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Parameters of radical resection in laparoscopic and open colon and rectal cancer surgery

Parametri radikalnosti kod laparoskopske i otvorene hirurgije karcinoma kolona i rektuma

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Abstract

Background/Aim. In colon and rectal cancer surgery, resection is considered radical when circumferential, proximal and distal resection margins are without the presence of tumor cells. Concept of total mesorectal excision in rectal surgery involves complete removal of the tumor with mesorectal fascia which surrounds lymph nodes, lymphatics and blood vessels. The aim of this study was to determine whether laparoscopic approach provides all parameters of oncological radicality as open surgery of colorectal cancer. **Methods.** The study included 122 patients with carcinoma of colon and rectum, divided into two equal groups: patients operated on by laparoscopic and those operated on by open approach. In colon surgery we analyzed proximal and distal resection margins, and the number of removed lymph nodes, and in rectal surgery: proximal, distal and circumferential resection margins, and the number of removed lymph nodes. **Results.** Both groups were comparable in age, sex, American Society of Anesthesiologists (ASA) score, tumor localization, tumor size, and type of surgical operation performed. According to localization of the tumor, the most commonly performed operation was anterior resection of the rectum (60.7% vs. 59%). There was no case of the tumor involvement of the distal margin. Average proximal distance from the tumor on the fixed specimen was 100 vs. 120 mm with statistical significance ($p < 0.001$). Distal margins were not significantly different, 40 mm in both groups ($p = 0.143$). In two cases we had circumferential resection margin (CRM) of 1 mm (7.7%) in the laparoscopic group, and in three cases operated conventionally CRM was 1 mm (8.8%). The average number of removed lymph nodes was 15 vs. 16, respectively. Length of hospital stay for patients assigned to the laparoscopic surgery was significantly shorter than for patients operated on by the open approach. Concerning postoperative complications, no significant difference was found between groups. The overall postoperative morbidity was 18% vs. 21.3%, respectively. **Conclusion.** With laparoscopic approach it is possible to provide all parameters of oncological radicality similarly to the open surgery of colorectal cancer.

Key words:
colon neoplasms; laparoscopy; laparotomy; rectal neoplasms; surgical procedures, operative; treatment outcome.

Apstrakt

Uvod/Cilj. Resekcija kod karcinoma kolona i rektuma smatra se radikalnom kada su proksimalna, distalna i radijalna linija resekcije bez prisustva tumorskih ćelija. Koncept totalne mezorektalne ekscizije podrazumeva kompletno uklanjanje tumora unutar fascijalnog omotača zajedno sa limfnim čvorovima, limfaticima i krvnim sudovima duž kojih tumor može da se širi. Cilj rada bio je da se utvrdi da li se laparoskopskim pristupom obezbeđuju svi parametri onkološke radikalnosti kao i u otvorenoj hirurgiji karcinoma kolona i rektuma. **Metode.** Studijom su bila obuhvaćena 122 bolesnika sa karcinomom kolona i rektuma svrstana u dve jednake grupe - bolesnici operisani laparoskopskim i oni operisani otvorenim pristupom. U hirurgiji kolona analizirali smo proksimalnu i distalnu resekcionu liniju i broj uklonjenih limfnih žlezda, a u hirurgiji rektuma proksimalnu, distalnu i cirkumferentnu resekcionu liniju kao i broj uklonjenih limfnih žlezda. **Rezultati.** Obe grupe su bile jednake u odnosu na životno doba, pol, rezultat klasifikacije Američkog društva anesteziologa, lokalizaciju, veličinu tumora i vrstu operativnog zahvata. Prema lokalizaciji tumora, naj-

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češće izvedena operacija bila je prednja resekcija rektuma (60,7% u odnosu na 59%). Nije bilo slučajeva sa pozitivnom distalnom linijom resekcije. Prosečno rastojanje tumora od proksimalne linije resekcije na fiksiranom preparatu bilo je 100 mm u odnosu na 120 mm, sa statistički značajnom razlikom ($p < 0,001$). Udaljenost od distalne linije resekcije bila je bez razlike, 40 mm u obe grupe ($p = 0,143$). Nađana je pozitivna cirkumferentna resekciona linija kod dva bolesnika u laparoskopskoj grupi (7,7%), a kod tri bolesnika u grupi operisanih otvorenom metodom (8,8%). Prosečan broj uklonjenih limfnih čvorova iznosio je 15 u laparoskopskoj grupi i 16 u grupi operisanoj otvorenim pristupom. Dužina boravka u bolnici kod bolesnika operisanih laparoskopskim pristupom bila je kraća, što je bilo visoko statistički značajno. U pogledu postoperativnih komplikacija, nije utvrđena značajna razlika između grupa. Ukupni postoperativni morbiditet iznosio je 18% prema 21,3%. **Zaključak.** Laparoskopskim pristupom je moguće obezbediti sve parametre onkološke radikalnosti jednako kao i u otvorenoj hirurgiji karcinoma kolona i rektuma.

Ključne reči:
kolon, neoplazme; laparoskopija; laparotomija; neoplazme, rektum; hirurgija, operativna, procedure; lečenje, ishod.

Introduction

Traditionally, surgical management of colon cancer entails removal of the tumor together with potentially metastatic nodes. Standard oncological principle involves removal of central lymph nodes with a negative line of resection.

Recently, concept of complete mesocolic excision (CME) [1] has been adopted as a more radical approach to the treatment of colon carcinoma. Dissection along embryonic layers (avoiding an incomplete excision, i.e. damaged mesentery) ensures complete removal of lymph nodes and nervous tissue found in the drainage area of tumor. High vascular tie, removal of specimen with intact fascia and peritoneum, and adequate distal and proximal resection margins with maximum number of lymph nodes show better results in terms of local recurrence and survival in comparison to standard colectomy [2, 3]. Patients at the stage II of the disease can also have a better prognosis with wider excision of mesentery with as many negative lymph nodes as possible [4]. Implementation of this technique, ensuring specimen with intact mesocolic fascia, is associated with 15% better five-year survival compared to specimens where there are defects in the mesocolon. The percentage of survival is even more pronounced in the stage III, up to 27% [5].

By the seventies of the last century, surgical technique of blind dissection along the presacral fascia was associated with frequent injuries of presacral venous plexus and conical narrowing of specimen. Lateral excision was generally insufficient with a high percentage of local recurrence, until the introduction concept of total mesorectal excision (TME) 1982 [6].

The TME concept involves complete removal of the tumor with mesorectal fascia with lymph nodes, lymphatics and blood vessels of the rectum. Resection is considered radical when circumferential, proximal and distal resection margins are without presence of tumor cells. If circumferential resection margin (CRM) is positive, local recurrence is increased three to four times [7]. By adopting the TME technique, rate of local recurrence was decreased to 4% [8]. The concept of TME remains the gold standard in rectal cancer surgery.

From oncological aspect, since the first recorded colon resection [9], laparoscopic colorectal surgery is still controversial. Several randomized multicenter studies have shown that there is no significant difference between laparoscopic and open colon surgery when discussing the parameters of radicality: proximal, distal and radial resection margins, and the number of removed lymph nodes [10, 11].

In laparoscopic surgery for rectal cancer, results of the first randomized trials are promising. The CRM status, quality of total mesorectal excision and the number of removed lymph nodes did not show a significant difference between open and laparoscopic surgery [12, 13]. However, long-term results are still missing in order to definitively determine routine use of laparoscopic surgery in this group of patients.

Analyzing the parameters of radical resection, the aim of this study was to determine whether laparoscopic surgery meets oncological principles as open surgery of colon and rectum carcinoma.

Methods

The study conducted at the Clinical Hospital Center „Zvezdara“, Belgrade included 122 patients with adenocarcinoma of the cecum, ascending, descending, sigmoid colon and adenocarcinoma of the rectum. Among all of the patients, 61 were operated by laparoscopic and 61 by open approach.

Mechanical preparation of intestine, antibiotic prophylaxis and prophylaxis of deep venous thrombosis were carried out by standard procedures, regardless of the applied method of operative treatment (laparoscopic or open surgery).

Inclusion criteria were: patients without distant metastases with solitary adenocarcinoma of the cecum, ascending, descending and sigmoid colon and patients with solitary adenocarcinoma of the rectum.

Exclusion criteria included: T4 tumors of the colon and rectum, tumors that are not adenocarcinomas, patients with clinical presentation of acute intestinal obstruction, preoperatively established metastases, absolute contraindication for general anesthesia or prolonged pneumoperitoneum.

In the colon surgery we analyzed proximal and distal resection margins, and the number of removed lymph nodes, while in the rectal surgery we analyzed: proximal, distal and circumferential resection margins, and the number of removed lymph nodes.

The following surgical procedures were performed: proximal ligation of a blood vessel that supplies the tumor or multiple blood vessels if the arterial distribution is such that tumor is at an equal distance between two blood vessels, appropriate proximal and distal resection lines (minimum 5-10 cm), and adequate lymphadenectomy [14]; partial mesorectal excision for tumors of the upper third of rectum (distal line of resection at least 5 cm); TME was performed for tumors of middle and lower third of rectum (distal line of resection 1–2 cm); ligation of the inferior mesenteric artery at the origin (1 cm from the aorta or after the separation of the left colic artery [15].

Microscopic analyses of specimens were determined by standard hematoxylin-eosin method by a pathologist at the University Clinical Center Zvezdara.

Results were presented as count (%), means ± standard deviation or median (25th-75th percentile) depending on data type and distribution. Groups were compared using parametric (*t*-test) and nonparametric (χ^2, Mann-Whitney *U* test, Fisher's exact test) tests. All *p* values less than 0.05 were considered significant. All data were analyzed using SPSS 20.0 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.).

Results

A total of 122 patients entered the study. The average age of patients was 67.3 ± 10.3 years. The youngest patient was 27 years old and the oldest one was 87 years old. Among all the patients, 77 (63.1%) were male and 45 (36.9%) female. Patients were divided into two equal groups, 61 patients in each (Table 1).

Both groups were comparable in age, sex, American Society of Anesthesiologists (ASA) score, tumor localization, tumor size, and type of surgical operation performed.

The ASA status of patients in both groups did not differ. In both groups, most frequent localization of the tumor was the rectum (39.3% vs. 52.5%). Only one patient (open technique) received neoadjuvant therapy (Table 1).

In both groups there was no statistically significant difference in relation to the type of surgical procedure (Table 2). According to the localization of the tumor, the most commonly performed operation was anterior resection of the rectum (60.7% vs. 59%). There was no case of the tumor involvement of the distal margin. Average proximal distance from the tumor on the fixed specimen was 100 vs. 120 mm with statistical significance ($p < 0.001$). Distal margins were not significantly different (40 mm in both groups) ($p = 0.143$). We had in two cases CRM of 1 mm (7.7%) in the laparoscopic group, and in three cases operated on conventionally, CRM was 1 mm (8.8%). The average number of removed lymph nodes was 15 vs. 16. The tumor size, stage distribution, and histological typing were similar in both groups. According to the TNM classification, in the laparoscopic group, 15 (24.6%) patients was in the stage I, 20 (32.8%) in the stage II, and 26 (42.6%) in the stage III. In the open surgicalgroup 7 (11.5%) patients were in the stage I, 20 (32.8%) in the stage II, and 34 (55.7%) in the stage III.

We had two conversions (3.27%) to laparotomy due to technical difficulties (Table 3). Some patients already had previous abdominal operations (13.1% of patients operated laparoscopically, and 9.8% with open surgery). Length of hospital stay for patients assigned to laparoscopic surgery was shorter than for patients of the open surgery group. This difference was highly statistically significant. The mean postoperative stay was 9 (range 5-58) vs. 12 (range 5-37) days, respectively. The prolonged hospital stay of 58 days was observed in one patient with high stoma output syndrome with consequent renal insufficiency after laparoscopic low rectal resection.

Table 1
Preoperative characteristics of patients with either laparoscopic or open approach

Parameter	Procedure		*p*
	laparoscopic	open	
Age (years), mean ± SD	68.0 ± 10.7	66.1 ± 9.9	0.448[a]
Sex (man), n (%)	41 (67.2)	36 (59.0)	0.348[b]
ASA, n (%)			
1	6 (9.8)	0	0.267[c]
2	28 (45.9)	31 (50.8)	
3	25 (41.0)	27 (44.3)	
4	2 (3.3)	3 (4.9)	
Localization of carcinoma, n (%)			
right colon	17 (27.9)	16 (26.2)	0.265[b]
left colon	20 (32.8)	13 (21.3)	
rectum	24 (39.3)	32 (52.5)	
Neoadjuvant therapy, n	0	1	–
Previous operations, n (%)	8 (13.1)	6 (9.8)	0.570[b]

ASA - American Society of Anesthesiologists; SD – standard deviation.
[a]*t* test; [b]Pearson χ^2 test; [c]Mann-Whitney *U* test.

Table 2

Operative characteristics of patients

Parameter	Procedure		*p*
	laparoscopic	open	
Operative procedure, n (%)			
subtotal colectomy	1 (1.6)	2 (3.3)	
right hemicolectomy	16 (26.2)	16 (26.2)	
left hemicolectomy	3 (4.9)	4 (6.6)	1.000[b]
resection of sigmoid colon	4 (6.6)	3 (4.9)	
rectal resection	37 (60.7)	36 (59.0)	
Anastomosis, n (%)			
stapler	39 (63.9)	31 (50.8)	0.290[b]
suture	17 (27.9)	21 (34.4)	
Tumor dimension (mm), mean ± SD	42.9 ± 16.6	45.6 ± 15.0	0.350[a]
Proximal resection line (mm), average (min-max)	100 (80–130)	120 (100–170)	< 0.001[c]
Distal resection line (mm), average (min-max)	40 (30–65)	40 (30–120)	0.143[c]
[1]CRM (mm), average (min-max)	17 (6–20)	12 (5–20)	0.697[d]
Positive, n (%)	2 (7.7)	3 (8.8)	1.000[b]
Number of harvested lymph nodes, average (min-max)	15 (2–65)	16 (3–42)	0.756[d]
Tumor differentiation, n (%)			
G1	5 (8.2)	1 (1.6)	
G2	52 (85.2)	53 (86.9)	0.092[c]
G3	4 (6.6)	7 (11.5)	
pT stage, n (%)			
I	7 (11.5)	1 (1.6)	
II	7 (11.5)	7 (11.5)	0.009[c]
III	41 (67.2)	47 (77.0)	
IV	2 (3.3)	6 (9.8)	
pN stage, n (%)			
0	35 (57.4)	27 (44.3)	
1	15 (24.6)	22 (36.1)	0.232[c]
2	11 (18.0)	12 (19.7)	
pM 1 stage, n	0	1	-
Stage of disease, n (%)			
I	15 (24.6)	7 (11.5)	
II	20 (32.8)	20 (32.8)	0.070[c]
III	26 (42.6)	34 (55.7)	

[1]CRM – circumferential resection margia: 1 mm was considered as positive; SD – standard deviation; pT – primary tumor; pN – regional lymph nodes; pM – distant metastasis; min – minimum; max – maximum.
[a]*t*-test; [b]Pearson χ^2 test/Fisher's exact test; [c]Mann-Whitney *U* test.

Table 3

Postoperative characteristics of patients

Parameter	Procedure		*p*
	laparoscopic	open	
Operative complications, n	0	1	
Conversion to laparotomy, n	2	0	
Length of hospital stay (days), median (min-max)	9 (5–58)	12 (5–37)	0.002[d]
Postoperative complications, n (%)			
no	50 (82)	48 (78.7)	
surgical	7 (11.5)	7 (11.5)	0.802[b]
non-surgical	4 (6.6)	6 (9.8)	
Reoperation, n (%)	4 (6.6)	2 (3.3)	0.680[b]
Death, n	1	1	
Rehospitalization, n (%)	2 (3.3%)	0	0.496[b]
Complications, n			
significant hemorrhage	3	0	0.244[e]
ileus	1	1	1.000[e]
anastomotic dehiscence	1	3	0.619[e]
wound infection	2	3	1.000[e]
clostridial colitis	1	2	1.000[e]
cardiac insufficiency	1	1	1.000[e]
renal insufficiency	1	0	0.496[e]
pulmonary insufficiency	0	1	1.000[e]

Among all of the patients, 61 were operated by laparoscopic and 61 by open approach.

Concerning postoperative complications, no significant difference was found between groups. The overall postoperative morbidity was 18% vs. 21.3%. Although reoperation was necessary in both groups of patients (6.6% vs. 3.3%), there was no statistically significant difference between groups ($p = 0.680$). Three patients operated by laparoscopy had postoperative bleeding and all of them were reoperated. There was one case of prolonged postoperative ileus in the laparoscopic group, solved surgically. In the open surgery group we reoperated two patients due to medically unresolved ileus and anastomotic leak. There were two infections of the mini-laparotomy incision site vs. three wound infections in the open surgery group. Rehospitalization was necessary in two patients after laparoscopic surgery, which was close to statistical significance ($p = 0.496$). The cause of rehospitalization was dehydration.

Overall anastomotic leakage rate was low in both groups, 1.64% vs. 4.91%. There was one case of anastomotic leakage in a patient with laparoscopic anterior rectal resection, and in three patients in the open surgery group (one with rectal resection and two with colon resection).

There was one death recorded in the laparoscopic group, due to cardiopulmonary complications after reoperation, and one in the open surgery group in case of respiratory failure.

Discussion

Open colectomy has been the standard treatment for colon cancer patients in the past 100 years. From perineal excision and first successful radical surgical treatment of rectal cancer reported by Miles in 1908 we are witnessing the great progress of surgery during the last century [16]. Over the last two decades, laparoscopic approach changed surgical treatments for colorectal cancers. At beginning, there was a lot of controversies in laparoscopic surgery for colorectal cancer. Several reports of early wound recurrence raised concerns about validity of this approach [17, 18]. Undoubtedly, less pain, shorter recovery, and quicker return to baseline functions are well known advantages of laparoscopic approach but concerns about oncological adequacy are still present. Recently, several randomized multicenter studies have shown that there is no significant difference between laparoscopic and open colorectal surgery regarding to parameters of radicality: proximal, distal and radial lines of resection, and number of removed lymph nodes [10, 11].

In our study, no differences were recorded between laparoscopic and open surgery with respect to tumor and nodal status, and short-term endpoints.

Concerning histopathological results of specimens, we can conclude that laparoscopic approach provides cancer clearance which is comparable to that of conventional surgery. In the present series there were no cases of the tumor involvement of the proximal or distal margins. Korolija et al. [19] showed a statistically significant difference in the average distal margin in a meta-analysis of 16 comparative series, 46 mm by the laparoscopic approach and 53 mm with the open approach. Schwenk et al. [20] found no difference in resection margins between two groups, what we confirmed in our study. For patients undergoing laparoscopic anterior resection for rectal cancer, the positivity rates of surgical CRMs were also similar between the two treatment groups.

Guillou et al. [11] noted positive CRMs in 12% of patients after laparoscopic anterior resection for cancer whereas only 6% of patients after open surgery had positive margins. Meta-analysis of Arezzo et al. [21] showed us that randomized-controlled trials reported a positive circumferential margin in 7.9 % of patients who underwent laparoscopic and 6.9 % of those undergoing open surgery. Data from the non-randomized-controlled trials reported a positive circumferential margin in 8.0 % vs. 12.7 % of patients. Using 1 mm margin as positive CRM, our results (7.7% vs. 8.8%) were without statistical differences between groups and comparable with so far published results in the literature [22-24].

On average, we removed fifteen lymph nodes per patient, with no significant differences between two groups, and it was also more than recommended to ensure radical resection [25]. Two prospective randomized trials from Europe (Barcelona, Spain [26], and Colon Cancer Laparoscopic or Open Resection (COLOR) trial [27]) demonstrated an equivalent number of lymph nodes retrieved from both groups.

Early randomized controlled trials for colorectal cancer published high conversion rates, up to 29%, with participating surgeons who already had 20 laparoscopic procedures [27, 28].

Meta-analysis by Noel et al. [29] reviewing all clinical studies published between 1994, and 2005, confirmed better conversion rates for malignancy, estimated at 14.8%. In our series, only two patients (3.27%) we had to convert to open surgery. The reason for such a low rate of conversion could be that all laparoscopic operations were performed by a surgeon who already has experience in the field of colorectal surgery and laparoscopy.

Although Stevenson et al. [30] have found no differences between the length of hospital stay, other studies [13, 31-33] have shown shorter hospital stay in laparoscopic surgeries of this type, which is confirmed by our results with high statistical significance ($p = 0.002$). Median hospital stays (9 vs. 12 days) in our study coincides with the results of Braga et al. [34] study.

Overall postoperative morbidity was 18% vs. 21.3% that is slightly lower than in published series of the Clinical Outcomes of Surgical Therapy (Cost) study [28] (21% vs. 20%) and lower than in the Medical Research Council Conerntional versus Laparoscopic-Assisted Surgery in Colorectal Cancer (MRC CLASICC) trial [11] (29% vs. 31%). Whereas overall anastomotic leakage rate was low, it was higher in the open group, 4.91% vs. 1.64%. For rectal resections, rate of leakage (2.7%) was the same in both groups, which was lower than Guillou et al. [11] reported. For colon resections in laparoscopic group we did not have clinical manifestations of anastomotic dehiscence.

In-hospital mortality also was without statistical difference in both groups (1.63%), which confirms the short-term clinical safety of the laparoscopic approach in our institution.

Conclusion

Based on our results, we can conclude that laparoscopic approach in the treatment of colorectal cancer provides valid oncological resection as the open surgery does.

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