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ORIGINAL ARTICLE

Laparoscopic resection of right colon cancer—a matched pairs analysis

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Abstract
Purpose Laparoscopy for colorectal cancer resection bares early post-operative advantages and results in equal oncologic long-term outcome. However, data on laparoscopic right hemi-colectomy is scarce. Aim of the present study was to analyze a well selected collective of patients with right-sided colon cancer treated open and laparoscopically with regard to peri-operative and long-term outcome.
Methods We analyzed all patients who underwent right-sided hemi-colectomy for colon cancer between January 1996 and March 2013. Data was extracted from our prospective database. Inclusion criteria were tumor localization in the ascending colon, oncologic resection, histology of an adenocarcinoma, tumors UICC I–III, and R0 resection. Exclusion criteria were multiple malignancies including colon, emergency operation, adenoma or pT0 status, and UICC IV. For the matched pairs approach between patients undergoing laparoscopic (LAP) or open (OPEN) surgery, the parameters age, UICC stage, tumor grading, and sex were applied.
Results A total of 188 patients was included in the analysis with $n = 94$ in both the LAP and the OPEN group. Some peri-operative results demonstrated advantages for laparoscopy including median return to liquid ($p < 0.0001$) and solid diet ($p = 0.008$), median length of ICU stay ($p < 0.0001$), and median length of hospital stay ($p = 0.022$). No significant differences were revealed for complication rates, rates of anastomotic leakage, or 30-day mortality. Lymph node yield was identical. Also, no differences in oncologic long-term outcome were detected. Rates for local recurrence were 4.3 and 2.0 %.
Conclusion This matched pairs analysis verifies peri-operative advantages of laparoscopy explicitly for the sub-group of CRC patients undergoing right-sided hemi-colectomy in comparison to open surgery while demonstrating equivalent oncologic long-term results.

Keywords Laparoscopic surgery · Open surgery · CRC patients · Hemi-colectomy

Introduction

Laparoscopy has emerged as the preferred operative approach for many intra-abdominal pathologic conditions and is well established for resectable colorectal cancer. Since its introduction in the early 1990s, it has been adopted as a safe and feasible technique and several trials could show that reservations towards a laparoscopic approach were negligible. Still, a North-American analysis revealed that even today, less than one-third of all colon cancer patients undergo surgery in a laparoscopic approach [1].

Large prospective multicenter trials as well as subsequent meta-analyses showed that oncologic long-term results were not inferior to those achieved by open surgery, some of the trials suggesting even slightly better oncologic outcome [2–5]. In addition, all trials showed advantages for laparoscopy regarding the peri-operative outcome such as intra-operative blood loss, post-operative bowel movement, use of analgesics, recovery, and length of hospital stay.

The above mentioned trials included patients with either colon cancer only or both colon and rectal malignancy.

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None of the trials presented results for sub-groups of colon cancer patients, i.e., the left or right hemi-colon. Especially for tumors located in the right hemi-colon, reservations towards a laparoscopic approach have persisted due to a more complex dissection technique in comparison to the left-sided colon. This aspect is underlined by the fact that some authors have promoted a more radical lymph node dissection for right-sided malignancy in open surgery which could further improve oncologic outcome [6]

Solid data on laparoscopic resection for colon cancer of the right hemi-colon is scarce. Published series cover very limited study populations. One small randomized trial with 145 patients in total, few case–control studies encompassing at most 100 laparoscopic procedures and one meta-analysis exist [7–16].

Aim of this study was therefore to perform a larger matched pairs analysis of patients receiving oncologic resection of the right hemi-colon in open and laparoscopic technique. We applied strictly defined inclusion criteria in order to compare the peri-operative outcome measures between patients treated laparoscopically with patients having undergone conventional open resection. Additionally, long-term outcome was analyzed between these groups.

Methods

Patients

This study initially involved all patients who underwent surgery for colon cancer of the right hemi-colon at the Department of Surgery, University Medical Center Schleswig-Holstein Campus Lübeck, Germany between January 1997 and June 2013. Prospectively documented demographic, clinical and follow-up data were obtained after patients' informed consent and in accordance to the approval of the local Ethical Committee (#07-124). Inclusion criteria were histopathologically proven adenocarcinoma of the right hemi-colon (coecum and ascending colon) treated by either laparoscopic (LAP) or open (OPEN) oncologic right hemicolectomy as defined by a central dissection of the ileocolic vein and artery, a central dissection of the right colic vein and artery if present, and a proximal dissection of the right branch of the mid colic vein and artery, respectively. Additional inclusion criteria were UICC stages I–III and resection status R0. Exclusion criteria were carcinomas treated by extended right hemicolectomy or mere ileocolic resection. Also, patients with other (pre-) existing malignancy including double carcinoma of the colorectum, patients treated as an emergency due to complications, histopathologically proven pT0-status or proven adenoma, stage UICC IV disease, and resection status R1 or R2 were excluded. In consequence, 94 patients could be identified who underwent an oncologic right hemicolectomy in laparoscopic technique. In a matched pairs design, 94 patients were then chosen out of a collective of 142 patients undergoing surgery in open technique. Matching criteria in order of their priority were age, UICC stage, histopathological grading, and sex. UICC stages were defined according to the consensus of 1997. The Karnofsky-Index was used to assess the patients' overall performance status with regard to their general well-being and their ability to undergo activities of daily life with a possible range from 10 to 100 %.

All patients were included in a regular post-operative surveillance program according to ASCO guidelines. Surveillance data of individual patients were recorded in a standardized questionnaire for the first 10 years after resection. Thereafter, the responsible physician was contacted, and the questionnaire was sent to each patient on a yearly basis. If there was any missing data, we addressed the registration office for residents for support.

Median time of follow-up for the entire collective study of 188 patients was 40 months (range 0–196), with 62 months (range 0–196) for the OPEN, and 35 months (range 0–99) for the LAP sub-group. Adjuvant treatment was considered for all stage III patients and for those stage I and II patients who had established risk factors for recurrence according to the German colorectal cancer guidelines. All patients were offered and motivated to participate in enhanced recovery programs. Demographic and clinical data for the entire collective as well as for the matched pairs sub-groups are summarized in Table 1.

Laparoscopic technique

We use one trocar for the camera placed just above the umbilicus and two additional trocars in the left lower and upper quadrant. In a lateral to medial approach, the cecum, mesenteric root of the ileum and the ascending colon are then mobilized leaving an intact plane of Toldt. The visceral and parietal fascias are then dissected to mobilize the right mesentery from the duodenum and the pancreatic head. Care is taken not to damage the fascial layers. Lateral transection of the greater omentum is followed by opening the lesser sac. Mobilization of the right flexure is completed by dissecting the hepato-colic ligament. We then open the peritoneal layer of the mesentery medially at the origin of the ileocolic artery and vein. The vessels are dissected between absorbable clips, and the mobilized mesentery is dissected parallel to the mesenteric vessels. If present, the right colic vessels are dissected centrally, otherwise, the right branch of the mid colic vessels at their origin. Through an epigastric mini-laparotomy, the colon is then exposed and the colon is transected distally to the right flexure. After transection of the terminal ileum, we re-construct the bowl with a hand-sewn isoperistaltic side-to-side anastomosis.

Table 1 Demographic and clinical data of the entire collective and the matched lap and open sub-group

	total ($n = 188$)	lap group ($n = 94$)	open group ($n = 94$)	p value
Med. age (range) [year][a]	73.5 (36–90)	73.5 (38–89)	73.5 (36–90)	ns
sex (m:f) [n][a]	89:99	45:49	44:50	ns
UICC [n (%)][a]				
I	44 (23.4)	29 (30.9)	15 (16.0)	.041
II	87 (46.3)	37 (39.4)	50 (53.2)	ns
III	57 (30.3)	28 (29.8)	29 (30.9)	ns
Grading [n (%)][a]				
1	8 (6.8)	4 (4.3)	4 (4.3)	ns
2	113 (60.1)	62 (66.0)	51 (54.3)	ns
3	67 (35.6)	28 (29.8)	39 (41.5)	ns
Mean Karnofsky-Index [%] (sd.)	85.5 (17.15)	89.0 (14.97)	82.1 (18.84)	.006
Med. follow-up [months] (range)	40 (0–196)	35 (0–99)	62 (0–196)	<.0001

med median, *sd* standard deviation, *ns* not significant

[a] Parameter used for matching

As a bleeding indicator, we place one drain intra-abdominally which is removed the day after surgery.

Statistics

Continuous variables were expressed as median with range or mean ± standard deviation (SD) and categorical variables in percent. The Kaplan-Meier curves for lap vs. open were calculated and assessed for significance by the log-rank test. The 5-year survival rates were estimated with the Kaplan-Meier method. Student *T*-test or Chi-squared test was performed to compare lap- vs. open-related differences. All results were considered significant with $p < 0.05$. All calculations were performed using IBM SPSS Statistics 22®.

Results

A total of 244 patients were identified from our database that fulfilled both the inclusion and exclusion criteria. In 102 (41.8 %) of these, laparoscopic resection was attempted. In eight (7.8 %) patients, conversion was necessary which resulted in a collective of 94 (39.8 %) patients undergoing complete laparoscopic and 142 (60.1 %) undergoing open resection. From the latter sub-group, 94 patients were chosen after application of the matched pair criteria as described above. The matching process resulted in indifferent or at least very comparable sub-groups as listed in Table 1.

In total, 99 (52.7 %) patients were female and 89 (47.3 %) were male with a median age of 73.5 (36–90) years. Between the LAP and the OPEN group there were no significant differences regarding gender or age distribution after application of the matching process (Table 1). Also, no significant differences in histopathological grading occurred. The rates of UICC II and III tumors showed no significant differences. For UICC I, the groups comprised 29 (30.9 %; lap) and 15 (16.0 %; open) patients, respectively ($p = 0.041$). The Karnofsky-Index also differed between the groups with $p = 0.006$. For the entire collective, the mean Karnofsky-Index was 85.5 % (±17.2) with 89.0 % (±15.0) for the LAP group and 82.1 % (±18.8) for the OPEN group.

With a median of 35 months (0–99) for the LAP and 62 months (0–196) for the OPEN group, a significant difference in follow-up was detected. This was due to a higher proportion of patients in the OPEN group throughout the earlier part of the time interval chosen for analysis.

We found significant differences in a number of peri-operative parameters (Table 2). As expected, median operation time was significantly longer in the LAP group than in the OPEN group with 175 min compared to 145 min ($p = 0.007$). In the OPEN group, peri-operative blood transfusions were necessary more often than in the LAP group ($p < 0.0001$). In the LAP group, the post-operative stay in the intensive care unit (ICU) was significantly shorter than in the OPEN group within median of 0 and 1 day, respectively ($p = 0.019$). There was no significant difference in the rate of anastomotic leakages with four (4.3 %) cases in the LAP and two (2.1 %) in the OPEN group. Overall, complications leading to surgical re-intervention occurred in both groups with no significant difference (LAP $n = 8$ [8.5 %] vs. OPEN $n = 6$ [6.4 %]). Reasons for surgical re-intervention were the above mentioned anastomotic leakages, post-operative bleeding, and a dislocated drainage. The number of total complications also revealed

Table 2 Peri-operative data

	total ($n = 188$)	lap group ($n = 94$)	open group ($n = 94$)	p value
Operation time [med. min (range)]	160 (65–320)	175 (85–320)	145 (65–260)	.007
Blood transfusion [n of patients (%)]	64 (34.0)	22 (23.4)	42 (44.7)	<.0001
ICU stay [med. days (range)]	0.0 (0–62)	0.0 (0–25)	1.0 (0–62)	.019
Total complications [n of patients (%)]	46 (24.5)	20 (21.3)	26 (27.7)	ns
Total complications[a] [n events]	83	32	51	ns
Cardiac [n (%)]	8 (9.6)	2 (6.3)	6 (11.8)	ns
Pulmonary [n (%)]	24 (28.9)	10 (37.0)	14 (27.5)	ns
Renal incl UTI [n (%)]	7 (8.4)	2 (6.5)	5 (9.8)	ns
Other [n (%)]	44 (53.0)	18 (58.0)	26 (51.0)	ns
Anastomotic leakage [n (%)]	6 (3.2)	4 (4.3)	2 (2.1)	ns
Surgical re-intervention [n (%)]	14 (7.4)	8 (8.5)	6 (6.4)	ns
30d-mortality [n (%)]	8 (4.3)	2 (2.1)	6 (6.4)	ns
Liquid diet [med. days (s.dev)]	1.0 (0–10)	1.0 (0–10)	2.0 (1–8)	<.0001
Diet solid [med. days (s.dev)]	5.0 (2–22)	4.0 (2–15)	7.0 (2–22)	.008
LOS [med. days (range)]	10.5 (4–92)	8.5 (4–69)	12 (5–92)	.022
Lymph node yield [med. n (range)]	16.0 (7–38)	16.0 (7–35)	17.0 (8–38)	ns

LOS length of stay, *med* median, *ns* not significant

[a] Multiple counts per patient possible

no significant difference with 20 (21.3 %) cases in the LAP and 26 (27.7 %) cases in the OPEN group.

The post-operative return to oral intake showed significant differences for both liquid and solid diets and was significantly faster in the LAP group than in the OPEN group. In median, the LAP group started liquid and solid intake on days 1 and 4 post-surgery, respectively, whereas the OPEN group started on days 2 and 7. Median length of hospital stay also was significantly shorter in the LAP group (8.5 days) than in the OPEN group (12 days). The 30-day mortality rate in the LAP group was 2.1 % with $n = 2$ patients. In the OPEN group there were $n = 6$ patients who died within this interval resulting in a rate of 6.4 %. Causes for mortality in the LAP group were a fulminant pulmonary embolism and a severe myocardial infarction whereas in the OPEN group, three patients suffered from a severe pneumonia with septic complications and multi-organ failure, two patients developed a fulminant pulmonary embolism, and one patient died of septic multi-organ failure due to severe peritonitis after anastomotic leakage. The difference in 30-day mortality rate was not significant. With a median of 16 (7–38; LAP) and 17 (8–38; OPEN), respectively, the number of lymph nodes harvested showed no difference between the groups.

There was no difference in overall survival between the groups (Fig. 1), neither regarding statistical testing of the Kaplan-Meier curves nor the calculation of the 5-year overall survival rates. For UICC I–III tumors, these were 68 vs. 65 % for the LAP and the OPEN group, respectively. Also, no significant differences were found when analyzing individual UICC stages (data not shown). Local recurrence occurred in $n = 4$ (4.3 %) patients in the LAP and $n = 2$ (2.1 %) patients in the OPEN group. This difference also showed no statistical significance.

Discussion

Colorectal cancer is the third most common malignancy within the Western countries. Several studies indicate the oncologic equivalence of the laparoscopic approach compared to open resection of colorectal carcinoma [2–4, 17]. For some of the studies, follow-up intervals exceeding 10 years are available by now. Moreover, short-term advantages concerning the peri- and early post-operative course were consistently reported [9, 10]. However, none of these studies analyzed possible outcome differences with regard to localization of colon tumors and the according surgical procedures. Aim of the present study was therefore to analyze our patient cohort undergoing oncologic right hemi-colectomy in laparoscopic technique compared to patients undergoing surgery in a conventional open approach by means of a highly selective extraction process combined with a matched pair approach.

The matching process resulted in non-different groups regarding age or sex distribution and histopathological grading. For UICC stage I, the groups encompassed 29 and 15 patients, respectively. When early (UICC I/II) and advanced stage (UICC III) tumors were dichotomized, the distribution was, however, equal with 66 UICC I/II and 28 UICC III tumors in

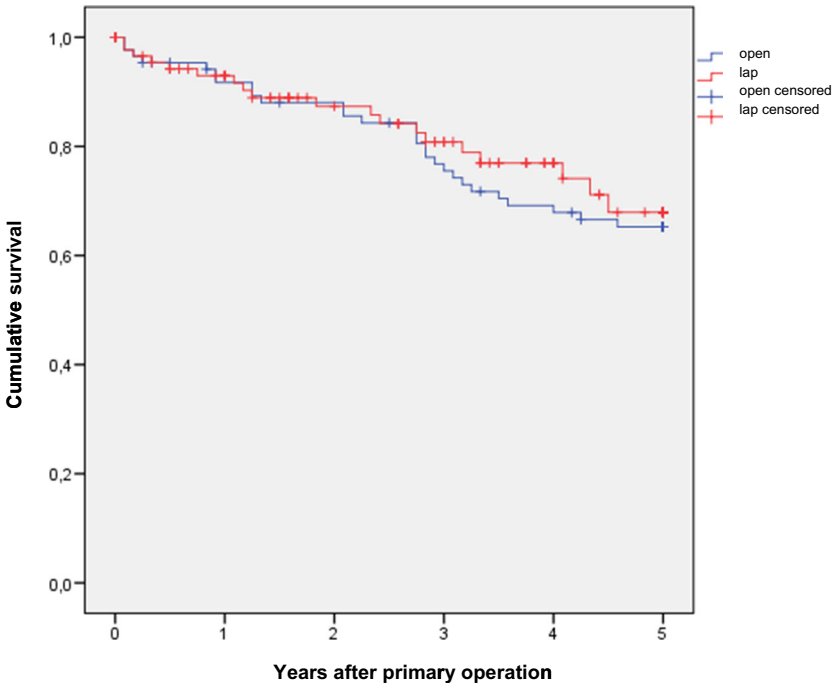

Fig. 1 Survival of all UICC stages

the laparoscopic and 65 UICC I/II and 29 UICC III tumors in the open group. Moreover, the difference in Karnofsky-Index with 89.0 % in the laparoscopic group and 82.1 % in open group was, albeit statistically significant, also minor when considering a possible range of 10–100 %. The reason for a longer follow-up in the open group is to be seen in the increasing share of patients undergoing surgery in laparoscopic technique throughout the later years of the interval analyzed. In sum, we therefore regarded the relevant characteristics of both sub-groups as equally or at least very similarly distributed which was essential for the subsequent analysis of peri- and post-operative outcome. Certainly, this study is still limited by its retrospective nature, although all data relevant for this analysis had been documented prospectively in our database. The above mentioned differences in sub-group characteristics may further limit possible conclusions drawn from our results. Also, in addition to the Karnofsky-Index, the ASA score, would have added a valuable parameter to the data with regard to evaluation of whether the two sub-groups indeed presented with similar co-morbidities. However, ASA score was available only for a small subset of patients, and we therefore decided not to include it in our dataset.

Other groups also applied age, sex, and tumor stage as matching criteria for their case–control studies and equally described minor differences in parameter distribution [12, 13] with combined cohort sizes of 77 and 49 patients. With 100 patients in both the laparoscopic and the open group, Nakamura et al. presented an equally large case–control study as the present one with non-significant differences in sex, age, ASA-status, and UICC stage [11]. However, their exclusion criteria were less strictly defined than ours. Carcinomas of the transverse colon were also included and fewer outcome parameters were analyzed.

The overall lymph node yield was 16 (range 7–38). To achieve a sufficient predictive value, a minimum of 12 lymph nodes should be harvested. Despite the equivalent technique, in four patients in the laparoscopic group and six patients in the open group less than 12 lymph nodes were described in the specimen. Concerning the lower range end of $n = 7$, it has been described that despite adequate oncologic surgical technique few lymph nodes may be harvested. In line with this, even in the detailed descriptions of complete mesocolic excision for right colon cancer, the minimum of lymph nodes retrieved was $n = 2$ [18].

Similar to previous results, we found several advantages in the peri- and early post-operative outcome in the laparoscopic group. The parameters with significant difference in favor of the minimally invasive approach encompassed blood transfusions, length of ICU stay, return to oral intake, and length of hospital stay. This is in line with most previous studies. Still, Li et al. could not find differences in intra-operative blood loss, Quyn et al. described an equal length of hospital stay for their study population of elderly patients, and Tan et al. found no difference for the return to oral diet [13, 19, 20]. The proportion of patients in the OPEN group was larger throughout the early period of the analyzed time interval where discharge management was less strict our results regarding the length of hospital stay have to be interpreted critically. Contrary to some other series [10, 11], we could not find a significantly smaller rate of post-operative complications in

the laparoscopic group. With 21.3 and 27.7 %, we found similar rates of overall complications as major prospective trials such as the COLOR-trial which included 48 % of right hemicolectomies but could also not reveal any differences between the open and the laparoscopic group [2]. Equally, the results of the COST-trial showed overall complication rates of 20 and 21 % with 54 % of right hemi-colectomies in the entire collective [3]. Classification according to Clavien-Dindo would have added further, possibly better information to the perioperative outcome results. However, Clavien-Dindo was available only for a subset of patients, and we decided to use the description displayed in the manuscript which is commonly used in many present studies on peri- and post-operative outcome analyses. Although Clavien-Dindo should be routinely applied in prospective data acquisition, the here presented entities of complications is in parts more detailed than results deriving from the Clavien-Dindo classification.

The time required for the laparoscopic procedure was significantly longer than for the open operation, a fact that has been frequently described [2, 4, 7, 9]. Although operation times of 217 min were reported [12], with 181 min in median, our operation time was slightly longer than that presented by others with i.e., 152 and 165 min [14, 16]. This may be due to the fact that we consider this operation a teaching procedure in the way that advancing visceral surgeons perform single steps of the procedure under the supervision of a surgeon skilled to perform the procedure. Also, as described above, we routinely perform an extra-corporal hand-sewn anastomosis requiring more time than a stapled anastomosis.

Whereas, the short-term advantages of laparoscopic surgery for the individual patient have been frequently shown, there is still debate about the related costs. In the late nineties, Philipson et al. described the direct costs for laparoscopic right hemi-colectomy to be significantly higher than the costs for the open procedure. This was explained by extended operation time and greater costs of disposals [10, 19]. Contrary to these findings, recently, a more detailed calculation including various indirect costs associated with the hospitalization revealed that the laparoscopic approach was more cost-efficient and resulted in progressive financial savings [21].

The merit of this study is the long-term observation and analysis of a matched pairs collective after right hemicolectomy. Our findings showed no differences in overall survival between the laparoscopic and the open group. The one small randomized trial by Chung et al. also showed non-different survival rates but with 30 and 28 months, respectively, their median follow-up was shorter than the interval of the present study. Neither could other retrospective studies find any survival differences between the two techniques [14–16]. This is in line with the large prospective trials; none of which detected survival differences between the patients undergoing open or laparoscopic resection for colon cancer, thereby documenting oncologic equivalence of the minimally invasive technique [2–4]. Still, the retrospective non-randomized character of our study together with the fact that we analyzed overall instead of cancer-specific survival limit the validity of conclusions drawn from the results. Another bias concerning the oncologic outcome arises from the fact that data on how many patients received the entire course of adjuvant treatment—where indicated—was incomplete and thus left out entirely.

Rates of local recurrence after oncologic resection of the right hemi-colon have been stated to be between 2.5 and 5.2 % [10, 14]. Overall, our recurrence rate was 3.2 % and showed no difference between the open and the laparoscopic groups. Interestingly, one large randomized prospective trial described differences in local recurrence rates between right and left colon resections with 14.7 % after right and 5.2 % following left hemi-colectomy [4]. Other long-term follow-ups revealed similar results [2, 3].

Despite the evident limitations of our retrospective study design, our results lead us to conclude that oncologic resection of the right hemi-colon entails advantages in the early postoperative outcome while showing no shortcomings in the oncologic long-term results. We thereby verify pre-described results in a larger and well-matched case–control study. Still, this should merely serve as a motivation to bring forward prospective trials on the particular aspect of right hemicolectomy further elucidating the possible advantages of laparoscopic surgery.

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