A single institutional experience in laparoscopic colorectal surgery: clinical and oncological outcomes over 10 years

Aleksandar Dermanović¹, Zoran Radovanović¹,², Dejan Lukić¹,², Mladen Đurić⁶, Danica Golijanin¹, Milan Ranisavljević¹,², Nemanja Petrović¹,²

SUMMARY
Introduction: The development of laparoscopic colorectal surgery began in 1991. Today, laparoscopic surgery presents standard approach in the surgical treatment of malignant colon and rectal diseases. Aim: Surgical and oncological outcomes and survival rates of laparoscopic colorectal surgery at the Oncology Institute of Vojvodina. Methods: Data were collected prospectively from 66 patients undergoing laparoscopic colorectal surgery between December 2009 and December 2019. Registered data included sex, age, surgical indication and type for the procedure, indication and reason for conversion to open surgery, operative time, performing temporary or permanent stoma, intraoperative bowel perforation, pathologic TNM grade, number of harvested lymph nodes, inclusion of positive resection margin, number of postoperative days at the hospital, postoperative complications, postoperative mortality, presence of distant metastases and survival rates. Results: Laparoscopic procedures were right hemicolectomy in 11/66 (16.7%), left hemicolectomy in 1/66 (1.5%), sigmoid colectomy in 19/66 (28.8%), high anterior rectal resection in 13/66 (19.7%), low anterior rectal resection in 12/66 (18.2%), abdominopерineal amputation of the rectum in 7/66 (10.6%), colectomy in 2/66 (3%) and proctocolectomy in 1/66 (1.5%) patient. The median follow-up was 37.5 months (range 6 to 128). The total number of surviving patients was 60 (90.9%). Conclusion: This study showed that laparoscopic colorectal surgery has good clinical and oncological outcomes. Keywords: laparoscopic colorectal surgery, colorectal cancer, surgical oncology

INTRODUCTION
Intensive technical and technological advances during the twentieth century resulted in rapid development of new surgery devices, endoscopy and laparoscopy which created a new modern field of surgery. The first descriptions of laparoscopic or minimally invasive surgery date back to the 1980s (1). The development of laparoscopic colorectal surgery began in 1991 when Jacobs et al. published the first batch of patients operated on by laparoscopic surgical technique. In the same year, Fowler et al. presented a laparoscopic resection of the sigmoid colon, then in 1994 Plasencia et al. resection of the sigmoid colon and low anterior resection of the rectum (2-5).

Following the publication of first studies, there was a period of non-acceptance of the laparoscopy in oncologic colorectal surgery due to the assumption of higher rates of disease relapse compared to conventional surgery. The assumptions of metastasis at the site of the placed ports, the long learning curve and the longer duration of surgery were also the main arguments against laparoscopy in colorectal cancer surgery (6-9).

In the past two decades, laparoscopic colorectal surgery has been proven to have numerous advantages over standard surgery. Less intraoperative blood loss, faster postoperative recovery, fewer complications, shorter hospital stay, better aesthetic result, faster return to work commitments with similar short and long-term clinical outcomes. The initial assumptions and arguments against laparoscopy in oncological colorectal surgery have been proven to be inaccurate in many studies (10-13).

Today, laparoscopic surgery presents the gold standard in the treatment of malignant colon and rectal diseases. With the further development of technology and the introduction of robotic colorectal surgery, a new era of modern surgical treatment begins (14,15).

Laparoscopic colorectal surgery was introduced at the Oncology Institute of Vojvodina in December 2009, when first laparoscopic procedure- a resection of the sigmoid colon due to cancer was performed. The purpose of this study was to analyze the clinical outcomes and survival rates of colorectal cancer patients operated by laparoscopic approach at the Oncology Institute of Vojvodina, Serbia.

METHODS
Data were collected prospectively from patients undergoing laparoscopic surgery for colon and rectal cancer or familial adenomatous colon polyposis (FAP) between December 2009 and December 2019. A total of 66 patients underwent laparoscopic surgery. Patient survival rate was measured in months from the surgery until death. Surviving patients were followed until June 2020.

Laparoscopic surgery was performed mainly in primary colon and rectal cancers and only in 2/66 (3%) cases due to FAP.

Registered data included sex, age, surgical indication and type for the procedure, indication and reason for conversion to open surgery, operative time, performing temporary or permanent stoma, intraoperative bowel perforation (IOP), pathologic TNM grade, number of harvested lymph nodes, inclusion of positive resection margin (CRM), number of postoperative days at the hospital, postoperative complications, postoperative mortality, presence of distant metastases and survival rates.

Preoperative diagnostics included digital rectal examination, colonoscopy with tumor biopsy, pelvic magnetic resonance imaging (MRI), abdominal computed tomography (CT). For each patient the treatment protocol was discussed by multidisciplinary team of oncologists, radiotherapists and surgeons. In some patients with locally advanced tumor a neoadjuvant therapy was applied according to the protocol which involved the Immediate technical and technological advances during the twentieth century resulted in rapid development of new surgery devices, endoscopy and laparoscopy which created a new modern field of surgery. The first descriptions of laparoscopic or minimally invasive surgery date back to the 1980s (1). The development of laparoscopic colorectal surgery began in 1991 when Jacobs et al. published the first batch of patients operated on by laparoscopic surgical technique. In the same year, Fowler et al. presented a laparoscopic resection of the sigmoid colon, then in 1994 Plasencia et al. resection of the sigmoid colon and low anterior resection of the rectum (2-5).

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Preoperative diagnostics included digital rectal examination, colonoscopy with tumor biopsy, pelvic magnetic resonance imaging (MRI), abdominal computed tomography (CT). For each patient the treatment protocol was discussed by multidisciplinary team of oncologists, radiotherapists and surgeons. In some patients with locally advanced tumor a neoadjuvant therapy was applied according to the protocol which involved the
application of fluorouracil and leucovorin (5 FU/LV) and radiotherapy at a dose of 50 Gy (25 x 2 Gy).

Patients were admitted to the hospital the day before the planned surgery. Preoperative preparation of patients included bowel cleansing, prevention of thrombosis with low molecular weight heparin and a single dose of dual antibiotic prophylaxis 30 min before surgery.

The surgeries performed were laparoscopic left and right hemicolectomy, sigmoid colectomy, high and low anterior rectal resection (HAR and LAR), abdominoperineal amputation of the rectum (APE), colectomy and proctocolectomy. The used approach during laparoscopic surgery was medial-to-lateral. The continuity of the digestive tract was established by extracorporeal intestinal anastomosis through mini laparotomy or double stapler technique. Permanent stoma procedure was performed in patients who underwent abdominoperineal amputation of the rectum (colostomy) and proctocolectomy (ileostomy), and in some patients a temporary colostomy was performed to protect the low colorectal anastomosis. In the second act, the continuity of the digestive tract was established with stoma closure.

In the early postoperative course, rapid mobilization and early translation to the oral diet were highly encouraged. Postoperative follow-up included regular routine medical check-ups, digital rectal examination, colonoscopy, tumor markers (CEA, CA 19-9), MRI of the abdomen and pelvis and CT of the chest. These follow-ups were every three months during the first year, twice per year for the second and third postoperative year and once annually after that.

This study showed overall characteristics and survival rates of patients who underwent laparoscopic surgery. The analysis and use of data for this retrospective study was approved by the Ethics Committee of the Oncology Institute of Vojvodina.

Data were presented as numbers with corresponding percentages, and the difference was determined by Chi-square and Fisher’s exact test. Patient age and number of lymphatic nodes were presented as mean values. Procedure time was presented as median (IKR 25-75 percentile). Overall survival rates were calculated using the Kaplan-Meier test. Patient age and number of lymphatic nodes were presented as median (IKR 25-75 percentile). Procedure time was presented as median (IKR 25-75 percentile). Overall survival rates were calculated using the Kaplan-Meier method. Follow-up time was measured as the time elapsed since the initial surgery. For statistical analysis SPSS Statistics 20 (IBM, USA) program was used.

RESULTS

Patient characteristics were shown in Table 1. In our study, 32/66 (48.5%) patients were male and 34 (51.5%) were female. The median age was 59 (range 18 to 84). The surgical indication in 64/66 (97%) of patients was colorectal adenocarcinoma, while in 2/66 (3%) cases the surgical indication was familial adenomatus polyposis and these were the youngest patients. The procedures performed by the laparoscopic method were right hemicolectomy in 11/66 (16.7%) patients, left hemicolectomy in 1/66 (1.5%), sigmoid colectomy in 19/66 (28.3%) patients, HAR in 13/66 (19.7%), LAR in 12/66 (18.2%), APE in 7/66 (10.6%), colectomy in 2/66 (3%) and proctocolectomy in 1/66 (1.5%) patient.

Neoadjuvant therapy received 3/66 (4.5%) patients, according to the long-course radiation protocol at a dose of 50 Gy (25 x 2 Gy) in combination with 5FU/LV. Out of all patients who received neoadjuvant therapy 2/3 had pT3 stage tumors that were operated laparoscopically using LAR and 1/3 of patients had pT4 stage of the tumors that were operated laparoscopically using APE.

Conversion rate to open surgery was 9.1% (6/66 patients). The reason for the conversion was the presence of intraperitoneal adhesions, tumor size and uncontrolled intraoperative bleeding. The median operative time (measured in minutes) was 150 min (range from 60 to 280). The longest surgical time was 280 min for laparoscopic proctocolectomy, and the shortest time was 60 min for laparoscopic right hemicolectomy. Overall 12/66 (18.2%) patients had postoperative complications. Surgical re-intervention due to intraperitoneal bleeding (one case) and anastomotic leak (two cases) was performed in 3/66 (4.5%) patients with open surgery. Prolonged postoperative fever had 1/66 (1.5%) patients, 1/66 (1.5%) patients had nausea and 2/66 (3%) patients had prolonged drainage. Postoperative wound infection was present in 3/66 (4.5%) patients. Enteroctaneous fistula was developed by 1/66 (1.5%) of the patients (operated by LAR) due to partial anastomotic leak which was treated conservatively. Ventral hernia was present in 1/66 (1.5%) patients. The mean duration of postoperative hospitalization was 6.69 days (range from 4 to 15; SD=2.227).

Intraoperative bowel perforation was present in 1/66 (1.5%) patients. Pathological report showed positive resection margin in 3/66 (4.5%) patients (R1 resection), of whom 1/66 (1.5%) had pT3 tumor stage after laparoscopic right hemicolectomy, 1/66 (1.5%) pT3 with laparoscopic LAR, and 1/66 (1.5%) patients had pT4 tumor stage after laparoscopic APE and who had IOP. In 95.5% of cases R0 resection was obtained. Histopathological T1 tumor stage was present in 10/66 (15.6%) patients, pT2 in 14/66 (21.9%) patients, pT3 in 38/66 (58.4%) and pT4 in 2/66 (3.1%) patients. In 43/66 (67.2%) patients histopathology verified N0 stage, N1 was present in 11/66 (17.2%) and N2 in 10/66 (15.6%) patients. The mean number of extracted lymphatic nodes was 16.95 (range from 6 to 41; SD=7.225). Stage M0 was present in 62/66 (96.9%) patients, 2/66 (3.1%) had M1, while 2/66 patients were not graded because they were operated on for FAP. Low-grade tumors were present in 59/66 (92.2%) and high-grade in 5/66 (7.8%) patients (Table 2).

Local recurrence was diagnosed in 3/66 (4.5%) patients and all had a positive resection margin with pT3 and pT4 stage tumors. Metastases were developed in 18/66 (28.1%) patients, of which 14/66 (21.9%) were...
present in the liver, 1/66 (1.5%) in the lungs, and 3/66 (4.5%) patients had both the liver and lung metastasis (Table 3).

The median follow-up was 37.50 months (range from 6 to 128). Total number of surviving patients was 60/66 (90.9%) (Figure 1). The highest survival rates were in patients operated on laparoscopic right hemicolec-tomy (p=0.007), sigmoid colectomy (p=0.003) and high anterior rectal resection (p=0.002), while all patients who had low anterior rectal resection have survived.

During follow-up 6/66 (9.1%) patients died. Of the deceased patients, 5 (83.3%) had pT3, and one (16.7%) had pT4 tumor stage that had a local recurrence. Patients with pT3 stage tumors had statistically significant low survival compared to patients with pT1 and pT2 tumors stage (p=0.000). All deceased patients had metastatic disease, 4 (66.7%) had solitary liver metastases, one (16.7%) had solitary lung metastases, and one (16.7%) had both liver and lung metastases.

**DISCUSSION**

As laparoscopic colorectal surgery evolved it has been accepted by a large number of surgeons and it was shown to have better short-term and similar long-term and oncological results compared to open surgery (16,17). Due to development of global technology surgery, which for many years has been based exclusively on classical open approaches, is also changing. With the introduction of laparoscopy in our hospital, we have gone a step further in surgery, although in many centers laparo-scopic colorectal surgery is being replaced by single-port, hand-assisted and robotic colorectal surgery (18-20).

Although laparoscopic colorectal surgery has become the standard in operative oncological treatment, open surgery still has its indications. Patient's preoperative staging, resectability and operative risk assessment are mandatory when deciding on a surgical approach. Oncological justified surgical resection is R0 resection. For locally advanced colorectal tumors where it is not possible to perform en-block (R0) resection by laparoscopy, an open surgical approach is an absolute indication (21).

In the meta-analysis of Hajibandeh et al. eight comparative studies were evaluated with a total of 1477 patients (626 with medial-to-lateral and 851 lateral-to-medial approach in laparoscopic colorectal surgery) (22). In the group with the medial-to-lateral approach, that we also practice, the total number of complications was 14.8%, but in our study it was 18.2%. Anatomotic leak in this meta-analysis was 2.5%, and 4.5% in our case. In the meta-analysis conversion to open surgery was 3.5%, the mean length of hospital stay was 9.3 days, and the mean number of lymph nodes removed was n=17.2 (22).

In our study, the conversion rate was 9.1%, median procedure time was 150 min, mean value of days of hospitalization was 6.89, and the number of removed lymph nodes was 16.95. From the above, we can conclude that although our sample had 66 patients compared to 626 in this meta-analysis, the results were similar.

In the study of Braga et al. a comparison of 26 patients operated using laparoscopic approach with 26 patients operated using open surgery due to colorectal pathology was made with the conclusion that there was no difference in oncological results between laparoscopic operations and open surgery for colorectal cancers and that postoperative recovery afterlaparoscopic surgery was faster (23). In this study conversion to

| Gender n (%) | Survivors1 | Died1 | Total2 | p* |
|-------------|------------|------|--------|---|
| Male        | 28 (87.5)  | 4 (12.5) | 32 (48.5) | 0.000 |
| Female      | 32 (84.1)  | 2 (5.9)  | 34 (51.5) | 0.000 |
| Total       | 60 (90.9)  | 6 (9.1)  | 66 (100)  | 0.000 |

| Age median (P25-P75) | Survivors1 | Died1 | Total2 | p* |
|----------------------|------------|------|--------|---|
| Cancer               | 58 (86.0)  | 6 (9.4)  | 64 (97.0) | 0.000 |
| FAP                  | 2 (100)    | 0 (0.0)  | 2 (3.0)  | 0.000 |

| Reason for surgery n (%) | Survivors1 | Died1 | Total2 | p* |
|--------------------------|------------|------|--------|---|
| Right hemicolectomy      | 10 (90.9)  | 1 (9.1)  | 11 (16.7) | 0.007 |
| Left hemicolectomy       | 1 (100)    | 0 (0.0)  | 1 (1.5)  | 0.003 |
| Sigmoid colectomy        | 16 (84.2)  | 3 (15.8) | 19 (28.8) | 0.002 |
| HARP                    | 12 (82.3)  | 1 (7.7)  | 13 (19.7) | 0.007 |
| LAR                     | 12 (100)   | 0 (0.0)  | 12 (18.2) | 0.059 |
| APE                     | 6 (85.7)   | 1 (14.3) | 7 (10.6)  | 0.000 |
| Colectomy               | 2 (100)    | 0 (0.0)  | 2 (3.0)  | 0.000 |
| Proctocolectomy         | 1 (100)    | 0 (0.0)  | 1 (1.5)  | 0.000 |

| Type of operation (%) | Survivors1 | Died1 | Total2 | p* |
|-----------------------|------------|------|--------|---|
| Operative time Median (P25-P75) | 150 (80-280) | 145 (80-180) | 150 (80-280) | 0.911 |

| Hospital day | Survivors1 | Died1 | Total2 | p* |
|--------------|------------|------|--------|---|
| Mean         | SD=2.102   | SD=2.714 | SD=2.227 | 0.179 |

† Percentage versus mortality; ‡ Percentage of total sample; & χ2 test and Fisher’s exact test; Bold values are statistically significant; FAP- familial adenomatous colon polyposis; HARP- high anterior rectal resection; LAR- low anterior rectal resection; APE- abdominopereineal amputation of the rectum

**Table 1. Patient and surgery characteristics**

| T stage n (%) | Survivors (n=60) | Died (n=6) | Total (N=66) | p* |
|--------------|-----------------|-----------|-------------|---|
| pT1          | 10 (17.2)       | 0 (0.0)   | 10 (15.6)   | 0.000 |
| pT2          | 14 (24.0)       | 0 (0.0)   | 14 (21.9)   | 0.035 |
| pT3          | 33 (55.9)       | 5 (83.3)  | 38 (59.4)   | 0.000 |
| pT4          | 1 (1.7)         | 1 (16.7)  | 2 (3.1)     | 0.058 |

| N stage n (%) | Survivors (n=60) | Died (n=6) | Total (N=66) | p* |
|---------------|-----------------|-----------|-------------|---|
| n0           | 41 (90.7)       | 3 (33.3)  | 43 (67.2)   | 0.000 |
| n1           | 9 (15.5)        | 2 (33.3)  | 11 (17.2)   | 0.035 |
| n2           | 8 (13.8)        | 2 (33.3)  | 10 (15.6)   | 0.000 |

| Lymphatic nodes Mean | Survivors (n=60) | Died (n=6) | Total (N=66) | p* |
|----------------------|-----------------|-----------|-------------|---|
| 17.63 (6-41)         | SD=7.138        | 10.17 (6-17) | SD=4.070   | 0.007 |

| M stage n (%) | Survivors (n=60) | Died (n=6) | Total (N=66) | p* |
|---------------|-----------------|-----------|-------------|---|
| M0           | 58 (100)        | 4 (66.7)  | 62 (99.9)   | 0.000 |
| M1           | 0 (0.0)         | 2 (33.3)  | 2 (3.1)     | 0.000 |

| Tumor differentiation n (%) | Survivors (n=60) | Died (n=6) | Total (N=66) | p* |
|------------------------------|-----------------|-----------|-------------|---|
| Low-grade                    | 54 (83.1)       | 5 (83.3)  | 59 (92.2)   | 0.000 |
| High-grade                   | 4 (6.9)         | 1 (16.7)  | 5 (7.8)     | 0.000 |

| Resection margin n (%) | Survivors (n=60) | Died (n=6) | Total (N=66) | p* |
|------------------------|-----------------|-----------|-------------|---|
| Positive – R1          | 0 (0.0)         | 3 (50.0)  | 3 (4.5)     | 0.000 |
| Negative – R0          | 60 (100)        | 3 (50.0)  | 63 (95.5)   | 0.000 |

| IOP n (%) | Survivors (n=60) | Died (n=6) | Total (N=66) | p* |
|-----------|-----------------|-----------|-------------|---|
| Yes       | 0 (0.0)         | 1 (16.7)  | 1 (1.5)     | 0.000 |
| No        | 60 (100)        | 5 (83.3)  | 65 (98.5)   | 0.000 |

† χ2 test and Fisher’s exact test; Bold values are statistically significant

**Table 2. Histopathological classification**

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open surgery was performed in 3.8% of cases, operative time was 190, the mean number of lymph nodes removed was 17 (SD = 9.76), and the mean hospital stay was 9.6 days; SD = 2.6. In our study conversion to open surgery was 4.5%, operative time 150 min, and mean of removed lymph nodes was 16.95 (SD = 7.22). In a meta-analysis by Dowson et al. laparoscopic and open colorectal surgery for postoperative quality of life were compared. The study reported outcomes for 3004 patients, of whom 1651 (50%) were from laparoscopic surgery. These results did not show advantage of laparoscopic surgery over open surgery (24). In an editorial by Coleman et al. 339 cases of laparoscopic colorectal surgery were presented, of which 268 of their own colon cancer patients (25). In this study conversion to open surgery was made in 7% of cases, while in our study it was 9.1% indicating good result concerning smaller number of patients.

Many countries have introduced mandatory laparoscopy training for surgeons. There are still indications for open surgery, but this percentage is much lower than before. It has been reported that more than 50% of operations in colorectal pathology can be started and completed with laparoscopic surgical technique (26,27). However, countries without operations in colorectal pathology can be started and completed with laparoscopic colorectal surgery (28). de'Angelis et al. compared 102 patients operated laparoscopically (LCRS) with 58 patients operated using robotic (RCRS) colorectal surgery (28).

No differences were found in postoperative morbidity, mortality, return to regular diet and length of hospital stay. Mean of operating time for LCRS compared to RCRS was 214.54 (SD = 42.73) versus 300.58 (SD = 142.5). Mean of hospital day was 14.78 (SD = 9.36) vs. 11.67 (SD = 8.17), and mean of removed lymph nodes was 17.97 (SD = 9.09) vs. 17.71 (SD = 9.25). Resection R0 was achieved in 95.3% of LCRS cases compared to 95.3% of RCRScases. Resection R1 was achieved in 4.7% vs. 4.7% cases, while local recurrence occurred in 7% vs. 6% of cases, respectively. The results of our study were very similar - R0 resection was achieved in 95.5%, R1 in 4.5%, and local recurrence in 4.5% of cases indicating very good results comparable to those from centers with advanced surgical technologies.

In conclusion, main limitations of this study were small number of analyzed patients. Our study showed that laparoscopic colorectal surgery has good clinical and oncological outcome. Based on our experience, the laparoscopic approach has an advantage over open surgery in resectable (R0) colorectal tumors. In cases when R0 resection cannot be performed, the method of choice is open surgery. The introduction of new technologies in colorectal cancer surgery is a great challenge for every surgeon. We will strive to increase the number of laparoscopic surgery cases in the future and to introduce the newest procedures into our surgical practice.

Declarations of Interests

Authors declare no conflicts of interest.

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