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ORIGINAL ARTICLE

Prospective multicenter registration study of colorectal cancer: significant variations in radicality and oncosurgical quality—Swiss Group for Clinical Cancer Research Protocol SAKK 40/00

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Abstract
Purpose This study aimed to investigate in a multicenter cohort study the radicality of colorectal cancer resections, to assess the oncosurgical quality of colorectal specimens, and to compare the performance between centers.
Methods One German and nine Swiss hospitals agreed to prospectively register all patients with primary colorectal cancer resected between September 2001 and June 2005. The median number of eligible patients with one primary tumor included per center was 95 (range 12–204).
Results The following variations of median values or percentages between centers were found: length of bowel specimen 20–39 cm (25.8 cm), maximum height of mesocolon 6.5–12.5 cm (9.0 cm), number of examined lymph nodes 9–24 (16), distance to nearer bowel resection margin in colon cancer 4.8–12 cm (7 cm), and in rectal cancer 2–3 cm (2.5 cm), central ligation of major artery 40–97 % (71 %), blood loss 200–500 ml (300 ml), need for perioperative blood transfusion 5–40 % (19 %), tumor opened during mobilization 0–11 % (5 %), T4-tumors not en-bloc resected 0–33 % (4 %), inadvertent perforation of mesocolon/mesorectum 0–8 % (4 %), no-touch isolation technique 36–86 % (67 %), abdominoperineal resection for rectal cancer 0–30 % (17 %), rectal cancer specimen with circumferential margin ≤1 mm 0–19 % (10 %), in-hospital mortality 0–6 % (2 %), anastomotic leak or intra-abdominal abscess 0–17 % (7 %), re-operation 0–17 % (8 %).
Conclusion In colorectal cancer, surgery considerable variations between different centers were found with regard to radicality

Parts of the study results have been presented at the annual congress of the Swiss Surgical Society in Lugano, Switzerland, June 2006, at the 7. BIC Biebrich International Conference on Colorectal Cancer in Wiesbaden, Germany, October 2010, and at the annual congress of the Swiss Surgical Society in Bern, Switzerland, May 2015.

Christian Klaiber is deceased October 2013

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and oncosurgical quality, suggesting a potential for targeted improvement of surgical technique.

Keywords Colorectal · Cancer · Surgery · Pathology · Radicality · Quality

Introduction

Short-term and long-term outcomes of patients with colorectal cancer (CRC) are strongly influenced by the quality of surgery. Many studies in this field including one of our group [1] have shown that the variability of performance among surgeons relates to the surgeon's special interest [2, 3], the surgeon's education and the annual case load [1, 3–9]. Hence, surgeons seem to be an important prognostic factor for their patients [6]. However, how an excellent or good CRC surgeon differs from an average or even a poorly performing one is only barely understood [10]. And since critical self-assessments among surgeons are rarely published, it seems difficult to obtain precise information with regard to the quality of their CRC surgery.

From the literature, only little evidence with regard to necessary surgical radicality or oncosurgical quality is available for cancer of the rectum, and even less for the colon [10–15]. Many issues of surgical technique such as the impact of total mesorectal excision, of blood loss, of short versus long segment colonic resection, of abdominoperineal versus sphincter preserving resection, of high versus intermediate or even low arterial tie, of inadvertent tumor opening will hardly ever be investigated in randomized controlled trials due to ethical and consent reasons. For many of the open scientific questions in CRC surgery, large prospective cohort studies remain an adequate tool for investigation. Adjuvant and neoadjuvant trials for CRC are in urgent need of standardization of surgery and of pathological work-up to reliably compare the specific anticancerous effect of different therapies.

The aim of the present multicenter cohort study in CRC patients was to assess meticulously and prospectively the surgical radicality and the oncosurgical quality of procedures and specimens, for the whole study population as well as for each participating center separately. Furthermore, we intended to identify the most important rules for obtaining long-term success in the future. As a consequence, this study might also create an instrument for quality control and for special education in this field of surgery.

Methods

Nine surgical departments from Switzerland and one from Germany agreed to prospectively register patients with resection of primary CRC within a central database of the Swiss Group for Clinical Cancer Research (SAKK) in Bern. The following categories of surgical institutions participated: one university hospital, five hospitals affiliated with a university, two district hospitals, and two small regional hospitals. The surgical units of all the participating hospitals had a special interest and special expertise in CRC surgery. A data manager of the SAKK periodically visited the participating hospitals to check that all consecutive patients had been registered, especially the emergency cases as well as the complicated cases. The study was approved by the scientific committee of the SAKK as well as by all responsible local ethics committees.

Between September 2001 and June 2005, 1502 patients with surgery for primary CRC were registered (initials, date of birth, and center, only). Informed consent was requested before surgery. Four hundred and sixty-two patients did not consent and hence no further data were collected and analyzed. In addition, thirthy-six patients were excluded from the analysis because the primary tumor was not resected ($n = 8$) or because the final diagnosis was not primary adenocarcinoma of the colorectum ($n = 28$). Patients with histologically proven rectal cancer and complete remission after combined neoadjuvant radiochemotherapy, and patients without any cancerous tissue left in the colorectal specimen following endoscopic removal of a malignant colorectal polyp were not excluded from the analysis. In total, the study population consists of 1004 patients, 965 patients with one resected and histologically proven primary adenocarcinoma of the colorectum forming the base of the present study, and 39 patients with two or more synchronous primary colorectal carcinomas which were analyzed separately.

The following underlying or concomitant colorectal diseases were recorded: six patients with ulcerative colitis, one patient with Crohn's disease, but no patient with familial adenomatous polyposis.

Special features of the standardized surgery form

To minimize discrepancies in nomenclature of the types of resection and of major arteries as well as to standardize reporting, the precise tumor location, the extent of bowel resection, and the ligature sites of major arterial blood supply had to be marked in a given figure of the colorectum including the arterial blood vessels (Fig. 1). The rectum was graduated in 1-cm steps.

Special features of the standardized pathology form

The pathologists had to declare the measuring conditions for each specimen, whether the measurement of the specimen was done in a native or in a formaline-fixed state and whether it was done under tension or not. For lymph node examination, no fat clearance method was used in any of the participating institutes of pathology. Furthermore, the maximum height of

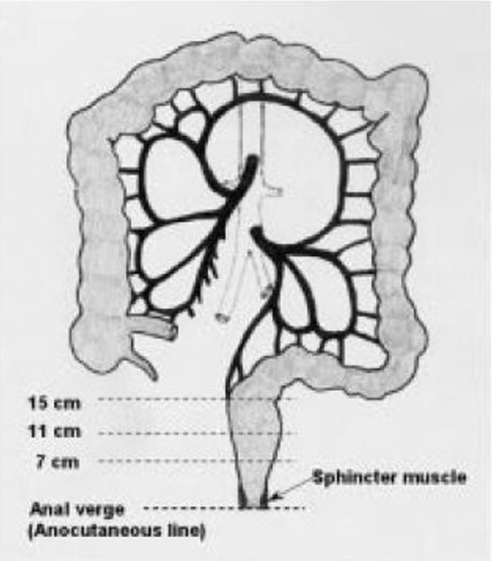

Fig. 1 Extract from the standardized surgery form: surgeons precisely had to mark tumor site, margins of bowel resection and site(s) of arterial ligation for each resection of colorectal cancer

the specimen's mesocolon had to be assessed, i.e., measurement of the distance from the most central arterial ligature perpendicularly to the bowel wall. The pathology form demanded a statement with regard to the presence of lymphatic, venous, and perineural invasion.

Special features of the standardized complication form

Within 2 weeks of discharge from the hospital, a completed standardized complication form including need of perioperative blood transfusion, re-operation, and in-hospital death had to be sent to the SAKK coordinating center for each patient.

Patients with multiple synchronous primary colorectal carcinomas

Thirty-nine (3.9 %) of 1004 patients had two or more synchronous primary CRCs. Even, there were 6 (0.6 %) out of these 39 patients with more than 2 synchronous adenocarcinomas of the colorectum. For each cancer, the pathologists had to send a separate pathology form. Five out of 39 patients with more than one synchronous primary CRC had two separate colorectal segments resected. For each resected and tumor-bearing segment of the colorectum, the surgeons had to send a separate surgery form. The primary with the highest tumor stage was relevant for further analyses [16].

Registration of data

The data from all forms was entered in a central database of the SAKK Coordinating Center in Bern by an independent data manager with medical education.

According to a key provided by the study chair, tumor locations, dissection sites of the bowel, and ligature sites of major arteries were then decoded from the figure of the surgery form (Fig. 1) by co-workers of the SAKK Coordinating Center and added to the database.

Furthermore, from all patients, copies of the surgical report and the pathology were stored in the SAKK Coordinating Center and used to clarify any potential discrepancies. All patient data was checked by at least two independent *people*, i.e., by a staff surgeon of the first author's surgical department (K.K.) and by a co-worker of the SAKK. The final review was done by the chairman of the study (C.A.M.) and the statisticians of the SAKK.

Definitions

The site of rectum was defined as 0–15 cm from anal verge. The site of rectosigmoid junction was defined as colonic section between >15 and 20 cm from anal verge. For determination of the tumor site, the lower border of the tumor was decisive, e.g., a carcinoma from 14 to 17 cm from anal verge was assigned to rectal cancer. The following ligature sites of major arteries, with respect to removal of the corresponding lymph node levels, have been discriminated: central, intermediate, peripheral.

Statistical methods

Exploratory analysis of prospective data was performed for the short-term outcome of this study. Summary statistics of all variables defining patient and tumor characteristics as well as the assessment of surgical radicality and oncosurgical quality are presented as median and range, or as a frequency and proportion. To compare the results across centers, Kruskal-Wallis rank sum test was applied to quantitative variables and chi-square test to qualitative/categorical variables. Monte Carlo approximation was used for low frequencies. The reported p values are two-sided without correction for multiple testing.

Associations between variables were checked by Wilcoxon rank sum tests or chi-square tests for frequency tables or for logistic regression models. Low frequencies were compared by Fisher's exact test. Correlations were evaluated using the Spearman method.

Results

Results regarding patient and tumor characteristics

Characteristics of participating centers are presented in Table 1. Patient and tumor characteristics of the study population of $N = 965$ evaluable patients with a single primary tumor are summarized in Table 2. In the latter, each criterion

Table 1 Characteristics of participating surgical departments

No.	Variable	Statistics	Total	Dept1	Dept2	Dept3	Dept4	Dept5	Dept6	Dept7	Dept8	Dept9	Dept 10
1	Case load per year per dept.	See[a]	263.5	46.8	9.9	67.7	133.8	25.1	4.0	27.4	76.0	50.3	21.0
2	Number of senior surgeons	Frequency	34	2	2	5	8	4	1	2	7	2	1
3	Evaluable patients with one primary CRC	Frequency	965	92	12	163	204	62	13	99	178	97	45
4	Evaluable patients with two or more primary CRC	Frequency	39	6	2	6	10	3	0	1	5	3	3

Dept. surgical department, *CRC* colorectal cancer

[a] For calculation of the annual case load per center, total numbers of colorectal cancer resections including the excluded patients have been considered, as well as the different lengths of study participation

Table 2 Patient and tumor characteristics, analyzed as overall statistics and per each surgical department

No.	Variable	Overall sample size	No. of centers	Statistics	Categories	Overall statistics	Range in statistics of centers	*P* value
1	Age (years)	965	10	Median		70	63–76	<.0001
2	Sex	965	10	Proportion	Female	0.39	0.34–0.51	0.3933
3	ASA score	965	10	Proportion	1	0.13	0.07–0.31	0.0005
					2	0.56	0.47–0.67	
					3	0.29	0.15–0.36	
					4–5	0.02	0–0.07	
4	Body mass index (kg/m^2)	965	10	Median		25.4	24.1–26.4	0.0079
5	Patients with rectal cancer	965	10	Proportion		0.40	0–0.53	<.0001
6	Rectal cancers treated with neoadjuvant radiotherapy	384	9	Proportion		0.28	0.09–0.63	<.0001
7	pT-stage	964	10	Proportion	0 + is	0.02	0–0.06	0.0004
					1	0.09	0–0.16	
					2	0.18	0.08–0.42	
					3	0.58	0.53–0.65	
					4	0.13	0–0.23	
8	pN-stage	960	10	Proportion	0	0.58	0.51–0.67	0.7917
					1	0.21	0.08–0.29	
					2	0.21	0.15–0.25	
9	M-stage	964	10	Proportion	0	0.83	0.77–0.92	0.4386
					1	0.17	0.08–0.23	
10	UICC-stage	959	10	Proportion	0	0.02	0–0.05	0.0166
					I	0.22	0.11–0.42	
					II	0.31	0.22–0.43	
					III	0.28	0.23–0.32	
					IV	0.17	0.08–0.23	
11	Grading	930	10	Proportion	1–2	0.76	0.55–0.92	<.0001
					3–4	0.24	0.08–0.45	
12	Maximum diameter of primary (cm)	922	10	Median		4	3–4.5	<.0001
13	Specimens measured after formaline fixation	961	10	Proportion		0.90	0.77–1	<.0001
14	Patients operated by laparoscopy	965	10	Proportion		0.08	0–0.65	<.0001
15	Conversion to open operation	80	8	Proportion		0.13	0–0.50	0.5948
16	Emergency large bowel resection	965	10	Proportion		0.07	0–0.16	<.0001
17	Stoma formation in colon cancer patients	581	10	Proportion		0.05	0–0.09	0.1960
18	Stoma formation in rectal cancer patients	384	9	Proportion		0.69	0.35–0.80	0.0001
19	Distance of rectal cancers from anal verge (cm)	384	9	Median		7	6–11	0.0234

Dept. surgical department, *ASA* American Society of Anesthesiology, *UICC* International Union Against Cancer

is presented as a result of the whole study population and as the range of the 10 participating centers. A detailed Table 5 with results for each center can be found in the Appendix. Figure 2 shows the distribution pattern primary tumors of the study population.

Surgical radicality and oncosurgical quality

The results regarding surgical radicality and oncosurgical quality are depicted in Tables 3 and 4, again for the study population and as range of the 10 participating centers. Detailed results for each center are depicted in the Appendix, Tables 6 and 7.

With regard to the no-touch isolation technique according to Turnbull [17], i.e., venous ligature, arterial ligature, and closure of bowel lumen close to the tumor before tumor mobilization, the frequency of these single steps is depicted in Table 4, item 15. All three steps of this no-touch isolation technique were completed in 404 resections (41.9 %), two steps in 251 resections (26.0 %), one step in 73 (7.6 %) resections, and zero steps in 236 resections (24.5 %).

In 50 resections (5.2 %), the tumor was opened during tumor mobilization or colorectal dissection, in 31 resections (3.2 %) iatrogenically and in 19 resections (2.0 %) due to underlying spontaneous perforation. Multivisceral resections due to potentially tumorous infiltration of adherent neighboring organs were performed in 59 resections (6.1 %), 52 of these 59 as en-bloc resection (88.1 %).

Microscopically, proximal or distal bowel resection margins were infiltrated by tumor in 15 specimens, i.e., 1.6 % of all specimens, 3 are colon cancer specimens (0.5 % of colon cancer specimens), and 12 are rectal cancer specimens (3.1 % of rectal cancer specimens). In addition, cancer was found within 3 stapler doughnuts. Of the patients without locoregional R2-resection and without transanal local excision (n = 930), 68 had either tumor infiltration of the bowel resection margin (n = 13), infiltration of the circumferential rectal resection margin (n = 25), spontaneous or iatrogenic tumor perforation (n = 38). Eight out of these 68 patients had a combination of such findings. This results in a R1-resection rate of 7.3 % (68/930), 2.9 % for colon cancer (16/557), and 13.9 % for rectal cancer (52/373).

Concomitant excision of liver metastases was done in 49 colorectal resections (5.1 %), in 24 of these 49 with a curative intent with no gross tumor left. Gross evidence of residual tumor was present following 145 colorectal resections (15.0 %), in 15 cases (1.5 %) locoregionally only, in 116 cases (11.8 %) at distant sites only and in 14 cases (1.5 %) both locoregionally and at distant sites, resulting in a locoregional R2-resection rate of 3.0 % (29/965), 4.0 % for colon cancer (23/581), and 1.6 % for rectal cancer (6/384).

Regarding the measurement conditions, 862 out of 965 specimens (89.3 %) were measured after fixation in formaline, 58 (6.0 %) prior to formaline fixation and without stretching, and 35 (3.6 %) prior to formaline fixation but with stretching, i.e., under tension. No information about stretching or formaline fixation or both was available in 10 (1.0 %) specimens.

Micrometastasis, defined as tumor deposits of up to 2 mm according to UICC [16], were detected as sole lymph node metastasis in an additional 14 (1.5 %) patients, 2 of them by immunohistochemistry only. *Serial* sections of lymph nodes were applied selectively in 130 (13.5 %) specimens.

A moderate correlation between the length of specimens and the number of examined lymph nodes was detected (Spearman correlation coefficient 0.34, $p < 0.001$). A weak correlation was found between the height of mesocolon and the number of examined lymph nodes (Spearman correlation coefficient 0.09, $p = 0.033$).

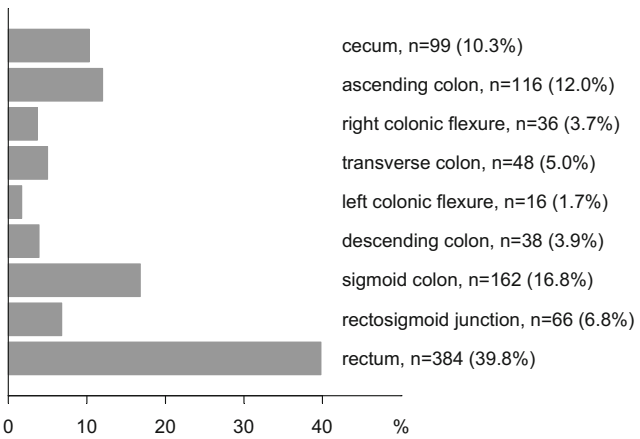

Fig. 2 Distribution of tumor locations (965 patients)

Mortality and surgical morbidity

The number of deaths during hospital stay was 24 (2.5 %), a median of 9.5 (1–61) days after surgery. Eighty-one patients (8.4 %) needed a re-operation after a median of 9 (0–121) days due to complications following primary surgery. The following frequencies of surgery-related complications were encountered: anastomotic leak and/or intra-abdominal abscess 64 (6.6 %), postoperative hemorrhage 21 (2.2 %), wound infection 97 (10.1 %), abdominal wall rupture 16 (1.7 %), bladder voiding difficulties longer than 10 days 81 (8 %), postoperative bowel paralysis longer than 7 days 80 (8.3 %), stoma complications 25 (2.6 %).

Table 3 Results regarding surgical radicality, analyzed as overall statistics and per each surgical department

No.	Variable	Overall sample size	No. of centers	Statistics	Categories	Overall statistics	Range in statistics of centers	*P* value
1	Length of specimen (cm)[a]	956	10	Median		25.8	20–39	<.0001
2	Maximum height of mesocolon (cm)[a]	514	10	Median		9	6.5–12.5	<.0001
3	Number of lymph nodes examined	957	10	Median		16	9–24	<.0001
4	Lymph node ratio[b] in node-positive patients	395	10	Median		0.22	0.16–0.36	0.2431
5	Lymph node ratio[b] in node-positive patients without distant metastasis (UICC stage III)	269	10	Median		0.16	0.13–0.41	0.4014
6	Distance to nearer bowel resection margin in *colon* cancer (excl. rectosigmoid junction, cm)	495	10	Median		8	5–12	<.0001
7	Distance to nearer bowel resection margin in cancer of *rectosigmoid junction* (cm)	64	9	Median		4	3–5.5	0.6835
8	Distance to nearer bowel resection margin in *rectal* cancer (cm)[a]	372	9	Median		2.5	2–3	0.0133
9	Height of major artery ligation[a]	960	10	Proportion	High (central)	0.71	0.40–0.97	<.0001
					Intermediate	0.25	0.02–0.53	
					Low (peripheral)	0.04	0–0.15	

Dept. surgical department, *LN* lymph nodes

[a] Patients with transanal local excision of rectal cancer are excluded from this analysis

[b] Lymph node ratio: proportion of positive LN among all LN examined

In a logistic regression model with center as stratification factor, a significant association between perioperative blood loss and need of blood transfusion was found ($p < 0.001$). An increase of 100-ml blood loss resulted in an odds ratio indicating a 1.11 times higher risk for a blood transfusion (95% confidence interval 1.06–1.16). Analyzing the association by center, the strongest associations were present in centers 3 and 4 (odd ratios 1.35 and 1.27).

Rectal cancer

Three hundred and eighty-four patients had primary rectal cancer defined as carcinoma of up to 15 cm from anal verge. Transanal local excision was performed in five patients (1.3 %), anterior resection in 312 patients (81.3 %), and abdominoperineal resection in 67 patients (17.4 %), resulting in an anal sphincter preservation rate of 82.6 %. Necessary mesorectal excision was done totally or longitudinally partially in 416 out of 445 patients (93.5 %) with carcinoma in the rectum or at the rectosigmoid junction. Of the 378 patients with carcinoma in the rectum or at the rectosigmoid junction who had anterior resection, a cytotoxic irrigation of the clamped rectum was performed in 277 patients (73.3 %) and the distal dissection site was completely within the irrigated section of the rectum in 263 patients (69.6 %). The additional resection of an involved distal resection margin was necessary in six patients (1.6 %) with rectal cancer. The anastomosis of the 312 patients with anterior resection for rectal cancer was protected by a temporary stoma in 199 patients (63.8 %). A leak of these anastomoses was encountered in 25 patients (8.0 %). An intra-abdominal or intrapelvic abscess was detected in 30 patients (7.8 %) of all rectal resections. Additional results regarding rectal cancer are listed in Table 2 (items 5, 6, 18, and 19), Table 3 (item 8), and Table 4 (items 5 and 11–14).

Influence of laparoscopic technique

Frequencies of the use of laparoscopic technique and conversion rates are mentioned in Table 2, items 15 and 16. The laparoscopically resected colorectal specimens were significantly shorter than the specimens of the open technique: given as medians 18 vs. 26 cm ($p < 0.001$). This was still true for the one center (center 9) with strong preference for the laparoscopic technique: 18 cm in laparoscopic and 25 cm in open technique. In 6 out of 7 centers performing laparoscopic resections for CRC, the median number of examined lymph nodes was smaller in the laparoscopic group. For the center with preference for the laparoscopic technique, the median number of lymph nodes was 16 in the laparoscopic group vs. 19 in the open group ($p = 0.011$), for node-positive patients in this center even 15 vs. 23.5 ($p = 0.009$). Interestingly, the median lymph node ratio (in node-positive patients) was smaller in the laparoscopic group than in the open group in this center (0.14 vs. 0.27, $p = 0.094$). Regarding the whole study population, other differences were noticed when comparing the laparoscopic versus the open technique: artery ligation before tumor mobilization in 83 vs. 66 %

Table 4 Results regarding oncosurgical quality, analyzed as overall statistics and per each surgical department

No.	Variable	Overall sample size	No. of centers	Statistics	Categories	Overall statistics	Range in statistics of centers	*P* value
1	In-hospital mortality	965	10	Proportion		0.02	0–0.06	0.0395
2	In-hospital mortality following emergency colorectal resection	965	10	Proportion		0.005	0–0.03	0.0841
3	Intra-abdominal septic complications (leak and/or abscess)	965	10	Proportion		0.07	0–0.17	0.0030
4	Reoperation	965	10	Proportion		0.08	0–0.17	0.0111
5	Abdominoperineal resection of rectal cancer	384	9	Proportion		0.17	0–0.30	0.1372
6	Perioperative blood loss (ml)	964	10	Median		300	200–500	<.0001
7	Patients needing perioperative blood transfusions	961	10	Proportion		0.19	0.05–0.40	<.0001
8	Perioperative blood loss for patients needing blood transfusion (ml)	180	10	Median		400	200–1000	0.0175
9	Tumors opened during mobilization	961	10	Proportion		0.05	0–0.11	0.0499
10	T4-tumors not en-bloc resected (% of T4)	121	9	Proportion		0.11	0–0.33	0.1272
11	Cytotoxic irrigations of anorectal stump (% of rectal and rectosigmoid cancers with anterior resection)	352	9	Proportion		0.79	0.14–1.0	0.0005
12	Principles of mesorectal excision applied (% of rectal and rectosigmoid cancers)[a]	445	9	Proportion		0.93	0.85–1.0	0.1226
13	Rectal cancer specimens with circumferential margin ≤1 mm[a]	301	9	Proportion		0.10	0–0.19	0.1113
14	Minimum histological distance from rectal cancer to circumferential resection margin (mm)[a]	206	9	Median		8	3–17	0.0011
15	No-touch isolation technique	964	10	Proportion	Arterial ligature	0.67	0.36–0.86	<.0001
					Venous ligature	0.68	0.36–0.86	<.0001
					Closure of bowel lumen	0.50	0.13–0.92	<.0001
16	Iatrogenically perforated mesocolon/mesorectum[a]	958	10	Proportion		0.04	0–0.08	0.2691

Dept. surgical department

[a] Patients with transanal local excisions are excluded from this analysis

of patients ($p = 0.002$), vein ligation before tumor mobilization in 81 vs. 67 % ($p = 0.008$), closure of bowel lumen before tumor mobilization in 9 vs. 54 % ($p < 0.001$)), central ligature of main blood vessels in 84 vs. 70 % ($p = 0.010$). All other parameters regarding radicality or oncosurgical quality were similar between the laparoscopic and open technique.

Influence of colorectal emergency resections

Sixty-three patients had their CRC resected as an emergency, defined as resection within 24 h after emergency admission. The following most obvious differences between emergency and elective resections of CRC were detected: in-hospital death rate 7.9 vs. 2.1 % ($p = 0.004$), macroscopic residual tumor (R2-resections) 27.0 vs. 14.2 % ($p = 0.006$). Macroscopic residual tumor was locoregional only in 29.4 vs. 7.9 % ($p = 0.019$), and locoregional with or without distant disease in 35.3 vs. 18.3 % ($p = 0.114$), inadvertent tumor perforation 12.7 vs. 4.7 % ($p = 0.013$), central ligature of major artery 82.5 vs. 70.5 % ($p = 0.041$), UICC stage 3/4 59.7 vs. 44.1 % ($p = 0.017$), median length of specimen 38 vs. 25 cm ($p < 0.001$), median height of resected mesocolon 8 vs. 9 cm ($p = 0.301$), median number of examined lymph nodes 20 vs. 15 ($p < 0.001$), blood loss ≥300 ml 69.8 vs. 56.8 % ($p = 0.043$).

Influence of the presence of multiple primary colorectal carcinomas

Comparing the group of 39 patients suffering from multiple primary CRCs with the population with one primary CRC ($n = 965$), the following differences were found: median length of resected bowel for multiple CRC 35.0 vs. 25.8 cm for single CRC, in-hospital mortality 5.1 vs. 2.5 %, anastomotic leak/abscess 15.4 vs. 6.6 %, re-operation 18.4 vs. 8.4 %, median blood loss 500 vs. 300 ml, and need for perioperative blood transfusion 26.3 vs. 18.7 %.

Discussion

In the past, many studies dealing with the outcome of surgical management in patients with CRC have been published. We have learned that satisfying results may depend on special training and sufficient annual case load in this type of surgery. However, it is still not yet clear which specific features make the difference between poor and excellent CRC surgery in daily practice. Therefore, from a public health point of view, benchmarking is needed. One may suppose that each surgical department and each multidisciplinary team would like to know how their quality of treatment compares with population-based or multicenter data on non-selected consecutive patients. To achieve this goal, reliable data from audits in large numbers of consecutive patients are required. To facilitate the comparison between centers, the selection of patients, the surgical treatment, the pathological work-up of the specimen as well as the outcome should be assessed in a standardized manner. This will allow the identification of high standards of performance, which should be the aim of each center. The knowledge of the benchmark and the average performance should motivate each center to improve its performance and to get as close as possible to or beyond the benchmark.

This study allowed us to assess prospectively—in detail and in a standardized manner—the surgical radicality and the oncosurgical quality of the specimens of patients with CRC from ten centers.

Although each center claimed to have special interest and expertise in CRC surgery, noteworthy differences in surgical radicality between different centers were detected. For example, the median lengths of the colorectal specimens varied from 20 to 40 cm between centers. To avoid any bias from different measuring conditions—the length of a stretched and natively measured colorectal specimen can shrink by up to 57 % in an unstretched and formaline-fixed state [18–20]—the pathologists of each center had to declare the measuring condition for each specimen on a standardized pathology form. In every center, at least 79 % of all specimens had been measured without tension and after formaline fixation; thus, the differences in median specimen lengths seem to reflect reality.

Increasing the length of colorectal specimens goes along with increasing number of harvested lymph nodes [21]. And a total number of lymph nodes ≥12 significantly improved the 5-year survival to 51 % in stage III colon cancer, compared with 45 % in patients with less than 12 lymph nodes examined [22]. Furthermore, the total number of examined lymph nodes seems to play an important prognostic role even in node negative patients [23, 24]. Thus, for the 648 node negative patients of the Intergroup Trial INT-0089 (trial of adjuvant chemotherapy for high-risk patients with stage II and stage III colon cancer) overall survival and cause-specific survival both increased significantly with the increasing number of analyzed lymph nodes [23]. In the present series, the median number of analyzed lymph nodes was 16 and compared well with other large series that

revealed medians of less than 12 lymph nodes [22, 25, 26]. The rather high number of lymph nodes in the present series may reflect the adequate length of specimens, the adequate amount of mesocolon resected, or both, always assuming careful pathological examination. However, important differences were detected again between different centers ranging from a median of 9 lymph nodes retrieved to 24, although none of the pathology institutes used a fat clearance technique to detect additional lymph nodes. Other factors such as the detected small differences in percentages of stage IV cancers or of neoadjuvant treatment are unlikely to explain the differences in examined lymph nodes between the centers.

Some authors promote the use of the lymph node ratio (LNR), i.e., the quotient of metastatic over total number of lymph nodes, as a predictor for prognosis rather than the total number of retrieved lymph nodes [22, 27–29]. This might especially be true for LNRs of ≥0.25 [22, 27, 30], indicating more advanced tumors, insufficient surgery, or both. Although we detected variable LNRs in our study, ranging from LNR values of 0.16 to 0.31, the rather low LNRs may again represent the relatively high radicality of surgery in the participating centers.

We postulate that another indicator of surgical radicality is the length of resected mesocolon, measured along the main artery from its central tie up to the bowel wall. Since almost all of the intermediate and central lymph nodes are found along the primary feeding arteries, as well as potential lymph node metastasis in those, central dissection of colonic arterial trunks seems to have prognostic relevance, especially for T3–T4 tumors, and even for T2 tumors that are sited in lengthening of the primary feeding artery [31]. To our knowledge, this is the first study that prospectively assessed the exact ligation level of the (primary) feeding artery/arteries and the height of resected mesocolon (i.e., the length of mesocolon perpendicularly measured to the colonic axis) as surrogate marker of central lymph node dissection. Further, this is the first study that demanded of the surgeons to mark the tumor site and the resection margins (bowel, blood vessels) in a standardized figure instead of a sole description of the surgical procedure. The intent of this measure was to minimize the well known discrepancies in anatomical nomenclature and in understanding of surgical anatomy between surgeons and to facilitate final analysis at the SAKK coordinating center. The 72 % overall rate of central ligation of primary feeding arteries seems to demonstrate that the participating surgeons were aware of the importance of this surgical step. Still, the percentages of specimens with central artery ligation differed between 39 and 97 % between centers. Accordingly, we observed a rather wide variation in median mesocolon lengths between centers, ranging from 6.5 to 12.0 cm. In a recent retrospective analysis of 399 specimens of resected colonic cancers, Quirke and colleagues noted a mean distance of 4.4 cm from the muscularis propria to the mesocolic resection margin in the best of their three groups, adding, however, that a high vascular tie close to the aorta or the superior mesenteric artery had never been done at their institution [32]. Although not proven in a prospective randomized trial, several papers indicate that more complete mesocolic excision and higher artery ligation in colon cancer result in a cancer-related 5-year survival advantage of 6–15 % [23, 32–35].

The distance of the tumor to the nearer bowel margin was of further interest as even a long specimen does not guarantee a priori adequate bowel margins on both sides. Excluding rectal cancer specimens, the median distances to the nearer bowel margin varied from 5.5 to 12.0 cm in the present series. Depending on the T-stage, a safety margin of 5.5 cm seems to be critical since pericolic lymph node metastasis up to 7 cm away from the primary occurs in 4 % [31], and more than 10 cm in 0.9–2.0 % [31, 36, 37].

Surgeons performing colorectal resection for cancer should precisely dissect along the mesenteric or mesorectal plane to avoid opening of the compartment of potential lymphatic spread [32, 33] and of mesenteric blood vessels. If this is done, and if no other accidental damage occurs, the expected blood loss is usually small. Therefore, the median blood loss and the need for perioperative blood transfusions seem to be indicators for oncosurgical quality and the surgeons' expertise and have been reported as prognostic factors [38]. Indeed, we found at least a tendential correlation between the average blood loss and the overall surgical performance per center, as well as between the number of patients needing blood transfusions and the overall surgical performance, as depicted in Table 4.

We noted a rather large variation in abdominoperineal resection (APR) rates, ranging from 6.3 to 29.6 %, between the eight centers treating patients with rectal cancers at all heights. Similarly, analysis of 31,223 patients receiving a major abdominal procedure for rectal cancer within the NHS in England between 1998 and 2004 revealed extensive and highly significant variation across hospital trusts with APR rates varying from 8.5 to 52.6 %, independently on patient case mix. Although the APR rate decreased from 30.5 % in 1998 to 23.0 %

in 2004 in that study, the authors conclude that this variation in APR rates is unacceptable and that rates of APR use could be a national performance measure [39]. The same is true for the APR rates in our series.

Interestingly, all centers had a few patients in whom inadvertent tumor opening occurred although some centers seemed to resect T4 tumors strictly en-bloc with parts of infiltrated neighboring organs. It is the first author's experience that inadvertent tumor opening may be difficult to avoid if covered tumor perforation to the pelvic side wall or the retroperitoneum is present. Several previous studies showed a significant reduction of the overall 5-year survival rate in patients with inadvertent tumor perforation, ranging from 20 to 26 % [40–42]. Therefore, inadvertent tumor perforation and the consecutive tumor cell spillage are adverse prognostic factors, and hence in some cases, another feature of oncosurgical quality.

Interpretation of morbidity and mortality in surgical oncology is delicate since more radical and more precise resections may be prone to more perioperative morbidity due to increased operating times and due to more demanding procedures. Therefore, morbidity, mortality, and re-operation rate of CRC surgery have to be evaluated for each center in context with case mix and with indicators of the center-specific surgical radicality and oncosurgical quality. The various treatment policies for emergencies due to CRC might further have influenced the center-specific mortality and morbidity rates in this series since only patients with tumor resection were included.

For rectal cancer, a high standard of surgical therapy with only small differences between the centers was found. Almost without exception, the technique of total or longitudinally partial excision of the mesorectum was applied by all centers and all surgeons. The median distal resection margin of at least 2.4 cm, measured without tension and after formaline fixation, in 8 out of 9 centers revealed reasonable surgical quality. All centers showed less than 15 % of rectal cancer specimens with a circumferential resection margin of <1 mm. It seems that the global efforts to propagate the TME-technique contributed to the fact that TME is now accepted in Switzerland and has been adopted as standard surgical procedure for rectal cancers [43–45]. Correspondingly, the prognosis for rectal cancer in Sweden has improved substantially and is now at least equal to the prognosis of colon cancer. Our study contributes to the identification of the surgical details in colon cancer that are crucial to improve the prognosis, similarly to what has been done for rectal cancer [6, 7, 42, 43]. Therefore, the long-term results of this study and especially the correlation of the long-term results with the issues of radicality and oncosurgical quality will be of interest.

Overall, the causes of the rather wide variations in radicality and oncosurgical quality between the centers remain speculative. Since 8 out of 10 centers have similar services, structural or process factors are unlikely to be responsible for the detected wide differences. Furthermore, largely differing case-mixes did not have been found as other possible explanation of the variations between the centers. Therefore, the crucial factors for the different radicalities and oncosurgical qualities seem to be the surgeons themselves or the specific surgical concepts of the different centers.

The following suggestions may be proposed to improve the performance of every surgeon and every surgical institution: meticulous anatomical knowledge by the surgeons is crucial, not only to identify and remove the important vascular and lymphatic structures but also to name them in the reports. Standardization of the surgical technique using a standardized procedure protocol and objective measuring tools is mandatory. And, standardization of the pathology work-up according to (future) guidelines will give the necessary feedback about the surgeons' performance. Supervision by regular audits may be an additional tool of quality control and may form the base for continuing improvement. Regular visits of workshops and life operations in highly specialized centers for colorectal cancer surgery are also recommended. Further, systematic long-term follow-up of the patients with careful analysis of potential reasons for tumor relapse should be declared obligatory.

Conclusions

The results obtained by the participating centers in Switzerland and Germany compare well with other series. The results may reflect the reality in CRC surgery, still far away from being satisfactory. Comparing the different centers, the top results for each single issue of radicality and oncosurgical quality may now serve as benchmarks for all other centers. The impressive differences in radicality and oncosurgical quality between the centers revealed that most of the centers still have a large potential for improvement.

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Appendix

Table 5 Patient and tumor characteristics, analyzed as overall statistics and per each surgical department

No.	Variable	Statistics	Total	Dept1	Dept2	Dept3	Dept4	Dept5	Dept6	Dept7	Dept8	Dept9	Dept10	*P* value
0	Evaluable patients with one tumor location	Sample size	965	92	12	163	204	62	13	99	178	97	45	–
1	Age (years)	Median	70	73	76	71	67	66	63	72	72	72	71	<.0001
		Min	21	33	61	27	34	44	48	42	21	33	29	
		Max	100	94	83	89	90	90	82	93	100	92	88	
2	Female sex	Frequency	378	37	5	55	74	21	6	39	74	49	18	0.3933
		Proportion	0.39	0.40	0.42	0.34	0.36	0.34	0.46	0.39	0.42	0.51	0.40	
3	ASA score													
	1	Proportion	0.13	0.07	0.25	0.10	0.07	0.29	0.31	0.08	0.19	0.13	0.18	0.0005
	2	Proportion	0.56	0.58	0.58	0.67	0.55	0.47	0.54	0.47	0.57	0.47	0.51	
	3	Proportion	0.29	0.33	0.17	0.22	0.36	0.23	0.15	0.39	0.22	0.32	0.29	
	4–5	Proportion	0.02	0.03	0	0.01	0.01	0.02	0	0.05	0.02	0.07	0.02	
4	Body mass index (kg/m^2)	Median	25.4	25.4	26.4	25.3	26.2	24.5	24.1	26.1	24.4	25.0	25.4	0.0079
		Min	14.7	17.8	19.4	16.5	14.7	18.2	18.0	16.7	15.6	15.6	18.7	
		Max	51.7	51.7	40.3	37.6	41.6	40.4	34.9	41.8	39.8	41.0	37.3	
5	Patients with rectal cancer	Frequency	384	37	5	57	109	27	0	23	83	28	15	<.0001
		Proportion	0.40	0.40	0.42	0.35	0.53	0.44	0	0.23	0.47	0.29	0.33	
6	Rectal cancers treated with neoadjuvant radiotherapy	Sample size	384	37	5	57	109	27	0	23	83	28	15	<.0001
		Frequency	106	10	3	5	16	17	–	5	37	8	5	
		Proportion	0.28	0.27	0.60	0.09	0.15	0.63	–	0.22	0.45	0.29	0.33	
7	T-stage	Sample size	964	92	12	163	203	62	13	99	178	97	45	0.0004
	0 + is	Proportion	0.02	0	0	0.05	0.01	0.06	0	0.01	0.01	0.04	0.04	
	1	Proportion	0.09	0.05	0	0.09	0.15	0.16	0.15	0.09	0.04	0.11	0.04	
	2	Proportion	0.18	0.17	0.42	0.17	0.24	0.16	0.08	0.15	0.20	0.09	0.09	
	3	Proportion	0.58	0.65	0.58	0.55	0.57	0.53	0.54	0.59	0.61	0.55	0.60	
	4	Proportion	0.13	0.12	0	0.15	0.03	0.08	0.23	0.16	0.14	0.21	0.22	
8	N-stage	Sample size	960	89	12	161	204	62	13	99	178	97	45	0.7917
	0	Proportion	0.58	0.61	0.67	0.51	0.58	0.63	0.62	0.59	0.59	0.63	0.56	
	1	Proportion	0.21	0.17	0.08	0.29	0.23	0.16	0.15	0.20	0.18	0.22	0.20	
	2	Proportion	0.21	0.22	0.25	0.20	0.19	0.21	0.23	0.21	0.23	0.15	0.24	
9	M-stage	Sample size	964	92	12	163	204	62	13	99	177	97	45	0.4386
	0	Proportion	0.83	0.84	0.92	0.80	0.82	0.90	0.92	0.77	0.86	0.86	0.82	
	1	Proportion	0.17	0.16	0.08	0.20	0.18	0.10	0.08	0.23	0.14	0.14	0.18	

Table 5 (continued)

No.	Variable	Statistics	Total	Dept1	Dept2	Dept3	Dept4	Dept5	Dept6	Dept7	Dept8	Dept9	Dept10	*P* value
10	UICC-stage	Sample size	959	89	12	161	204	62	13	99	177	97	45	0.0166
	0	Proportion	0.02	0	0	0.04	0.01	0.05	0	0.01	0.01	0.03	0	
	I	Proportion	0.22	0.16	0.42	0.18	0.31	0.29	0.23	0.20	0.20	0.16	0.11	
	II	Proportion	0.31	0.43	0.25	0.25	0.22	0.27	0.38	0.32	0.35	0.40	0.40	
	III	Proportion	0.28	0.25	0.25	0.32	0.28	0.29	0.31	0.23	0.30	0.26	0.31	
	IV	Proportion	0.17	0.17	0.08	0.20	0.18	0.10	0.08	0.23	0.14	0.14	0.18	
11	Grading	Sample size	930	86	12	159	192	59	13	97	175	94	43	<.0001
	1–2	Proportion	0.76	0.81	0.92	0.77	0.55	0.90	0.77	0.84	0.82	0.76	0.81	
	3–4	Proportion	0.24	0.19	0.08	0.23	0.45	0.10	0.23	0.16	0.18	0.24	0.19	
12	Maximum diameter of primary (cm)	Sample size	922	89	12	160	194	60	13	98	178	79	39	<.0001
		Median	4	4.5	3.5	4	3	3.5	4	4	4	4	4.5	
		Min	0	0.2	2.5	0.3	0.1	0	1	0	0	0	0	
		Max	15	15	9	12	15	13	10	15	12.5	12	14	
13	Specimens measured after formaline fixation	Sample size	961	92	12	163	203	62	13	99	177	95	45	<.0001
		Frequency	862	71	12	132	197	61	13	95	143	95	43	
		Proportion	0.90	0.77	1.0	0.81	0.97	0.98	1.0	0.96	0.81	1.0	0.96	
14	Patients operated by laparoscopy	Frequency	80	2	4	6	1	0	0	1	3	63	0	<.0001
		Proportion	0.08	0.02	0.33	0.04	0.00	0	0	0.01	0.02	0.65	0	
15	Conversion to open operation	Sample size	80	2	4	6	1	0	0	1	3	63	0	0.5948
		Frequency	10	1	0	1	0	–	–	0	0	8	.	
		Proportion	0.13	0.50	0	0.17	0	–	–	0	0	0.13	.	
16	Emergency large bowel resection	Frequency	63	15	0	9	3	0	0	11	17	6	2	<.0001
		Proportion	0.07	0.16	0	0.06	0.01	0	0	0.11	0.10	0.06	0.04	
17	Stoma formation in colon cancer patients	Sample size	581	55	7	106	95	35	13	76	95	69	30	0.1960
		Frequency	28	2	0	9	9	1	0	1	3	2	1	
		Proportion	0.05	0.04	0	0.08	0.09	0.03	0	0.01	0.03	0.03	0.03	
18	Stoma formation in rectal cancer patients	Sample size	384	37	5	57	109	27	0	23	83	28	15	0.0001
		Frequency	265	27	4	45	85	21	–	8	52	14	9	
		Proportion	0.69	0.73	0.80	0.79	0.78	0.78	–	0.35	0.63	0.50	0.60	
19	Distance of rectal cancers from anal verge (cm)	Sample size	384	37	5	57	109	27	0	23	83	28	15	0.0234
		Median	7	8	8	7	6	6	–	9	6	9	11	
		Min	0	1	4	1	0	1	–	0	0	1	3	
		Max	15	15	14	15	15	14	–	15	15	14	14	

The sample sizes for a variable are given only if it differs from the overall sample sizes in No. 0. *P* values: chi-square tests for frequencies, Monte Carlo approximation for low frequencies; Kruskal-Wallis tests for measurements (summarized by median, min, max). Missing items excluded from analyses

Dept. surgical department, *ASA* American Society of Anesthesiology, *UICC* International Union Against Cancer

Table 6 Results regarding surgical radicality, analyzed as overall statistics and per each surgical department

No.	Variable	Statistics	Total	Dept1	Dept2	Dept3	Dept4	Dept5	Dept6	Dept7	Dept8	Dept9	Dept10	*P* value
0	Evaluable patients with one tumor location	Sample size	965	92	12	163	204	62	13	99	178	97	45	–
1	Length of specimen (cm)[a]	Sample size	956	89	12	161	202	62	13	99	178	97	43	<.0001
		Median	25.8	39	25.5	26	25	22	21	33	22	20	22	
		Min	8.5	13	13	11	8.5	11	11.2	13	9	9.5	12	
		Max	160	160	52	154	140	50	30	120	95	65	60	
2	Maximum height of mesocolon (cm)[a]	Sample size	514	55	6	17	76	42	8	98	177	21	14	<.0001
		Median	9	12.2	7.5	9	9	8.3	8	10	7	6.5	12.5	
		Min	1	2.5	3	4	3	3	6	1	1.5	1.7	3.5	
		Max	44	44	10	26	42	22	16	31	18	15	17	
3	Number of lymph nodes examined	Sample size	957	88	12	161	203	62	13	99	178	96	45	<.0001
		Median	16	24	16	15	13	9	12	19	15	17	18	
		Min	0	7	6	3	0	0	0	4	2	3	2	
		Max	78	60	34	48	37	39	35	78	52	54	31	
4	Lymph node ratio[b] in node-positive patients	Sample size	395	34	4	78	84	23	5	41	72	35	19	0.2431
		Median	0.22	0.16	0.36	0.18	0.25	0.31	0.31	0.21	0.29	0.16	0.21	
		Min	0.02	0.03	0.04	0.03	0.03	0.06	0.04	0.03	0.02	0.02	0.04	
		Max	1.00	1.00	0.55	1.00	1.00	1.00	0.51	0.88	1.00	0.88	1.00	
5	Lymph node ratio[b] in node-positive patients without distant metastasis (UICC stage III)	Sample size	269	22	3	51	57	18	4	23	52	25	14	0.4014
		Median	0.16	0.14	0.41	0.12	0.15	0.28	0.25	0.17	0.20	0.15	0.17	
		Min	0.02	0.03	0.04	0.03	0.03	0.06	0.04	0.03	0.02	0.02	0.04	
		Max	1.00	0.79	0.55	0.87	1.00	1.00	0.51	0.58	1.00	0.54	0.50	
6	Distance to nearer bowel resection margin in colon cancer (excl. Rectosigmoid junction, cm)	Sample size	495	48	6	90	80	27	13	71	82	58	20	<.0001
		Median	8	9.5	5.8	8	6	5	6.5	12	7	6	7.3	
		Min	0	0	3	0.5	0.5	1.5	2	1.5	2.2	1.5	1.1	
		Max	46	19	10	29	27	20	15.5	41.5	46	17	22	
7	Distance to nearer bowel resection margin in cancer of rectosigmoid junction (cm)	Sample size	64	7	1	14	10	5	0	4	13	5	5	0.6835
		Median	4	5.5	3.5	4	3.3	3.5	–	4.8	4	3	5.5	
		Min	0.5	2.1	–	2	0.5	0.7	–	3	1.5	2	4	
		Max	9	6	–	7	6	8	–	6	9	8	6	
8	Distance to nearer bowel resection margin in rectal cancer, only (cm)[a]	Sample size	372	33	5	53	106	27	0	23	83	27	15	0.0133
		Median	2.5	3	2	2.2	2.2	2	–	3	3	2.2	2.8	
		Min	0	0.5	0.4	0.2	0	0	–	0.9	0	0	0	
		Max	14	8	4	8.5	7	6	–	8	12	14	9	
9	Height of major artery ligation:	Sample size	960	89	12	161	204	62	13	99	178	97	45	<.0001

Table 6 (continued)

No.	Variable	Statistics	Total	Dept1	Dept2	Dept3	Dept4	Dept5	Dept6	Dept7	Dept8	Dept9	Dept10	*P* value
	- high (central)	Proportion	0.71	0.90	0.92	0.47	0.82	0.40	0.61	0.97	0.65	0.80	0.60	
	- intermediate	Proportion	0.25	0.10	0.08	0.48	0.16	0.53	0.23	0.02	0.30	0.11	0.31	
	- low (peripheral)[a]	Proportion	0.04	0	0	0.04	0.02	0.06	0.15	0.01	0.04	0.08	0.09	

The sample sizes for a variable are given only if it differs from the overall sample sizes in No. 0. *P* values: chi-square tests for frequencies, Monte Carlo approximation for low frequencies; Kruskal-Wallis tests for measurements (summarized by median, min, max). Missing items excluded from analyses

Dept. surgical department, *LN* lymph nodes

[a] Patients with transanal local excision of rectal cancer are excluded from this analysis

[b] Lymph node ratio: proportion of positive LN among all LN examined

Table 7 Results regarding oncosurgical quality, analyzed as overall statistics and per each surgical department

No.	Variable	Statistics	Total	Dept1	Dept2	Dept3	Dept4	Dept5	Dept6	Dept7	Dept8	Dept9	Dept10	*P* value
0	Evaluable patients with one tumor location	Sample size	965	92	12	163	204	62	13	99	178	97	45	–
1	In-hospital mortality	Frequency	24	5	0	9	2	0	0	0	2	4	2	0.0395
		Proportion	0.02	0.05	0	0.06	0.01	0	0	0	0.01	0.04	0.04	
2	In-hospital mortality following emergency colorectal resection	Frequency	5	3	0	2	0	0	0	0	0	0	0	0.0841
		Proportion	0.005	0.03	0	0.01	0	0	0	0	0	0	0	
3	Intra-abdominal septic complications (leak and/or abscess)	Frequency	64	3	2	4	19	5	0	1	19	10	1	0.0030
		Proportion	0.07	0.03	0.17	0.02	0.09	0.08	0	0.01	0.11	0.10	0.02	
4	Reoperation	Frequency	81	4	2	8	22	6	0	1	23	11	4	0.0111
		Proportion	0.08	0.04	0.17	0.05	0.11	0.10	0	0.01	0.13	0.11	0.09	
5	Abdominoperineal resection of rectal cancer	Sample size	384	37	5	57	109	27	0	23	83	28	15	0.1372
		Frequency	67	4	0	10	27	8	.	3	11	3	1	
		Proportion	0.17	0.11	0	0.18	0.25	0.30	.	0.13	0.13	0.11	0.07	
6	Perioperative blood loss (ml)	Sample size	964	92	12	163	204	62	13	99	178	96	45	<.0001
		Median	300	250	500	300	200	500	500	300	400	300	500	
		Min	0	10	100	2	10	100	100	50	0	20	50	
		Max	4200	3500	1000	3000	2600	4000	1000	700	2500	4200	1800	
7	Patients needing perioperative blood transfusions	Sample size	961	92	12	161	203	62	13	99	177	97	45	<.0001
		Frequency	180	5	1	16	25	16	1	22	70	17	7	
		Proportion	0.19	0.05	0.08	0.10	0.12	0.26	0.08	0.22	0.40	0.18	0.16	
8	Perioperative blood loss for patients needing blood transfusion (ml)	Sample Size	180	5	1	16	25	16	1	22	70	17	7	0.0175
		Median	400	200	1000	550	500	500	200	300	400	300	500	
		Min	0	100	1000	50	30	150	200	150	0	50	50	
		Max	4200	500	1000	3000	2000	2300	200	700	1700	4200	1000	
9	Tumors opened during mobilization	Sample size	961	90	12	163	204	62	13	99	176	97	45	0.0499
		Frequency	50	6	0	14	9	7	1	2	3	4	4	
		Proportion	0.05	0.07	0	0.09	0.04	0.11	0.08	0.02	0.02	0.04	0.09	
10	T4-tumors not en-bloc resected (% of T4)	Sample size	121	11	0	24	7	5	3	16	25	20	10	0.1272
		Frequency	13	0	.	5	0	0	1	0	1	4	2	
		Proportion	0.11	0	.	0.21	0	0	0.33	0	0.04	0.20	0.20	
11	Cytotoxic irrigations of anorectal stump (% of rectal and rectosigmoid cancers with anterior resection)	Sample size	352	37	6	52	90	22	0	21	76	29	19	0.0005
		Frequency	277	37	4	49	59	3	–	16	68	24	17	
		Proportion	0.79	1.0	0.67	0.94	0.66	0.14	–	0.76	0.89	0.83	0.89	
12	Principles of mesorectal excision applied (% of rectal and rectosigmoid cancers)[a]	Sample size	445	41	6	69	119	33	0	27	96	33	21	0.1226
		Frequency	416	41	6	63	115	28	–	24	87	32	20	
		Proportion	0.93	1.0	1.0	0.91	0.97	0.85	–	0.90	0.91	0.97	0.95	

Table 7 (continued)

No.	Variable	Statistics	Total	Dept1	Dept2	Dept3	Dept4	Dept5	Dept6	Dept7	Dept8	Dept9	Dept10	*P* value
13	Rectal cancer specimens with circumferential margin ≤1 mm[a]	Sample size	301	27	4	47	86	22	0	19	69	17	10	0.1113
		Frequency	29	5	0	6	2	1	–	3	10	2	0	
		Proportion	0.10	0.19	0	0.13	0.02	0.05	–	0.16	0.14	0.12	0	
14	Minimum histological distance from rectal cancer to circumferential resection margin (mm)[a]	Sample size	206	30	3	36	27	14	0	16	69	9	2	0.0011
		Median	8	6	10	5	17	10	–	11.5	10	3	3	
		Min	0	0	0.4	0	0.2	0.5	–	0	0	0.7	0	
		Max	65	65	15	30	60	50	–	40	45	28	6	
15	No-touch isolation technique:	Sample size	964	91	12	163	204	62	13	99	178	97	45	
	- arterial ligature	Proportion	0.67	0.60	0.50	0.36	0.78	0.71	0.38	0.86	0.76	0.81	0.47	<.0001
	- venous ligature	Proportion	0.68	0.68	0.50	0.36	0.80	0.73	0.38	0.86	0.76	0.81	0.40	<.0001
	- closure of bowel lumen	Proportion	0.50	0.75	0.33	0.34	0.51	0.58	0.92	0.75	0.52	0.13	0.49	<.0001
16	Iatrogenically perforated mesocolon/mesorectum[a]	Sample size	958	89	12	161	203	61	13	99	178	97	45	0.2691
		Frequency	37	4	0	5	9	4	0	2	3	8	2	
		Proportion	0.04	0.04	0	0.03	0.04	0.07	0	0.02	0.02	0.08	0.04	

The sample sizes for a variable are given only if it differs from the overall sample sizes in No. 0. *P* values: chi-square tests for frequencies, Monte Carlo approximation for low frequencies; Kruskal-Wallis tests for measurements (summarized by median, min, max). Missing items excluded from analyses

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[a] Patients with transanal local excisions are excluded from this analysis

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