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**The importance of laparoscopic surgery for early postoperative course in patients with colorectal carcinoma**

Значај лапароскопске хирургије за рани постоперативни ток пацијената са колоректалним карциномом

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## The importance of laparoscopic surgery for early postoperative course in patients with colorectal carcinoma

Значај лапароскопске хирургије за рани постоперативни ток пацијената са колоректалним карциномом

### SUMMARY

**Introduction/Objective** The aim of our study was to compare early postoperative recovery in patients operated using laparoscopically assisted and open method in colorectal carcinoma surgery.

**Methods** The study involved 60 patients, that were divided into two groups of 30 patients treated by open or laparoscopically assisted colorectal surgery. Three groups of factors were collected and analyzed for all patients. The first group of factors: age, sex, ASA score, preoperative hemoglobin, localization. The second group: intraoperative complications, the duration of operations, blood and blood derivatives compensation. The third group: complications, length of stay in intensive care, rate of peristaltic establishment and the time needed for unobstructed oral intake, number of hospitalization days, analgesic use and verticalization time.

**Results:** The patients who underwent laparoscopic-assisted surgery showed significant advantages in early postoperative recovery compared with those who underwent open surgery. In terms of the number of postoperative days of hospitalization ( $p < 0,001$ ), the duration of the operation ( $p < 0,001$ ), the day of establishment of peristalsis ( $p = 0,009$ ) and the day of establishment of unobstructed oral intake ( $p < 0,001$ ), the time of verticalization of patients ( $p = 0,001$ ), the use of analgesics ( $p < 0,001$ ).

**Conclusions:** Laparoscopically assisted surgery has an advantage over open surgery colorectal cancer, as regards of early postoperative recovery of the patient.

**Keywords:** laparoscopic colorectal surgery; open colorectal surgery; colorectal cancer

### САЖЕТАК

**Увод/циљ** Циљ наше студије био је поређење раног постоперативног опоравка код пацијената оперисаних лапароскопски асистираним и отвореном методом код преоперативно хистопатолошки дијагностикованог колоректалног карцинома.

**Метод** У истраживању је учествовало 60 пацијената са колоректалним карцином, који су подељени у две групе од 30 пацијената лечених отвореним или лапароскопским путем. Три групе фактора су прикупљене и анализирани за све пацијенте. Прва група фактора били су: старост, пол, ASA оцена, преоперативни хемоглобин, локализација тумора. Друга група параметра су: интраоперативне компликације, трајање операције, надокнада крви и крвних деривата. Трећа група били су: постоперативне компликације, дужина боравка на интензивној нези, време отпочињања перисталтике и пер оралног уноса, дужина хоспитализације, употреба аналгетика и време вертикализације.

**Резултати** Пацијенти који су били подвргнути лапароскопским операцијама показали су значајне предности у раном постоперативном опоравку у поређењу с онима који су били подвргнути отвореној операцији. У погледу броја постоперативних дана хоспитализације ( $p < 0,001$ ), трајања операције ( $p < 0,001$ ), дана успостављања перисталтике ( $p = 0,009$ ) и дана успостављања несметаног оралног уноса ( $p < 0,001$ ), време вертикације пацијената ( $p = 0,001$ ) и употребе аналгетика ( $p < 0,001$ ).

**Закључак** На основу наших резултата може се закључити да лапароскопска хирургија карцинома колоректума има предност у односу на отворени оперативни приступ, што се тиче раног постоперативног опоравка пацијента.

**Кључне речи:** лапароскопска колоректална хирургија; отворена колоректална хирургија; колоректални карцином

## INTRODUCTION

Colorectal cancer is the third most common cancer in men (746,000 patients per year, 10% of total cancer patients) and second most prevalent in women (614,000 patients per year, 9,2% of total cancer patients). It is represented in 8.5% of all patients with malignant tumors

in the world [1]. With continuous improvement of modern medicine and technology, the aims are set to faster recovery time, as well as the reduction of postoperative morbidity and mortality.

Laparoscopic colorectal surgery had been routinely performed by the surgeons of the Department for General Surgery, Clinical Hospital Center of Zemun since 2013. The aim of our study was to compare early postoperative recovery in patients treated with laparoscopically assisted and classical-open method in colorectal cancer surgery.

## METHODS

The study was performed as a clinical retrospective study. This study included 60 patients who underwent elective laparoscopic assisted or open colorectal surgery at the Clinic for Surgery, Clinical Hospital Center of Zemun in Belgrade from January 2013 to September 2016. The study involved 60 patients with acceptable general operability and diagnostics verified malignant colorectal neoplasm. Patients were divided into two groups, each of 30 patients: first group- patients treated by open colorectal surgery; second group- patients undergoing laparoscopically-assisted colorectal surgery.

Three groups of factors were analyzed for all patients. The first group of factors was known preoperatively: age, gender, ASA score, preoperative values of hemoglobin and localization. Second group of factors was known intraoperatively: we analyzed the potential differences of intraoperative complications, the duration of operations, blood and blood derivatives compensation. The third group of factors that were known postoperatively: complications, length of stay in intensive care, rate of peristaltic establishment and the time needed for unobstructed oral intake, number of hospitalization days, analgesic use and verticalization time. The criteria for patient involvement in the study for both groups were as

follows: patients with histopathologically diagnosed colorectal cancer, both sexes, age over 18 years, acceptable general operability, written consent for operative treatment.

Indications for surgical treatment were based on the guidelines issued by the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) [2]. Preoperatively, all patients were prepared in terms of complete diagnostics for diagnosis of colorectal malignancies. A colonoscopy was performed with biopsy and pathohistological analysis of the material, analysis of blood count and biochemistry, blood group. Then supplementary diagnostic methods in the form of MSCT/MRI abdomen and pelvis, X-ray of chest, due to preoperative determination of disease stage. Immediately the day before surgery patients were discontinued oral administration, fluid reimbursement by infusion was administered in the form of solutions 0.9% NaCl, Ringer, Hartman or 5% Glucose solution. Patients were preoperatively administered an antibiotic in the form of cephalosporins of II / III generation and metronidazole, as well as mandatory thromboembolic prophylaxis. Patients were operated on a regular operating program - electively in general endotracheal anesthesia. The following details of the surgical procedure were recorded in all patients: duration of operation, amount of homologous blood transfused. Transfusion of blood products in the perioperative period was based on the hemoglobin level 80 g/L or on an individual basis according to the clinical condition. All patients were treated on a strictly controlled protocol with regard to analgesic administration, feeding, and postoperative care. Postoperative recovery of bowel function was evaluated by first flatus and bowel movement. Postoperatively, patients were transferred to the intensive care unit and then as needed transferred to the Department of General Surgery. Any anastomotic dehiscence with clinical and/or radiologic evidence has been considered. Patients were discharged after meeting the following conditions: bowel movement and full recovery of both ambulation and oral food

intake. Follow-up for infectious and noninfectious complications was carried out for 30 days after hospital discharge by weekly office visits.

The data required for this study were taken from the protocol of surgical treatment, patient medical history, therapy list of the patients, anesthesiology lists conducting surgical treatment and pathologist reports. All data were grouped into two tables, which were subsequently used for statistical purposes processing. The first table was patients operated on by open surgical technique, the second the table is patients operated on by a laparoscopically assisted surgical technique.

Descriptive and analytical statistical methods were used in this study. Of the descriptive ones used were: absolute and relative numbers (n, %), measures of central tendency (arithmetic mean, median), dispersion measures (standard deviation, interval of variation). Of the analytical statistical methods, the difference tests were used: parametric (t test), non-parametric (Hi-square test, Fisher's exact probability test, Mann-Whitney U test). The choice of test to test the difference depended on the data type and distribution.

Parametric methods were used in a situation where the distribution was normal, while non-parametric ones were used in a situation where the distribution is not normal. The normality of the distribution was examined on the basis of descriptive ones parameters, normality distribution tests (Kolmogorov-Smirnov and Shapiro-Wilks test) and graphical methods (histogram, boxplot, QQ plot). The results are presented in tables and graphs. All data were processed in SPSS 20.0 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp. ) software package.

The study was done in accordance with the standards of the institutional committee on ethics.

## RESULTS

The mean age of the patients was 67.5 years. With the oldest patient in both groups having 86 years, while the youngest patient was 25 years old and underwent open surgery.

There was no statistically significant difference between the groups ( $t = -0.697$ ;  $p = 0.489$ ).

In the laparoscopic group of patients, 14 men and 16 women were represented. In the open patient group, 19 men and 11 women were represented. There was no statistically significant difference between the groups ( $X^2 = 1.684$ ;  $p = 0.194$ ). The third group of ASA score patients was the highest in both groups, in as much as 68%. There was no statistically significant difference between the groups ( $Z = -1.695$ ;  $p = 0.090$ ). The mean hemoglobin in both groups was 126. There was no statistically significant difference between the groups ( $t = 0.050$ ;  $p = 0.960$ ). In laparoscopic group, the largest percentage of malignancy was present in the region of sigmoid colon with 36.7%, while in the open group of the patient the largest percentage of malignancy were in the area of the proximal third of the rectum with 43.3%. In laparoscopic group the rectum was represented in 36%. All patients had a diagnosed colorectal adenocarcinoma.

In the intraoperative group of factors, there were no significant intraoperative complications of the examined patient groups such as abundant abdominal bleeding and intraoperative lesions of surrounding organs. The average operative time in the open group was 120 minutes, while in the laparoscopic group was 156 minutes. The duration of laparoscopic surgery is statistically significantly longer than open surgery group ( $t = -4.783$ ;  $p < 0.001$ ). (Table 1.)

In the open group, blood transfusion was administered in 9 patients. In the laparoscopic group, blood transfusion was administered in 10 patients. Intraoperatively in the laparoscopic group was administered in 2 patients one dose of blood, while in the open group

in 2 patients were administered one dose of blood and in one patient 2 doses of blood.

Postoperatively, in the laparoscopic group, 4 patients were administered one dose of blood each, and 3 patients with two doses of blood. In the open group, 2 patients were administered a single dose of blood, in 3 patients with 2 doses of blood. There was no statistically significant difference ( $X^2 = 0.077$ ;  $p = 0.781$ ). (Table 2.)

In the second group of factors, by analyzing postoperative complications in the two observed groups, there were no statistically significant difference between the groups ( $X^2 = 0$ ;  $p = 1,000$ ). There were two lethal outcomes in the laparoscopic group and one in the open group. Two patients in the laparoscopic group and three patients in the open group had anastomosis dehiscence ( $X^2 = 0.218$ ;  $p = 1.000$ ). In the laparoscopic group of patients, both dehiscence were treated by reoperation. One dehiscence in patients of the laparoscopic group was due to increased bleeding from stapler anastomosis. In the classic group, two dehiscence were treated by reoperation, while one was treated conservatively. Postoperative intraabdominal hemorrhage was verified in the laparoscopic group of patients. In one case it was treated conservatively, while in another it was treated by reoperation. In the laparoscopic group subcutaneous emphysema was verified in one patient, was spontaneously resolved. In the classic patient group one patient had wound infection, as well as one dehiscence of wound, which were treated with suture. In the laparoscopic group of patients, a complication of necrotizing fasciitis was verified, which led to a lethal outcome. Clostridial intestinal infection in the form of pseudomembranous colitis has been verified in open group in one patient.

Two urinary retention rates were verified in the open and one in the laparoscopic group of patients. (Table 3.)

There was no statistically significant difference between the groups in length of stay in intensive care unit ( $Z = -1,466$ ;  $p = 0.143$ ). There is a difference, which is not statistically

significant, patients in the laparoscopic group averaged stay in ICU 1.77 days, while the classic group patients 1.93 days. A statistically significant ( $Z = -2.630$ ;  $p = 0.009$ ) earlier establishment of peristalsis was in a group of laparoscopically operated patients. Peristalsis established averaged 1.93 days in the laparoscopic group while in the open group established an average of 2.47 days. There is a statistically significant difference in the rate of establishment of undisturbed oral intake ( $Z = -4.399$ ;  $p < 0.001$ ), the average of the second postoperative day in our study in the laparoscopic group, while in the open group, a third postoperative day. In the laparoscopic group, an unhindered oral intake was established in 7 patients first postoperative day, while in the open group of patients unhindered oral intake was not established before the second postoperative day. Patients in both groups received a stool on average after the fourth postoperative day ( $Z = -0.811$ ;  $p = 0.418$ ). Patients of the laparoscopic group were statistically significantly ( $Z = -4.607$ ;  $p < 0.001$ ) shorter hospitalized postoperatively relative to open group of patients. In the laparoscopic group were hospitalized for 5 days on average. While in the open group were hospitalized on average for 9 days.

First degree analgesics were on average administered in the laparoscopic group of patients in the amount of 12 doses, in patients undergoing open surgery, an average of 20 doses were administered. Second-degree analgesics are administered in less than one dose in a laparoscopic group of patients, and an average of 2.72 analgesics in the open group.

Analgesics of first ( $Z = -3.896$ ;  $p < 0.001$ ) and second degree ( $Z = -2.303$ ;  $p = 0.021$ ) were statistically significantly less ordained in the laparoscopic group of patients than in the classic group of patients. We found a statistically significant difference ( $Z = -3.341$ ;  $p = 0.001$ ) per patient verticalization day. Patients of the laparoscopic group were on average one day earlier verticalized than the open group. In the laparoscopic group, patients were average 2.9 days verticalized, whereas in the open group 3.9 days on average. The earliest verticalization in the



patients of the laparoscopic group was on the first postoperative day, while in the classic group on the second postoperative day.

## DISCUSSION

Following the introduction of laparoscopic cholecystectomy and its success in the treatment of gallbladder disease, laparoscopic surgery began to be applied in other fields as well. Open colorectal cancer surgery has been considered as the gold standard surgical treatment for this disease, in decades ago. With the advancement of technology and modern medicine, and the emergence and progression of minimally invasive surgery, it is becoming the next step in the treatment of this disease. With the advent of laparoscopic procedures in the treatment of colorectal cancer, numerous papers on this topic have been published. They showed an improvement in the quality of operative technique, and especially an advantage in the early postoperative recovery after this type of operative treatment [3, 4, 5]. The very beginning laparoscopically assisted colorectal surgery was promising, studies were done that confirmed that this type of surgery was less traumatic than open surgery. Leung in their study examined the systemic response of cytokines after laparoscopically assisted and classic resections of rectosigmoid carcinoma in 34 patients. They got results that shows that trauma of the tissue, which is reflected in the response of the cytokine, is smaller after laparoscopic surgery [6]. Theoretical advantage in colorectal cancer laparoscopic surgery over classic surgery is less painful operative wounds, and therefore less use of analgesics, earlier recovery of both bowel function and oral feeding, lower percentage infections of surgical wounds, faster mobilization and shorter hospitalization of patients. Numerous studies have been done and some are ongoing, examining whether laparoscopic surgery has grown open surgery and is it able to fulfil adequately oncological radicality, which is essentially of paramount importance. [6, 7, 8].

In this study, the objective benefit of early postoperative recovery were evaluated in the patient treated with laparoscopic surgery compared to classic colorectal surgery. We compared preoperative parameters between these two groups of patients, to show homogeneity in patient choice for both procedures. The mean age of the patients was 67.5 years. Regarding on some studies that dealt with comparison of laparoscopic and open colorectal surgery, we can see benefits in patients over 70 years treated with laparoscopic surgery, which shows a lower rate of postoperative mortality and morbidity. For Elderly patients of great importance is early mobilization, which is faster established in patients operated by laparoscopic surgery [9,10]. In several studies that analyzed risk factors for laparoscopic conversion colorectal surgery, one of the factors that proved statistically significant was obese male gender [11,12]. The third group of ASA patients had the highest prevalence in both groups, in as much as 68%. A multicenter randomized MRC CLASICC study concluded that the risk of conversion laparoscopic colorectal to open surgery rises in patients with ASA score over 3 [13] The ASA score is also an elevated independent predictor of postoperative mortality and morbidity [14]. Preoperative anemia is associated with poorer cancer response to therapy, poorer locoregional disease control, and overall shorter patient survival [14,15]. The intraoperative and postoperative parameters that we compared showed a number of similarities with world studies done on this topic. In this study, there is a statistically significant difference in the operating time. The shorter operating time was in open surgery. We find similar data in a number of randomized studies, but conclusion of this studies is that laparoscopic colectomies are associated with improved outcomes compared with open operations that do not exceed an operative time of 6 hours. [16,17]. Average operating time, in the open group was 120 minutes, while in the laparoscopic group, 156 minutes. Comparisons with other studies, we didn't find significant difference between the duration of laparoscopic surgery compared to our study. Nelson and al. in the study that

involved 435 laparoscopic colorectal operations, had an average operating time 150 minutes[17]. However, numerous studies indicate that continuous training of teams which are dealing with laparoscopic colorectal surgery, after multiple operations, reduces the duration of the operation [18,19]. So, we can expect in the future approximately the same duration of surgery for these two types of surgical treatment. In terms of reimbursement of blood and blood derivatives, we compared intraoperative and postoperative administrations of these products. The result of our research is that we did not get statistically significant difference in the ratio of the study groups. Our results coincide with a large meta-analysis of Japanese authors, who compared 12 papers - randomized studies - by comparison laparoscopic and classic colorectal surgery from 1990-2011. This study is included 4458 patients, also no statistically significant difference in reimbursement of blood transfusion [20]. It is considered that advantages of laparoscopic surgery is the optical magnification of the operative fields, therefore, making the operational field, substrate and surrounding structures more transparent. This one the fact should be in favor of lower intraoperative blood loss, and therefore reduced intraoperative and postoperative blood supply, which is confirmed by some papers [21]. Regarding to intraoperative and postoperative complication, there were no statistical difference. This result show that laparoscopic colorectal surgery is safe like open surgery. There is a difference, but no statistical, in stay in the intensive care unit. Patients in laparoscopic groups spent 1.77 days in the intensive care unit, while patients in open group spent 1.93 days. A statistically significant difference was verified regarding the number of postoperative days hospitalizations. We can agree with most studies that speak in favor of shorter postoperative hospitalizations in patients operated by laparoscopic surgery [22,23]. The mean length of hospital stay in the laparoscopic group was 5 days. Similar results shown the study conducted by Lacy et al. [24], where average hospital stay was 5.2 days Compared to some other randomized studies, there is the difference from the Braga et al study, where

the mean length of hospital stay was 7 days for colon and 10 days for rectum, and in relation to the COLOR study where patients were hospitalized on average 8.2 days [23,25]. By comparing the recovery of bowel function and recovery of oral food intake we found a statistically significant difference between the two groups. As one of the advantages of laparoscopic surgery is precisely in these two categories. Peristalsis was established in the laparoscopic group after 1.93 days, while in the open group was established after 2.47 days. In a study by Koch et al, the recovery of bowel function in the laparoscopic group is after 2.57 days [26]. The COLOR II study has a slightly different results, with 1103 patients operated laparoscopically, recovery of bowel function was on the second day [27]. On the average of the second postoperative day in our study, unobstructed oral intake was established in laparoscopic group, while in the open group was established on the third postoperative day. In the laparoscopic group, recovery of oral food intake on the first postoperative day was established in 7 patients, while in the classic group was not established before the second postoperative day. Compared to other studies, the time of recovery of oral food intake in the study by Lacy et al., the average intake was established on the second day, while at COLOR studies almost on the third day [23]. In the laparoscopic group, patients were verticalized on average 2.9 days, while in the classic group averaged 3.9 days. Most studies that compare laparoscopically assisted and classic colorectal cancer surgery, speaks in support of our results [23,25,26,27]. As well as most other studies and we have tried to express the degree of pain in patients through quantity dose of a particular analgesic that was administered. Pain management after colorectal surgery varies widely and predicts significant differences in patient-reported pain and clinical outcomes. Enhanced postoperative pain management requires dissemination of multimodal analgesia practices [28]. In our study the analgesics we used were divided into two groups. First-degree analgesics of non-opioid analgesics: metamizole-sodium, ketorolac, diclofenac, and second-degree analgesics of

opioid analgesics: tramadol. Studies showed statistically significant difference in the administration of second-degree analgesics, in terms of less administration analgesics in laparoscopic colorectal surgery.

## CONCLUSION

Laparoscopically assisted surgery has an advantage over classical surgery colorectal cancer, as regards of early postoperative recovery of the patient.

**Conflict of interest:** None declared.

Paper accepted

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**Table 1.** Intraoperative factors in analyzed groups

Intraoperative factors	Open group (n = 30)	Laparoscopic group (n = 30)	p
Operative time (minutes)	120	156	< 0.001
Complications Organ injury Massive hemorrhage	/	/	/
Blood transfusion one dose two doses	2 1	2	0.781



**Table 2.** Postoperative complications in analyzed groups

Complications postoperative	Open group (n = 30)	Laparoscopic group (n = 30)	p
Lethal outcome	1	2	1.000
Anastomotic dehiscences	3	2	
Intraabdominal hemorrhage	0	2	
Subcutaneous emphysema	0	1	
Wound infection	1	0	
Necrotizing fasciitis	0	1	
Clostridium difficult-colitis	1	0	
Urinary retention	2	1	

**Table 3.** Postoperative factors in analyzed groups

Postoperative factors	Open group (n = 30)	Laparoscopic group (n = 30)	p
ICU stay (days)	1.93	1.77	0.143
Peristalsis (days)	2.47	1.9	0.009
Oral intake (days)	3	2	< 0.001
Blood transfusion one dose	4	2	0.781
two doses	3	3	
Hospitalization (days)	9	5	< 0.001
Analgesics First degree	20	12	< 0.001
Second degree	2.72	< 1	< 0.001
Verticalization (days)	2.9	1.9	0.001