Gastrointestinal Tumors

Research Article

Gastrointest Tumors 2021;8:16–24
DOI: 10.1159/000511104

Received: June 22, 2020
Accepted: August 24, 2020
Published online: November 18, 2020

The Effect of Laparoscopic Technique on the Surgical Outcome of Colorectal Cancer in a Small-Volume Rural Finnish Lapland Central Hospital

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Keywords

Laparoscopy · Colorectal surgery · Single-center study · Retrospective · Small-volume center · Enhanced recovery after surgery

Abstract

Introduction: Laparoscopic colorectal surgery has become widely used in treating colorectal cancer. Multicenter studies have shown that laparoscopy decreases postoperative complications and provides equivalent long-term oncological results compared to open surgery. Previous studies were conducted in high-volume institutions, with selected patients, which may influence the reported outcome of laparoscopy. ***Methods:*** All patients with colorectal cancer that underwent surgery for a primary tumor between 2005 and 2015 in the Lapland Central Hospital were retrospectively collected. We retrieved data on the primary surgical outcome and complications within the first 30 days after surgery from patient records. We surveyed the national patient registry to determine long-term oncological results and patient survival. ***Results:*** We identified 349 patients treated for colorectal cancer during 2005–2015. Of these, 219 patients (median age 71 years) underwent laparoscopy and 130 (median age 72 years) underwent open surgery. The 5-year disease-specific survival rates for stages I–III colon cancer were 83.3 and 87.7%, respectively. The 3-year disease-specific survival rates for stages I–III rectal cancer were 86.1 and 65.0%, respectively. ***Conclusion:*** Our results showed that the introduction of laparoscopic colorectal surgery for treating cancer in a rural, small-volume hospital provided short- and long-term results comparable to findings from previous studies conducted in high-volume centers. Therefore, laparoscopy should be considered the treatment of choice for colorectal cancer in small, rural clinics.

Introduction

Colorectal cancer (CRC) is the third most common cancer in the world and the second most common cause of cancer-related death in Europe [1]. The CRC incidence is 27.3/100,000 individuals among men and 21.1/100,000 among women [2]. The 5-year overall survival, currently 66%, has increased significantly in the 21st century [3].

Laparoscopic surgery is commonly practiced for various diseases that require a bowel resection. Compared to

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open surgery, laparoscopic surgery reduces intraoperative bleeding, postoperative pain, postoperative hospitalization time [4, 5], and overall morbidity, and it enables earlier bowel function [6]. Moreover, laparoscopic surgery and open surgery achieved equivalent long-term oncological results [7, 8]. Consequently, laparoscopic colorectal surgery has become the prevailing trend for CRC surgery.

Most randomized trials for laparoscopic CRC surgery were performed in multiple high-volume institutions, with highly specialized operation units and operative personnel [7, 8]. In addition, those trials included patients selected with strict exclusion criteria, which might have influenced the reported outcomes of laparoscopic colorectal resections [7, 8]. The laparoscopic technique for CRC is also used in small-volume hospitals with unselected patients. Few studies have investigated the long-term oncological results of laparoscopic CRC surgery in middle- or low-volume hospitals with unselected patients [9, 10].

Lapland Central Hospital is a small, rural teaching hospital in Rovaniemi, in the Lapland region of Finland. Our unit began performing laparoscopic bowel resections in 2005; we performed our first laparoscopic bowel resection for CRC in October 2006. Routine laparoscopic CRC surgery started in 2008. During the past 5 years, we performed between 50 and 60 laparoscopic colorectal resections annually; of these, 30–38 resections per year were performed to treat CRC. Our short-term laparoscopic surgery results were described previously [11].

The present study described the long-term oncological results of CRC surgery performed in unselected patients in our small-volume institution. We evaluated these results according to measures used previously in high-volume, multicenter studies.

Materials and Methods

Patients and Data Collection

We included all patients with CRC that underwent open or laparoscopic surgery, between January 2005 and December 2015, in Lapland Central Hospital. The final cohort comprised 349 patients with CRC. We acquired data from patient records on the study populations, American Society of Anesthesiologists (ASA) scores, hospital stays, readmissions, intra-abdominal abscesses near the anastomosis, and possible anastomotic leakages. Patient survival and cause of death data were acquired from the national registry (Statistics Finland). The use of patient samples and the data inquiry were approved by the Oulu University Hospital Ethics Committee (EETTMK: 81/2008). The need to obtain a written or oral consent from the patients for using the samples in research was waived by the Finnish National Authority for Medicolegal Affairs (VALVIRA, Dnro 10832/06.01.03.01/2014).

Surgical Procedure

Right Hemicolectomy

Dissection was performed medial to lateral with laparoscopy-assisted approach and lateral to medial with open surgery following a plane between visceral (Told's) and parietal (Gerota's) fascia. The dissection line traversed the head of the pancreas but gastroepiploic or infrapyloric lymph nodes were not routinely dissected. The dissection line followed the superior mesenteric vein keeping lateral to it in the D2 dissection plane. The anastomotic sites were located at the terminal ileum and the midsection of the colon transversum, unless otherwise selected by the operator. Anastomoses were stapled side to side, either via a laparotomy or outside the abdominal cavity, after extending the umbilical trocar port used in the laparoscopic approach.

Left Hemicolectomy and Anterior Rectosigmoid Resection

The left hemicolectomy and anterior sigmoid resections were performed by dissecting the inferior mesenteric artery 1–2 cm from the aorta to preserve the hypogastric nerves. Five-centimeter bowel margins were accepted and splenic flexure mobilization was optional. For sigmoid resections, anastomoses were performed extracorporeally, side to side, with a linear stapler. For anterior sigmoid resections, anastomoses were performed intra-luminally, with a circular stapler. Anastomoses were stapled end to end, for high rectosigmoid anastomoses, and side to end for low rectal anastomoses, with the aim of preserving anastomotic circulation. Total mesorectal excisions were performed in patients with rectal cancer (RC). A diversionary loop ileostomy was performed when selected for individual patients.

Abdominal Perineal Rectum Resection

Abdominal perineal rectum resections (APRs) were performed with either a laparotomy or a laparoscopic approach for a total mesorectal excision. The patient was placed in a prone, jackknife position for the perineal resection and specimen removal. The tissue incision was closed, according to the judgment of the operator. A biological mesh was used when deemed appropriate.

Radiological and Pathological Evaluations

Preoperative computed tomography (CT) was performed to detect potential distant metastasis and regional adenopathy. Preoperative rectal MRI was performed for patients with RC. After surgery, pathological anatomic examinations were performed on the cancer specimens, and TNM staging was performed according to the 7th edition of the American Joint Committee on Cancer (AJCC). For the present study, all patients that experienced cancer recurrences were reevaluated (by P.T.), based on CT or MRI scans. All tumors recurrences were classified according to their location, relative to the sacral promontorium; thus, all residual tumors located on the caudal side of the sacral promontorium were defined as local residuals. Moreover, circumferential resection margins were reevaluated in patients with T3 and T4 RC (by H.H.) A R0 resection was defined as a circumferential resection margin >1 mm, between the deepest point of tumor invasion and the margin of resection.

Statistical Analysis

Statistical analyses were performed with IBM SPSS Statistics 24.0 (IBM Corp., Armonk, NY, USA). All values are presented as the mean and 95% confidence intervals (95% CI) or the median

Table 1. Patient characteristics

	CC, *n*/241	%	RC, *n*/108	%
Age at diagnosis				
<70 years	89	37	57	53
70–80 years	107	44	36	33
>80 years	45	19	15	14
BMI	Median (IQR)			
Male	26.2 (24–29)		25.6 (24–28)	
Female	25.7 (23–30)		27.3 (23–30)	
Sex				
Male	126	52	66	61
Female	115	48	42	39
ASA				
I	7	2.9	1	0.9
II	74	31	40	37
III	118	49	48	44
IV	26	11	11	10
Missing data	16	6.6	8	7.4

ASA, American Society of Anesthesiologists; CC, colon cancer; RC, rectal cancer.

Table 2. Combined laparoscopic and open surgery postoperative complications

	CC patients		RC patients	
	n/241	%	*n*/108	%
30-d mortality	2	0.8	3	2.8
90-d mortality	2	0.8	4	3.7
30-d reoperation rate	21	8.7	22	20
Clavien-Dindo classification				
IIIa	18	7.5	20	19
IIIb	21	8.4	22	20
IV	4	1.7	2	1.9
V	4	1.7	3	2.8

CC, colon cancer; RC, rectal cancer.

and interquartile range (IQR). Kaplan-Meier was used to calculate overall, disease-specific, and disease-free survival (DFS); curves were compared with the log-rank test, and hazard ratios were calculated with Cox regression analyses, performed with the enter method of selection. Survival rates were calculated from the date of surgery to the time of death or the end of follow-up.

Results

Laparoscopic Surgery

The median operative time was 135 min (range 45–345), and the median intraoperative blood loss was 100 mL (IQR 0–250). The median hospital stay was 6 days after the operation (IQR 4–9). The rate of conversion from laparoscopic to open surgery was 14.5%. Patients' baseline characteristics are described in Table 1.

Open Surgery

The median operative time was 87 min (range 30–272), and the median intraoperative blood loss was 200 mL (IQR 100–450). The median hospital stay was 7 days (IQR 6–10). Patients' baseline characteristics are described in Table 1.

Follow-Up

The median follow-up time was 36 months (range 0–131) for all surviving patients (i.e., both open and laparoscopic groups). We could not retrieve survival data from 6 patients. Patient characteristics are described more specifically in Table 1.

Short-Term Surgical Results

Laparoscopic Surgery

Among the 219 laparoscopic colorectal resections for CRC during 2005–2015, 34.2% were right hemicolectomies, 1.4% were transversal resections, 31.5% were left hemicolectomies, and 32.9% were anterior rectosigmoid resection or APRs. One patient with colon cancer (CC) (0.71%) and 57 patients with RC (72.2%) received primary intestinal stomas after the operation. Anastomotic leakage, diagnosed with CT or endoscopy, occurred in 14 patients with CC (5.8%) and 10 with RC (9.3%). Postoperative hemorrhages occurred in 10 patients with CC (7.1%) and 2 with RC (2.5%). Wound dehiscence/infection occurred in 4 patients with CC (2.8%) and 3 with RC (3.8%). Perioperative ureter injuries occurred in no patients with CC and 2 with RC (0.9%). Complications are presented with Clavien-Dindo classification [12] in Table 2. Readmissions were necessary for 9 patients with CC (6.4%) and 7 with RC (8.9%).

Open Surgery

During the period 2005–2015, we performed 130 open bowel resections for cancer, and of those, 41.5% were right hemicolectomies, 3.8% were transversal resections, 26.2% were left hemicolectomies, and 28.5% were anterior rectosigmoid resection or APRs. Three (3.5%) patients with CC and 39 (81.3%) with RC received primary enterostomas. Wound infections occurred in 3 (3.5%) patients with CC and 4 (8.3%) with RC. Postoperative hem-

Table 3. Tumor characteristics

	CC		RC	
	n/241	%	*n*/108	%
Tumor grade				
1	56	25.2	34	31
2	120	54.1	54	50
3	41	18.5	19	18
Missing data			1	1.0
Tumor stage				
I	91	38	42	39
II	66	27	23	21
III	45	19	20	19
IV	38	16	23	20
Missing data	1	0.5	1	1.0
T Class				
1	21	8.7	8	7.4
2	82	34	35	32
3	73	30	36	33
4	61	25	25	23
Missing data	4	1.7	4	3.7
Lymph nodes				
0	170	71	69	64
1	53	22	26	24
2	16	6.6	12	11
Missing data	2	0.8	1	1.0
Number of harvested lymph nodes (mean)	11		12	
Distal metastases				
Negative	200	83	86	80
Positive	40	17	22	19
Missing data	1	0.4	1	1.0

CC, colon cancer; RC, rectal cancer.

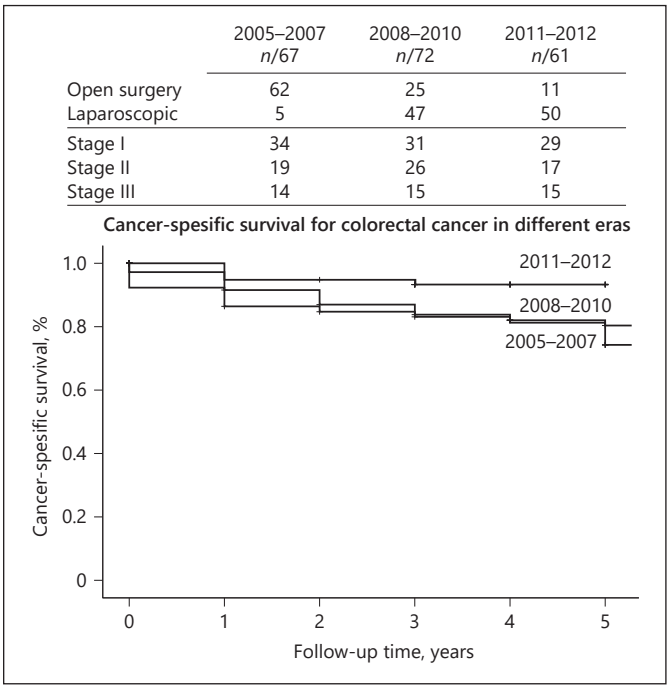

Fig. 1. DSS in different eras. CRC, colorectal cancer; DSS, disease-specific survival.

orrhages occurred in 4 (4.7%) patients with CC and 3 (6.3%) with RC. Anastomosis leakage occurred in 6 patients (6.5%) with CC and 8 (5.4%) with RC. Ureter injuries occurred in no patient with CC and 1 (2.1%) patient with RC. Complications are presented with Clavien-Dindo classification [12] in Table 2. Readmissions were necessary for 5 (5.8%) patients with CC and 5 (10.4%) with RC.

Long-Term Oncological Results

Eighty-three percentage of the patients with stage III CC (*n*/*N*, 38/46) and 81% with stage IV CC (30/37) received postoperative chemotherapy. Separately in the laparoscopic group, 24 patients with stage III CC (83%) and 20 with stage IV CC (95%) received postoperative chemotherapy and in the open surgery group, 14 patients with stage III CC (82%) and 10 with stage IV CC (63%), respectively. Eleven (17%) patients with stage II CC received postoperative adjuvant chemotherapy. The main reasons for abandoning chemotherapy were older age, comorbidity, and patient preference. Fifty-five percentage of the patients with stage III RC (11/20) and 82% with stage IV RC (18/22) received postoperative chemotherapy. Separately in the laparoscopic group, 10 patients with stage III RC (71%) and 14% with stage IV (88%) received postoperative chemotherapy (of these, 3 patients also received preoperative chemotherapy) and in the open surgery group, 1 (17%) with stage III RC and 4 (68%) with stage IV, respectively. Seven (30%) patients with stage II RC received adjuvant chemotherapy. Among patients with clinical stage T3N0-2 and T2N1-2 RC that underwent laparoscopic surgery, 22 (44%) received preoperative chemotherapy. In contrast, no patients that underwent open surgery received preoperative chemotherapy. Chemotherapy consisted of oral capecitabine and oxaliplatin or capecitabine alone, according to patient comorbidity. Four patients received irinotecan + 5-fluorouracil + leucovorin treatment.

In our hospital, preoperative radiation therapy for patients with RC was started in 2008. Preoperative clinical staging was performed with rectal MRI and body CT. Among patients with stages T3N0-2 and T2N1-2 RC, 36

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Table 4. Long-term oncological results from laparoscopic and open surgery for colon and rectal cancer

Laparoscopic					Open surgery			
CC	Patients, *n*	5-year DSS, %	HR	95% CI	Patients, *n*	5-year DSS, %	HR	95% CI
Stage I	55	83.3	1.0	Reference	36	91.8	1	Reference
Stage II	43	89.8	0.8	0.2–3.4	23	90.7	1.7	0.2–12.3
Stage III	29	76.6	2.0	0.6–7.0	16	75.0	8.4	1.7–41.8
		5-year DFS, %				5-year DFS, %		
Stage I	55	89.9	1	Reference	36	88.1	1	Reference
Stage II	43	82.9	2.6	0.7–8.7	22	80.3	2.6	0.7–9.3
Stage III	29	60.7	5.3	1.6–17.5	16	62.5	4.6	1.3–16.4
Laparoscopic					Open surgery			
RC	Patients, *n*	3-year DSS, %	HR	95% CI	Patients, *n*	3-year DSS, %	HR	95% CI
Stage I	28	91.1	1	Reference	14	90.0	1	Reference
Stage II	11	100	0.0	0.0	12	83.3	5.5	0.6–47.2
Stage III	14	85.7	1.1	0.1–10.7	6	60.0	22.7	2.1–239.3
		3-year DFS, %				3-year DFS, %		
Stage I	28	84.6	1	Reference	14	72.5	1	Reference
Stage II	11	100	0.0	0.1	12	90.1	0.8	0.2–3.6
Stage III	14	77.1	2.2	0.6–8.0	6	80.0	0.7	0.1–6.2

No statistical difference between laparoscopic and open surgery groups within stages; data not shown. CC, colon cancer; RC, rectal cancer; DSS, disease-specific survival; DFS, disease-free survival; CI, confidence interval; HR, hazard ratio.

(72%) and 4 (40%) patients received preoperative radiation in the laparoscopic and open surgery groups, respectively. The main reasons for abandoning preoperative radiation despite the staging were older age and comorbidity 3 (5.0%), palliative operation for metastatic disease 9 (15.0%), and unknown reason 8 (13%). The distribution of TNM classifications, stages, and differentiation grades are summarized for both groups in Table 3.

We investigated the influence of a laparoscopic learning curve on long-term survival. Patients were divided into 3 different eras, according to the prevalent surgical technique used in that time period. The 3 eras were as follows: 2005–2007: open surgery era (92% open surgery and 8% laparoscopic); 2008–2010: learning phase for laparoscopic surgery era (36% open and 64% laparoscopic); and 2011–2013: laparoscopic era (18% open and 82% laparoscopic). The survival analyses showed that the 5-year disease-specific survival (DSS) trend was similar in all eras (Fig. 1).

Colon Cancer

A total of 241 colon resections for cancer were performed during 2005–2015, and 200 of those were stages I–III CC. The overall 5-year survival rates for stages I–III CC were 74.5 and 70.0% for the laparoscopic ($n = 125$) and open surgery ($n = 75$) groups, respectively, and there was no statistical difference between groups ($p = 0.1$, log rank). The 5-year DSS rates for stages I–III CC were 83.3 and 87.7% in the laparoscopic and open surgery groups, respectively. The 5-year DFS rates were 80.9 and 80.3% in the laparoscopic and open surgery groups, respectively. Between right side CC (89%) and left side CC (64%), DSS survival rates differ significantly for stages I–IV ($p = 0.034$, log rank) in the laparoscopic group. However, within stages I–III, no difference between the right and the left side CC was seen. In the open surgery group, overall survival rates for stages I–III differ significantly between the right (45%) and left (61%) side CC ($p = 0.016$, log rank). The 5-year survival data are presented more specifically in Table 4 and in Figures 2 and 3. There was no statistically significant difference in cancer survival between the laparoscopic and open surgery groups.

Rectal Cancer

A total of 108 bowel resections for RC were performed during 200–2015, and 85 of those were stages I–III. The overall 3-year survival rates for stages I–III of RC were 84.8 and 54.8% in the laparoscopic and open

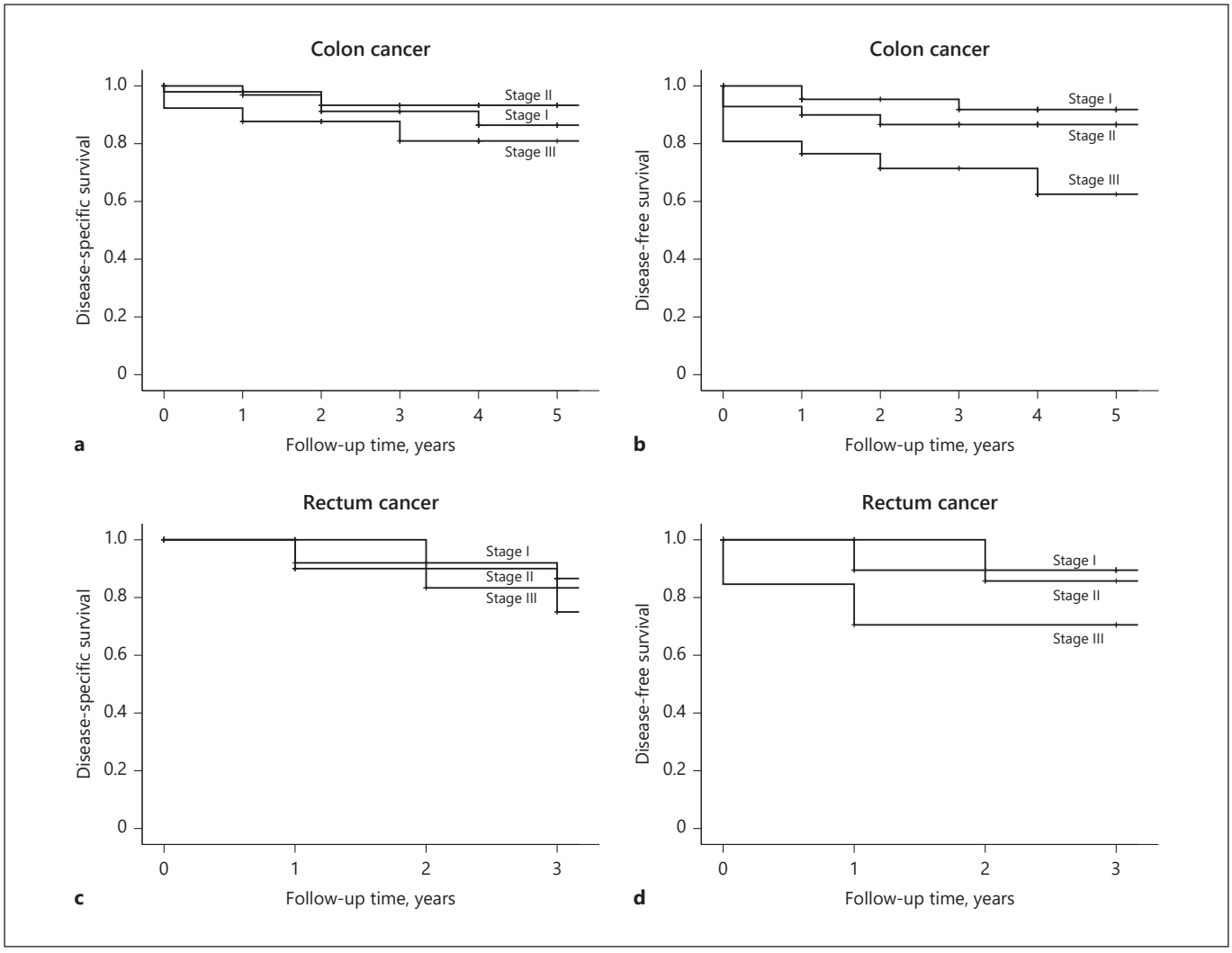

Fig. 2. DSS (**a**, **c**) and DFS (**b**, **d**) by stages for the laparoscopic colon and rectal cancer. DSS, disease-specific survival; DFS, disease-free survival; RC, rectum cancer.

surgery groups, respectively, and there was no statistical difference between groups (p = 0.4, log rank). The 3-year DSS rates (stages I–III) were 86.1 and 65.0% for the laparoscopic (n = 53) and open surgery (n = 32) groups, respectively. The 3-year DFS rates were 77.8 and 86.4% for the laparoscopic and open surgery groups, respectively. There was no statistically significant difference in overall or DSS survival between the laparoscopic and open surgery groups. The 3-year DSS and DFS rates are presented more specifically in Table 4 and in Figures 2 and 3.

In the laparoscopic group (n = 70), the 3-year local recurrence rate was (n = 70) 8.6% (95% CI 2.6–16) for R0 resections (n = 68) and 5.4% (0.0–14.3) in the open surgery group (n = 38) and 2.7% (0.0–9.4) for R0 resections (n = 31), respectively.

Discussion

Laparoscopic surgery for CRC was shown to decrease postoperative complications and preserve oncological long-term results, compared to open surgery. However, most studies were performed in large-volume centers, which might have affected the results [7–9]. In clinical settings, the choice between laparoscopy and open sur-

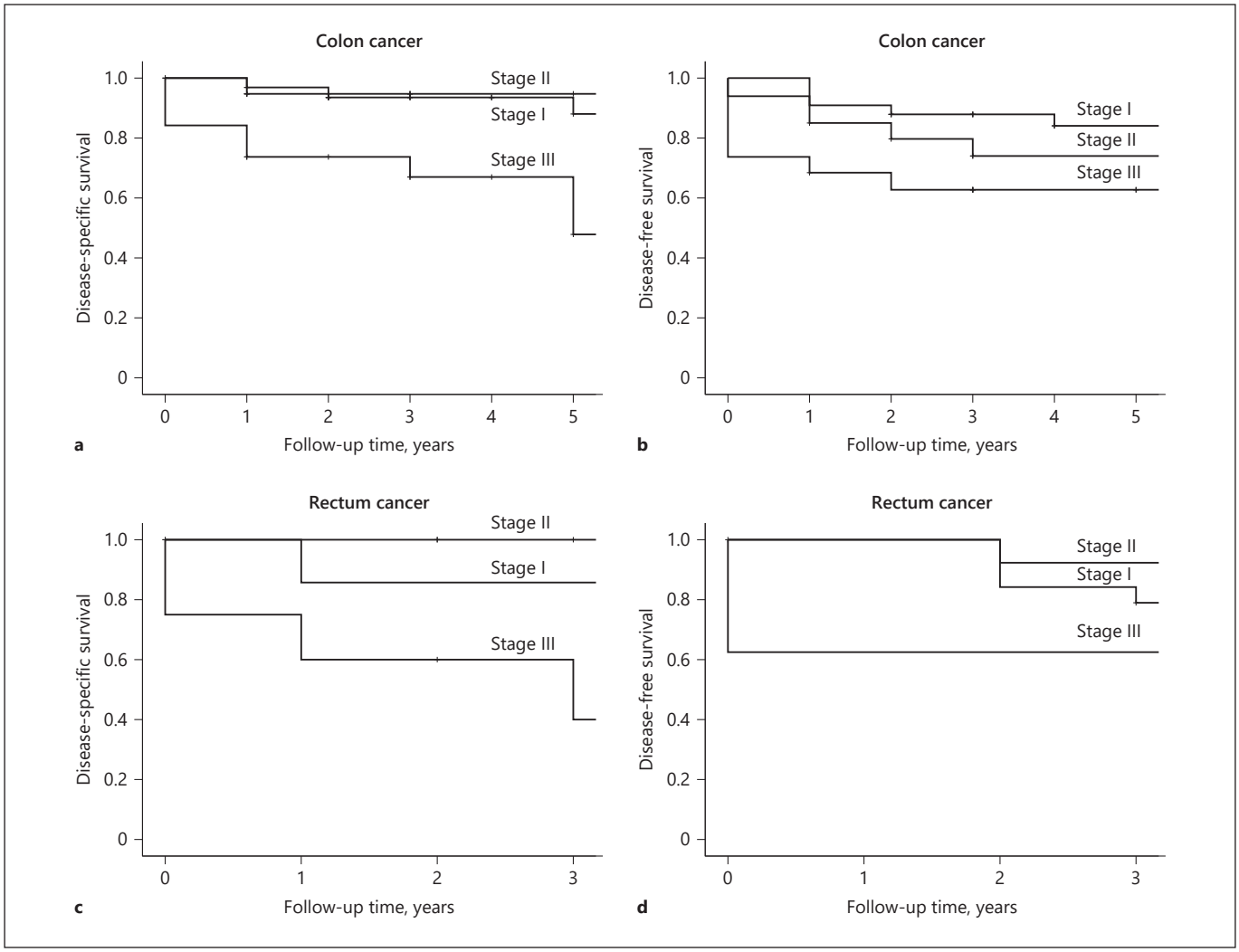

Fig. 3. DSS (**a**, **c**) and DFS (**b**, **d**) by stages for the open surgery colon and rectal cancer. DSS, disease-specific survival; DFS, disease-free survival; RC, rectum cancer.

gery is never random. Thus, patient selection is skewed, and retrospectively, these groups are rarely comparable. Therefore, our primary aim here was not to compare the laparoscopic and open surgery groups. However, their survival results were similar as in previous studies. Instead, our aim was to evaluate how introducing laparoscopic surgery as an alternative treatment for CRC affected long-term survival, which is the main indicator of surgical quality among patients with cancer. We investigated RC and CC results separately, due to differences in surgical techniques and perioperative treatments.

Our 5-year survival rate was similar to that of previous studies, despite our somewhat older patients. Our 5-year DSS for CC stages I–III was 86%, consistent with previous findings [7, 9]. In the laparoscopic group DSS, rates for stages I–IV were significantly worse in left side CC (64%) compared to right side CC (89%), and furthermore, in the open surgery group, overall survival rates for stages I–III differ between right (45%) and left (61%) side CC. Meguid et al. [13] have shown poorer survival for right side CC. However, stage IV left side CC patients exhibited a poorer survival rate compared to right side CC. Our results are in a line with this finding because, in the laparoscopic group, there were 15 patients with stage IV left side CC compared to 5 patients with right side stage IV CC.

Within 2 years of introducing laparoscopic cancer surgery in our institution, the 5-year survival rate decreased. This could be explained by the learning curve in laparoscopic colon surgery, which lasts for 30–60 operations [14–16]. After only a 2-year learning period, the 5-year survival rate was similar to or better than survival after open surgery. However, because surgery is only part of CRC treatment, we cannot exclude other possibilities that could contribute to the improved 5-year survival during the switch from open to laparoscopic surgery. For instance, in our study, patients with RC treated with laparoscopic surgery (81%) received postoperative chemotherapy more often than those in the open surgery group (29%), which definitely has an influence on survival trends. Moreover, improvements in the oncological regimen and overall healthcare systems could contribute to patient survival [17, 18]. However, in our hospital, the chemotherapy protocol did not change during the study period. Moreover, a somewhat large number of patients (22%) did not receive oncological adjuvant treatment, despite an indication based on cancer stage. This clinical reality emphasized the fact that treatments are based on individual considerations. Importantly, in an unselected patient cohort, comorbidities and quality-of-life issues can limit oncological treatments that might otherwise be suggested [18, 19]. Despite these limitations in oncological treatment for stage III CRC, our 5-year survival was comparable to that reported in recent publications [3, 7–9].

RC is a somewhat special entity in CRC. Low rectal anastomoses require a diversifying stoma, which is known to prolong the primary hospital stay and might contraindicate some advances in laparoscopy [20]. Therefore, the laparoscopic approach has not been rapidly introduced in RC surgery, despite promising results [8, 21]. We started laparoscopic rectal surgery in 2008. Here, we found that, among patients with RC, laparoscopy achieved a 3-year survival rate comparable to that achieved with open surgery, but with the postoperative advantages of laparoscopic surgery. Thus, a laparoscopic approach for RC provided high-quality results in a small-volume center.

Our study had several limitations. The retrospective study design prevented inclusion of some surgical complications, due to insufficient records. Similarly, we might have missed some cancer recurrences, due to the lack of a diagnosis or other relevant information in hospital records. However, patient survival data were acquired from Statistics Finland; survival data were missing for only 6 patients in that database.

Conclusion

Taken together, this study showed that like every new surgical treatment option, laparoscopic colorectal surgery required a learning period during implementation, before showing its true potential. However, introduction of the laparoscopic approach in our unit achieved similar survival rate comparable to that achieved with open surgery, but with the postoperative advantages of laparoscopic surgery of patients with CRC. Moreover, survival rates were equivalent to those observed in high-volume surgical institutions. Therefore, laparoscopy may also be considered the treatment of choice in small-volume centers.

Acknowledgements

We thank Katri Vuopala, PhD, Specialist in Pathology, for serving as a consultant in the reevaluation of pathological specimens, and we thank Erja Tomperi for her excellent technical assistance.

Statement of Ethics

This study has Oulu University Hospital Ethics Committee's (EETTMK: 81/2008) and Lapland Central hospitals (Tut46/2015) permissions, and research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The need to obtain a written or oral consent from the patients for using the samples in research was waived by the Finnish National Authority for Medicolegal Affairs (VALVIRA, Dnro 10832/06.01.03.01/2014).

Conflict of Interest Statement

The authors declare no conflict of interest.

Funding Sources

This work was supported by grants from the Thelma Mäkikyrö Foundation and the Mary and Georg Ehrnrooth Foundation.

Author Contributions

J.R. and H.H. had full access to all of the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: J.R. and H.H. Acquisition of data: J.R. and H.H. Analysis and interpretation of data: J.R. and H.H. Drafting of the manuscript: all authors. Critical revision of the manuscript for important intellectual content: all authors. Statistical analysis: H.H.

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