ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

DOI: 10.5336/medsci.2021-84099

Evaluation of the Feasibility and Safety of Laparoscopic Resection in Elderly Colorectal Cancer Patients: A Retrospective Study

Yaşlı Kolorektal Kanserli Hastalarda Laparoskopik Rezeksiyonun Uygulanabilirliği ve Güvenliğinin Değerlendirilmesi: Retrospektif Çalışma

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ABSTRACT Objective: The incidence of colorectal cancer gradually increases with age. The fact that elderly patients have frequent comorbidities and limited functional reserve requires surgeons to choose the most optimal surgical method. The aim of this study is to investigate the safety and applicability of laparoscopic surgery in elderly colorectal cancer patients ≥70 years old. **Material and Methods:** The data of 153 patients, who underwent laparoscopic resection for colorectal cancer in our clinic in the period between January 2014 and January 2019, were retrospectively investigated. We divided patients into 2 groups by age; elderly patients (≥70 years old, 55 cases) and non-elderly patients (<70 years old, 98 cases). Patient characteristics, clinicopathological findings, surgical findings, short-term and long-term outcomes were compared between the age groups. **Results:** The rate of patients with high American Society of Anesthesiologists score (p<0.001) and the rate of comorbid diseases (87.3%) were found to be higher in the elderly group (p<0.001). There was no difference between the groups in terms of postoperative complications other than atelectasis (p=0.037). In-hospital mortality rates (p=0.423), re-operation rates (p=0.999), intensive care unit (p=0.741) and hospital stay (p=0.997) of the groups were similar. When the long-term results are examined, no statistically significant differences were found between the age groups in terms of overall survival (p=0.150) and disease-free survival (p=0.449). **Conclusion:** Laparoscopic surgery is a safe and applicable surgical method for elderly colorectal cancer patients in terms of both short and long term oncologic results.

Keywords: Aged; colorectal neoplasms; laparoscopy; surgery

ÖZET Amaç: Kolorektal kanser insidansı yaşla birlikte giderek artmaktadır. Yaşlı hastaların komorbiditelerinin sık olması ve fonksiyonel rezervin sınırlı olması, cerrahların en uygun cerrahi yöntemi seçmesini gerektirmektedir. Bu çalışmanın amacı, ≥70 yaşındaki kolorektal kanser hastalarında laparoskopik cerrahinin güvenliğini ve uygulanabilirliğini araştırmaktır. **Gereç ve Yöntemler:** Ocak 2014-Ocak 2019 tarihleri arasında kliniğimizde kolorektal kanser nedeniyle laparoskopik rezeksiyon yapılan 153 hastanın verileri, retrospektif olarak incelendi. Hastaları yaşa göre 2 gruba ayırdık; yaşlı hastalar (≥70 yaş, 55 vaka) ve yaşlı olmayan hastalar (<70 yaş, 98 vaka). Hasta özellikleri, klinikopatolojik bulgular, cerrahi bulgular, kısa ve uzun dönem sonuçlar yaş grupları arasında karşılaştırıldı. **Bulgular:** Amerikan Anestezistler Derneği skoru yüksek olan hasta oranı (p<0,001) ve komorbid hastalık oranı (%87,3) yaşlı grupta daha yüksek bulundu (p<0,001). Atelektazi dışında postoperatif komplikasyonlar açısından gruplar arasında fark yoktu (p=0,037). Grupların hastane içi mortalite oranları (p=0,423), re-operasyon oranları (p=0,999), yoğun bakım ünitesi (p=0,741) ve hastanede kalış (p=0,997) süreleri benzerdi. Uzun dönem sonuçlar incelendiğinde genel sağkalım (p=0,150) ve hastalıksız sağkalım (p=0,449) açısından yaş grupları arasında istatistiksel olarak anlamlı fark bulunmadı. **Sonuç:** Laparoskopik cerrahi, hem kısa hem de uzun dönem onkolojik sonuçlar açısından yaşlı kolorektal kanserli hastalar için güvenli ve uygulanabilir bir cerrahi yöntemdir.

Anahtar Kelimeler: Yaşlı; kolorektal neoplazmlar; laparoskopi; cerrahi

Colorectal (CRC) cancer are common malignancies found in the elderly population. Nearly 50% of CRC individuals are over 75 years old.[1] Elderly CRC individuals have severe comorbid diseases and limited functional capacity, which affects treatment and expectation.[2] Surgical treatment is still the only curative treatment method. Factors such as the development of surgery and the emergence of a multidisciplinary approach in recent years have led to promising results by allowing major surgeries to be performed in elderly CRC patients.[3] Some studies have reported a high mortality and complication rate

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Peer review under responsibility of Turkiye Klinikleri Journal of Medical Sciences.

Received: 28 Apr 2021 ***Received in revised form:*** 22 Nov 2021 ***Accepted:*** 23 Nov 2021 ***Available online:*** 24 Nov 2021

in elderly CRC patients who undergo open surgery.[4-6] Recently, there has been an increasing trend towards laparoscopic surgery, especially in gastrointestinal cancers. Laparoscopic surgery have several advantages such as less postoperative pain, earlier mobilization of patient, shorter hospital stays, and earlier return of bodily functions.[7-9] However, the use of the minimal invasive surgery in elderly patients with multimorbidity continues to be a question of debate because of several reasons such as long operative times and circulatory and respiratory system disorders induced by the CO_2 pneumoperitoneum in laparoscopic colectomy. Therefore, it is important to choose the optimal operation method.

In this study, we aimed to investigate the feasibility and safety of laparoscopic surgery in elderly CRC patients.

MATERIAL AND METHODS

Throughout the work, the principles of the Declaration of Helsinki were adhered to. This retrospective study was approved by the Human Research Ethics Committee of Ankara University Faculty of Medicine (decision no: İl-75-21, decision date: 29.01.2021). The data of 153 patients, who underwent laparoscopic operation for colorectal cancer in the Surgical Oncology Clinic of Ankara University Medical Faculty in the period between January 2014 and January 2019, were retrospectively studied.

We categorized patients into 2 groups by age based on the previous study; elderly patients (≥70 years old, 55 cases) and non-elderly patients (<70 years old, 98 cases).[10] The criteria for inclusion in the study were as follows: patients with a preoperative diagnosis of histologically proven colorectal adenocarcinoma; there was no missing patient data; the type of the operation, including conversion to intraoperative laparotomy was laparoscopic resection; absence of distant metastases; and R0 resection was performed depending on pathological findings. Patients with pathological diagnosis other than adenocarcinoma in preoperative or postoperative pathological examination; with a history of comorbid malignant tumors; who have a distant metastasis; and patients with missing data were excluded from the study. Patient characteristics, clinicopathological findings, surgical findings, short-term and long-term outcomes were compared between the 2 patient groups. The evaluation of patient characteristics and clinicopathological findings included the analysis of demographic data, body mass index (BMI), albumin levels, American Society of Anesthesiologists (ASA) scores, comorbidities, neoadjuvant status and pathological stages. In this study, comorbidities were evaluated in the following four different categories: cardiovascular diseases, diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), and other diseases (cerebrovascular events, chronic kidney failure, chronic liver disease).

The following operative details were evaluated: the procedures performed, conversion to open surgery, operative time (minutes), blood loss, the transfusion requirement, stoma creation and the ostomy type. On the other hand, the short-term outcomes were evaluated using the following findings: 30-day postoperative morbidity, mortality, hospital stay and intensive care unit (ICU) stay. Postoperative morbidity was classified under the following four categories: surgical complications, cardiovascular complications, pulmonary complications, and acute kidney failure.

Moreover, overall survival and disease-free survival findings were evaluated as long-term outcomes, and these findings were compared between the 2 groups.

STATISTICAL ANALYSIS

Descriptive analyses were presented using mean±standard deviation, median (minimum-maximum) or n (%), where appropriate. The normality assumptions were controlled by the Shapiro-Wilk test. Categorical data were compared with Pearson chi-square and Fisher's exact test. Mann-Whitney U test and independent t-test were used for analysis of non-normally and normally distributed numerical data, respectively. Survival curves were made by the Kaplan-Meier method and the log-rank test was performed to compare overall and disease-free survival between the age groups. p value less than 0.05 was denoted statistically significant. Statistical analysis was made using IBM SPSS (Corp., Armonk, NY, USA), Version 23.0.

RESULTS

The mean age of the (n=153) patients was 64.6±11.3 (minimum: 36; maximum: 93) years. Approximately 62% of the patients were male and 35.9% were ≥70 years old. The gender (p=0.690) and BMI values (p=0.513) of the groups were similar. In the elderly group, the rate of patients with ASA score of 2 (58.2%) and 3 (29.1%) was higher (p<0.001). The rate of cardiovascular disease (p<0.001) and DM (p=0.019) was significantly higher in elderly individuals. There was no significant difference between the groups in terms of tumor localization (p=0.990), TNM Stage (p=0.612) and neoadjuvant treatment status (p=0.258). Patient characteristics are shown in Table 1.

When the operative details were compared, no significant differences were found between the groups in terms of operation type (p=0.977), operating time (p=0.426), blood loss (p=0.221), transfusion requirment (p=0.999), conversion to laparotomy (p=0.272), creating a stoma (p=0.345) and ostomy type (p=0.324). Surgery details are summarized in Table 2.

No significant differences were detected between the elderly and non-elderly individuals in terms of postoperative complications (p=0.816). When the complications were evaluated according to subtitles, the rate of atelectasis in elderly individuals (7.3%) was observed to be significantly higher (p=0.037). In-hospital mortality rates (p=0.423), re-operation rates (p=0.999), ICU (p=0.741) and hospital stay (p=0.997) of the groups were similar. Postoperative and short-term outcomes are shown in Table 3.

The follow-up time in the study ranged between 0.1 and 86 months. The overall survival rates in the 1st, 3rd, and 5th years were found to be 97.3%, 93.2%, and 91.1%, respectively. The disease-free survival rates in the 1st, 3rd, and 5th years were calculated as 96.1%, 88.1%, and 85.3%, respectively. The mean overall survival and disease-free survival time in the study population were 79.8 months and 77.1 months, respectively. No statistically significant differences were detected between the age groups in terms of overall survival rate [non-elderly group: 77.9 months (95% confidence interval "CI": 73.2-82.6) versus elderly group: 81.1 months (95% CI: 77.2-85.1); p=0.150] and disease-free survival [non-elderly group: 75.9 months (95% CI: 70.7-81.3) versus elderly group: 77.5 months (95% CI: 72.1-82.9); p=0.449]. The Kaplan-Meier curves are presented in Figure 1 and Figure 2.

TABLE 1: Comparison of patient characteristics.

Variables	Non-elderly (<70) (n=98)	Elderly (≥70) (n=55)	p value
Age (years)	58.1±7.6	76.3±6.1	**<0.001**
Gender			
Male	62 (63.3)	33 (60)	0.690
Female	36 (36.7)	22 (40)	
BMI (kg/m²)	24.9±4.9	24.7±5.2	0.513
ASA			
1	70 (71.4)	7 (12.7)	**<0.001**
2	25 (25.5)	32 (58.2)	
3	3 (3.1)	16 (29.1)	
Comorbid diseases	32 (32.7)	48 (87.3)	**<0.001**
Cardiovascular	15 (15.3)	36 (65.5)	**<0.001**
Diabetes mellitus	12 (12.2)	15 (27.3)	**0.019**
COPD	1 (1)	3 (5.5)	0.133
Other	12 (12.2)	9 (16.4)	0.477
Tumor localization			
Rectum	49 (50)	30 (54.5)	0.990
Right colon	27 (27.6)	14 (25.5)	
Sigmoid	13 (13.3)	7 (12.7)	
Left colon	7 (7.1)	3 (5.5)	
Transvers colon	2 (2)	1 (1.8)	
TNM Stage			
0	4 (4.1)	5 (9.1)	0.612
I	13 (13.3)	6 (10.9)	
II	45 (45.9)	23 (41.8)	
III	36 (36.7)	21 (38.2)	
Neoadjuvant status			
No	85 (86.7)	51 (92.7)	0.258
Yes	13 (13.3)	4 (7.3)	
Albumin (g/dL)	4.02±0.43	3.78±0.57	**0.004**

Values are expressed as means±standard deviation or n (%).
Student's t-test, Pearson chi-square test, Fisher's exact test.
BMI: Body mass index; ASA: American Society of Anesthesiologists;
COPD: Chronic obstructive pulmonary disease; TNM: Tumor, nodule, metastasis.

DISCUSSION

The fact that CRC is mostly encountered in elderly individuals makes it difficult for surgeons to perform

TABLE 2: Comparison of operative details.

Variables	Non-elderly (<70) (n=98)	Elderly (≥70) (n=55)	p value
Operation type			
Left hemicolectomy	7 (7.1)	3 (5.5)	0.977
Right hemicolectomy	27 (27.6)	14 (25.5)	
Anterior and low anterior resection	60 (61.2)	36 (65.5)	
Abdominoperineal excision of rectum	2 (2)	1 (1.8)	
Subtotal colectomy	2 (2)	1 (1.8)	
Operation time (minutes)	143.2±23.5	146.4±24.4	0.426
Blood loss (mL)	100 (50-400)	100 (50-700)	0.221
Transfusion requirement	2 (2)	1 (1.8)	0.999
Conversion to laparotomy	8 (8.2)	8 (14.5)	0.272
Creating a stoma	34 (34.7)	15 (27.3)	0.345
Ostomy type			
Ileostomy	21 (61.8)	12 (80)	0.324
Colostomy	13 (38.2)	3 (20)	

Values are expressed as means±standard deviation, median (range) or n (%).
Student's t-test, Mann-Whitney U test, Pearson chi-square test, Fisher's exact test.

TABLE 3: Comparison of operative details.

Variables	Non-elderly (<70) (n=98)	Elderly (≥70) (n=55)	p value
Postoperative complications	23 (23.5)	12 (21.8)	0.816
Surgical complications			
Anastomotic leakage	4 (4.1)	1 (1.8)	0.128
Postoperative ileus	2 (2)	1 (1.8)	0.920
Surgical site infeciton	6 (6.1)	2 (3.6)	0.509
Bleeding	0 (0)	1 (1.8)	0.180
Restless leg syndrome	1 (1)	1 (1.8)	0.675
Eventration	1 (1)	0 (0)	0.453
Urinary dysfunction	2 (2)	0 (0)	0.285
Urinary leakage from ureteroneocystostomy	1 (1)	0 (0)	0.453
Urinary leak due to iatrogenic ureter injury	1 (1)	0 (0)	0.453
Cardiovascular complications			
Atrial fibrillation	1 (1)	1 (1.8)	0.675
Pulmonary complications			
Atelectasis	1 (1)	4 (7.3)	**0.037**
Pleural effusion	1 (1)	1 (1.8)	0.675
Acute kidney failure	2 (1)	1 (1.8)	0.920
In-hospital mortality	4 (4.1)	1 (1.8)	0.423
Hospital stay (day)	9 (4-35)	9 (3-25)	0.997
ICU stay (day)	1 (1-6)	1 (1-7)	0.741
Re-operation	3 (3.1)	2 (3.6)	0.999

Values are expressed as, median (range) or n (%).
Mann-Whitney U test, Pearson chi-square test, Fisher's exact test.
ICU: Intensive care unit.

major surgery. Despite the development of a multidisciplinary approach, surgery is still the basis of CRC treatment. Laparoscopic colorectal operations are major surgical procedures. The development of surgical instruments, improvements in intraoperative monitoring and postoperative patient care facilitates laparoscopic colorectal resection in elderly patients.

The World Health Organization defines a 65-year-old individual as an elderly person. In surgical publications, the cut-off value used for the definition of elderly patients is different.[11] In previous studies on colorectal cancer surgery in elderly patients, several different age criteria were used, for example, Chautard et al. used the age criteria of ≥70 years, Fiscon et al. and Tan et al. used the age criteria of ≥75 years, Ueda et al. and Kvasnovsky et al. used the age

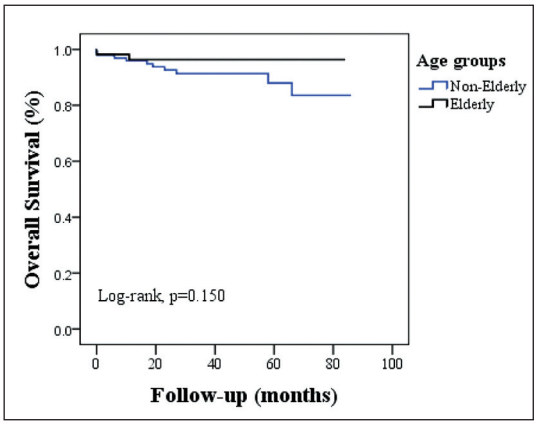

FIGURE 1: Overall survival curve in matched cohort of elderly and non-elderly groups.

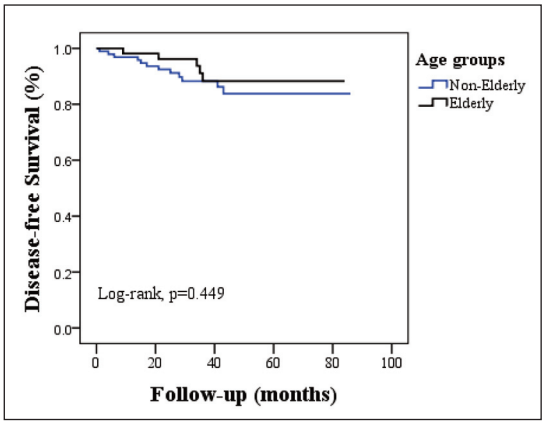

FIGURE 2: Disease-free survival curve in matched cohort of elderly and non-elderly groups.

criteria of ≥80 years.[10,12-15] In the present study, we determined the age of 70 as the cut-off value and divided the patients into elderly and non-elderly groups.

Elderly patients are usually more likely to have comorbid diseases that may be associated with postoperative complicaitons, such as cardiovascular diseases, DM, or COPD. Most of our "elderly" patients had cardiovascular disease (p<0.001), DM (p=0.019) and significantly higher ASA scores preoperatively. Despite all these negative factors, in our study, no significant differences were detected between the elderly and non-elderly groups in terms of postoperative complications other than atelectasis. The high incidence of atelectasis (p=0.037) in the elderly group may be relatead to the limited functional reserve and limited performance of elderly patients. In the present study, there was no difference in terms of mortality. In the literature, there are different results in terms of postoperative morbidity and mortality after laparocopic colorectal cancer operation in elderly individuals. In line with our study, Ueda et al. and Inoue et al. reported that, despite high comorbidity, there were no differences in terms of postoperative morbidity and mortality.[1,14] Tokuhara et al. showed that the elderly colorectal cancer individuals had similar morbidity rate with non-elderly patients after laparoscopic operation.[16] In a study by Tan et al. despite high comorbidity in elderly patients, there was no difference in terms of development of postoperative complications between the age groups.[13] In another study by Chautard and et al. it was described that, overall postoperative complications were similar between age groups.[10] In some studies, it is stated that advanced age is an independent risk factor for postoperative complication and mortality.[17,18] In contrast with our study, in the study by Fiscon et al. comorbidity and high ASA score accompanied increased morbidity in elderly colorectal cancer patients.[12] In the study by Kvasnovsky et al. elderly patients have higher ASA scores and have more infectious postoperative complications.[15]

Examining the operative findings of the patients, no differences were detected between the groups in terms of the surgery type, operating time, blood loss, transfusion requirment, conversion to laparotomy, stoma creation and ostomy type. This is similar to the results of previous studies.[12-15,19]

In line with previous studies, in this study mortality rates (p=0.423), re-operation rates (p=0.999), ICU stay (p=0.741) and hospital stay (p=0.997) of the groups were similar.[14,20]

In our study, no significant difference was found between age groups in terms of overall survival (p=0.150) and disease-free survival (p=0.449). Unfortunately, there are not many studies in the literature investigating the long-term outcomes of laparoscopic operation in elderly CRC patients. In the study conducted by Tokuhara et al., it was found that disease-free survival and overall survival were similar between elderly and non-elderly individuals.[16] Jeong et al. described that although overall survival was lower in the elderly group, there was no difference in terms of disease-free survival.[21] Ueda et al. reported that overall survival was lower in elderly individuals.[14]

The limitations of our study were that it was a retrospective single-center investigation, the operations were performed by different surgeons, and the sample size may be small. Multi-center studies with large sample sizes are needed in the future.

CONCLUSION

Laparoscopic operation for elderly CRC patients aged ≥70 years was technically and oncological safe method as it is for younger patients. Although our study partially sheds light on this issue, prospective multi-center studies are needed with a large sample size.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Afig Gojayev;* ***Design:*** *Afig Gojayev;* ***Control/Supervision:*** *Ali Ekrem Ünal;* ***Data Collection and/or Processing:*** *Afig Gojayev;* ***Analysis and/or Interpretation:*** *Afig Gojayev;* ***Literature Review:*** *Afig Gojayev;* ***Writing the Article:*** *Afig Gojayev;* ***Critical Review:*** *Ali Ekrem Ünal*.

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