

**Postgraduate Study Program
Surgical Oncology**

**COMPARISON OF THE LAPAROSCOPIC
VERSUS OPEN SURGERY IN COLORECTAL
CANCER IN PATIENT AGED OVER 75 YEARS
OLD. LONG-TERM OUTCOMES**

**MSC THESIS
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ΕΥΧΑΡΙΣΤΙΕΣ

Η εκπόνηση της παρούσας διπλωματικής δεν θα ήταν εφικτή δίχως την πολύτιμη βοήθεια πολλών ανθρώπων.

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ABSTRACT

Background

Colorectal cancer is the second most common cancer in men and third commonest in women of all ages. Life expectancy has increased and this has created a challenge for surgeons today to decide which approach is better for the elderly patient with colorectal neoplastic disease. The benefit of minimally invasive surgery in colorectal cancer patients has been established, however it is not clear whether these benefits apply to older patients as well.

The aim of this study is to present short- and mid-term outcomes in elderly patients, over the age of 75 years, with colorectal cancer who were treated with the laparoscopic approach in comparison with patients that were treated with open surgery in a tertiary hospital.

Methods

This is a midterm retrospective study of selected patients over the age of seventy-five who underwent laparoscopic and open surgery for colorectal cancer between January 2013 until December 2018 in a tertiary referral center.

All patients were > 75 years of age, treated for colorectal cancer, and categorized in two groups: Group 1 patients who had open surgery and Group 2, patients underwent laparoscopic surgery.

Demographic, clinical and postoperative data were retrospectively collected and analyzed between the two study groups.

Results

A minimally invasive procedure in colorectal cancer is equally safe in comparison with the open procedure, considering the similar postoperative complication rate (p-value 0.184). The overall hospital stay postoperatively was in favor of the laparoscopic approach (p-value 0.001). The overall survival in short- and midterm outcomes represents equal results among open and laparoscopic surgical access.

Conclusion

Laparoscopic surgery is as safe and implementable approach for the elderly patients with colorectal cancer, with equal oncological results, maintaining the benefit of a shorter postoperative hospital stay.

Summary

This retrospective study compared short and midterm outcomes in elderly patients that underwent elective open or laparoscopic surgery for colorectal cancer.

Keywords: Colorectal cancer, Laparoscopic colectomy, Open colectomy, Elderly patients, Retrospective study

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Introduction

Colorectal cancer (CRC) is a very common disease in surgical practice. Statistically, it is the second cancer for men and the third in women population of all ages¹

In the era of minimally invasive surgery, it has been established that laparoscopic surgery is as safe and equally efficient to open procedure regarding the achievement of negative resection margins, rate of metastasis, port-site and wound-site recurrence, local recurrence, overall survival, and blood loss during surgery^{2,3}.

Because of the unprecedented aging of the human population with this trend set to continue, during the last decades the number of operations, which were performed on elderly patients has increased dramatically⁴. Age by itself is an independent risk factor of mortality⁵. Comorbidities in elderly patients can significantly increase perioperative risk and therefore the choice of the best approach is crucial for this group of patients.

The aim of this study is to present the short and midterm results of laparoscopic versus open surgery in the elderly patients (>75 years of age) with CRC that were treated in a tertiary University hospital.

Material and Method

Study selection

This a retrospective, single tertiary center study, comparing laparoscopic versus open surgery in the over seventy-five years of age group of CRC patients. All patient's data were retrieved from the hospital's archives and prospectively maintained database, after obtaining informed consent from the patients. This study was approved by the hospital Research Scientific Committee.

Characteristics on preoperative data include Charlson Comorbidity index score, while functional status was quantified using a metabolic equivalent score (METs); in addition, the Body Mass Index (BMI) was measured. Similarly, all analgesic agents used intraoperatively, like fentanyl, remifentanyl, non-steroidal anti-inflammatory drugs, were measured and converted into morphine equivalent doses.

Postoperative data include common postoperative complications (postoperative ileus, urinary retention, postoperative hernia formation), need for intensive care unit admission, overall postoperative hospital stay, mobilization, number of retrieved lymph nodes as well as histopathological data as a measure of surgery quality (Table 1). Overall survival was calculated and analyzed.

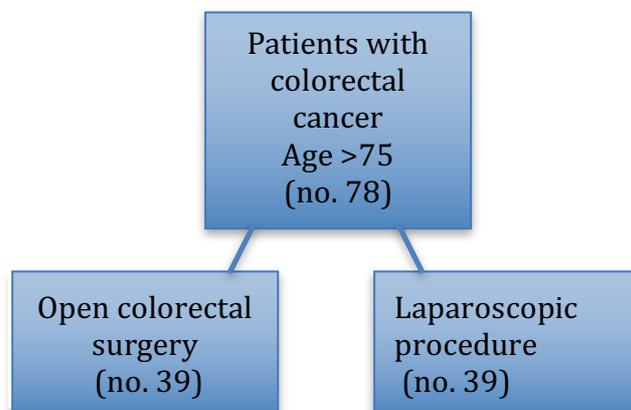


Figure 1. *Flowchart of patient selection.*

Preoperative work up

Before surgery, all patients had a physical exam, full blood count, liver and renal function tests and measurement of carcinoembryonic antigen levels (CEA). Multidetector computer tomography (CT) of the abdomen, pelvis and chest was performed to reveal the presence of distant metastasis and define the functional status of patients.

Preoperative colonoscopy to the caecal pole was performed almost in all patients except those with partial obstruction, where virtual colonoscopy was used to exclude the appearance of the synchronous colonic tumors. Histological evaluation of tumor biopsy was applied to all our patients.

In case of rectal cancer, we performed pelvic magnetic resonance imaging, since it is the most accurate test for locoregional staging. We do not use positron emission tomography routinely except in cases with an abnormality in the CT scan and where findings may change the surgical management.

All CRC patients were discussed pre- and postoperatively at Multidisciplinary meetings (MDT) which consist of surgeons, pathologists, clinical oncologists, radiologists and radiation oncologists.

Preoperative care

All of the study patients were subjected to mechanical bowel preparation (polyethylene glycol or sodium phosphate) except for those with partial obstruction, where an enema was used. Antibiotic prophylaxis was given intravenously at the induction of general anesthesia (2nd generation cephalosporin and metronidazole). Low molecular weight heparin (such as enoxaparin or bemiparin) was given before surgery as prophylaxis for deep-vein thrombosis. This regimen was continued after surgery in combination with the use of graded compression stockings^{6,7}.

Meticulous preoperative cardiovascular evaluation was performed with electrocardiograms and ultrasonic cardiograms as well as a pulmonary function tests (spirometry) where indicated.

Surgical approach

All operations were performed by experienced colorectal surgeons. The decision for laparoscopic or open surgery was based upon surgeon's preference and experience for each individual case.

For the right-sided cancer cases, a laparoscopic colectomy with medial-to-lateral approach was performed. Specimen extraction was made through a mini laparotomy with upper midline incision and anastomosis was performed extracorporeally using a hand-sewn or stapling technique.

For the left-sided cancer, the distal bowel was divided intracorporeally with laparoscopic staplers and anastomosis was performed with transanally inserted circular stapler (staple diameter 29 or 31mm). The specimen was extracted via a small Pfannenstiel incision.

The concept of total mesorectal excision for rectal cancer and total mesocolic excision and for colonic cancer was followed in all cases either laparoscopic or open procedure

Follow-up

Data collection was performed in direct consultation with the patient, from hospital medical database or through a telephone interview.

Statistical analysis

Categorical variables are presented as absolute and relative frequencies (%). Normality of distribution was evaluated with the Kolmogorov-Smirnov test. Normally distributed quantitative variables are presented as means (\pm standard deviation) whereas non-normally ones as medians (range). Pearson's chi-square test was used for the comparison of categorical variables. Student's t-test and Mann-Whitney test were performed for parametrical and non-parametrical variables respectively. The survival curve was evaluated with the Kaplan-Meier method and the log-rank was used for comparison between laparoscopic and open procedures. All p-values were two-sided, whereas p-values of <0.05 were considered statistically significant.

All tests were performed with SPSS version 22 (SPSS, Chicago, IL).

Results

(Table 1)

We selected a total number of 78 patients who underwent surgical resection for CRC between January 2013 until December 2018 in Aretaieion Hospital. This included two groups of thirty-nine patients over the age of seventy-five; the patients in group 1 underwent open procedure (OP), and the patients in group 2 had laparoscopic procedure (LP). Overall median age was equal in both groups, 79 years (range:76-84) in LP group and 79 years in OP group (range:77 – 83) respectively, with no statistical differences (p-value 0,549); the statistical analysis of the gender distribution in both groups showed similar results (p-value 0,496).

Preoperative measurements showed no differences between the two study groups in Charlson score (p-value 0,113), Body Mass Index (p-value 0,544) as well as in MET score measurements (p-value 0,583).

Surgery (Table 2, Fig 2)

All selected patients underwent a scheduled procedure. Urgent colectomies were excluded from the study. There were no differences in both groups in the type of surgical approach (p-value 0,990).

Postoperative data

The postoperative data are presented in table 3. The two groups did not have differences in the histopathological staging (p-value 0,153), and the number of extracted lymph nodes was equal. More precisely, LP retrieved 20,0 nodes in comparison with 20,54 nodes in OP (p-value 0,816).

Intraoperative use of analgesics was measured in morphine equivalents and compared between two group without significant differences (OP 37,23mg, LP 35,62mg).

There was no difference in the patient's mobilization between the two study groups which was in the first postoperative day (p-value 0,693). The need for Intensive care unit admission did not differ in the study population [OP 8 patients (22,2%) related to LP 7 patients (18,4%), p-value 0,776].

The median length of the postoperative hospital stay differed statistically between the two groups; in the open procedure group it was significantly higher compared to the

laparoscopy group [OP 8 days (range:7 – 12) versus LS 6 days (4 – 8,5) with p-value 0,001].

Additional finding of this research is that the amount of total complications in two groups did not present any statistically significant differences with p-value 0,224 (Table 4)

Overall survival (Figure 3, Table 5)

Survival analysis and the Kaplan-Meier plot demonstrate that overall survival rate in 12 and 24 months was without significant statistical difference in both groups (p-value 0,098 and 0,387 for 12 and 24 months respectively).

Discussion

Surgery is the cornerstone of CRC treatment. Nowadays, two main standards of surgical treatment are followed worldwide, the classic open procedure and the so-called minimally invasive technique represented mainly by laparoscopic surgery.

After the first description of laparoscopically performed colectomy in 1991 by Jacobs et al.⁸, the interest for minimally invasive surgery was constantly growing worldwide, especially after the publication of the COLOR, COST and CLASICC trials that showed oncological equality in the short- and long-term outcomes of CRC^{9,10,11}. Since then, many variations of the minimally invasive technique have been adopted, from classical laparoscopy to the less invasive access for colorectal surgery like a Transanal Total Mesorectal Incision (TME) and Single Incision Laparoscopic surgery (SILS)^{12,13}.

Nowadays, minimally invasive techniques in CRC surgery, despite a steep learning curve and longer operative time, became the standard choice of colorectal surgeons. Devoto et al. demonstrated in their systematic review that the age is not a contraindication for colorectal surgery itself, but more than that, the morbidity in the laparoscopic group in elderly patient was reduced¹⁴.

In the past ten to fifteen years a number of studies were published, thus confirming equality of the oncological outcomes in laparoscopic surgery in comparison to open surgery for CRC in short- midterm and long-term outcomes^{15,16,17}.

The aim of this study was to evaluate whether laparoscopic surgery for colorectal cancer in the elderly is as safe and effective as that for open colorectal surgery patients, which gives as an opportunity to improve the treatment of CRC in this fragile group of patients. This study analysis revealed that laparoscopic resection is associated with equal short-term and mid-term outcomes in comparison with open procedures. It is also shown that there is a trend of slightly better survival in the mid-term outcomes without reaching a statistically significant difference. The above statement is probably because of small number of patients in the LP group. That can be explained also with the fact that the selection of the patient's for laparoscopic procedure was depended of the surgeon preference, we are more selective – by possible selection bias in the laparoscopy group.

Proper selection of patients for LS is a 'sine qua non', however in comparison to OP group LS achieved similar number of harvested lymph nodes (p-value 0,816). Shiha et al. described in his propensity score matching study that there is less aggressive surgical resection (p-value=0,01) in the elderly laparoscopic group despite equal preoperative features in comparison with younger patients¹⁸.

In our study also there were no statistically significant differences in survival in the compared groups, but it can be concluded that there is a definite tendency for a higher risk of death in the open surgery group. This is confirmed by the following figure 3.

It is still unclear whether it is necessary to harvest the higher lymph node, especially if we weigh on scales the likelihood of postoperative complications after D3 lymph node dissection according to Japanese staging system and its unknown implication on overall survival^{19,20}. This question still remains unanswered.

The long-term outcome of radical treatment correlates mostly with the tumor stage, as it shows in the study of Sheridan et al., but this also is in strong correlation with ASA score and patient's performance status²¹.

The total complication rate in this study does not show statistically significant differences in total complications between the two groups (p-value 0,224), which corresponds with results of the complications rate in the literature^{22,23}.

The overall hospital stay postoperatively has considerable inequality between the groups (p-value 0.001) that corresponds to systematic review study by the Li et al. where this parameter was significantly better in the laparoscopic group²⁴.

Study limitations

The retrospective nature of the study by itself is a subject of assessment bias. Particularly, the limitation of this study is the small number of patients in comparison with other studies of similar nature.

Follow up of both patient's groups was difficult due to the fact that the patients were elderly and also suffered from many other comorbidities.

Conclusion

This is the first study of laparoscopic surgery in the elderly patients in Greece. Similarly to the findings of the earlier studies in other countries, the postoperative hospital stay was less in the laparoscopic group. Furthermore, this study confirmed that oncological outcome was same in both groups. It can be concluded that laparoscopic surgery appears to be a safe and applicable option for elderly patients with CRC.

Conflict of interest statement

The authors have no conflict of interest to disclose and received no financial support for this study.

TABLES

Table 1. Perioperative data and short-term outcomes between minimally invasive procedure and open approach in elderly (aged ≥ 75 years) patients

	Laparoscopic surgery (n=39)	Open surgery (n=39)	P value
Age, years (Me [Q₁-Q₃])	79 (76 – 84)	79 (77 – 83)	0,549
Gender, no. (%)			
men	22 (56,4)	19 (48,7)	0,496
women	17 (43,6)	20 (51,3)	
BMI, abs. (%)			
1	3 (7,9)	1 (2,8)	0,544
2	9 (23,7)	13 (36,1)	
3	14 (36,8)	13 (36,1)	
4	12 (31,6)	9 (25,0)	
METS score, >4 events / total (%)	15 / 38 (39,5)	12 / 36 (33,3)	0,583
CHARLSON score, Me [Q₁-Q₃]	6 [6 – 7]	7 [6 – 8]	0,113

Table 1. Perioperative data and short-term outcomes between minimally invasive procedure and open approach in elderly (aged ≥ 75 years) patients (continue)

	Laparoscopic surgery (n=39)	Open surgery (n=39)	P value
Pathological stage, no. (%)			0,153
Tis	3 (7,9)	1 (2,6)	
I	7 (18,4)	7 (17,9)	
II	18 (47,4)	10 (25,6)	
III	8 (21,1)	15 (38,5)	
IV	2 (5,3)	5 (12,8)	
N, no. (%)			0,008*
N0	10 (76,9)	2 (40,0)	
N1	3 (23,1)	0 (0,0)	
N2	0 (0,0)	3 (60,0)	

Table 2. Type of selective surgical procedure

	Laparoscopic surgery (n=40)	Open surgery (n=39)	P value
Procedure			0.990
Right Colectomy	16 (40%)	16(41%)	
Left colectomy	2(5%)	2 (5.1%)	
Sigmoidectomy	11 (27,5%)	10 (25%)	
Low Anterior resection	8(20%)	9 (23.1%)	
Abdominoperineal resection	3(7%)	2(5.1%)	

Table 3. Comparison of surgical results between minimally invasive procedure and laparoscopic approach in elderly (aged ≥ 75 years) patients.

	Laparoscopic surgery (n=39)	Open surgery (n=39)	P value
No. of lymph nodes	20,0 \pm 9,26	20,54 \pm 10,59	0,816
Mean \pm SD			
Post-operative hospital stay (days)	6 [4 – 8,5]	8 [7 – 12]	0,001*
Me [Q₁-Q₃]			
Morphine use, mg	35,62 \pm 11,45	37,23 \pm 11,8	0,555
Mean \pm SD			
Mobilization (days)	1 [1 – 2]	1 [1 – 2]	0,693
Median [Q₁-Q₃]			
ICU need, abs. (%)	7 (18,4)	8 (22,2)	0,776
Total complications, no. (%)	9 / 26 (34,6)	5 / 27 (18,5)	0,224

Table 4. Comparison of complication between minimally invasive procedure and laparoscopic approach in elderly (aged ≥ 75 years) patients.

	Lap colectomy n=26, no (%)	Open colectomy n=27, no (%)	p-value
Total complications, no. (%)	9 / 26 (34,6)	5 / 27 (18,5)	0,224
Ileus	2 (7,7)	0 (0,0)	0,236
Urinary distension	3 (11,5)	0 (0,0)	0,111
Anastomotic leak	2 (7,7)	1 (3,7)	0,61
Postoperative hernia	2 (7,7)	4 (14,8)	0,669

Fig 2. Comparison of a type of performed surgical procedure between minimally invasive procedure and laparoscopic approach in elderly (aged ≥ 75 years) patients.

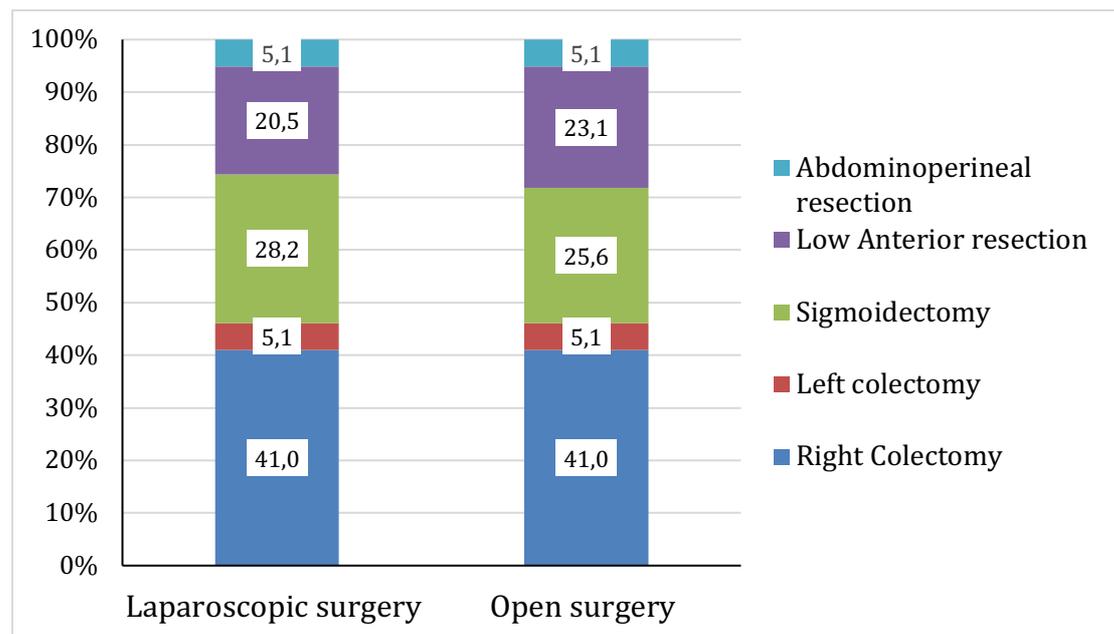


Table 5. Overall survival

Time period, months	Lap colectomy n=26, no (%)	Open colectomy n=27, no (%)	p-value
12	91,8±5,6%	85,9±6,5%	0,098
24	91,8±5,6%	80,9±7,9%	0,387

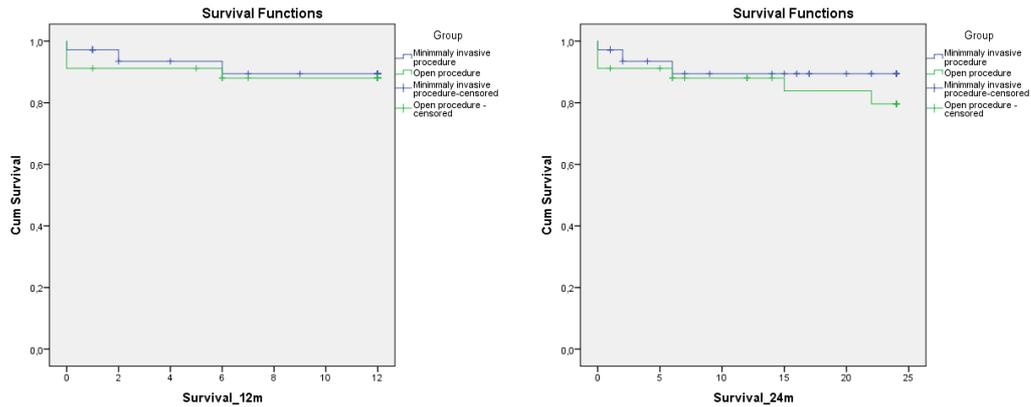


Fig. 3 (A) Kaplan-Meier curve for 12 months survival in the laparoscopic group (blue line) and in the open procedure group (green-line), p-value 0,098. X-axis=months. Y-axis=percentage. (B) Kaplan-Meier for 24 months survival in the laparoscopic group (blue line) and in the open procedure group (green line), p-value 0,387. X-axis=months. Y-axis=percentage. Significance was defined as $p < 0,005$. The figure shows tick marks for censored patients due to the larger number of patients on the study.

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