)pN0	177 (66.8%)
(y)pN1	59 (22.3%)
(y)pN2	29 (10.9%)
CRM/LN-positive/negative groups	
Sub-group classification	
CRM negative	236 (89.0%)
CRM positive	29 (11%)
CRMI (T)	16 (6.0%)[a]
CRMI (LN)	13 (4.9%)[a]
30-day mortality (total)	6 (2.3%)
90-day mortality (total)	7 (2.6%)
Overall survival (5 years)	72.5%
Cancer-specific survival (5 years)	82.8%
Follow-up period	
Median months (IQR)	53 (29–74)

CRM circumferentiala resection margin, CRMI CRM involvement, CRMI(T) tumour involving the CRM, CRMI (LN) lymph node involving the CRM, APER abdominoperineal resection, TME total mesorectal excision

aIs the % of the cohort

Table 2 Demographics and clinical details of patients with positive and negative CRM

Cohort = 265	CRM negative	CRM positive	*p* value
Number	236 (89%)	29 (11%)	
Gender			
Female	72 (30.5%)	10 (34.5%)	0.457[a]
Male	164 (69.9%)	19 (65.5%)	
Age (cohort median = 69 years)			
Median years (IQR)	69 (60–75)	70 (60–76)	0.576[c]
≤ 69 years	121 (51.3%)	14 (48.3%)	0.764[a]
> 69 years	115 (48.7%)	15 (51.7%)	
Neoadjuvant treatment			
None	84 (35.6%)	12 (41.4%)	0.543[a]
Short course	83 (35.2%)	5 (17.2%)	0.053[a]
Long course	69 (29.2%)	12 (41.4%)	0.181[a]
Procedures			
AR	163 (69.1%)	15 (51.7%)	0.061[a]
APER	73 (30.9%)	14 (48.3%)	
TME grade			
Muscularis propria	46 (19.5%)	11 (37.9%)	0.022[a]
Intramesorectal	63 (26.7%)	9 (31.0%)	0.617[a]
Mesorectal	127 (53.8%)	9 (31.0%)	0.020[a]
T stage			
(y)pT0	6 (2.5%)	0	0.626[b]
(y)pT1	35 (14.8%)	0	0.035[b]
(y)pT2	79 (33.5%)	6 (20.7%)	0.163[a]
(y)pT3	103 (43.6%)	16 (55.2%)	0.238[a]
(y)pT4	13 (5.5%)	7 (24.1%)	0.002[b]
Lymph node yield (IQR)	39 (29–51)	33 (23–46)	0.087[c]
N Stage			
(y)pN0	170 (72.0%)	7 (24.1%)	0.001[a]
(y)pN1	46 (19.5%)	13 (44.8%)	0.003[a]
(y)pN2	20 (8.5%)	9 (31.0%)	0.001[b]

CRM circumferential resection margin, *AR* anterior resection, *APER* abdominoperineal resection, *TME* total mesorectal excision

[a]Pearson's chi−square test

[b]Fishers exact test and

[c]Mann−Whitney *U* test (Pearson's chi-square test is done for frequency data & if any of the expected cell frequency is less than 5, the Fishers exact test is done)

treatment. Of the 16 patients with a tumour threatening the CRM, 6 (37.5%) had no pre-operative radiotherapy and 10 had long course (62.5%). Of the patients with a negative CRM, 84 (35.6%) did not have preoperative radiotherapy, 83 (35.1%) had short course and 69 (29.2%) had long course treatment.

Local recurrence and distant metastases

The 5-year cumulative incidence of LR and DM was 10.5% and 16.5% respectively (see Table 4). LR was detected in

Table 3 Patient demographics and clinical details of patients with CRMI secondary to tumour [CRMI (T)] versus those with CRMI due to positive lymph nodes [CRMI (LN)]

Sub group total = 29	CRMI(T)	CRMI(LN)	*p* value
Frequency	16 (6.0%)	13 (4.9%)	
Gender			
Female	5 (31.3%)	5 (38.5%)	0.714[b]
Male	11 (68.8%)	8 (61.5%)	
Age			
Median (IQR)	66 years (60–77)	72 years (58–77)	0.846[c]
≤ 69 years	9 (56.3%)	5 (38.5%)	0.340[a]
> 69 years	7 (43.8%)	8 (61.5%)	
Neoadjuvant treatment			
None	6 (37.5%)	6 (46.2%)	0.639[a]
Short course	0	5 (38.5%)	0.010[b]
Long course	10 (62.5%)	2 (15.4%)	0.010[a]
Procedures			
AR	4 (25.0%)	11 (84.6%)	0.002[b]
APER	12 (75.0%)	2 (15.4%)	
TME grade			
Muscularis propria	7 (43.8%)	4 (30.8%)	0.702[b]
Intra-mesorectal	3 (18.8%)	6 (46.2%)	0.225[b]
Mesorectal	6 (37.5%)	3 (23.1)	0.454[b]
T stage			
(y)pT0	–	–	
(y)pT1	–	–	
(y)pT2	2 (12.5%)	4 (30.8%)	0.363[b]
(y)pT3	9 (56.3%)	7 (53.8%)	0.887[a]
(y)pT4	5 (31.3%)	2 (15.4%)	0.410[b]
Lymph node yield	30 (9–56)	41 (15–71)	0.215[c]
N Stage			
(y)pN0	7 (43.8%)	–	0.008[c]
(y)pN1	3 (18.8%)	10 (76.9%)	0.001[a]
(y)pN2	6 (37.5%)	3 (23.1%)	0.454[b]

Usually Pearson's Chi−square test is done for frequency data and if any of the expected cell frequency is less than 5, the Fishers exact test is done

CRM circumferential resection margin, *CRMI* CRM involvement, *CRMI(T)* tumour involving the CRM, *CRMI (LN)* lymph node involving the CRM, *AR* anterior resection, *APER* abdominoperineal resection, *TME* total mesorectal excision

[a]Pearson's Chi−square test

[b]Fishers exact test and

[c]Mann−Whitney *U* test

22/269 (8%) of patients, of which 12 patients also had DM. There were 39 (14%) additional patients who only had DM.

There was a significant difference in the 5-year cumulative incidence of both LR and DM between patients with CRM involvement compared to those with a negative CRM (LR 26.5% % versus 8.8%, $p = 0.001$; DM 52.5% versus 13.6%, $p < 0.001$ respectively). Similarly, when patients with tumour involving the CRM (CRMI(T)) were compared to patients with a negative CRM, a similar difference in LR (43.7% versus 8.8%, $p = 0.001$) and DM (62% versus 15.3%, $p = 0.001$) was observed. However, CRMI due to positive lymph nodes (CRMI(LN)) was only associated with a higher DM rate (41.3% versus 13.6%, $p = 0.004$) and comparable rate of LR in both groups (8.3% versus 8.8%, $p = 0.694$).

The patients with CRMI(LN) were compared to CRM-negative, node-positive patients ($n = 63$). This showed no difference in LR (8.3% versus 15.5%, $p = 0.846$) or any difference in DM (41.3% versus 19.8%, $p = 0.135$).

Clinical factors affecting local recurrence and distant metastases

Univariate analysis of other clinical and pathological factors that affect LR and DM is shown in Table 5. T-stage, N-stage and CRM resection margin status were associated with differences in both LR and DM -free survival. Extramural vascular invasion was only associated with shorter DM-free survival [HR 3.11 (1.74–5.56), $p = 0.001$] and no differences were found in LR (HR 2.18 (0.92–5.18), $p = 0.080$). On multivariate analysis, short course radiotherapy was the only independent predictor for LR [HR 0.264 (95% CI 0.073–0.960), $p = 0.043$]. In comparison, nodal positivity [N1 HR 2.323 (95% CI 1.040–5.185), $p = 0.040$] and N2 [HR 2.620 (95% CI 1.118–6.134), $p = 0.027$] and a positive CRM [HR 3.350 (95% CI: 1.625–6.906), $p = 0.001$] were independent predictors of poorer DM-free survival.

Overall (OS) and cancer-specific survival (CSS)

CRMI(T) was associated with poorer 5-year OS and CSS compared to CRM-negative patients (20.0% versus 77.5%, $p = 0.001$; 32.0% versus 87.8%, $p = 0.001$, respectively) (see Figs. 1, 2). There was no difference in 5-year OS between patients with CRMI(LN) compared to CRM-negative patients (49.4% versus 77.5%, $p = 0.694$), though these patients did have poorer 5-year cancer-specific survival (59.3% versus 87.8%, $p = 0.038$). However, if CRM-negative patients with nodal disease are compared to CRMI(LN), there was no difference in 5-year OS (69.5% versus 49.4%, $p = 0.134$) or CSS (86.5% versus 59.3%, $p = 0.228$) (see Table 6).

Discussion

Involvement of the CRM in rectal cancer is an important prognostic factor as it predicts higher LR which results in poorer overall and cancer-specific survival [2–4, 17, 18]. However, our study illustrates that if there are positive lymph nodes involving the CRM, patients have outcomes similar

Table 4 Five-year cumulative incidence of local recurrence and distant metastases

	Local recurrence (%)	95% CI	*p* value	Distance metastases (%)	95% CI	*p* value
Overall (Cohort)	10.5	6.2–14.8%		16.5%	11.6–21.4%	
CRM negative	8.8	4.5–13.1%	0.001	13.6%	8.9–18.3%	0.001
CRM positive	26.5	8.1–45.0%		52.5%	47.8–57.2%	
CRMI (LN)	8.3	0–18.3%	0.077	41.3%	13.4–69.1%	0.391
CRMI (T)	43.7	14.7–72.7%		62.0%	47.5–76.5%	

CRM circumferential resection margin, *CRMI* CRM involvement, *CRMI(T)* tumour involving the CRM, *CRMI (LN)* lymph node involving the CRM

Table 5 Univariate analysis of clinical and pathological variables affecting Kaplan–Meier-predicted mean local recurrence-free survival and distant metastases-free survival

Kaplan–Meier-predicted mean survival (95% CI) (months)	Local recurrence-free survival	*p* value	Distant metastases-free survival	*p* value
Gender				
Female	104.0 (99.0–109.0)	0.328	93.6 (85.8–101.4)	0.47
Male	103.6 (99.0–108.5)		93.2 (87.0–99.3)	
Age				
≤ 69 years	101.5 (95.8–107.1)	0.158	93.5 (87.0–103.4)	0.966
> 69 years	107.6 (103.1–112.2)		94.2 (87.1–101.2)	
Neoadjuvant treatment				
None	102.1 (96.5–107.7)	0.038	94.0 (86.7–101.4)	0.221
Short course	110.3 (106.1–114.4)		97.1 (89.1–105.2)	
Long course	97.0 (88.3–105.6)		87.0 (77.2–97.0)	
Procedures				
AR	101.6 (94.5–106.0)	0.828	94.0 (88.5–93.4)	0.098
APER	103.9 (96.3–111.0)		88.1 (78.6–98.0)	
TME grade				
Muscularis propria	102.6 (94.0–111.2)	0.928	84.4 (75.6–96.2)	0.123
Intra-mesorectal	106.0 (99.0–112.7)		95.5 (86.1–105.0)	
Mesorectal	104.0 (99.0–109.0)		97.0 (90.5–103.2)	
T stage				
(y)pT0	92.8 (57.4–128.2)	0.001	92.8 (57.4–128.2)	0.001
(y)pT1	94.3 (87.2–101.5)		94.3 (87.2–101.5)	
(y)pT2	93.0 (86.0–99.7)		95.0 (88.4–101.3)	
(y)pT3	83.3 (75.0–91.7)		87.4 (79.2–96.0)	
(y)pT4	53.2 (38.6–68.1)		59.4 (45.0–74.0)	
N Stage				
(y)pN0	98.56 (93.1–104.0)	0.001	100.1 (94.8–105.3)	0.001
(y)pN1	78.5 (68.0–89.1)		86.7 (77.0–96.4)	
(y)pN2	48.1 (33.6–62.5)		50.1 (35.4–64.7)	
CRM Status				
Negative	107.0 (103.2–110.3)	0.001	98.6 (94.0–103.4)	0.001
Positive	70.7 (57.0–85.0)		43.1 (32.7–62.6)	
EMVI				
Negative	107.0 (103.0–110.7)	0.080	101.4 (96.5–106.3)	0.001
Positive	86.7 (79.3–94.1)		70.5 (61.2–80.0)	

CRM circumferential resection margin, *EMVI* extramural venous invasion, *TME* total mesorectal excision

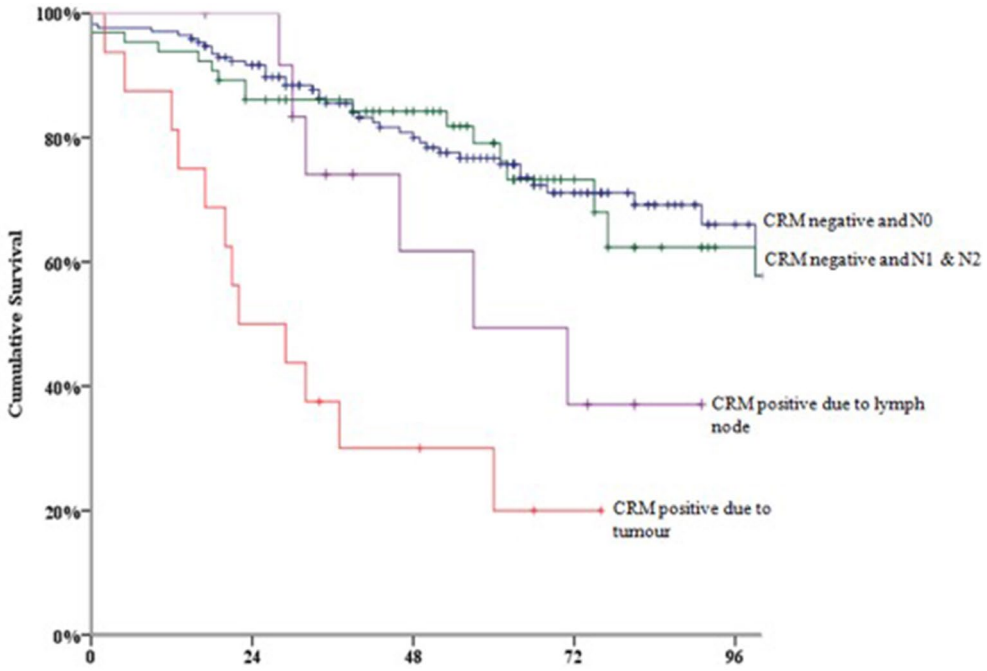
Table 6 Multivariate analysis using Cox regression model to identify independent predictors for local recurrence-free survival and distant metastases-free survival

Variables included	Local Recurrence	p-value
Neoadjuvant treatment[a] (short course radiotherapy)	HR 0.264 (95% CI: 0.073–0.960)	0.043
T-stage		
N-stage		
CRM status		

Variables included	Distant metastasis	p-value
T-stage		
N-stage[a] pN1	HR 2.323 (95% CI: 1.040–5.185)	0.040
N-stage[a] pN2	HR 2.620 (95% CI: 1.118–6.134)	0.027
CRM status[a]	HR 3.350 (95% CI: 1.625–6.906)	0.001
EMVI		

CRM circumferential resection margin, *EMVI* extramural venous invasion

[a]Denotes significant predictors

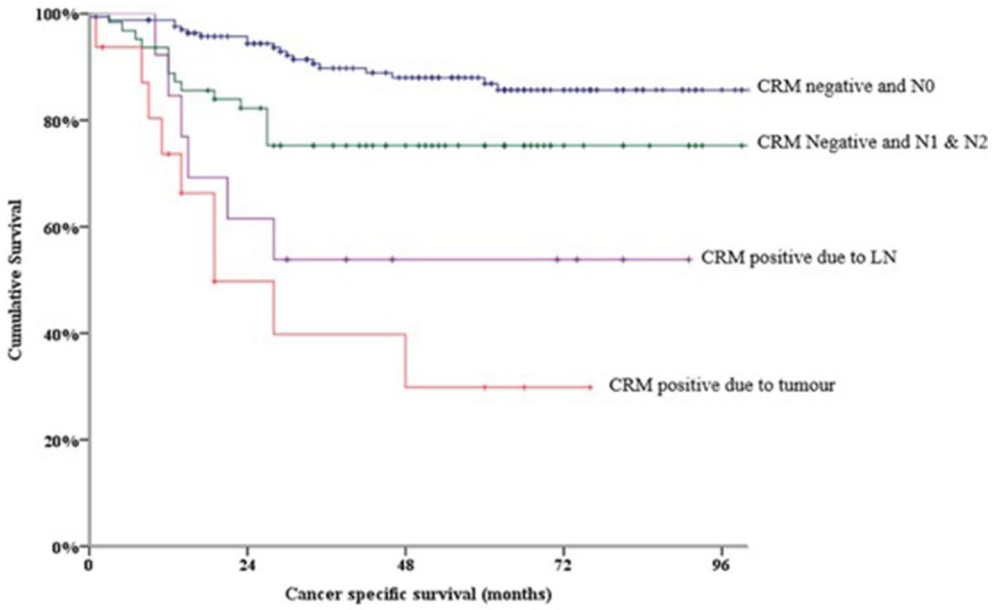


Number at Risk					
CRM -ive and N0	171	142	96	47	16
CRM- ive and N1& N2	65	54	36	14	3
CRM +ive due to LN	16	7	3	1	0
CRM +ive due to Tumour	13	12	4	2	0

Fig. 1 Kaplan–Meier 5-year overall survival

to those with a negative CRM, node-positive cancer. In comparison, tumour involvement of the CRM is associated with significantly higher LR and poorer survival. Thus, our findings imply that the nature of CRM involvement may be an important prognostic marker and needs to be evaluated further in studies reporting outcomes in rectal cancer.

The proportion of patients with a positive CRM (11%) recorded in our study is comparable to previous reports



Number at Risk					
CRM -ive andN0	171	145	97	50	16
CRM-ive andN1& N2	65	58	36	14	3
CRM +ive due to LN	16	7	3	1	0
CRM +ive due to Tumour	13	12	4	3	0

Fig. 2 Kaplan–Meier 5-year cancer-specific survival

which have described rates varying between 8 and 17% [9, 10, 19–22]. Independent predictors of CRMI that have been described in the literature include T stage, nodal involvement, operative procedure, tumour grade, lymphovascular invasion and perineural invasion [8, 10, 23]. Our analysis revealed that CRM positivity was associated with similar factors including T4 stage, N1/N2 disease, dissection in the muscularis propria/intramesorectal plane and abdominoperineal excision. Patients with a positive CRM had poorer oncological outcomes compared to patients with a negative CRM; however, on multivariate analysis, CRM status was only a predictor of poorer DM-free survival. This is similar to a recent analysis which found LR rates to be similar in CRM-positive and CRM-negative patients; the authors concluded that CRM positivity only affects the incidence of DM [13]. Our results on multivariate modelling are likely to have been influenced by the use of short course radiotherapy. CRM status may have failed to reach statistical significance as an independent prognostic marker of LR due to the protective effect of short course radiotherapy, as described previously [7].

There have been a few reports where the nature of CRMI has been considered. The incidence of CRMI due to positive lymph nodes varies considerably across the literature and is comparable to the incidence found in our study (4.8%). In a study investigating CRMI and prognosis, 67/656 (10%) patients were found to have CRMI due to lymph nodes involving the CRM [14]. A more recent evaluation of magnetic resonance imaging assessment for rectal cancer demonstrated that only 5/396 (1.26%) patients had a positive CRM solely due to an involved lymph node on pathological analysis [24]. The overall CRMI rate in both these studies is noticeably different (18.3% in former versus 12.6% in latter) probably reflecting improvements in surgical technique and better selection for neoadjuvant therapy.

Our study has highlighted that patients with positive lymph nodes located within 1 mm of the CRM have similar outcomes in terms of LR compared to patients with a negative CRM, node-positive cancer. These findings are similar to those reported previously [3, 14] which concluded that involvement of the CRM by lymph nodes was not associated with adverse outcomes. Thus, these patients should not be considered in the same category as those with tumour involving the CRM as they have a risk of LR which is similar to CRM-negative (lymph node-positive) patients. The risk of distant metastases, however, is higher in CRM involvement with LN than CRM-negative patients but comparable to CRM negative, lymph node-positive patients implying that it is the nodal spread which is associated with DM rather than CRM positivity. Hence, our findings suggest that nodal

involvement of the CRM does not influence risk of LR but is associated with DM and a poorer cancer-specific survival in a similar manner to any node-positive patient. The nature of CRM involvement, therefore, may be important in determining prognosis in these patients and requires further exploration in prospective, multicentre studies.

All resection specimens included in this study were analysed by a single histopathologist who has a specialist interest in rectal cancer. The meticulous nature of the pathological workup and standardised approach can be appreciated by the high nodal count and low pathological complete response rate (7%) when comparison is made to previous reports. However, the following limitations need to be considered. Patients who were CRM positive had poorer TME quality which may have contributed to the poorer survival outcomes observed in this group, though our univariate analysis did not show any measurable differences in survival amongst different TME grades. The numbers of CRM-positive patients in each group is too small to be able to perform multivariate analysis to determine if this is an independent prognostic factor affecting disease recurrence and survival; however, the results do suggest that the nature of CRM involvement should be recorded and investigated further to allow comparison of outcomes in different populations and direct different approaches to treatment of rectal cancer.

Our study has highlighted the importance of recording the nature of CRM involvement in patients undergoing rectal cancer surgery as lymph nodes involving the CRM do not pose the same threat to LR as CRM involvement by direct tumour extension.

Conclusions

CRM involvement in rectal cancer surgery is associated with an adverse clinical outcome. However, our results imply that CRM involvement from LN affects the incidence of distant metastases rather than local recurrence. We suggest that studies investigating rectal cancer treatment consider this distinction and patients with CRMI secondary to positive lymph nodes could be a separate high-risk group compared to those with CRMI due to direct tumour extension.

Acknowledgements We would like to thank the colorectal multidisciplinary teams at Heartlands Hospital and Good Hope Hospital who were responsible for treating the patients investigated in this study.

Funding None.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This study does not require direct contact with human participants or animals.

Informed consent For this type of study, informed consent is not required.

References

1. Parfitt JR, Driman DK (2007) The total mesorectal excision specimen for rectal cancer: a review of its pathological assessment. J Clin Pathol 60(8):849–855
2. Quirke P, Durdey P, Dixon MF, Williams NS (1986) Local recurrence of rectal adenocarcinoma due to inadequate surgical resection. Histopathological study of lateral tumour spread and surgical excision. Lancet 2(8514):996–999
3. Birbeck KF, Macklin CP, Tiffin NJ, Parsons W, Dixon MF, Mapstone NP et al (2002) Rates of circumferential resection margin involvement vary between surgeons and predict outcomes in rectal cancer surgery. Ann Surg 235(4):449–457
4. Bernstein TE, Endreseth BH, Romundstad P, Wibe A, Group NCC (2009) Circumferential resection margin as a prognostic factor in rectal cancer. Br J Surg 96(11):1348–1357
5. Heald RJ, Ryall RD (1986) Recurrence and survival after total mesorectal excision for rectal cancer. Lancet 1(8496):1479–1482
6. Sauer R, Becker H, Hohenberger W, Rödel C, Wittekind C, Fietkau R et al (2004) Preoperative versus postoperative chemoradiotherapy for rectal cancer. N Engl J Med 351(17):1731–1740
7. van Gijn W, Marijnen CA, Nagtegaal ID, Kranenbarg EM, Putter H, Wiggers T et al (2011) Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer: 12-year follow-up of the multicentre, randomised controlled TME trial. Lancet Oncol 12(6):575–582
8. Tilney HS, Tekkis PP, Sains PS, Constantinides VA, Heriot AG, Ireland AoCoGBa (2007) Factors affecting circumferential resection margin involvement after rectal cancer excision. Dis Colon Rectum 50(1):29–36
9. Youssef H, Collantes EC, Rashid SH, Wong LS, Baragwanath P (2009) Rectal cancer: involved circumferential resection margin—a root cause analysis. Colorectal Dis 11(5):470–474
10. Rickles AS, Dietz DW, Chang GJ, Wexner SD, Berho ME, Remzi FH et al (2015) High rate of positive circumferential resection margins following rectal cancer surgery: a call to action. Ann Surg 262(6):891–898
11. Hall NR, Finan PJ, al-Jaberi T, Tsang CS, Brown SR, Dixon MF et al (1998) Circumferential margin involvement after mesorectal excision of rectal cancer with curative intent. Predictor of survival but not local recurrence? Dis Colon Rectum 41(8):979–983
12. Nikberg M, Kindler C, Chabok A, Letocha H, Shetye J, Smedh K (2015) Circumferential resection margin as a prognostic marker in the modern multidisciplinary management of rectal cancer. Dis Colon Rectum 58(3):275–282
13. Tilly C, Lefevre JH, Svrcek M, Shields C, Flejou JF, Tiret E, Parc Y (2014) R1 rectal resection: look up and don't look down. Ann Surg 260(5):794–799
14. Nagtegaal ID, Marijnen CA, Kranenbarg EK, van de Velde CJ, van Krieken JH, Committee PR et al (2002) Circumferential margin involvement is still an important predictor of local recurrence in rectal carcinoma: not one millimeter but two millimeters is the limit. Am J Surg Pathol 26(3):350–357
15. Association of Coloproctology of Great Britain and Ireland (2007). Guidelines for the management of colorectal cancer. 3rd edn. https://www.acpgbi.org.uk

16. Langman G, Patel A, Bowley DM (2015) Size and distribution of lymph nodes in rectal cancer resection specimens. Dis Colon Rectum 58(4):406–414
17. Adam IJ, Mohamdee MO, Martin IG, Scott N, Finan PJ, Johnston D et al (1994) Role of circumferential margin involvement in the local recurrence of rectal cancer. Lancet 344(8924):707–711
18. Wibe A, Møller B, Norstein J, Carlsen E, Wiig JN, Heald RJ et al (2002) A national strategic change in treatment policy for rectal cancer–implementation of total mesorectal excision as routine treatment in Norway. A national audit. Dis Colon Rectum 45(7):857–866
19. Wibe A, Syse A, Andersen E, Tretli S, Myrvold HE, Søreide O et al (2004) Oncological outcomes after total mesorectal excision for cure for cancer of the lower rectum: anterior vs. abdominoperineal resection. Dis Colon Rectum 47(1):48–58
20. Tekkis PP, Heriot AG, Smith J, Thompson MR, Finan P, Stamatakis JD et al (2005) Comparison of circumferential margin involvement between restorative and nonrestorative resections for rectal cancer. Colorectal Dis 7(4):369–374
21. Nagtegaal ID, Quirke P (2008) What is the role for the circumferential margin in the modern treatment of rectal cancer? J Clin Oncol 26(2):303–312
22. Phang PT, McGahan CE, McGregor G, MacFarlane JK, Brown CJ, Raval MJ et al (2010) Effects of change in rectal cancer management on outcomes in British Columbia. Can J Surg 53(4):225–231
23. Al-Sukhni E, Attwood K, Gabriel E, Nurkin SJ (2016) Predictors of circumferential resection margin involvement in surgically resected rectal cancer: a retrospective review of 23,464 patients in the US National Cancer Database. Int J Surg 28:112–117
24. Shihab OC, Quirke P, Heald RJ, Moran BJ, Brown G (2010) Magnetic resonance imaging-detected lymph nodes close to the mesorectal fascia are rarely a cause of margin involvement after total mesorectal excision. Br J Surg 97(9):1431–1436