

Oncological surgical outcomes for colorectal cancer surgery with loco-regional anesthesia

A feasibility study

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ABSTRACT

الأهداف: قمنا بتقييم النتائج المرضية لمرضى سرطان القولون والمستقيم الذين لم يتمكنوا من الحصول على تخدير عام وخضعوا للتخدير الموضعي من حيث الملاءمة للجراحة الأورام.

المنهجية: تم فحص ثلاثة وخمسين مريضاً خضعوا لجراحة القولون والمستقيم المتوسطة والمستقيمة تحت التخدير الموضعي في مستشفى مدينة أنقرة بيلكنت بأثر رجعي. قمنا بتحليل العقد الليمفاوية القريبة والبعيدة والمحيطية وعدد العقد الليمفاوية المتأصلة لكل عينة.

النتائج: كان لدى جميع المرضى الذين أجريت لهم الجراحة هوامش جراحية واضحة قريبة وبعيدة ومحيطية. كان متوسط عدد العقد الليمفاوية التي تمت إزالتها من المرضى 23.45 (الحد الأدنى والحد الأقصى: 3-97). عندما تم استبعاد المرضى الذين يتلقون العلاج المساعد، تم إزالة عدد غير كافٍ (أقل من 12) من العقد الليمفاوية في 3 من المرضى (7.69%). كان معدل الوفيات بعد 30 يوماً من العملية (5.6%).

الخلاصة: بالنسبة للمرضى المسنين والمصابين بأمراض مصاحبة بسرطان القولون والمستقيم، يمكن استخدام التخدير الموضعي لإجراء جراحة مناسبة للأورام.

Objectives: To evaluate the pathological outcomes of colorectal cancer (CRC) patients who were unsuitable for general anesthesia and underwent regional anesthesia in terms of their suitability for oncological surgery.

Methods: A total of 53 patients who underwent mesocolicomesorectal surgery under regional anesthesia at Ankara Bilkent City Hospital, Ankara, Turkey, between May 2019 and May 2023 were retrospectively examined. The negative margins of the proximal, distal, and circumferential margins of specimens, as well as the number of lymph nodes removed, were analyzed.

Results: All the patients had clear proximal, distal, and circumferential surgical margins. The median number of lymph nodes removed was 23.45 (min-max: 3-97). When patients (n=24) who received neoadjuvant therapy were excluded, an insufficient number (<12)

of lymph nodes were removed in 3 (7.69%) patients. A total of 3 patients died postsurgery, resulting in a 30-day mortality rate of 5.6%.

Conclusion: For elderly and comorbid individuals with CRC, regional anesthesia can be used to carry out surgery with oncological principles.

Keywords: colon cancer, spinal anesthesia, oncological surgery

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Colorectal cancer (CRC) is the third most common cancer in men and the second most common cancer in women, according to GLOBACAN data statistics.¹ Age is a major risk factor for CRC, and modifiable risk factors include smoking, excessive alcohol consumption, an unhealthy diet, physical inactivity, and a high body mass index.^{2,3} The treatment of CRC requires a multidisciplinary approach, but surgery remains the most effective curative method.⁴ According to oncological standards, the standard approach in CRC treatment is complete mesocolic excision (CME) and total mesorectal excision (TME), defined as the complete removal of the tumor, along with vascular structures and lymph nodes following embryological planes.^{5,6} For CMEs, open, laparoscopic, and robotic procedures provide equivalent oncological outcomes.^{5,7,8}

Elderly individuals and those with comorbidities who are diagnosed with CRC may experience higher risk of complications as a result of both surgical procedures and anesthesia.^{9,10} The American Society of Anesthesiologists (ASA) score is frequently used to assess anesthesia risk and anesthesia-related complications.¹¹ Due to the increased risks posed by CRC surgery and anesthesia to the above-mentioned groups, patient-specific planning should be undertaken prior to surgery. Whenever possible regional anesthesia rather than general anesthesia should be used for anesthesia management to preserve lung and heart functions.^{12,13}

The aim of this study was to analyze pathology specimens from patients who underwent CRC surgery under regional anesthesia due to advanced age or comorbidities to determine whether these specimens adhered to oncological standards for CRC treatment.

Methods. In this retrospective cohort study, 75 patients with an ASA score of 3-4 who underwent surgery for CRC at Ankara Bilkent City Hospital, Ankara, Turkey, between May 2019 and May 2023 were analyzed. Of these, 10 (13.33%) were emergency cases, 8 (10.66%) were elective cases carried out under general anesthesia (or conversion to general anesthesia), and 4 (5.33%) were patients who underwent palliative surgery. After excluding these patients, the remaining 53 (70.66%) patients were included in the study. The ethics committee of Ankara Bilkent City Hospital, Ankara, Turkey, approved the study (ref. no.: E1-23-3694). Open surgery was carried out for all patients based on the localization of the tumor.

The data on the patients were obtained from electronic records. All patients switched to a clear liquid diet 3 days before the surgery. During this period, they received intravenous fluids and enteral/parenteral nutrition support. The night before the surgery, bowel preparation was administered orally and rectally. In addition to nutritional support, patients were enrolled in a prehabilitation program that included breathing exercises and walking exercises. Standard preoperative antibiotic prophylaxis with 1g ceftriaxone and 500mg metronidazole was initiated one hour before the surgery and repeated every 4 hours during the procedure. All patients undergoing low anterior resection for rectal cancer had an ileostomy. In cases of colon cancer, the decision to carry out an anastomosis or create a stoma

was left to the surgeon's discretion. The pathology results were examined to determine whether they adhered to oncological standards. The negative margins of the proximal, distal, and circumferential margins (CRMs), as well as the number of lymph nodes (>12) removed, were assessed. Prior to undergoing surgery for mid- and lower rectal tumors, 24 of the 53 patients in the study received neoadjuvant chemoradiotherapy.

All patients underwent complete mesocolic and mesorectal resection in accordance with oncological standards for CRC treatment.

An epidural catheter was inserted at T7/8 intervals. For epidural anesthesia, 3cc of heavy bupivacaine was administered. Following the negative aspiration, 7ml of injectable epidural analgesia, 5ml of bupivacaine 0.5%, and 2ml of epidural saline were delivered. A 3cc of 0.5% bupivacaine was administered intraoperatively at 2-hour intervals, and controlled analgesia was maintained until the second postoperative day. After the spinal block, ketamine-propofol (ketofol [1:1]) with a Ramsay sedation score of 3 was delivered.

Statistical analysis. Data were analyzed using the Statistical Package for the Social Sciences Statistics for Windows, version 24.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to describe demographic data. The Shapiro-Wilk test was used to test the normality of the data. Continuous variables are presented as median (min-max) or mean \pm standard deviation. Categorical variables are reported as absolute frequencies and percentages.

Results. The median age of the patients (N=53) included in the study was 75 years (min-max: 53-94). There were 27 (50.9%) females and 26 (49.1%) males. **Table 1** provides information on the surgical techniques that were carried out and the number of patients.

Postsurgery, 15 (28.30%) patients were followed in the ward without any intensive care unit (ICU) stay. A total of 20 (37%) patients were followed in the ICU for one day. The remaining 18 (33.3%) patients were followed for more than one day, and one (1.82%) patient was followed for 26 days. In the postoperative period, 3 of the 53 patients died, resulting in a mortality rate of 5.6%. Among the patients who died, 2 deaths were attributed to myocardial infarction (MI), and one death was due to COVID-19 pneumonia (**Table 2**).

Interestingly, noanastomotic leaks were observed in any of the patients who underwent anastomosis during postoperative follow-up. Out of 53 patients, 22 (41.53%) developed wound infections; 30 (56.6%) experienced pulmonary complications; 4 (7.54%) had urinary tract infections; 12 (22.64%) experienced

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Table 1 - Comparative baseline characteristics of the patients.

Parameters	n (%)
Age (years), median (min-max)	75 (53-94)
Gender	
Female	27 (50.9)
Male	26 (49.1)
Cigarette smoking	32 (60.4)
Major comorbidities	
Coronary artery disease	22 (41.5)
Hypertension	36 (67.9)
Diabetes mellitus	39 (75.6)
COPD	28 (52.8)
Heart failure	18 (34.0)
ASA score	
ASA 3	33 (62.3)
ASA 4	20 (37.7)
Preoperative stage	
I	3 (5.7)
II	19 (35.8)
III	26 (49.0)
IV	5 (9.4)
Operations	
Right hemicolectomy	9 (17.0)
Extended right hemicolectomy	5 (9.4)
Left hemicolectomy	5 (9.4)
Extended left hemicolectomy	1 (1.9)
Low anterior resection	22 (41.5)
Abdominoperineal resection	4 (7.5)
Total colectomy	7 (13.2)
Values are presented as numbers and percentages (%), COPD: chronic obstructive pulmonary disease, ASA: America Association of Anesthesiology	

Table 2 - Time of stay in the intensive care unit and mortality.

Parameters	n (%)
Time of stay ICU (day)	
0	15 (28.3)
1	20 (37.7)
2	3 (5.7)
3	3 (5.7)
4	2 (3.8)
5	2 (3.8)
7	1 (1.9)
10	1 (1.9)
15	1 (1.9)
26	1 (1.9)
Mortality	
Myocardial infarct	
ASA 3	1 (1.9)
ASA 4	1 (1.9)
Total	2 (3.8)
COVID-19 pneumonia	
ASA 3	1 (1.9)
ASA 4	0 (0.0)
Mortality (overall)	3 (5.7)
Values are presented as numbers and percentages (%). ICU: intensive care unit, ASA: America Association of Anesthesiology	

urinary dysfunction; 18 (33.96%) developed ileus; and 4 (7.54%) developed intra-abdominal abscesses. All complications, except for 12 (22.64%) patients who required wound debridement due to wound abscess and 4 (7.54%) patients who required radiological drainage for intra-abdominal abscess, resolved with medical treatment. All patients resumed oral intake 8 hours postoperatively. In the 18 patients who developed ileus, discharge was achieved with conservative management, and no radiological or surgical intervention was required (Table 3).

All the patients had negative proximal, distal, and circumferential surgical margins. The mean number of removed lymph nodes was 23.45 (min-max: 3-97). The median number was 19 (IQR%: 25-75: 13-27) (Table 3). In 10 (18.9%) of the 53 patients, the number of lymph nodes (<12) retrieved was insufficient. When the patients who received neoadjuvant therapy were excluded, an insufficient number (<12) of lymph nodes were removed in 3 (7.69%) of 10 patients. Among these, 7 (70%) had local advanced rectal cancer and received neoadjuvant treatment with subsequent low anterior resection, 2 (20%) had a left hemicolectomy, and one (10%) had a right hemicolectomy (Table 4).

In our series, 8 patients with an ASA score of 3-4 underwent surgery under general anesthesia. Complete mesocolic excision was carried out in only 2 of these patients. Postoperative mortality was observed in a total of 4 (50%) patients, including 2 who underwent oncological resection and 2 who did not undergo oncological resection.

Discussion. Complete mesocolic/mesorectal excision is a crucial requirement for optimal survival in patients with colorectal carcinomas. While patients classified as ASA3 and above have a higher risk of morbidity and mortality associated with general anesthesia, this risk is further elevated in CRC patients due to the need for a wide surgical dissection area in line with oncological standards and associated prolonged

Table 3 - Complications after surgery.

Complications	n (%)
Cardiac*	13 (24.5)
Respiratory**	30 (56.6)
Wound infection/abscess	22 (41.5)
Urinary dysfunction	12 (22.6)
Urinary tract infection	4 (7.5)
Postoperative ileus	18 (34.0)
Intraabdominal abscess	4 (7.5)

Values are presented as numbers and percentages (%). *Hypotension, hypertension, acute heart failure, and myocardial infarction.

**Athelectasy, pneumonia, and nasal oxygen requirement.

Table 4 - Removed lymph nodes.

Operations	Median	Mean	Min-max	IQR (25-75%)
Right hemicolectomy	19	20.22	11-34	11-19
Extended right hemicolectomy	26	26.60	20-32	20-24
Left hemicolectomy	16	24.20	7-66	7-10
Extended left hemicolectomy	28	28.00	-	-
Low anterior resection	14	13.80	3-29	7-17
Abdominoperineal resection	21	28.25	12-59	12-
Total colectomy	48	45.86	14-97	14-48
Overall	19	23.45	3-97	13-27

IQR: interquartile range

operative times. The present study shows that surgeries for high-risk CRC patients can be carried out in accordance with oncological standards using regional anesthesia.

Colorectal cancer patients generally have a mortality rate of approximately 2%.¹⁴ Patients classified as ASA3 and above, including those with CRC, exhibit perioperative mortality rates in the range of 8%.¹⁴ One major reason for the elevated mortality rate is the intolerance of these patients to general anesthesia. Hecket et al¹⁵ emphasized that the ASA score is a simple and useful predictor of morbidity and mortality, highlighting that patients classified as ASA3 and above are at high risk. In a study carried out by Skipworth et al,¹⁶ high-risk patients were administered spinal/epidural anesthesia as an alternative approach to general anesthesia. Skipworth et al¹⁶ reported that surgical treatment under spinal-epidural anesthesia can be safely carried out without early additional morbidity and mortality in patients with ASA scores of 3-4. In another study on 68 CRC patients who underwent elective surgery with spinal anesthesia and a continuous catheter, Kumar et al¹⁷ examined parameters, such as early-term morbidity, mortality, and return to normal life. Kumar et al¹⁷ included 29 patients with an ASA score of 4 in this research, and none of these patients had died 30 days postsurgery. However, Kumar et al¹⁷ did not specify whether the procedures involved CME or whether they were palliative (namely, carrying out ileostomy or non mesocolic resection). In the current study, one ASA4 patient died from MI. Of 2 ASA3 patients who died, one death was due to MI and the other to COVID-19. The present study differs from similar studies in the literature in that it assessed only CRC patients who underwent elective major surgery according to standard oncological standards. In our study, the surgical procedures were carried out under regional anesthesia and had no effect on mortality in these high-risk patients.

Complete mesocolic excision and TME are effective methods in terms of specimen quality and survival.¹⁸

Applying this technique, the 5-year survival rate increases from approximately 45-75%, while recurrence rates decrease from 30% to 5-8%.¹⁹ For this reason, CME/TME is the standard treatment for colorectal carcinomas. The most significant disadvantage of this treatment is the higher complication rate compared to patients who do not undergo CME/TME.^{18,19} In addition to complications, other disadvantages include prolonged operative time, increased blood loss, and greater insensible fluid loss and CME/TME is more difficult than other colectomies.²⁰ Despite these challenges associated with the CME/TME technique, it remains the standard surgical approach for patients with colorectal carcinomas. In our study, the complication rates in patients who underwent CME/TME under spinal-epidural anesthesia were similar to those reported in the literature for patients with lower ASA scores. Despite all these challenges, results from our study suggested that CME/TME with spinal-epidural anesthesia can be safely carried out without higher complication rate and mortality in patients with high ASA scores.

Lymph node metastasis is the most important prognostic factor in CRC.²¹ Consequently, it is recommended that the surgeon should remove a minimum of 12 lymph nodes.^{22,23} Indeed, inadequate lymph node retrieval has been reported in 14.7-52% of all CRC patients.²⁴ In a population-based study by Baxter et al,²⁵ the rate of adequate lymph node removal was 37%. In a study, inadequate lymph node excision occurred in 34.6% of patients undergoing surgery for colon cancer. Other than inadequate lymph node removal due to surgical techniques, there are also problems with pathological evaluations.²⁶ Lymph node dissection should be repeated on specimen by pathologists if the pathology results indicate that the number of lymph nodes in the specimen is inadequate. If this problem recurs after re-examination, the second lymph node dissection attempt should be documented in the pathology report.^{22,23} In this study, one patient with insufficient lymph node retrieval had a tumor

located in the right colon, and 2 patients had tumors in the left colon. Neoadjuvant therapy for rectal cancer patients may result in inadequate lymph node retrieval in 40-80% of cases.²⁷ In this study, lymph node retrieval was insufficient in 29.16% of the patients with rectal cancer, which is lower than the rate reported in the literature. The present study suggests that spinal/epidural anesthesia is not a barrier to achieving adequate lymph node dissection.

In rectal cancers, positivity of the CRM is the most critical factor associated with rectal cancer recurrences.²⁸ Circumferential margin positivity for rectal cancers of 5-41% has been reported in the literature.²⁸⁻³¹ Despite the small number of patients in our study, it shows that rectal cancer surgery can be carried out under regional anesthesia with a negative CRM and acceptable lymph node recovery.

Study limitations. The study's retrospective design and small patient population are the main limitations. Although this study included patients with complete medical records, retrospective designs are nevertheless susceptible to medical record challenges, such as missing or inaccurate data. Another limitation is the small number of patients in the control group, as all patients were not suitable for general anesthesia, making it difficult to carry out a case-control study. Therefore, it was not possible to form and compare 2 groups. Only a feasibility study could be carried out through retrospective cohort analysis. Prospective research may be useful in confirming the findings of this study.

In conclusion, regional anesthesia in elderly and comorbid CRC patients is sufficient in terms of oncological surgical principles, and it offers substantial benefits in terms of postoperative morbidity and mortality. Nonetheless, additional prospective studies on this topic is required.

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