Locally recurrent rectal cancer; long-term outcome of curative surgical and non-surgical treatment of 447 consecutive patients in a tertiary referral centre

J.A.W. Hagemans, J.M. van Rees, W J. Alberda, J. Rothbarth, J.J.M.E. Nuyttens, E. van Meerten, C. Verhoef, J.W.A. Burger

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ABSTRACT

Introduction

The majority of patients with locally recurrent rectal cancer (LRRC) present with extensive metastatic disease or an unresectable recurrence, and will be treated palliatively. Only a minority of patients will be eligible for potential cure by surgical treatment. The aim of this study is to evaluate the long-term outcome of surgical treatment and non-surgical treatment of patients with LRRC.

Methods

All patients with LRRC referred to our tertiary institute between 2000 and 2015 were retrospectively analysed. Patients were discussed in a multidisciplinary tumour board (MDT) and eventually received curative surgical or non-surgical treatment. Overall survival (OS) was compared by resection margin status and non-surgical treatment.

Results

A total of 447 patients were discussed in our MDT of which 193 patients underwent surgical treatment and 254 patients received non-surgical treatment. Surgically treated patients were significantly younger, received less neoadjuvant therapy for the primary tumour, had less metastasis at diagnosis and more central recurrences. The 5-year OS was 51% for R0-resections and 34% for R1-resections. Although numbers with R2-resections were too small to implicate prognostic significance, there was no difference in 5-year OS between R2-resections and non-surgical treatment (10% vs. 4%, p=0.282). In a subgroup analysis the OS of R2-patients was even poorer compared to optimal palliative treated patients with combined chemotherapy and radiotherapy(22 vs 29 months, p=0.413).

Conclusions

R2-resections do not result in a survival benefit compared to non-surgical treatment in this non-randomized series. Patients with a high chance on a R2-resection could be offered non-surgical treatment, without local resection.

INTRODUCTION

The introduction of total mesorectal excision (TME) and neoadjuvant (chemo-) radiotherapy have drastically decreased local recurrence rates after surgery for rectal cancer over the last decades. Locally recurrent rectal cancer (LRRC) still occurs in 6-10% of the surgically treated patients.(1-5) The development of LRRC has a major impact on quality of life, mostly by the occurrence of severe pain, bleeding and fistulation.(6)

Most patients with LRRC present with extensive metastatic disease or an unresectable local recurrence.(7-10) These patients can be offered non-surgical treatment, consisting of external beam radiotherapy, chemotherapy, a combination of both or comfort care.(11) Palliative external beam radiotherapy may relief pelvic pain complaints and chemotherapy may delay disease progression and prolong survival.(7, 8, 11-13) A minority of patients presenting with LRRC can potentially be cured by surgical resection. The long-term outcome of surgical treatment mainly depends on the ability to achieve a clear resection margin.(10, 14, 15) Management of LRRC remains a challenge both for curative surgical treatment and non-surgical treatment.

The aim of the current study is to evaluate the long-term outcome of a large cohort of patients with LRRC and determining the outcome of curative surgical treatment and non-surgical treatment in these patients.

Patients and Methods

All consecutive patients with confirmed LRRC discussed in the multidisciplinary tumour board (MDT) of the Erasmus MC Cancer Institute, a tertiary referral hospital, from 2000-2015 were retrospectively analysed. LRRC was defined as local recurrence of rectal cancer in the pelvic area. This MDT included experienced surgeons, radiologists, radiation oncologists and medical oncologists. If needed, gynaecologists, urologists, pathologists and plastic surgeons were invited to join the meeting.

Data was collected from all referring hospitals, general practitioners and obtained from hospital notes, operation notes, histopathological and imaging reports. The local medical ethics committee of our institution approved this study (MEC-2017-448).

Surgical treatment

Surgical treatment was considered feasible in patients with resectable metastatic disease and/or non-metastasized LRRC with a realistic chance of a R0/R1-resection, as discussed by the MDT. R0-resections were defined as any radical resection (no tumour invasion in the resection plane, tumour-free margin of >1 mm); R1-resections as microscopically involved

margins (tumour invasion in resection plane on microscopic assessment, tumour-free margin of ≤1 mm); R2-resections as macroscopically involved margins or massive invasion into the resection surface on pathology report.

Patients were usually scheduled for neoadjuvant (chemo) radiotherapy. Radiotherapy-naïve patients were planned for long course radiotherapy (44.6-52Gy) and previously irradiated patients received a short course re-irradiation (27-30Gy). From 2006 onwards, all patients received concurrent Capecitabine during radiotherapy as reported previously.(16) Induction chemotherapy was occasionally administered. After neoadjuvant therapy, patients were restaged (CT Thorax/Abdomen and Pelvic MRI) and discussed in the MDT to evaluate development of distant metastases, tumour response of the local recurrence and clinical condition, which may alter the decision for surgical treatment to palliative treatment.(17) Surgical planning was made by the MDT based on imaging after restaging after neoadjuvant therapy.

Surgical procedures included low anterior resection (LAR), abdominoperineal resection (APR) with and without multivisceral resection (MVR), and both posterior exenteration and total pelvic exenteration. Surgery was usually performed at our institute and in some cases in the referring hospital. In our institute, the multimodality approach for LRRC included intra-operative brachytherapy (IOBT) with a single dose of 10Gy. Patients received IOBT in case of a positive circumferential resection margin (CRM) or a narrow margin (CRM ≤ 2mm) on frozen sections taken preoperatively. In addition, patients received IOBT in case of peroperatively expected or uncertain achievement of radical margins, i.e. due to fibrosis and patient with an expected peroperative R2-resection.(18, 19) Surgical complications were scored according to the Clavien-Dindo classification.(20)

Non-surgical treatment

Patients receiving non-surgical treatment usually had extensive metastatic disease, unresectable local recurrence or a poor clinical condition. There was no standard policy regarding the choice of non-surgical treatment. Non-surgical treatment consisted of radiotherapy or chemotherapy, either with or without hyperthermia or a combination of both and comfort care. Generally, patients with symptomatic LRRC were treated with radiotherapy and those with asymptomatic metastasized or unresectable LRRC were treated with chemotherapy. Hyperthermia was usually administered to previously irradiated patients due to the limited radiation dose available for their local recurrence. The choice of dose and fractioning of radiotherapy was largely based on the clinical judgment of the radiation oncologists and this resulted in heterogeneity in the radiotherapy management. Comfort care was provided for patients who were unable to receive or did not desire any treatment with radiotherapy or chemotherapy.

Statistical analysis

Continuous data were reported as median (interquartile range or 95% confidence interval) and categorical data were reported as count (percentage). Group comparisons were made using Chi-square or Mann-Whitney-U-test as appropriate. Survival and follow-up were calculated from the date of LRRC diagnosis until death or last follow-up. Survival rates and follow-up were calculated by the (reversed) method of Kaplan-Meier and comparisons by log-rank test. For all analyses, patients were divided into two groups: 1) patients who underwent surgery and 2) patients who received non-surgical treatment including those patients who were previously considered eligible for surgical treatment. Statistical analyses were performed using IBM SPSS Statistics v24.0.0 for Windows (IBM Corp, Armonk, New York, USA).

RESULTS

A total of 447 consecutive patients with LRRC were discussed in our MDT. A flowchart of included patients is displayed in figure 1. After discussion in the MDT, 244 patients (55%) were considered candidates for surgery. This decision was reversed in 51 patients after restaging after neoadjuvant therapy, as described in figure 1. In total, 193 patients underwent surgical treatment and 254 patients received non-surgical treatment. Patient, primary and recurrent tumour characteristics are outlined in table 1. Treatment and follow-up are depicted in table 2.

Time to recurrence after primary rectal cancer resection

The median time from primary tumour resection to the diagnosis of LRRC was 23 months (IQR 11 – 39 months). In more than half of the patients (55%) LRRC developed within 2 years and in almost all patients within 5 years (88%). A total of 162 patients (36%) presented with synchronous metastases at diagnosis of LRRC: the predominant location was lung only (34%), followed by liver only (28%), other (24%) or liver and lung (14%).

The median time to diagnosis of LRRC was significantly shorter in patients with incomplete primary tumour resections compared to patients with complete resections (10 vs. 24 months, $p<0.001$) and in patients who had received neoadjuvant radiotherapy for the primary tumour compared to no radiotherapy (21 vs. 24 months, $p=0.039$). More advanced primary pathological T-stage (T3-4 vs. T1-2) did not influence the median time to LRRC (21 vs. 24 months, $p=0.172$), nor lymph node positivity (21 vs. 23 months, $p=0.776$).

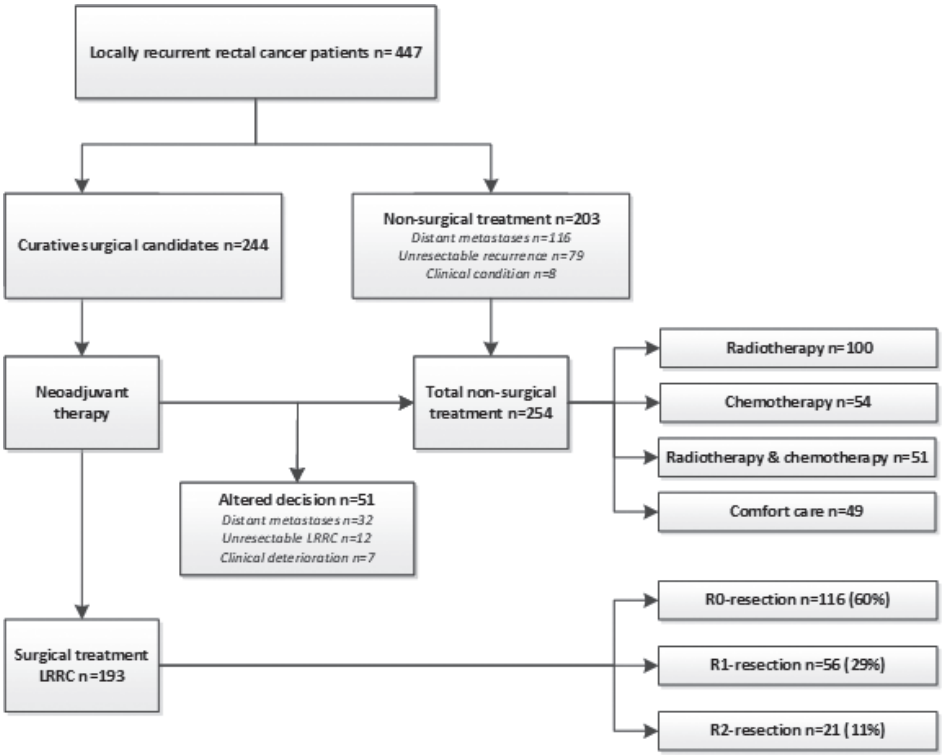

Figure 1. Flowchart of all referred LRRC patients

Surgical and non-surgical patients

There were significant baseline differences for patients who eventually underwent surgery (n=193) compared to all non-surgically treated patients (n=254) (Table 1). Surgically treated patients were significantly younger, less symptomatic at presentation of LRRC, received less radiotherapy for the primary tumour, had fewer incomplete primary tumour resections, had less frequent synchronous distant metastasis, more differences in terms of localization of the local recurrence and underwent different procedures for the primary rectal tumour. Patients with a central localization of the local recurrence were more likely to be scheduled for surgical treatment, whereas patients with a pre-sacral recurrence were more likely to receive non-surgical treatment.

Table 1. Patients, primary and recurrent tumour characteristics of surgical and palliative treatment

		Total (N=447)	Surgical (N=193)	Palliative (N=254)	P-value
Gender	Male	289 (65%)	125 (65%)	164 (65%)	0.965
	Female	158 (35%)	68 (35%)	90 (35%)	
Age at primary tumour resection	Median (IQR)	63 (56-70)	62 (54-67.5)	64 (56-72)	0.016*
Age at diagnosis LRRC	Median (IQR)	66 (58-73)	65 (57-71)	67 (58-75)	<0.001*
Neoadjuvant treatment primary tumour	None	256 (57%)	126 (65%)	130 (51%)	0.002**
	Short course RTx	49 (11%)	18 (9%)	31 (12%)	
	Long course RTx	62 (14%)	14 (7%)	48 (19%)	
	Chemoradiotherapy	80 (18%)	35 (18%)	45 (18%)	
Primary tumour resection	LAR	244 (55%)	112 (58%)	132 (52%)	<0.001**
	APR	106 (24%)	30 (16%)	76 (30%)	
	Rectosigmoid	55 (12%)	32 (17%)	23 (9%)	
	Exenterative surgery	21 (5%)	4 (2%)	17 (7%)	
	TEM	21 (5%)	15 (8%)	6 (2%)	
Primary tumour stage	Stage I	52 (13%)	30 (16%)	22 (10%)	0.076
	Stage II	139 (34%)	58 (31%)	81 (35%)	
	Stage III	186 (45%)	86 (46%)	100 (44%)	
	Stage IV	38 (9%)	12 (7%)	26 (11%)	
	Missing***	32	7	25	
Resection margin primary tumour	R0	381 (88%)	174 (96%)	207 (83%)	<0.001**
	R1	50 (12%)	8 (4%)	42 (17%)	
	Missing***	16	11	5	
Interval primary - LRRC	Median (IQR)	23 (11-39)	24 (12-40)	21 (10-37)	0.154
Recurrence within	24 months	246 (55%)	99 (52%)	147 (58%)	
	5 years	393 (88%)	174 (90%)	219 (86%)	
	10 years	433 (97%)	191 (99%)	242 (95%)	
Symptoms at diagnosis LRRC	Yes	262 (55%)	86 (45%)	176 (69%)	<0.001**
	No	185 (45%)	107 (55%)	78 (31%)	
Metastases at diagnosis LRRC	None	285 (64%)	172 (89%)	113 (45%)	<0.001**
	Lung	55 (12%)	11 (6%)	44 (17%)	
	Liver	45 (10%)	7 (4%)	38 (15%)	
	Lung & Liver	23 (5%)	0 (0%)	23 (9%)	
	Other	39 (9%)	3 (2%)	36 (13%)	
Location LRRC	Central	74 (18%)	54 (29%)	20 (9%)	<0.001**
	Anterior	62 (15%)	31 (17%)	31 (14%)	
	Posterolateral	53 (13%)	24 (13%)	29 (13%)	
	Anterolateral	34 (8%)	14 (8%)	20 (9%)	
	Lateral	59 (14%)	29 (16%)	30 (13%)	
	Pre-sacral	133 (31%)	33 (18%)	100 (44%)	
	Missing***	32	8	24	

*Mann Whitney U test ** Chi squared test *** *missing's not included in group comparison, percentages-might not add up due to rounding*

LRRC: Locally recurrent rectal cancer; IQR: interquartile range; RTx: radiotherapy; LAR: low anterior resection;APR: abdominoperineal resection; TEM: transanal endoscopic microsurgery

Surgical treatment

The majority of surgically treated patients received neoadjuvant therapy (90%) and more than half of the patients received (re-)chemoradiotherapy (62%). Some patients received induction chemotherapy (n=13) or radiation (n=38) or re-irradiation (n=9) without concurrent Capecitabine and 7 patients received solely induction chemotherapy. In 175 patients (91%) the surgical procedure was performed at our institute, while 18 procedures (9%) were performed in the referring hospitals. Neoadjuvant therapy and surgical procedures are described in Table 2.

Table 2. Treatment and follow up of LRRC in surgical and palliative treatment

	Surgical (N=193)	Palliative (N=254)
Neoadjuvant therapy LRRC		
None	19 (10%)	205 (81%)
Irradiation (50Gy)	38 (20%)	13 (5%)
Re-irradiation (30Gy)	9 (5%)	3 (1%)
Induction chemotherapy*	20 (10%)	9 (2%)
Chemoradiotherapy (50Gy)	61 (32%)	14 (6%)
Re-Chemoradiotherapy (30Gy)	59 (31%)	15 (6%)
Surgical procedure		
Total pelvic exenteration	43 (22%)	N/A
Posterior pelvic exenteration	27 (14%)	N/A
APR with MVR	26 (14%)	N/A
LAR with MVR	18 (9%)	N/A
Local resection with MVR	11 (5%)	N/A
APR only	25 (13%)	N/A
LAR only	26 (13%)	N/A
Local resection only	17 (7%)	N/A
IORT	86 (45%)	N/A
Follow up		
Alive at last FU	65 (34%)	9 (4%)
No evidence of disease at last FU	47 (24%)	N/A
Local re-recurrence	62 (32%)	N/A
Metastases (any)	88 (46%)	186 (73%)
Metastases (synchronous)	14 (7%)	138 (54%)
Metastases (metachronous)	74 (38%)	48 (19%)
Lung**	47 (53%)	63 (34%)
Liver	15 (17%)	46 (25%)
Lung and liver	10 (11%)	26 (14%)
Peritoneal	6 (7%)	15 (8%)
Lymphogenic	7 (8%)	20 (11%)
Other	3 (3%)	16 (9%)

* Combined with (chemo-)radiotherapy in 13 patients for surgical patients and 5 non-surgical patients; ** Location of metastases are reported as percentage within metastases; N/A: not applicable; APR: abdominoperineal resection; MVR: multivis ceral resection; LAR: low anterior resection; IORT: intraoperative radiation therapy; FU: follow up

Surgical results

R0-resections were achieved in 116 patients (60%), R1-resections in 56 patients (29%) and R2-resections in 21 patients (11%). The 30-day mortality and the in-hospital mortality rate were both 3% (n=5). Four patients died within 22 days and one patient died during admission at 67 days after surgery. Postoperative complications were registered in 176 out of 193 patients. A total of 59 (34%) patients experienced major complications (Clavien-Dindo ≥ 3). Most common complications were wound complications (23%), pre-sacral abscesses (11%) and urinary tract infections (9%). Surgical re-intervention was required in 26 patients (13%) and abscess drainage (i.e. pre-sacral or abdominal abscess) in 25 patients (13%). Complications for surgically treated patients are displayed in Table 3.

Table 3. Surgical complications

	Total (N=193)
Clavien-Dindo	
No complication	59 (34%)
Clavien-Dindo I	31 (18%)
Clavien-Dindo II	27 (15%)
Clavien-Dindo IIIA	21 (12%)
Clavien-Dindo IIIB	25 (14%)
Clavien-Dindo IVA	3 (2%)
Clavien-Dindo IVB	4 (2%)
Clavien-Dindo V	5 (3%)
Most common complications	
Wound complication	45 (23%)
Pre-sacral abscess	22 (11%)
Urinary tract infection	18 (9%)
Relaparotomy	18 (9%)
Pneumonia	15 (8%)
Sepsis	13 (7%)
Cardiac complication	12 (6%)
Nephrostomy	12 (6%)
Reintervention stoma	3 (2%)
Anastomotic leakage	3 (2%)
Any surgical reintervention	26 (13%)
Any abscess drainage	25 (13%)

Non-surgical treatment

A total of 254 patients received non-surgical treatment, including 51 patients who were first considered candidates for surgical treatment. These patients had received neoadjuvant therapy, but the aim of the treatment was altered as described previously. Patients were

treated by radiotherapy (n=100), by chemotherapy only (n=54), by combined radiotherapy and chemotherapy (n=51) or comfort care (n=49).

In 63 previously irradiated patients, re-irradiation was administered in varying doses of 15 to 48 Gy delivered in 3-15 fractions. Radiotherapy-naïve patients (n=88) received radiotherapy doses varying from 6-66Gy in 4-28 fractions. Almost half of the patients experienced pain (48%) of whom the majority (56%) needed pain consultation.

Follow-up and survival surgical and non-surgical treatment

The median follow-up time for the whole cohort was 26 months (IQR 11 – 45) and median follow-up for survivors was 120 months (IQR 68 – 142).

Survival surgically treated patients

The median follow-up of the 193 surgically treated patients was 42 months (IQR 29 - 70) and the median follow-up for survivors was 117 months (IQR 67 - 140). The estimated 1-, 3- and 5-year overall survival rates were 93%, 65% and 41%, respectively. The median overall survival was 47 months (IQR 29 – 156). The estimated 1-, 3- and 5-year local re-recurrence free survival rates were 81%, 64% and 63%, respectively. The median local re-recurrence free survival was not reached. At last follow-up 65 (34%) patients were alive, of whom 50 patients with no evidence of disease. Sixty-two patients developed a local re-recurrence and 74 patients developed metastases after surgery. Thirty-one patients were diagnosed with both. Recurrence patterns and death by resection margin are demonstrated in Table 4.

Survival non-surgically treated patients

The median follow-up of the 254 non-surgically treated patients was 15 months (IQR 7 – 29) and the median follow-up for survivors was 145 months (IQR 142-162). The estimated 1-, 3-, 5-year overall survival rates were 60%, 19%, 4%, respectively. The median survival was the highest for patients treated with combined radiotherapy and chemotherapy, followed by chemotherapy only, radiotherapy only and comfort care (29, 18, 14 and 7 months, respectively). There was no significant difference in median survival of metastasized and non-metastasized patients at diagnosis (14 vs. 18 months, p=0.293). Nine patients were alive at last follow-up. One patient, with a proven LRRC on imaging, had a complete radiologic response of the recurrence after treatment with radiotherapy and was alive at 162 months follow-up. Two patients, with histologically confirmed LRRCs, were alive at 145 and 142 months with stable systemic and local disease after an experimental chemotherapeutic treatment. Two patients, with histologically proven LRRC and systemic disease, were alive at 44- and 32-months follow-up, both receiving experimental chemotherapeutic treatment. Two patients with proven LRRC on imaging with systemic disease with highly

elevated carcinoembryonic antigen were alive at 44 and 32 months with slowly progressive systemic and local disease without treatment. Another two patients with histologically proven LRRC and systemic disease were alive, but were lost to follow-up at 21 and 10 months. Distant metastases were diagnosed in 186 patients. In 141 patients, distant metastases were diagnosed at presentation and 45 patients developed distant metastases during follow-up of non-surgical treatment.

Survival by resection margin vs. non-surgical treatment

Compared to patients treated non-surgically, there was a significant difference in 5-year overall survival in favour of patients with R0-resections (51% vs. 4%, p<0.001) and R1-resections (34% vs. 4%, p<0.001). There was no difference in overall survival between R2-resections and non-surgical treatment (10% vs. 4%, p=0.282). This is shown in figure 2. In a subgroup analysis, patients with a R2-resection had a prolonged median survival of 29 months (IQR 16 – 41) compared to 22 months (IQR 14 – 37) of the patients who were treated with palliative radiotherapy and chemotherapy, although this difference was not significant (p=0.413).

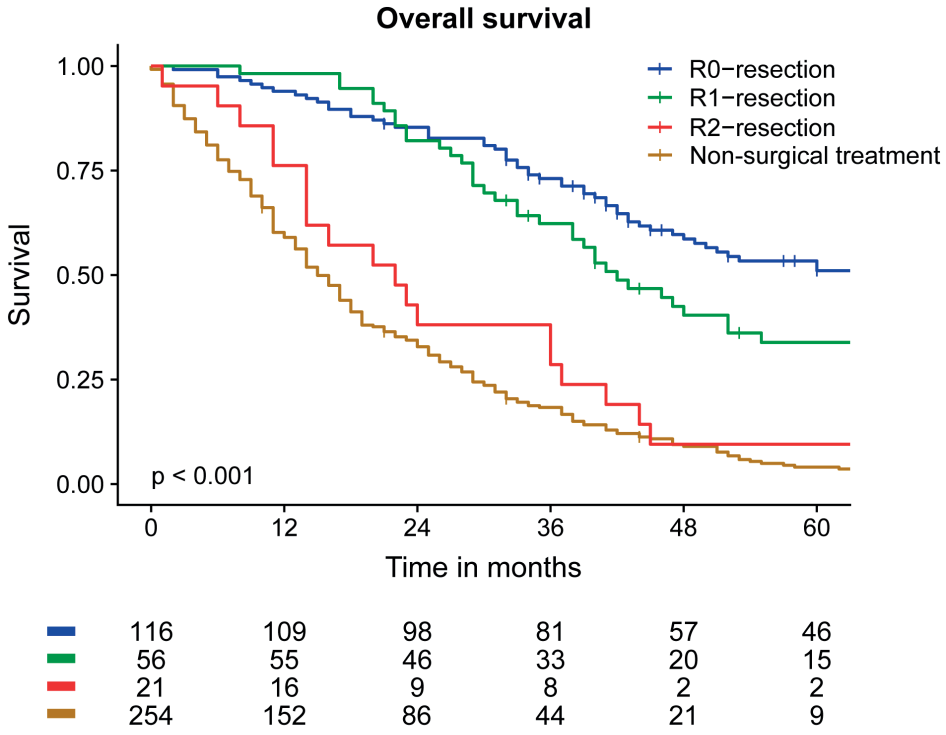

Figure 2. Overall survival according to surgical resection margin and non-surgical treatment

DISCUSSION

This large cohort of patients with LRRC, treated by surgical or non-surgical treatment, have demonstrated that R0- and R1-resections result in a 5-year overall survival rate of 51% and 34%, respectively. These survival rates are significantly prolonged compared to non-surgical treatment. Although numbers were too small to implicate prognostic significance, R2-resections did not result in a 5-year overall survival benefit compared to non-surgical treatment with a rate of 10% vs. 4%. Moreover, the overall survival of patients who underwent a R2-resection was poorer compared to patients who were treated non-surgically with combined radiotherapy and chemotherapy.

The 5-year overall survival rate for R0-resections in the present study is in line with previously reported outcomes of population-based studies and meta-analyses within a range of 43%-60%. Additionally, the poorer overall survival rate of R1-resections (range 14-36%) and the dismal overall survival rate of R2-resections (range 0-16%) are in line with the overall survival rates reported by others.(7-11, 14, 15) This confirms that resection margin status after surgical treatment for LRRC is the most important prognostic factor for overall survival. Unfortunately, not all LRRC patients are eligible for curative surgery.

The 5-year survival rate of 4% for all non-surgically treated patients in this study seems relative high compared to other series, which rarely exceeds 4%.(21, 22) However, a recently published study by Bhangu et al.(23) demonstrated a 3-year overall of approximately 35% for patients who did not undergo surgery, which is even higher compared to our 3-year overall survival of 19%. In line with our study, they reported an overall survival benefit in favour of R0- and R1-resections compared to non-operative management. In R2-resections, they were not able to find a survival benefit compared to non-operative management. Neither a large meta-analysis by their group was able to demonstrate a survival benefit for R2-resections compared to non-surgical treatment.(14, 23). These results are similar to our study, where we were not able to find a survival benefit of R2-resection compared to non-surgical treated patients. In a subgroup of patients who were treated by radiotherapy and systemic chemotherapy, a prolonged median survival was found compared to R2-resections (29 vs 22 months). Nevertheless, in our study the results of R-resections our limited by the small number of patients and cannot implicate statistical significance.

The survival benefit of R0- and R1-resections compared to non-surgical treatment seems clear in the current study. However, it is important to realize that these results may be influenced by a selection bias. This study includes patients who are referred and discussed in our MDT, the number of patients not suitable for surgery, and not referred to our MDT, may be even higher. The group of non-surgically treated patients contains a higher propor-

tion of patients with unfavourable characteristics compared to the surgically treated patients. Non-surgically treated patients had more synchronous distant metastases and more advanced local recurrences. These unfavourable characteristics may contribute to a poorer prognosis of the non-surgical group. In line with others, the overall survival of patients receiving only comfort care was poor with a median survival of 7 months. This median survival was poorer compared to R2-resections.(8, 10, 14, 23) However, it is important to realize these patients were generally in such poor clinical condition that they were not able to receive any form of treatment.

Untreated LRRC can cause severe impairment in quality of life mainly due to severe pain, but also fistula, obstruction or bleeding.(6, 24) There may be a role for palliative surgery in these patients to reduce pain, and relief symptoms of obstruction by stenting or a diverting stoma as reported by others.(11, 25, 26) However, surgery is accompanied by high morbidity and mortality rates, occurring mainly perioperative or in the first 3 months after surgical treatment. This impairment in quality of life persists until one year after surgery. Thereafter, surgically treated patients tends to have a better quality of life.(27) This fact and the lack of a survival benefit of R2-resections suggest that LRRC surgery with a high chance on R2-resections should be abandoned and should only be performed when the potential benefit is clear.

Regarding the secondary findings, this study identified several factors associated with resectability of LRRC. Obviously, age is a factor to be considered candidate for LRRC surgery due to the high morbidity and mortality rates of LRRC surgery. Previous irradiation for the primary tumour was also associated with resectability. Presumably, neoadjuvant radiotherapy for the primary tumour is not able to prevent local recurrences in patients with unfavourable primary tumour characteristics, such as more residual disease or higher tumour load. These patients do also have a higher risk of developing distant metastases and were therefore disqualified for LRRC surgery.(28) Patients with a more extensive primary procedure had a lower chance to be considered candidates for LRRC surgery. Extensive primary surgery leads to local recurrences closely related to structures, which cannot be resected completely, while low anterior resections or local excisions (TEM, transanal endoscopic microsurgery) may lead to central recurrences. This makes localization of the local recurrence also associated with resectability, because central recurrences results more often into R0-resections.(29)

A promising strategy to improve resectability of LRRC is induction chemotherapy. However, improved resectability does not automatically guarantee a survival benefit. Other factors, such as tumour behaviour, have more impact on overall survival as well. In our study few patients received induction chemotherapy, but a retrospective cohort study by van Zoggel et

al.(30) compared outcomes of resection of LRRC in patients with induction chemotherapy followed by chemoradiotherapy to patients who received solely chemoradiotherapy. The R0-resection rate did not differ significantly, but a higher rate of pathologic complete response was found in patients with combined treatment. Van Zoggel et al.(30) suggested that response rate to induction chemotherapy may be used as guidance to avoid overtreatment in patients with progressive disease under induction chemotherapy. Otherwise, in a previous study, our institute showed a lower response to chemotherapy of the local recurrence compared to the response of distant metastases in a small cohort of previously irradiated rectal cancer patients.(31) Further research is warranted to evaluate the potential benefit of induction chemotherapy for treatment of LRRC.

Due to the retrospective nature of this analysis, this study has drawbacks. There was no standard protocol for non-surgical treatment. The choice of non-surgical treatment consisting of radiotherapy, chemotherapy, or only comfort care was judged on clinical factors. This resulted in a heterogenetic group of patients from critical ill patients not able to receive any form of treatment, to patients in good clinical condition, refusing surgery. Follow-up data of patients treated non-surgically was limited, because treatment was usually performed in the referring hospitals. Therefore, data of complication rates and quality of life in non-surgically treated patients was limited.

Furthermore, this study was only able to demonstrate survival differences. As mentioned above, quality of life may be even more important in the management of LRRC. Future research should focus on quality of life of surgical or palliative management of LRRC.

In conclusion, R0- and R1-resections of LRRC resulted in 5-year overall survival rates of 51% and 34%, respectively. Although numbers with R2-resections were too small to implicate prognostic significance, there was no significant difference between the 5-year overall survival for R2-resections and palliative treatment (10% vs. 4%). Moreover, the median survival may be poorer for surgically treated patients with a R2-resection compared to optimal palliatively treated patients. Patients with a high chance on a R2-resection could be offered palliative treatment, without local resection.

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