Nikola JANKULOVSKI¹ Svetozar ANTOVIC¹, Vladimir JOKSIMOVIC¹, Biljana KUZMANOVSKA²

PERIOPERATIVE OUTCOMES OF THE LAPAROSCOPIC TREATMENT FOR COLORECTAL CANCER AT THE CLINIC FOR DIGESTIVE SURGERY, SKOPJE IN A 5-YEAR INTERVAL

Abstract

Colorectal cancer (CRC) is the third leading cause of cancer related death in the world, and its incidence is rising in developing nations. Taking into account the increase in the incidence of this disease, the purpose of this review was to evaluate perioperative outcomes (in the first 30 days after surgery) for **laparoscopic treatment** of this malignancy, a treatment that is steadily becoming standard of patient care in the world.

Our review showed that at the Clinic for Digestive Surgery, from 2015 to 2019, 115 patients with colorectal cancer were treated laparoscopically. The figures show a growing trend during this period. 10% of all colorectal cancers in 2019 were completed laparoscopically. In most cases (88.7%) tumor staging was pT2 and pT3. Perioperative outcomes showed wound infection in 2 patients, pulmonary complications in 1, anastomotic leakage in 1, bleeding in 1 patient, no readmission, and no mortality. The rate of conversion to open access is 5.7%, the operating time was 198 minutes on average, the average number of hospital stays was 9 days, and the average number of extirpated lymph nodes 13. There was no need for blood transfusion.

¹ University Clinic for Digestive Surgery, Medical Faculty, University of Ss. Cyrill and Methodius, Skopje, R. North Macedonia

² University Clinic for Anesthesiology, Reanimatology and Intensive Care, Medical Faculty, University of Ss. Cyril and Methodius, Skopje, R. North Macedonia

Perioperative results for laparoscopic treatment of colorectal cancer at our institution show a low morbidity and mortality rate in these patients, with a clearly rising number in laparoscopically operated patients each year. Long term results are yet to be seen. Follow up with these patients will provide results later.

Key words: colorectal cancer, laparoscopy, outcomes

Introduction

CRC is the third most commonly diagnosed cancer in males and the second most in females. The global incidence of CRC in 2018 was 1.8 million new cases and nearly 860,000 deaths (World Health Organization GLOBOCAN database). Age-standardized (world) incidence rates per 100,000 of CRC in both sexes is 19.7: 23.7 in males, and 16.2 in females. Rates of colorectal cancer in younger patients have been increasing over the past few years, making this disease even more important to observe. Recent advances in screening for early detection and treatment have reduced CRC mortality in developed nations, despite the circumstances of growing incidence.

The emergence of laparoscopy has brought forth a revolution in the surgical approach to colonic resections for cancers. Laparoscopic colectomy was first established in 1991. Initially, it was not widely accepted as a cancer treatment because there were some technical difficulties (working in multiple intra-abdominal quadrants, ligation of vessels and re-establishment of intestinal continuity, as well as oncological concerns which included the retrieval of lymph nodes, surgical resection margin and survival results). These controversies died down as surgeons gained more experience as well as the technological progress of instrumentation.¹ Large prospective randomized trials comparing these two approaches of treatment (Lap vs Open) have found no significant differences between open and laparoscopic colectomy, with regards to the intraoperative or postoperative complications (perioperative mortality rates, readmission or reoperation rates, or rate of surgical wound recurrence). Also the results of oncologic outcomes (causespecific survival, disease recurrence, number of gathered lymph nodes), are likewise comparable.² Although laparoscopic surgery continues to be considered the foremost common approach for the treatment of colorectal cancer, new surgical technologies are emerging including transanal total mesorectal

excision, laparoscopic lateral pelvic lymphatic node tissue dissection and robotic surgery.

Implementing laparoscopic treatment for CRC is by no means an easy task for even experienced surgeons and hospitals. It involves a steep learning curve and requires a dedicated team that, with persistent endurance, will accumulate enough skills for a safe and quality laparoscopy. This is why perioperative outcomes are very important in assessing the quality of laparoscopy itself as a treatment method for this disease.

The aim of this study is not to compare laparoscopic with the open treatment of colorectal cancer, nor to establish which is better, since many studies have already addressed this issue. It is simply to show our ability to perform laparoscopy for colorectal cancer in our clinic and to show the perioperative results from it.

Materials and methods

Our paper represents a retrospective analysis of laparoscopic surgical treatment in patients with colorectal cancer who were operated on at the Clinic for Digestive Surgery, Skopje in the period from 2015 to 2019. The analysis covers the trend of the number of operated patients in the given period, the proportion of different surgical procedures, the relationship between laparoscopic and open access, the rates of perioperative morbidity and perioperative outcomes.

The incidence of patients with colorectal cancer in R.N. Macedonia is 25.7/100,000 inhabitants. The number of annual newly diagnosed cases is around 600, of which about 300-350 are surgically treated at the Clinic for Digestive Surgery in Skopje. Three-quarters of patients have advanced stages of the disease, at least stage III.

As a developing country, the first case of laparoscopic surgery at our Clinic coincides with the year when the world's first laparoscopic colectomy was performed, 1991. The first laparoscopic resection of the rectum in our country was performed in 2003.

The review of our data shows that in the period of 2015-2019, a total of 115 laparoscopic operations for colon and rectal cancer were performed at our Clinic. The numbers of laparoscopic treatment of the colon and rectum show a yearly upward trend. This trend has increased thus: 16 (2015),

18 (2016), 22 (2017), 30 (2018), 29 (2019). In 2019, 10% of all surgically treated patients with colorectal cancer at our Clinic were treated laparoscopically (29 out of 290 operated patients). Out of a total of 115 cases for the 5-year time interval, 28 (24.3%) patients underwent right hemicolectomy, 37 (32.1%) left hemicolectomy, anterior resection of the rectum was observed in 32 (27.8%) patients, while 18 (15.6%) patients underwent rectal amputation. As for the tumor staging, among 115 patients, the distribution of cases is 5.2% (pT1), 34.7% (pT2), 53% (pT3), 6.95% (pT4).

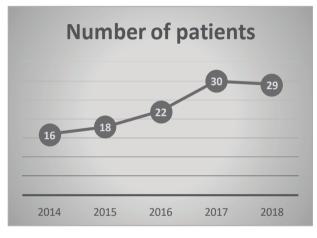


Figure 1 – Number of patients

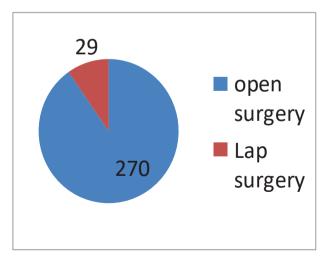


Figure 2 - Laparoscopy for colon/rectum 2019

Table 1

Laparoscopy for colon/rectum - 5 year period

Operation performed	Number of cases
Right hemicolectomy	28
Left hemicolectomy	37
Anterior resection	32
Amputation of rectum	18
Total	115

Table 2

Laparoscopy for colon/rectum- Tumor stage

Tumor stage	Number of cases
pT1	6 5,2%
pT2	40 34.7%
pT3	61 53%
pT4	8 6,95%
Total	115 100%

The analysis of the perioperative outcomes gave the following results: conversion to open surgery 5.7%, average duration of the operation 198 min (125-285 min), the need for blood transfusions - 0%, hospital stay an average of 9 days (7-16), and the average number of dissected lymph nodes 13 (8–25).

Perioperative morbidity analysis, on the other hand, covered the following variables: wound infection 1.7% (2 patients), pulmonary complications in only 1 patient, bleeding, stepler port bleeding in only 1 patient, anastomotic leakage in 1 patient (conservative care), readmission to hospital 0, mortality 0.

Variable	Number (%)
Conversion to open	7/122 (5.7%)
Operative time (min)	198 min (125-285)
Blood transfusion	0
Length of stay (day	9 (7-16)
Lymph node yield	13 (8-25)

Table 3

Perioperative outcomes

Table 4

Perioperative morbidity

Variable	Number (%)
Wound infection	2 (1.7%)
Pulmonary	1
Bleeding	1Stapler port bleeding (operated)
Anastomotic leakage	1 Conservative treatment
Readmission to hospital	0
Mortality	0

Discussion

Although this paper reflects our perioperative experience with the laparoscopic treatment of colorectal cancer within the 5-year interval, without direct comparison with open surgical access, the results show that patients who receive laparoscopic treatment have a short hospital stay, operating time equivalent to the open surgery approach, very low rates of wound infections, bleeding and anastomotic leakage, low pulmonary complications, no admission to the ICU unit or need for mechanical ventilation, no need for blood transfusions, no repeated hospitalizations and no mortality. Although our clinical long-term oncological outcomes of laparoscopic vs. open surgery remain to be seen, these perioperative results show that recovery, physiological function, and other short-term outcome measures are improved with the laparoscopic approach.³⁻⁶

It has been reported that hospital volume, surgeon volume, and, therefore, the rate of laparoscopic surgery may affect the results of colorectal surgery. Higher hospital and surgeon volume are generally related to better outcomes after laparoscopic surgery for colorectal cancer⁷ However, what is evident is that although our Clinic does not have a high rate of laparoscopic colorectal surgery, the rates of complications are still very low. This could be result of the high rate of laparoscopic treatment for other digestive pathologies at our clinic and the right selection of cases for laparoscopy.

In our study, laparoscopic surgery for colorectal cancer was associated with comparable operation time to the open access surgery, which was slightly lower but generally compatible with most previous reports. ^{4,15} Although prolonged operation time was a suggested possible risk factor for the development of postoperative pulmonary complications, our results show that laparoscopic surgery was associated with no ICU admission and postoperative mechanical ventilation. This was outweighed by other factors like incision size and pain. Conversion from laparoscopic to open surgery has been related to worse outcome, but this has probably been associated with issues stemming from the learning curve. Risk factors for conversion for various populations are widely reported within the literature. Clancy et al. recently performed a meta-analysis of 15 studies and reported a mean conversion rate of 17.9% ($\pm 10.1\%$) with males, rectal tumor, T3/T4 stage and node-positive disease as factors that negatively influence the completion

of laparoscopic surgery.¹⁶ Our analysis, however, shows that although most of our cases - 53% - were T3, the conversion rate remained low - only 5.7%. Conversion rates are expected to scale back over time. The CLASICC trial, for example, had a conversion rate of 34% ¹⁷ for rectal cancer, while this was 16% ¹⁸ in additional recently published trials from Western population regions. Surgical experience is one of the most crucial elements for quality patient care in laparoscopic procedures. Recent studies show that with increasing laparoscopic hospital volume, conversion decreases below 10% with only a minimal impact of conversion on short-term postoperative outcome. To perform an early conversion may be an appropriate decision, and this kind of conversion should not be considered a failure.¹⁹

Some oncological parameters like tumor size, number of lymph nodes retrieved, and surgical margin, are important to assess the oncological adequacy of the operation. Of those, lymph node status is probably the strongest pathologic predictor of patient outcome, and it represents a high quality indicator for cancer care. Sufficient node staging (TNM) is absolutely essential to establish definitive diagnosis and prognosis of the patient and is essential for planning further oncologic treatment. Several studies support that number of lymph nodes harvested during an operation (minimum 12 lymph nodes) is one of the strongest predictor for cancer treatment because it is associated with a better survival rate. In our study, the average number of harvested lymph nodes was 13, which is a very important result. showing adequate oncological resection. In terms of tumor size, our data shows that almost all of the operated patients had PT2, PT3 lesions (87.7% together), which is a reflection of the low screening rate within our population. Laparoscopic surgery for advanced colorectal cancer has become widespread, with demonstrated short-term benefits and better long-term oncological outcomes than open surgery.^{4,16,21-23}However, for locally advanced pathological T4 (pT4) carcinoma based on the American Joint Committee on Cancer (AJCC) TNM staging system,²⁴ the safety and feasibility of laparoscopic procedures remain controversial. In pT4 carcinoma, technically demanding surgical procedures, including en bloc resection of adjacent infiltrated organs or structures, are generally required. It is well-known that open multivisceral resection for pT4 colon cancer includes a high postoperative morbidity and a high risk of microscopically positive surgical margins.²⁵ For these reasons, some authors consider pT4 colon cancer to be a relative contraindication to laparoscopic surgery which could lead to prolon-352

ged operative time, an increased conversion rate, higher postoperative morbidity, and, most significantly, suboptimal oncological results.²⁶ In our case, the selective approach provided a comparatively low rate of operated patients in pT4 colorectal cancer of only 6.5%.

It is essential to perform strict oncologic resections and for pathologists to conduct a meticulous evaluation of specimens.²⁷

Conclusion

Laparoscopic surgery, which is becoming a standard treatment for colon and rectal cancer in the USA and Europe, has several benefits over open surgery in terms of short-term outcomes such as decreased pain, improved pulmonary function in the postoperative period, lower rates of postoperative ileus, lower incidence of wound infection, faster recovery, and shorter hospital stay. Further, as shown by the results of several randomized controlled trials, the long-term outcomes after laparoscopic surgery for colorectal cancer are comparable to those after open surgery. An overview of our data has shown excellent short-term perioperative outcomes as well as solid oncological surgical parameters. The long-term outcome of these cases remains to be considered.

REFERENCES

- Clinical Outcomes of Surgical Therapy Study Group. A comparison of laparoscopically assisted and open colectomy for colon cancer. N Engl J Med. 2004 May 13; 350(20): 2050–9
- 2. Veldkamp R, Kuhry E, Hop WC, et al. *Laparoscopic surgery versus open* surgery for colon cancer: short-term outcomes of a randomised trial. *Lancet Oncol.* 2005 Jul. 6(7): 477-84.
- 3. Clinical Outcomes of Surgical Therapy Study, G. et al. A comparison of laparoscopically assisted and open colectomy for colon cancer. N. Engl. J. Med., 2004; 350, 2050–2059,
- 4. Lacy, A. M. et al. Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial. Lancet, 2002; 359, 2224–2229,

- 5. Veldkamp, R. *et al.* Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial. *Lancet Oncol.*, 2005; 6 477–484,
- 6. Jayne, D. G. et al. Randomized trial of laparoscopic-assisted resection of colorectal carcinoma: 3-year results of the UK MRC CLASICC Trial Group. J. Clin. Oncol., 2007; 253061–3068,
- 7. Huo, Y. R., Phan, K., Morris, D. L. & Liauw, W. Systematic review and a meta-analysis of hospital and surgeon volume/outcome relationships in colorectal cancer surgery. J. Gastrointest. Oncol. 2017; 8 534–546,
- 8. Doyle, R. L. Assessing and modifying the risk of postoperative pulmonary complications. Chest 1999; 115.77S–81S
- 9. Fougeres, E. et al. Hemodynamic impact of a positive end-expiratory pressure setting in acute respiratory distress syndrome: importance of the volume status. Crit. Care Med. 2010; 38 802–807,
- 10. Schweickert, W. D. et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet, 2010; 3731874–1882,
- Southall J C, Lee S W, Allendorf J D, Bessler M, Whelan R L. Colon adenocarcinoma and B-16 melanoma grow larger following laparotomy vs. pneumoperitoneum in a murine model. Dis Colon Rectum. 1998; 41(5): 564–569
- 12. Allendorf J DF, Bessler M, Kayton M L, et al. *Increased tumor establishment and growth after laparotomy vs laparoscopy in a murine model. Arch Surg.* 1995; 130(6): 649–653
- 13. Lee S W, Feingold D L, Carter J J, et al. *Peritoneal macrophage and blood monocyte functions after open and laparoscopic-assisted cecectomy in rats. Surg Endosc.* 2003; 17(12): 1996–2002.
- 14. Fleshman J, Sargent DJ, Green E, Anvari M, Stryker SJ, Beart RW, Jr, et al. *Laparoscopic colectomy for cancer is not inferior to open surgery based on 5-year data from the COST Study Group trial. Ann Surg.* 2007; 246: 655–662.
- 15. Shantha Kumara H M, Feingold D, Kalady M, et al. *Colorectal resection is associated with persistent proangiogenic plasma protein changes: posto-perative plasma stimulates in vitro endothelial cell growth, migration, and invasion. Ann Surg.* 2009; 249(6): 973–977.
- 16. Jayne, D. G. et al. Randomized trial of laparoscopic-assisted resection of colorectal carcinoma: 3-year results of the UK MRC CLASICC Trial Group. J. Clin. Oncol. 2007; 25: 3061–3068,

- 17. Clancy C, O'Leary DP, Burke JP, Redmond HP, Coffey JC, Kerin MJ, et al. *A meta-analysis to determine the oncological implications of conversion in laparoscopic colorectal cancer surgery. Colorectal Dis.* 2015; 17: 482–490.
- 18. Guillou PJ, Quirke P, Thorpe H, Walker J, Jayne DG, Smith AM, et al. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. Lancet. 2005; 365: 1718–1726.
- 19. van der Pas MHGM, Deijen CL, Abis GSA, de Lange-de Klerk ESM, Haglind E, Fürst A, Lacy AM, Cuesta MA, Bonjer HJ *Conversions in laparoscopic surgery for rectal cancer. Surg Endosc* 2017; 31: 2263–2270
- Michael P. M. de Neree tot Babberich, Julia T. van Groningen, Evelien Dekker, Theo Wiggers, Michel W. J. M. Wouters, Willem A. Bemelman, Pieter J. Tanis, Laparoscopic *Surg Endosc.* 2018; 32(7): 3234–3246Surg Endosc. 2018; 32(7): 3234–3246
- Baxter NN, Virgin D, et al. Lymph Node Evaluation in Colorectal Cancer Patients: A Population-Based Study. Journal of the National Cancer Institute. 2005; 97(3): 219–225
- 22. Yamamoto S, Inomata M, Katayama H, Mizusawa J, Etoh T, Konishi F, et al. *Short-term surgical outcomes from a randomized controlled trial to evaluate laparoscopic and open D3 dissection for stage II/III colon cancer: Japan Clinical Oncology Group Study JCOG 0404.* Ann Surg. 2014; 260: 23–30.
- 23. Kitano S, Inomata M, Mizusawa J, Katayama H, Watanabe M, Yamamoto S, et al. Survival outcomes following laparoscopic versus open D3 dissection for stage II or III colon cancer (JCOG0404): a phase 3, randomised controlled trial. Lancet Gastroenterol Hepatol. 2017; 2: 261–268.
- 24. Edge SB, Compton CC. *The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol.* 2010; 17: 1471–1474.
- 25. Mohan HM, Evans MD, Larkin JO, Beynon J, Winter DC. *Multivisceral resection in colorectal cancer: a systematic review. Ann Surg Oncol.* 2013; 20: 2929–2936.
- 26. Buunen M, Veldkamp R, Hop WC, Kuhry E, Jeekel J, Haglind E, et al. Survival after laparoscopic surgery versus open surgery for colon cancer: long-term outcome of a randomised clinical trial. Lancet Oncol. 2009; 10: 44–52.
- 27. Wong S. Lymph Node Counts and Survival Rates After Resection for Colon and Rectal Cancer. Gastrointestinal Cancer Research. 2009; 2(3) Supplement 1: S33–35.