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Oncological outcome of carcinomas in the rectosigmoid junction compared to the upper rectum or sigmoid colon – A retrospective cohort study

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ABSTRACT

Introduction: Although carcinomas of the rectosigmoid junction are frequent, specific data on these tumors are sparse because assignment either to the colon or rectum is common. The objective of this study is to determine whether carcinomas of the rectosigmoid junction can be assigned to the sigmoid colon or to the upper rectum in terms of tumor characteristics and oncological outcome.
Materials and methods: 337 consecutive patients undergoing resection of carcinomas in the sigmoid colon, the rectosigmoid junction and the upper third of the rectum were analyzed retrospectively and additionally followed-up for oncological outcome.
Results: 185 patients (54.9%) showed carcinoma in the sigmoid colon, 41 (12.2%) in the rectosigmoid junction and 111 (32.9%) in the upper rectum. Synchronous liver metastases (rectosigmoid junction 31.7%, sigmoid colon 16.2%, upper rectum 11.7%; $P = 0.01$), lymphovascular invasion (rectosigmoid junction 46.3%, sigmoid colon 25.4%, upper rectum 32.4%; $P = 0.03$) and pN2 (rectosigmoid junction 31.7%, sigmoid colon 10.3%, upper rectum 13.5%; $P = 0.002$) were more common in carcinomas of the rectosigmoid junction. The median follow-up period was 44 (22–75.5) months. Five-year overall survival was 44.6% in patients with carcinomas in the rectosigmoid junction, 70.9% in the sigmoid colon, and 70.2% in the upper rectum.
Conclusion: Carcinomas of the rectosigmoid junction reveal a deviant behavioral pattern compared to its adjacent bowel segments.

Introduction

Adenocarcinomas of the rectosigmoid junction represent up to ten percent of colorectal carcinomas [1,2]. The Classification of Diseases for Oncology, ICD-O, Third Edition of the World Health Organization (www.who.int) encodes the rectosigmoid junction (C19) as an independent segment of the large intestine. In most studies on colorectal carcinomas, the rectosigmoid junction is not evaluated separately, but rather added to the rectum [3–5] or colon [6]. Only few studies are available that analyzed adenocarcinomas of the rectosigmoid junction, especially comparing the region to the adjacent colorectal segments regarding tumor characteristics and parameters dealing with the oncological outcome [7–10]. Studies, which subdivide the upper third of the rectum as the directly adjacent segment are rare [10], and randomized controlled trials on the subject are still not available. Because therapy of colorectal tumors becomes more and more differentiated and individualized, it is important to obtain more information about tumor characteristics and the post-therapeutic behavior of cancer in the rectosigmoid junction.

The objective of this study is to determine whether carcinomas of the rectosigmoid junction can be assigned to the sigmoid colon or the upper rectum or even have to be considered independently, taking into account tumor characteristics and the oncological

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outcome.

Material and methods

All patients who underwent resection of a primary colorectal carcinoma between the years 2004 and 2014 at the University Hospital of Tuebingen were retrospectively analyzed. The patients were identified by using the clinical documentation system (i.s.h.med® (Siemens Medical Solutions GSD GmbH, Berlin, Germany), SAP for Healthcare® (SAP SE, Walldorf, Germany)). For final data analysis, patients with a primary carcinoma of the sigmoid colon, the rectosigmoid junction and the upper third of the rectum were considered. MRI imaging was only available for patients with rectal cancer. But in all patients, pre-operative endoscopy/rectoscopy was performed. Endoscopy/rectoscopy and MRI are comparable for measuring the distance from the distal tumor margin to the anocutaneous line [11–13]. So, assignment to one of the three bowel segments was performed taking into account the pretherapeutic distance between the anocutaneous line and the distal tumor margin, measured by rectoscopy [14]. For allocation of the tumors to the rectum or the sigmoid colon, common used definitions were applied [5,15]. So, the upper third of the rectum was defined between 12 cm and 16 cm. Based on previous studies, a 4 cm bowel segment proximal to the rectum between 16.1 cm and 20 cm was defined as the rectosigmoid junction [16]. Tumors, with its distal tumor margin more than 20 cm distant from the anocutaneous line, were considered as carcinomas of the sigmoid colon [15,16].

All patients underwent a standardized oncological tumor resection including lymphadenectomy by specialists in colorectal surgery according to current evidenced-based guidelines for colorectal cancer adapted to the individual tumor site [17]. Multimodal therapies were performed in accordance with the recommendations of the interdisciplinary tumor board of the University Hospital of Tuebingen (Comprehensive Cancer Center). Exclusion criteria to achieve homogenization of the data were tumors, which could not be clearly assigned to one of the three segments, as well as carcinoma in situ, resection without anastomosis (e.g. Hartmann's procedure, transanal minimally invasive surgery) and emergency resections. The patient collective is shown in the flow chart in Fig. 1.

Patient characteristics and comorbidities, as well as parameters including preoperative staging, therapy, histopathology, morbidity as documented and hospital mortality were extracted from the electronic patient records. The comorbidities were assessed by using the Charlson Comorbidity Index (CCI) [18] and the patients physical condition was rated by ASA classification (American Society of Anesthesiologists) [19]. After bowel resection, the specimen was histopathologically reviewed and classified according to the American Joint Committee on Cancer (AJCC, 7th edition) by a specialized pathologist (Institute of Pathology and Neuropathology, University of Tuebingen). Postoperatively occurring events such as tumor recurrence and death were determined by means of a standardized questionnaire, requested via mail or telephone interviews. Missing data were supplemented by a query from the Cancer Registry.

Statistical analysis

All statistical analyses were performed with IBM® SPSS® Statistics Version 24.0.0.1 (IBM Corporation, NY, USA). Categorical data are

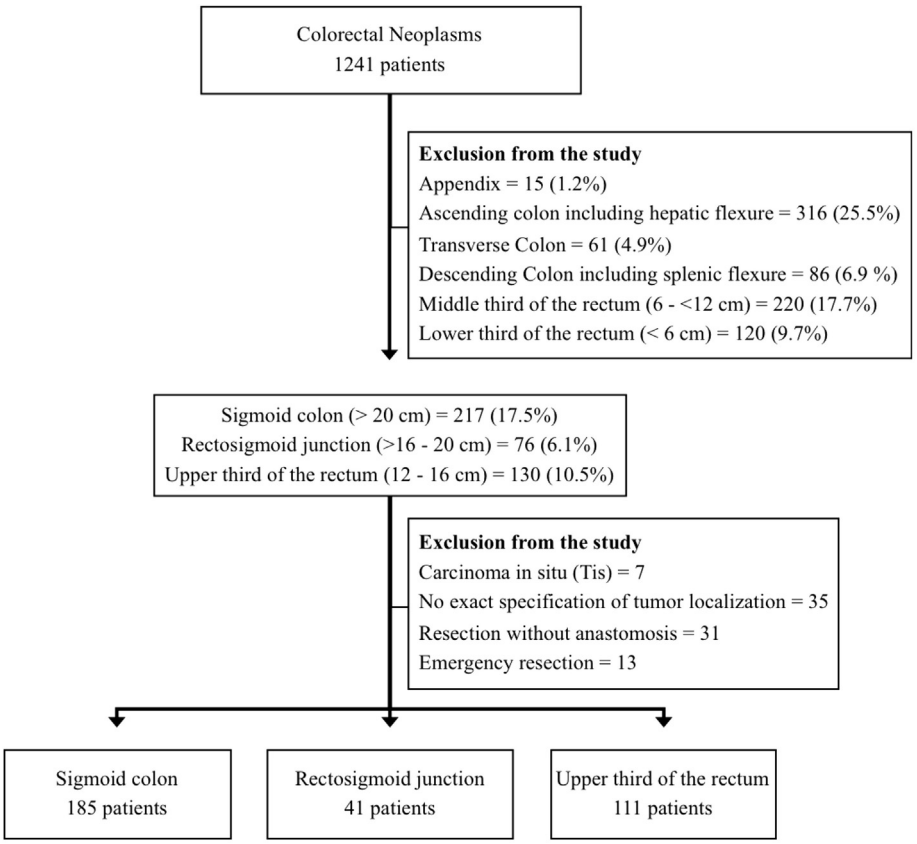

Fig. 1. Flow chart of the study collective.

presented as absolute values and percentages. Continuous data are shown as median and interquartile range (IQR). A comparison of categorical data between the three groups was performed with the Chi^2 test and the medians with the Kruskal-Wallis-Test. Survival curves were calculated according to the Kaplan-Meier method. Differences in survival between the groups were statistically assessed by using the log-rank test. Univariable and multivariable Cox regression analyses were performed to determine the prognostic implications of variables on the overall survival and disease-free survival, and hazard ratios with 95% confidence intervals were calculated. Age, sex, CCI-Score, UICC stage, completeness of resection, tumor differentiation, lymphovascular invasion and the three tumor localizations were included in the univariable analyses. Into the multivariable analyses, all variables were entered showing a p value less than 0.1 in univariable analysis. All p values listed are two-sided and p values < 0.05 were deemed to denote statistical significance. The starting point for the calculation of survival curves or time intervals until tumor recurrence was the day of tumor resection. For the analysis of tumor recurrence, including local recurrence and metachronous tumor dissemination, only patients with tumor stage 0-III and histopathologically proven tumor free resection margins (R0) were considered. No patient was included who underwent previous, simultaneous or subsequent metastasectomy.

The study was carried out in accordance with the ethical requirements regarding the protection of the rights and welfare of human subjects participating in medical research (Ethics Review Board of the University of Tübingen, Germany) and complies with the criteria of the STROCSS guideline for cohort studies in surgery [20]. The study was registered in the German Clinical Trials Register (DRKS00015052).

Results

Within an 11-year interval, a total of 1241 patients underwent oncological bowel resection. The final analysis included 337 patients with carcinomas in the sigmoid colon (185 patients), the rectosigmoid junction (41 patients), and the upper third of the rectum (111 patients) (Fig. 1). Patient characteristics, comorbidity, therapy data, postoperative morbidity and mortality according to tumor site are shown in Table 1. There was no statistical difference between patients suffering from carcinoma in the sigmoid colon, the rectosigmoid junction and the upper third of the rectum for gender distribution, age, BMI, CCI-Score, ASA score and HNPCC (Hereditary NonPolyposis Colorectal Cancer). Neoadjuvant therapy was only performed in patients suffering from carcinoma in the upper third of the rectum (one patient radiotherapy alone, 18 patients chemoradiotherapy).

Staging and histopathology

Tumor characteristics and histopathological findings according to the three tumor localizations are listed in Table 1. A complete histopathological tumor remission (ypT0 ypN0) was detected in four of 18 patients (22.2%) with a carcinoma of the upper third of the rectum after neoadjuvant chemoradiotherapy. In another patient with ypT0 stage, vital tumor cells were seen in one regional lymph node (ypN1). Patients with a carcinoma in the rectosigmoid junction were more rarely node-negative (pN0) and had significantly more frequently four or more lymph node metastases (pN2) ($P = 0.002$). Similarly, carcinomas in the rectosigmoid junction showed a significantly higher lymphovascular invasion ($P = 0.03$).

In addition, patients with a carcinoma in the rectosigmoid junction showed a significantly higher rate of synchronous distant metastasis in general and were affected more frequently by synchronous liver metastases (sigmoid colon: 16.2%, rectosigmoid junction: 31.7%, upper third of the rectum: 11.7%, $P = 0.01$).

Ulcerative tumors were more common in the sigmoid colon (59.5%) than in the rectosigmoid junction (43.9%) and the upper third of the rectum (39.6%) ($P = 0.003$). On the other hand, carcinomas in the rectosigmoid junction (56.1%) and the upper third of the rectum (51.4%) were more frequently polypoid tumors than in the sigmoid colon (34.1%) ($P = 0.002$). Tumor perforation verified by histopathology was seen significantly more often in carcinomas of the rectosigmoid junction (12.2%) than in the sigmoid colon (3.2%) and the upper third of the rectum (2.7%) ($P = 0.02$). No differences between the three bowel segments were registered in tumor size, tumor differentiation, incidence of mucinous adenocarcinoma, perineural invasion, tumor stenosis and inflammation.

Tumor recurrence

262 of 337 patients (77.7%) showing UICC stage 0-III tumors and clear resection margins (R0) after bowel resection were reexamined for local recurrence and metachronous tumor dissemination, as displayed in Table 2. The median follow-up period was 44 (22–75.5) months. Adjuvant therapy was more often performed in patients with carcinomas in the rectosigmoid junction and the upper third of the rectum (7/25 patients, 28%; 30/92 patients, 32.6%) than in carcinomas of the sigmoid colon (27/152 patients, 17.8%; $P = 0.04$).

Of the 262 patients, 40 patients (15.3%) developed recurrent disease, of which six patients (2.3%) showed only local recurrence, 28 patients (10.7%) distant metastasis alone and six patients (2.3%) local recurrence as well as distant metastasis. Although the rate of local recurrence did not differ between the three segments, patients with carcinomas in the rectosigmoid junction revealed more often metachronous liver metastases (20%) than the two adjacent segments (sigmoid colon: 6.9%, upper third of the rectum: 8.7%), however, this was not statistically significant ($P = 0.10$). In contrast, metachronous metastases of the lung were more common in carcinomas of the upper third of the rectum (10.9%) than in carcinomas of the sigmoid colon (4.8%) and the rectosigmoid junction (4.0%) ($P = 0.17$).

19 of the patients suffering from a carcinoma in the upper third of the rectum underwent neoadjuvant therapy and no patient in the two other groups did. In the patients with a carcinoma of the upper third of the rectum undergoing neoadjuvant therapy, the overall rate of recurrent tumors, local recurrence and metachronous distant metastasis did not differ in a statistically significant manner compared to patients without neoadjuvant therapy.

Overall survival

The overall survival of patients with a carcinoma of the rectosigmoid junction differs significantly from carcinomas of the sigmoid colon ($P = 0.02$) and the upper third of the rectum ($P = 0.02$), as shown in the Kaplan-Meier survival curves in Fig. 2. This is reflected in the five-year overall survival, which was 44.6% in patients with carcinomas in the rectosigmoid junction, 70.9% in the sigmoid colon, and 70.2% in the upper third of the rectum. Univariable analysis identified the rectosigmoid junction as a risk factor for a worse overall survival (HR 1.92, 95% CI 1.17–3.17, $P = 0.01$), whereas, the sigmoid colon and the upper third of the rectum were not (Table 3). However, in the multivariable analysis the rectosigmoid junction was not an independent risk factor for poorer overall survival (Table 3). Older age, higher CCI score, positive resection margins (R+) and a lymphovascular invasion were identified as independent risk factors for poorer overall survival by multivariable analysis.

Table 1
Patient characteristics, therapy data, postoperative morbidity and mortality, tumor characteristics and histopathological finding according to tumor site.

	Total (n = 337)	Sigmoid Colon (n = 185/ 54.9%)	Rectosigmoid Junction (n = 41/ 12.2%)	Upper Rectum (n = 111/ 32.9%)	P
Patient characteristics					
Sex					
male	199 (59.1)	107 (57.8)	26 (63.4)	66 (59.5)	0.80
female	138 (40.9)	78 (42.2)	15 (36.6)	45 (40.5)	
Age (years)	67 (59–75)	67 (58–76)	64 (57–76)	68 (61–75)	0.78
BMI (kg/m^2)	26 (23–29)	26 (23–29)	26 (23–28)	26 (23–28)	0.37
CCI Score	1 (0–4)	1 (0–4)	3 (0–6)	1 (0–4)	0.12
ASA-Score[a]					0.75
< 3	224 (68.3)	118 (66.7)	28 (68.3)	78 (70.9)	
≥ 3	104 (31.7)	59 (33.3)	13 (31.7)	32 (29.1)	
Therapy data,					
Preoperative therapy (total)	33 (9.8)	9 (4.9)	0	24 (21.6)	<0.001
Neoadjuvant Chemoradiotherapy	18 (5.3)	0	0	18 (16.2)	<0.001
Neoadjuvant Radiotherapy	1 (0.3)	0	0	1 (0.9)	0.36
Palliative Chemotherapy**	14 (4.2)	9 (4.9)	0	5 (4.5)	0.36
Surgery					
Resection with protective loop ileostomy	53 (15.7)	8 (4.3)	4 (9.8)	41 (36.9)	<0.001
Resection without protective loop ileostomy	284 (84.3)	177 (95.7)	37 (90.2)	70 (63.1)	
Anastomotic leakage	10 (3.0)	3 (1.6)	2 (4.9)	5 (4.5)	0.27
In-hospital mortality rate	1 (0.3)	1 (0.5)	0	0	0.66
Tumor characteristics					
Synchronous multifocal colorectal carcinoma	15 (4.5)	8 (4.3)	5 (12.2)	2 (1.8)	0.02
HNPCC	7 (2.1)	4 (2.2)	0	3 (2.7)	0.58
Primary tumor (pT)					0.03
T0[b]	5 (1.5)	0	0	5 (4.5)	
T1	42 (12.5)	21 (11.4)	8 (19.5)	13 (11.7)	
T2	55 (16.3)	29 (15.7)	4 (9.8)	22 (19.8)	
T3	191 (56.7)	107 (57.8)	22 (53.7)	62 (55.9)	
T4	44 (13.1)	28 (15.1)	7 (17.1)	9 (8.1)	
Regional lymph nodes (pN)					0.01
pN0	205 (60.8)	116 (62.7)	20 (48.8)	69 (62.2)	
pN1	85 (25.2)	50 (27.0)	8 (19.5)	27 (24.3)	
pN2	47 (13.9)	19 (10.3)	13 (31.7)	15 (13.5)	0.002
Examined lymph nodes	16 (13–21)	16 (13–21)	17 (13–22)	16 (13–21)	0.92
Distant metastasis (M)	73 (21.7)	39 (21.1)	16 (39.0)	18 (16.2)	0.01
Liver	56 (16.6)	30 (16.2)	13 (31.7)	13 (11.7)	0.01
Lung	17 (5.0)	9 (4.9)	4 (9.8)	4 (3.6)	0.30
Peritoneum	15 (4.5)	8 (4.3)	3 (7.3)	4 (3.6)	0.61
Others	12 (3.6)	6 (3.2)	3 (7.3)	3 (2.7)	0.37
UICC stage					0.004
0	4 (1.2)	0	0	4 (3.6)	
I	85 (25.2)	44 (23.8)	10 (24.4)	31 (27.9)	
II	100 (29.7)	65 (35.1)	7 (17.1)	28 (25.2)	
III	75 (22.3)	37 (20.0)	8 (19.5)	30 (27.0)	
IV	73 (21.7)	39 (21.1)	16 (39.0)	18 (16.2)	
Tumor diameter (cm)[c]	3.7 (2.5–5.0)	3.5 (2.5–5.0)	3.6 (2.8–5.0)	4.0 (2.5–5.0)	0.78
Tumor differentiation###					0.52
G1 (well)	19 (5.8)	13 (7.1)	3 (7.5)	3 (2.9)	
G2 (moderate)	251 (76.5)	140 (76.1)	28 (70.0)	83 (79.8)	
G3 (poor)	58 (17.7)	31 (16.8)	9 (22.5)	18 (17.3)	
not available	9	1	1	7	
Mucinous adenocarcinoma	50 (14.8)	33 (17.8)	5 (12.2)	12 (10.8)	0.23
Lymphovascular invasion (L)	102 (30.3)	47 (25.4)	19 (46.3)	36 (32.4)	0.03
Perineural invasion (Pn)	14 (4.2)	9 (4.9)	2 (4.9)	3 (2.7)	0.65
Tumor growth pattern and behavior					
Ulcerative	172 (51.0)	110 (59.5)	18 (43.9)	44 (39.6)	0.003
Polypoid	143 (42.4)	63 (34.1)	23 (56.1)	57 (51.4)	0.002
Stenosing	168 (49.9)	94 (50.8)	21 (51.2)	53 (47.7)	0.86
Perforation	14 (4.2)	6 (3.2)	5 (12.2)	3 (2.7)	0.02
Inflammation	53 (15.7)	27 (14.6)	6 (14.6)	20 (18.0)	0.72
Completeness of resection (R)					0.88
R0	325 (96.4)	179 (96.8)	39 (95.1)	107 (96.4)	
R+	12 (3.6)	6 (3.2)	2 (4.9)	4 (3.6)	

BMI, Body Mass Index; HNPCC, Hereditary Non-Polyposis Colorectal Cancer; ASA, American Society of Anesthesiologists; CCI, Charlson Comorbidity Index.
[a] n = 328; ** All patients suffering from distant metastasis.
[b] All patients following neoadjuvant chemoradiotherapy. In one out of the five patients, vital tumor cells were seen in a regional lymph node.
[c] Tumor diameter measured on specimen. Patients showing a complete response in histopathology (pCR) following neoadjuvant chemoradiotherapy are excluded.### If neoadjuvant therapy was performed, differentiation detected in preoperative biopsy is shown.

Table 2
Follow up data of 262 patients showing UICC stage 0-III tumors and clear resection margins (R0) after surgery.

	Total (n = 262)	Sigmoid Colon (n = 145/ 55.3%)	Rectosigmoid Junction (n = 25/ 9.2%)	Upper Third of the Rectum (n = 92/ 35.1%)	P
Overall rate of recurrent tumor[a]	40 (15.3)	17 (11.7)	5 (20.0)	18 (19.6)	0.21
Time from surgery to diagnosis (months)	19 (10–37)	27 (11–41)	7 (4–17)	20 (10–46)	0.10
Local recurrence	12 (4.6)	5 (3.4)	1 (4.0)	6 (6.5)	0.54
Time from surgery to diagnosis (months)	16.5 (11–31)	19 (7–38)	7	16.5 (12–31)	0.42
Distant recurrence[b]	34 (13.0)	14 (9.7)	5 (20.0)	15 (16.3)	0.18
Liver	23 (8.8)	10 (6.9)	5 (20.0)	8 (8.7)	0.10
Lung	18 (6.9)	7 (4.8)	1 (4.0)	10 (10.9)	0.17
Peritoneum	3 (1.1)	2 (1.4)	0	1 (1.1)	0.83
Distant lymph node	5 (1.9)	2 (1.4)	0	3 (3.3)	0.45
Bone	3 (1.1)	0	0	3 (3.3)	0.06
Brain	1 (0.4)	0	0	1 (1.1)	0.40
Further localizations	2 (0.8)	1 (0.7)	0	1 (1.1)	0.85
Time from surgery to diagnosis (months)	20 (10–40)	27.5 (11–41)	7 (4–17)	21 (8–51)	0.11

[a] Overall rate of local recurrence and distant recurrence. Time interval is defined as time interval between tumor resection and diagnosis of local recurrence or distant recurrence, respectively.
[b] Multiple nominations of metachronous metastases are possible. However, all patients who were affected by metachronous peritoneal carcinomatosis showed metachronous tumor dissemination at this site exclusively.

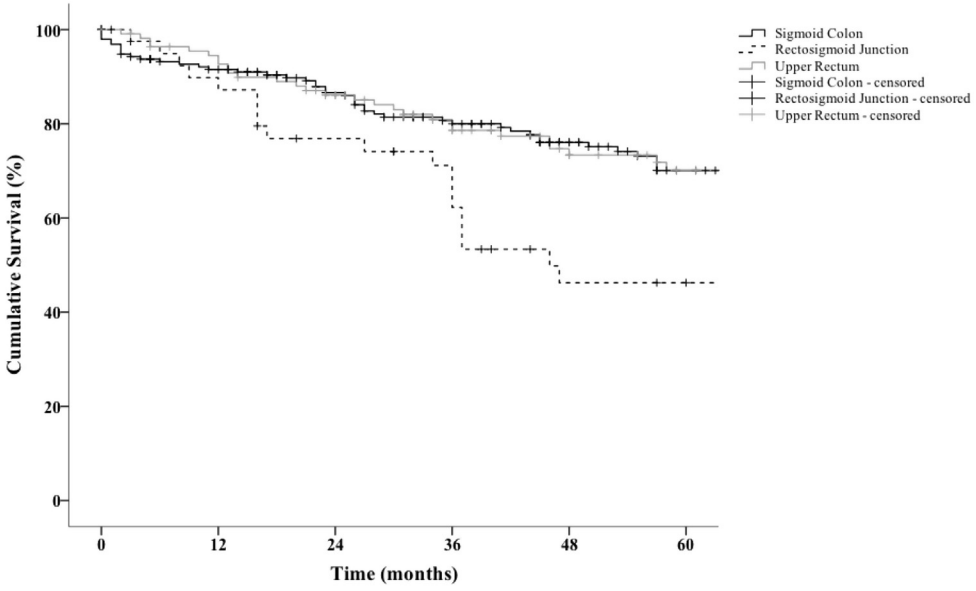

Fig. 2. Overall Kaplan-Meier survival curves for primary cancer in the sigmoid colon, rectosigmoid junction and the upper third of the rectum.

Disease-free survival

In all patients with stage 0-III tumors and clear resection margins in histopathology (R0), the Kaplan-Meier curves showed no statistically significant difference in disease-free survival between the three localizations (Fig. 3). The disease-free five-year survival was as follows: sigmoid colon 77.4%, rectosigmoid junction 64.3%, upper third of the rectum 72.9%. The rectosigmoid junction had no prognostic influence on disease-free survival in the univariable analysis, as did the two other segments. Independent risk factors associated with a poor disease-free survival identified by the multivariable analysis were an older age, male gender and a higher CCI score.

Discussion

Considering the pathological findings such as tumor ulceration and polypoid tumor growth, tumors of the rectosigmoid junction resembled rather rectal carcinomas than those of the sigmoid colon. Whereas the lymphatic spread and the rate of tumor

Table 3
Univariable and multivariable Cox regression analysis for overall survival and disease-free survival (UICC stage 0-III and R0).

	Overall survival (n = 337)				Disease-free survival (n = 262)			
	Univariable analysis		Multivariable analysis[a]		Univariable analysis		Multivariable analysis[a]	
	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P
Age (years)[b]	1.02 (1.00–1.04)	0.07	1.02 (1.00-1-04)	0.03	1.04 (1.02–1.07)	0.002	1.03 (1.01–1.06)	0.02
Sex								
female	1.00 (reference)				1.00 (reference)		1.00 (reference)	
male	1.27 (0.84–1.92)	0.26			1.63 (0.96–2.75)	0.07	1.81 (1.04–3.14)	0.04
CCI Score[b]	1.33 (1.26–1.39)	<0.001	1.20 (1.09–1.32)	<0.001	1.41 (1.27–1.57)	<0.001	1.34 (1.20–1.50)	<0.001
UICC stage								
UICC 0-I	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
UICC II	1.70 (0.88–3.29)	0.12	1.54 (0.78–2.99)	0.20	2.12 (1.16–3.86)	0.01	1.72 (0.93–3.12)	0.08
UICC III	1.08 (0.50–2.33)	0.85	0.67 (0.30–1.51)	0.33	1.41 (0.71–2.79)	0.33	1.23 (0.64–2.53)	0.49
UICC IV	11.25 (6.05–20.93)	<0.001	2.36 (0.96–5.78)	0.06	-	-	-	-
Completeness of resection								
R0	1.00 (reference)		1.00 (reference)					
R1/2	4.77 (2.30–9.91)	<0.001	3.99 (1.75–9.08)	0.001				
Tumor differentiation								
G1/G2 (well-moderate)	1.00 (reference)		1.00 (reference)		1.00 (reference)			
G3 (poor)	2.20 (1.42–3.41)	<0.001	1.18 (0.72–1.94)	0.51	1.58 (0.84–2.95)	0.15		
Lymphovascular invasion								
No	1.00 (reference)		1.00 (reference)		1.00 (reference)			
Yes	2.55 (1.72–3.79)	<0.001	2.17 (1.37–3.43)	0.001	1.36 (0.79–2.35)	0.26		
Sigmoid Colon								
No	1.00 (reference)				1.00 (reference)			
Yes	0.87 (0.59–1.29)	0.48			0.86 (0.53–1.40)	0.55		
Rectosigmoid Junction								
No	1.00 (reference)		1.00 (reference)		1.00 (reference)			
Yes	1.92 (1.17–3.17)	0.01	1.17 (0.69–1.99)	0.57	1.46 (0.70–3.07)	0.32		
Upper Third of the Rectum								
No	1.00 (reference)				1.00 (reference)			
Yes	0.81 (0.53–1.24)	0.34			1.01 (0.61–1.66)	0.98		

CCI, Charlson comorbidity index; HR, hazard ratio. 95%CI, 95% confidence interval.
[a] Variables with a p value less than 0.1 in the univariable analysis were entered into the multivariable analysis.
[b] Continuous variable, β coefficient = +0.01.

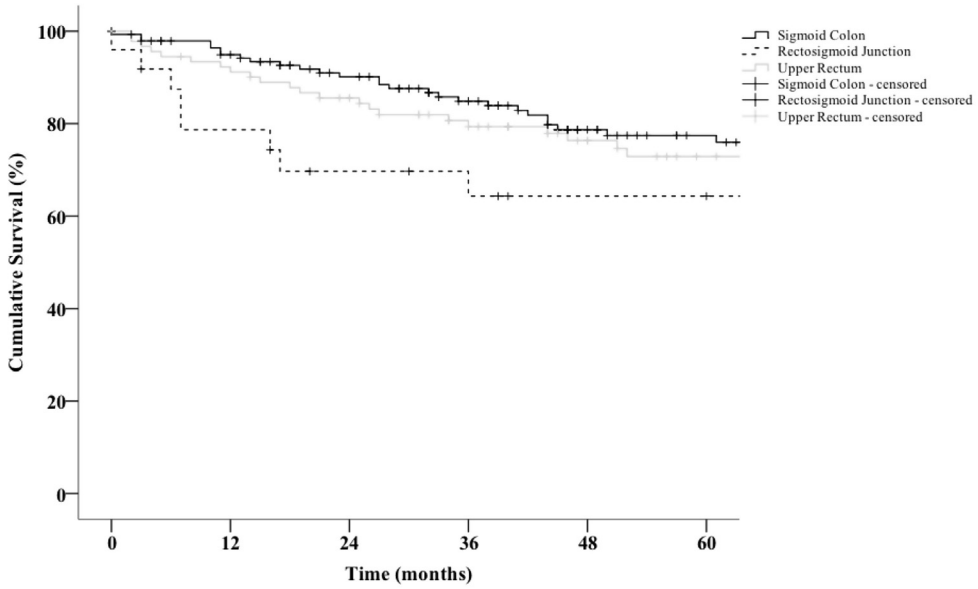

Fig. 3. Disease-free Kaplan-Meier survival curves for primary cancer in the sigmoid colon, rectosigmoid junction and the upper third of the rectum of all patients with stage 0-III tumors and clear resection margins (R0) after surgery.

perforation distinguished carcinomas in the rectosigmoid junction from both adjacent sites. All other investigated features did not differ between the three localizations. The published literature up to now either did not identify any differences between the three localizations [1] or described only a moderate variability of the rectosigmoid junction to the sigmoid colon but also to the rectum [10].

In comparison to the sigmoid colon and the upper third of the rectum, we observed a significantly higher rate of synchronous liver metastases in tumors of the rectosigmoid junction. This also might be due to the higher rate of lymphovascular invasion in tumors of the rectosigmoid junction. The frequent occurrence of liver metastases in tumors of this segment is responsible for the significantly higher overall rate of synchronous distant metastases compared to the sigmoid colon and the upper third of the rectum. An analysis of the Surveillance, Epidemiology, and End Results (SEER) database reports on a rate of synchronous liver metastases in tumors of the left colon of 15.3% and in rectal cancer of 12.3% [21]. The data are consistent with our rates in carcinoma of the sigmoid colon and the upper third of the rectum, respectively. However, there is little known about the ratio of synchronous distant metastasis in carcinomas of the rectosigmoid junction. Analyzing a Korean study population, Bae et al. described a rate of 17.6% of synchronous distant metastasis in carcinomas of the rectosigmoid junction [1]. Compared to our rate of 39.0%, this is lower, whereas the rates of synchronous metastasis in carcinomas of the sigmoid colon and rectum are more similar to our data [1]. Published data of German cancer registries reported a rate of synchronous distant metastasis in advanced cancers of the rectosigmoid junction of 27.7%, which is more similar to the results of our cohort [22]. However, in this population, synchronous distant metastasis in cancer of the sigmoid colon (28.7%) and rectum (24.7%) were more frequent as well, and thus not relevantly increased compared to carcinomas of the rectosigmoid junction [22]. Data published on synchronous liver metastasis in carcinomas of the rectosigmoid junction are lacking to our knowledge.

Metachronous liver metastases in our population also tended to be more frequent in carcinomas of the rectosigmoid junction (20%), compared to tumors in the sigmoid colon (6.9%) and the upper third of the rectum (8.7%), though not statistically significant. While also no data concerning metachronous dissemination in tumors of the rectosigmoid junction are available, metachronous liver metastasis in tumors of the entire colon are reported between 8.4 and 48.6% and in rectal carcinomas between 19.6 and 32.6% [23–25]. The rates of local recurrence in our study did not differ between the three localizations and are in accordance with published studies [6,26].

Metastatic colonic and rectal carcinomas show a poorer five-year survival than non-metastatic tumors in these colon segments [27]. Therefore, the greater frequency of synchronous distant metastasis in patients suffering from carcinomas within the rectosigmoid junction is very likely the reason for the significantly worse five-year overall survival, compared to patients with cancer localized in the adjacent bowl segments in our study population. Although the Kaplan-Meier survival curves for disease-free survival in patients with stage 0-III cancer seem to be similar, and patients with carcinoma of the rectosigmoid junction also showed a higher rate of metachronous liver metastases in comparison to the adjacent bowel segments, the differences are not statistically significant. Mukai et al. compared stage II/III carcinomas of the rectosigmoid junction with cancer of the rectum and the colon in terms of five-year overall survival and five-year disease-free survival [28]. Hereby, stage III carcinomas of the rectosigmoid junction and the rectum differed significantly. So, the authors concluded that the rectosigmoid junction should not be regarded as an independent tumor type, but rather assigned to the colon.

Except for very few publications, tumors in the rectosigmoid junction are not investigated differentiatedly and are usually assigned either to the colon or the rectum. Because up to day both is practiced, an interpretation of the data of these tumors is not possible. Additionally, the few available data on tumors of the rectosigmoid junction are very inhomogeneous and of moderate quality. But detailed information on the individual colorectal segments is indispensable for an individualized treatment of colorectal carcinomas in future. Contributing to this, there is no uniformly used definition for analyzation of tumors in this region. If cancer in the rectosigmoid junction can be assigned to the sigmoid colon or the upper rectum or even have to be handled individually, in this retrospective study only patients were considered for analyzation, in which the tumors clearly could be assigned to this transition zone. The small number of tumors in the rectosigmoid junction in our study population limits the generalization of the results shown. And based on the different numbers of patients within the three groups due to the natural distribution of the tumors, a comparison is of limited nature. But of note, the data including the follow-up data, are comprehensive and nearly complete. And until today, no major collectives showing detailed data on tumors in the rectosigmoid junction are available in the literature, in particular no randomized controlled trials.

Taking into account the histopathological findings, the rectosigmoid junction differed from the adjacent bowel segments in particular in terms of a more aggressive lymphatic spread and a more frequent tumor perforation. Features that are known to be risk factors for a poor disease-free survival and overall survival [29,30]. Also, the higher rates of synchronous multifocal colorectal carcinomas and liver metastasis (synchronous and metachronous) in carcinomas of the rectosigmoid junction confirm that the different tumor behavior as the bowel segments nearby. Although the rectosigmoid junction is identified as a risk factor for poorer overall survival in the univariable analysis but is not an independent risk factor in the multivariable analysis, a multifactorial influenced process seems to underlie.

Conclusions

The rectosigmoid junction shows a deviant behavioral pattern of its carcinomas in comparison to the adjacent bowel segments. A clear assignment to the sigmoid colon or upper rectum is not possible. The data have to be approved by larger collectives in randomized controlled trials. In particular, since no detailed data on carcinomas of the rectosigmoid junction with larger case numbers are available. To characterize the carcinomas in a more detailed fashion, comparative molecular biological investigations and studies which examine gene expression of the carcinomas in that bowel segment could help to treat patients with carcinomas in the rectosigmoid junction more individually in future. In addition, anatomical examinations for local lymphatic drainage for example by lymphoscintigraphy may be valuable.

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Author contribution

Claudius Falch, Sven Mueller and Andreas Kirschniak drafted the manuscript and contributed to the study conception and design as well as the acquisition and analyzing of data. Claudius Falch, Sven Mueller, Manuel Braun, Cihan Gani, Falko Fend, Alfred Koenigsrainer and Andreas Kirschniak contributed by interpretation of data, critical revising of the manuscript and its final approval.

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Appendix A. Supplementary data

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