Original article

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Palliative resection of the primary tumour in stage IV rectal cancer

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Abstract

Aim The aim of this study was to investigate the use of resection in a cohort of palliatively treated patients with stage IV rectal cancer. To avoid selection bias, particular attention was paid to correction for comorbidity and extent of disease.

Method Patients with stage IV rectal cancer in two hospitals in Groningen were consecutively included over a 5-year period. Comorbidity was defined as major (dementia, cardiac failure or left ventricle ejection fraction < 30%, or severe chronic obstructive pulmonary disease), minor (diabetes, hypertension, mild renal disease or mild pulmonary disease) or none. The effect of patient and disease characteristics on survival was assessed using Kaplan–Meier and Cox regression analyses.

Results Of 88 patients, 11 (13%) underwent elective surgical resection without chemotherapy, 15 (17%) received both elective resection and chemotherapy, 21 (24%) underwent palliative chemotherapy only and 41 (47%) had supportive care only. The extent of disease ($P < 0.01$), hospital ($P = 0.02$) and comorbidity ($P = 0.04$) were correlated with worse survival. Patients treated surgically survived for longer than patients treated nonsurgically, when the data were corrected for age, comorbidity, extent of disease and hospital [hazard ratio (HR) = 0.4 (95% CI = 0.2–0.7)]. Perioperative morbidity was seen in 38% of the patients, and 30-day mortality was 0%.

Conclusion In this retrospective cohort, resection was associated with longer survival independently of the extent of distant metastases, age and comorbidity.

Keywords Metastatic rectal cancer, palliative resection

What is new in this paper?

The use of resection of the primary tumour in stage IV rectal cancer is investigated. The outcome is corrected for comorbidity and extent of disease. A scoring system for extent of disease has been introduced and has proved to be a useful tool, which makes the decision regarding treatment less difficult.

Introduction

Rectal cancer accounts for about one-third of colorectal cancers, with 14–18% of patients having synchronous metastatic disease (stage IV) at first presentation http://nbocap.org.uk/resources/reports/NBOCAP_2009.pdf.

In stage IV disease, a curative strategy can only be carried out in selected patients when the primary tumour and distant metastases are both resectable. For patients with extensive nonresectable metastatic disease, the treatment strategy will mostly be palliative, prolonging survival with the best possible quality of life as the goal. Chemotherapy is effective in prolonging the time to disease progression and survival in patients with advanced rectal cancer [1].

Whether or not resection of the primary tumour in palliative care is beneficial remains a clinical dilemma. Palliative rectal resection may relieve symptoms and avoid potential complications such as obstruction. This symptom-directed intervention can be a safe and effective approach [2,3]. Resection is sometimes recommended because radical surgery can provide durable local control with acceptable morbidity [4,5]. However, in patients presenting with a locally advanced tumour or extensive comorbidity, palliative resection is associated with a poorer survival [6]. In the case of resection, the postoperative recovery period and hospital stay may

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worsen quality of life, and palliative resection of the primary tumour might be associated with significant postoperative morbidity and mortality [7,8]. Moreover, postoperative recovery can delay the start of palliative chemotherapy [9].

The retrospective nature of studies comparing surgical with nonsurgical treatment imply a risk of selection bias.

The aim of this study was to assess the benefit of palliative resection in stage IV rectal cancer. Selection bias in the analysis was adjusted as much as possible by introducing a score that included comorbidity, age and extent of disease.

Method

Patients

A consecutive series of patients with stage IV rectal cancer, diagnosed between January 2002 and December 2006 in a university hospital and a large teaching hospital in Groningen, the Netherlands, was selected from the regional cancer registry database. In this database, all newly diagnosed malignancies are registered based on the main sources of notification, including the automated pathological archive (PALGA) and haematology departments. Information on patient characteristics, tumour characteristics, treatment and hospital was recorded. Only rectal cancers below the rectal fold were included. Rectal cancer was the primary tumour and a diagnosis was made premortem and based on pathology. Patients in whom a curative strategy was adopted were excluded from the study. Clinical and follow-up data were obtained during standard treatment and follow up. According to Dutch law and the Medical Ethical Committee, no further Institutional Review Board (IRB) approval was needed for this study.

Treatment protocol

The treatment strategy for each patient was discussed by a multidisciplinary team. The different therapies were palliative resection with or without chemotherapy, or chemotherapy alone. Patients with severe comorbidity, patients who had end-stage disease or who were in a poor clinical condition, and patients who did not want to be treated, were also included and received only supportive care. This regimen could include a diverting colostomy, radiotherapy on a primary or a metastatic tumour or no therapy at all.

Data collection

Patients and their disease characteristics were collected, including extent of metastatic disease, length of hospital stay, comorbidity and information on perioperative complications and side-effects of chemotherapy. Each patient was scored on comorbidity, which was classified as major, minor or none. Major comorbidity included dementia, cardiac failure or left-ventricle ejection fraction < 30%, and severe chronic obstructive pulmonary disease. Minor comorbidity included diabetes mellitus, hypertension, mild renal disease and mild pulmonary disease. For determining preoperative extensiveness of disease, all CT examinations of the abdomen and thorax were revised by one radiologist (M.P.) and scored on extent of primary tumour growth, nodal metastases and other distal metastases.

Extent of disease scale

These data were then categorized and scored using a self-developed scoring system, indicating the total amount of primary, nodal and metastatic disease. The classification and the scoring system are given in Table 1. For patients who did not undergo a CT scan ($n = 10$), all other diagnostic imaging tools were revised to obtain the preoperative extent of disease as accurately as possible.

Analysis

The use of the scoring system was investigated by comparing the scores for the different treatment groups using Fisher's exact test. For survival, the Kaplan–Meier survival curves were constructed and a log-rank test was performed. The influences of patient and tumour

Table 1 Self-developed scoring system for CT scans of the thorax and abdomen.

Location	Classification	Score (points)
Primary tumour	T < 4	0
	T = 4	1
Nodal metastases	None	0
	Mesenteric	0
	Para-aortic	1
Liver metastases	None	0
	Single	1
	Multiple	2
Lung metastases	None	0
	Single or multiple	1
Ascites	Absent	0
	Present	1
Peritoneal carcinomatosis	Absent	0
	Present	1
Other distant metastases	Absent	0
	Present	2
	Maximum	9

characteristics on survival were studied for each treatment group using Cox regression survival analysis. All statistical analyses were performed using SPSS 16.0 for Windows (Gorinchen, the Netherlands).

Results

Treatment strategies

Of the 96 patients, eight (7%) were lost to follow up because of incomplete medical records. This resulted in a cohort of 88 patients. The median age at which stage IV rectal cancer was diagnosed was 60 (range, 30–93) years. Patient and tumour characteristics are listed in Table 2.

Twenty-six (30%) patients had a surgical resection of the primary tumour, followed by chemotherapy in 15 (58%). Twenty-one (24%) patients underwent palliative chemotherapeutic treatment only and 41 (46%) received supportive care. Supportive care consisted of diverting colostomy in 22 patients, of whom 12 received radiotherapy to the primary tumour or metastasis. Fifteen patients received palliative radiotherapy only. Four patients did not receive any form of palliative care at all.

Of the 88 patients, 86 died during the study period, with an overall median survival time of 382 (range 13–1599) days. One patient was alive 1151 days after treatment with palliative resection and chemotherapy, and one patient survived for 551 days after supportive care with diverting colostomy and radiotherapy to the primary tumour.

Extent of disease and choice of treatment

CT scans were accessible for 78 (87%) patients. Using the self-constructed scoring system for extent of disease (Table 1), the median score was 3 (range 1–8) points. The scores are shown in Fig. 1. In the group undergoing resection with chemotherapy, the median extent of disease was 2.53 (range 1–4) points, and in the supportive care group the median score was 3.44 (range 1–8) points. The reasons for performing a certain type of treatment, as extracted from the multidisciplinary reports, are summarized in Table 3. The poor clinical state of the patient affected treatment choice in only 12 patients.

Mortality and morbidity

Twenty-six patients received palliative resection. The mean hospital stay was 17 days, with a maximum of

Table 2 Patient characteristics per patient group.

Characteristic	All $n = 88$	Treatment				
		Resection $n = 11$	Resection with chemotherapy $n = 15$	Chemotherapy $n = 21$	Supportive care $n = 41$	P
Gender	49 (56)					
Male						
Age						
< 60 years	28 (31)	1 (4)	7 (25)	9 (32)	11 (39)	**0.004**
60–75 years	42 (48)	7 (17)	8 (19)	12 (29)	15 (35)	
> 75 years	18 (21)	3 (17)	0 (0)	0 (0)	15 (83)	
Comorbidity						
Major	8 (9)	0 (0)	1 (12.5)	1 (12.5)	6 (75)	0.71
Minor/none	80 (83)	11 (14)	14 (18)	20 (25)	35 (43)	
Hospital						
University hospital	35 (40)	0 (0)	3 (9)	8 (23)	24 (68)	**0.001**
Teaching hospital	53 (60)	11 (21)	12 (22)	13 (25)	17 (32)	
Location of metastases						
Liver	51 (58)	7 (14)	10 (20)	10 (20)	24 (46)	0.218
Lung	7 (8)	1 (14)	2 (29)	3 (43)	1 (14)	
Liver and lung	21 (24)	1 (5)	2 (10)	7 (33)	11 (52)	
Other	9 (10)	2 (22)	1 (11)	1 (11)	5 (56)	
Type of resection	$N = 26$					
APR	10 (38)	7 (70)	3 (30)	Not applicable	Not applicable	**0.02**
LAR	16 (62)	4 (25)	12 (75)			

Data are given as n (%). Statistically significant differences are given in bold.
APR, abdominoperineal resection; LAR, low anterior resection.

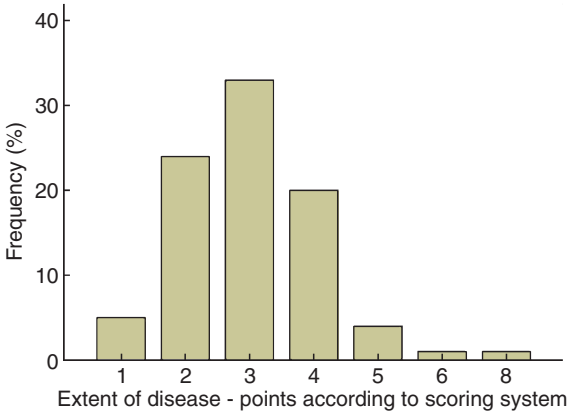

Figure 1 Distribution of the extent of disease according to the scoring system presented in Table 1.

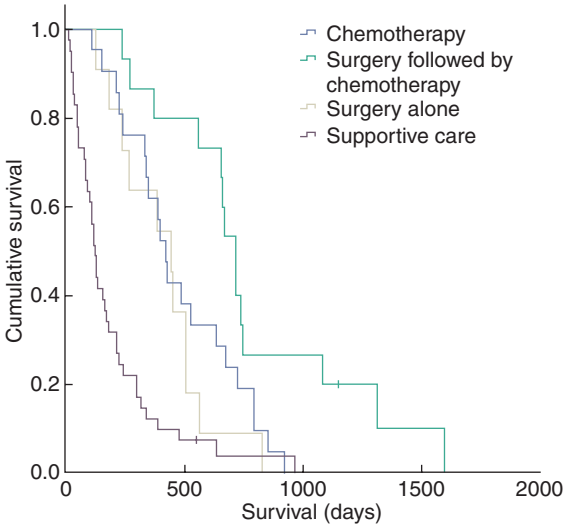

Figure 2 Median length of survival in each treatment group.

66 days. Perioperative complications occurred in nine (38%) patients. Minor complications consisted of urine retention (three patients), urinary tract infection (one patient) and pulmonary infection (one patient). Major complications were respiratory insufficiency with the need for mechanical ventilation in one patient, septic shock with multiorgan failure in one patient, fascia dehiscence in one patient and faecal impaction requiring readmission in one patient. None of the patients died within 30 days after surgery. Of the patients receiving chemotherapy, six discontinued chemotherapy because of severe side effects or the desire to stop.

Survival

The median survival for all patients was 300 days. Patients treated by resection of the primary tumour had a significantly better survival than patients who were not treated surgically ($P < 0.001$). Survival analysis is shown in Fig. 2.

In a Cox regression analysis, resection of the primary tumour followed by chemotherapy led to a longer survival, which was independent of age, comorbidity, extent of disease and hospital [hazard ratio (HR) = 0.4; 95% CI = 0.2–0.7] (Table 4). In a subgroup analysis excluding patients receiving only supportive care, this effect remained (HR = 0.5; 95% CI = 0.2–1.1). The survival rates in the two hospitals were significantly different, in favour of the general hospital ($P = 0.02$; HR = 0.6; 95% CI = 0.4–0.9).

Discussion

No uniform strategy for the treatment of surgically incurable, metastatic rectal cancer has yet been defined. The purpose of this study was to determine the value of palliative resection. Resection of the primary tumour was found to be associated with longer survival, and this was independent of the preoperative extent of disease, age and comorbidity.

Table 3 Considerations in the multidisciplinary meeting on treatment choice.

Treatment	Main argument according to multidisciplinary meeting report	*n* (%)
Surgery ± chemotherapy	Physical symptoms of primary tumour	7
	Local control	18
	Acute presentation with palliative resection	1
Chemotherapy	No symptoms of primary tumour	3
	Extensiveness of disease	15
	Unknown	3
Supportive care	Disease too extensive, including peritoneal carcinomatosis	21
	Comorbidity/poor physical condition	12
	Patient's wish	7
	Unknown	1

Table 4 Multivariate regression analysis showing the influence of treatment and clinical characteristics on survival.

	OR	95% CI	
		Lower	Upper
Treatment			
Treatment (resection *vs* no resection/supportive care)	0.380	0.173	0.831
Age (> 75 years *vs* < 75 years)	0.616	0.431	0.879
Comorbidity (major *vs* minor/none)	0.576	0.268	1.240
Metastases (extent of disease)	1.213	0.992	1.485

The main problem when comparing different treatment strategies, incorporated in the retrospective character of the study, is the bias in decision-making for individual patients [10]. We recognize this as a limitation of our study. We described and defined, to the best of our knowledge, the exact preoperative conditions of each patient, according to comorbidity and the extent of the tumour, by revising and scoring each CT scan, and combined this information with the results obtained by revising the outcome of multidisciplinary reports of each patient, strengthening the interpretation of the results. The decision regarding whether or not to operate on a patient was based on the poor clinical condition of the patient in a minority of cases.

No randomized control trials are available on this topic. Several studies have not found a difference in survival between patients with rectal cancer who have been operated on and those who have not [2,3,11]. Low rates (7–9%) of perforation or bleeding leading to surgical action in the nonoperated groups have led to the recommendation of a nonresection approach for selected patients [2,12].

However, in a large multicentre study of both colon and rectal cancer, median and 1-year survival after resection of the primary tumour were significantly higher than for those patients treated with oncological nonsurgical care [13]. In other retrospective studies comparing patients undergoing elective surgery for metastatic colorectal cancer with those receiving nonsurgical treatment, the authors found a significantly better median survival for the resection group [14–18]. In these studies, comorbidity of the patients is not taken into account in survival analysis, which can bias the favourable outcome of the selected, surgically managed patients. Moreover, the extent of distant metastatic disease is not defined in some of these studies [16–18].

Liver involvement, size and number of lymph nodes (as determined by pretreatment CT scans) and extent of the primary tumour have been found to be clinical prognostic factors in patients with rectal cancer [19–22]. We constructed a categorical scale for extensiveness of disease by giving points for the presence of cancer activity, thereby combining extent of disease on tumour (T), node (N) and metastases (M) stages. This gives notably more information on the extensiveness of disease than only liver or nodal involvement.

Perioperative morbidity was seen in 38% of surgical patients, ranging from minor to major. In a review on both colon and rectal cancers in noncurable metastatic disease, postoperative morbidity was found to range from 19 to 47%, with an incidence of 12% for major complications [23]. Postoperative mortality was not seen in the present retrospective study, although its incidence in the literature ranges from 0 to 14% for rectal cancer [2,8,11]. Furthermore, perioperative morbidity is known to be higher with worse comorbidity. Severe complications of chemotherapy were also seen, resulting in the death of one patient from a pyrimidine metabolism disorder.

We performed a noncase-matched retrospective study comparing outcomes of surgical and nonsurgical treatment modalities in patients with stage IV rectal cancer. To allow for the impact of case selection, we were particularly interested in the preoperative extent of metastatic disease and comorbidity, and their effects on survival. We found that resection of the primary tumour was associated with longer survival, which was independent of age, comorbidity or extent of disease.

Conflict of interest statement

The authors have no conflict of interest.

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