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RESEARCH ARTICLE

Comparison of Minimally Invasive and Open Colon Surgery for the Treatment of T4 Colon Cancer in a Tertiary Care Institution Using Propensity Score Matching Analysis

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ABSTRACT

Aim: Despite the increasing popularity of minimally invasive surgery (MIS) in recent years, its efficacy in treating T4 colon cancer remains a subject of ongoing debate. This study aimed to assess the perioperative and oncological outcomes of MIS for T4 colon cancer in comparison with open surgery (OP).

Method: We conducted a retrospective cohort analysis on 181 consecutive patients who underwent a T4 colon cancer resection through either MIS or OP between December 2014 and September 2021. Converted patients were evaluated in the MIS group according to the intention-to-treat principle. Propensity score matching (PSM) was employed based on age, gender, American Society of Anesthesiologists score, and the T-stage subgroup (T4a and T4b) to control for potentially confounding factors. Demographics short-term and long-term oncological outcomes were evaluated and compared between the two groups.

Results: Post-PSM resulted in 49 patients in each group. Both groups were comparable in terms of patient demographics, clinical stage at diagnosis, and postoperative morbidity. The median operative time was longer in the MIS group (167 vs. 132 minutes, p<0.01). The lymph node yield and the quality of complete mesocolic excision did not differ significantly between the two groups. The conversion rate was 8.2%. The 5-year overall survival (85.0% for the MIS group vs. 88.5% for the OP group, p=0.7) and the disease-free survival (62.5% for the MIS group vs. 70.0% for the OP group, p=0.33) rates were comparable between the groups.

Conclusion: MIS is a safe approach for treating T4 colon cancer, demonstrating satisfactory outcomes. The method offers oncologically acceptable results, reinforcing its potential advantages.

Keywords: Colorectal neoplasms, colorectal surgery, minimally invasive surgical procedures

Introduction

Colorectal cancer is a serious cause of mortality and morbidity and is the third most common type of cancer and the fourth leading cause of cancer-related deaths in both men and women.[1]

The primary treatment for non-metastatic, localized colon cancer is surgery. While historically open surgery (OP) had been preferred, the first-ever laparoscopic resection of colorectal cancer was performed in 1991 by Jacobs et al.[2] Laparoscopic surgery has been popularized since 1991 and provides advantages over OP in terms of short-term outcomes, such as reduced postoperative pain, decreased blood loss, shorter hospital stay, earlier resumption of bowel function, early mobilization, and better cosmesis[3-7] without any compromise in long-term oncologic outcomes.[3,8-11] Due to these advantages,

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the laparoscopic approach is becoming more extensively used in treating colorectal cancer at all stages except T4.

No consensus has yet been reached on the optimal surgical approach in T4 colorectal tumors, and there is still an ongoing debate. Data in the literature that compare the results of open and laparoscopic resection of T4 tumors in depth are rare. According to the American Joint Committee on Cancer (AJCC),[4] European Association of Endoscopic Surgery,[12] and National Comprehensive Cancer Network[13] guidelines, laparoscopic treatment of T4 colorectal cancers is not recommended due to technical difficulties of en bloc resection, longer operative times, higher perioperative morbidity, and questionable oncologic outcomes.[14] These guidelines recommend OP, which enables easier extensive en bloc resection and avoids suspicion of tumor seeding due to excessive manipulation used in the laparoscopic technique.

In recent years, there has been significant improvement in minimally invasive surgery (MIS) techniques and surgeons' experience. Parallel to these advances, growing literature on this topic demonstrated that the laparoscopic technique is safe and feasible in locally advanced cancers,[15-18] and other research demonstrated good surgical and oncologic outcomes.[15,17,19,20] However, these studies have certain limitations: a low number of cases, retrospective design, and lack of long-term oncological results.[15,16,18,21,22] Therefore, although these articles show promising results, they still provide insufficient evidence to support laparoscopic resections.

This study aims to retrospectively demonstrate our experience in the MIS of T4 colorectal cancer. Furthermore, we compare R0 resection rates, perioperative results, and short- and long-term oncologic outcomes between propensity score-matched MIS and OP groups with T4 tumors.

Materials and Methods

Patients who underwent elective MIS or OP in Koç University Hospital and VKF American Hospital between January 2014 and September 2021 were recorded and their data were prospectively gathered and retrospectively analyzed. This study was approved by Koç University Institutional Board of Review (approval code: 2020.491.IRB1.181, date: 04.03.2021) and was conducted in compliance with the 1964 Helsinki Declaration. All participants agreed to a written informed consent before their participation. All methods were carried out according to the institutional review board's relevant guidelines and regulations. Each patient was also discussed in the multidisciplinary team consisting of general surgery, medical oncology, radiation oncology, gastroenterology, radiology, pathology, and nuclear medicine. This study included patients aged >18 years with a T4 tumor located between the cecum and rectosigmoid colon. Patients undergoing emergency surgery, patients presenting with perforated tumors, patients with metastatic disease or underlying inflammatory bowel disease, and familial adenomatous polyposis were excluded. Patient demographics, including age, gender, body mass index (BMI), and history of previous abdominal surgery, were recorded. The American Society of Anesthesiologists (ASA) Physical Status Classification, length of stay, biochemical results, complications (anastomotic leakage, wound dehiscence, bleeding, ileus), operative details (type and duration of surgery), pathology reports (tumor location and dimensions, lymph node status, tumor invasion depth, number of harvested lymph nodes, apical lymph node status, surgical margin status, AJCC stages, and distance between vascular tie and tumor epicenter/colon wall), intensive care unit stay, readmission, data related with follow-up visits, morbidity, and perioperative mortality status were recorded.

The patients' routine preoperative evaluation included a complete physical examination, colonoscopy and biopsy, computerized tomography (CT) of the chest and abdomen, and positron emission tomography with 2-deoxy-2-(fluorine-18) fluoro-D-glucose integrated with CT if necessary. Surgical procedures were performed using oncological resection principles. The extent of the surgery was decided according to the tumor location and adjacent organ involvement, and an en bloc resection was preferred in the case of adjoining organ involvement. The conversion was defined as performing laparotomy during MIS due to factors such as bleeding, adhesions, and tumor perforation to achieve R0 resection and critical alterations in patients' vital status (Figures 1, 2). En bloc resections, cholecystectomy, and stoma-creation were accepted as additional procedures. Patients with postoperative complications within 30 days of colectomy were graded using the Clavien-Dindo grading system.[23]

At the joint discretion of the surgeon and the patient, a decision was made on whether the surgery would be performed with an MIS or an OP technique. MIS was offered regardless of the presence of a history of previous abdominal surgery. Whereas the MIS strategy included high ligation, mediolateral dissection, radical lymphadenectomy, and en bloc multi-visceral resection, the open approach consisted of vein and artery ligation, followed by lateral-to-medial dissection, radical lymphadenectomy, and an en bloc multi-visceral resection.

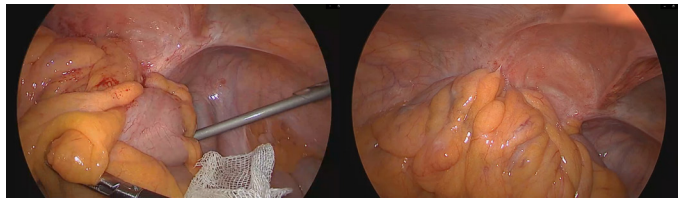

Figure 1. Laparoscopic view of a tumor in the sigmoid colon. Due to the invasion of the urinary bladder by the tumor, the procedure is converted to open surgery

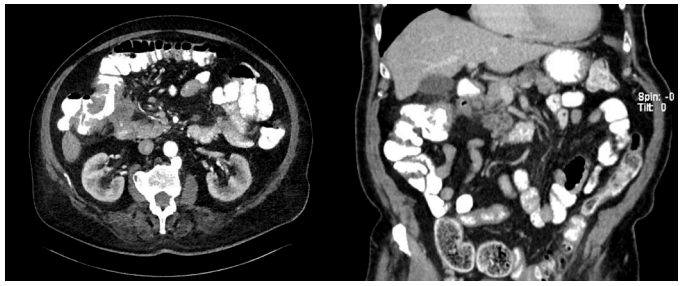

Figure 2. Computerized tomography scan showing a tumor in the right colon directly invading the pancreas and the second part of the duodenum

Patients meeting the criteria were split into two groups: the MIS group, consisting of patients who underwent laparoscopic or robotic surgery, and the OP group, consisting of patients who underwent OP. Patients who converted from MIS procedures to OP procedures were evaluated in the MIS group based on the intention-to-treat principle. Propensity score matching was performed to minimize the confounding factors and selection bias. Age, gender, ASA score, and pathological T-stage subgroup (pT4a or pT4b) were the variables included in the score matching. Nearest neighbor matching was performed in a 1:1 ratio, with the caliper width set at 0.2. Postoperative outcomes were assessed and compared between the two groups.

The patients' oncological follow-up was carried out in accordance with the American Society of Clinical Oncology and American Society of Colon and Rectal Surgeons guidelines.[24,25] Follow-up visits were scheduled every 3 months for the first 2 years and then every 6 months for the next 2 years. A physical examination was performed, and tumor marker levels (CEA, Ca-125, Ca 19-9) were measured during every follow-up visit. An annual control colonoscopy and CT scan of the chest and abdomen to check for recurrent cancer in the lymph nodes, lungs, and liver were performed for the first 3 years after surgery. The frequency of follow-up visits and tests was adjusted according to the disease's progression.

The primary outcomes were oncological, such as R0 resection rates, overall survival (OS), disease-free survival (DFS), short and long-term mortality, and morbidity.

Statistical Analysis

Statistical analysis of the results was carried out using SPSS version 21.0 (IBM, Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) or median (range) based on data distribution, whereas categorical variables were presented as absolute values and percentages. Student's t-test and the Mann-Whitney U test were used to compare normally and non-normally distributed variables, respectively. Fisher's exact test and the chi-squared test were used to analyze categorical variables. The Kaplan-Meier curve was utilized to evaluate OS, and survival differences between ages were compared using the log-rank method. Cox's proportional hazards regression model was used for the combined effect of different parameters on survival. Statistical significance was defined by a p-value of <0.05.

Results

Between January 2014 and September 2021, 181 patients with colon cancer clinically staged as T4 were operated upon, and 51 patients were excluded because of distant metastasis. Thus, the total sample size was 130 before matching, and after matching, 49 patients were selected for each group (Chart 1). The patients were followed up for 75 months on average. The

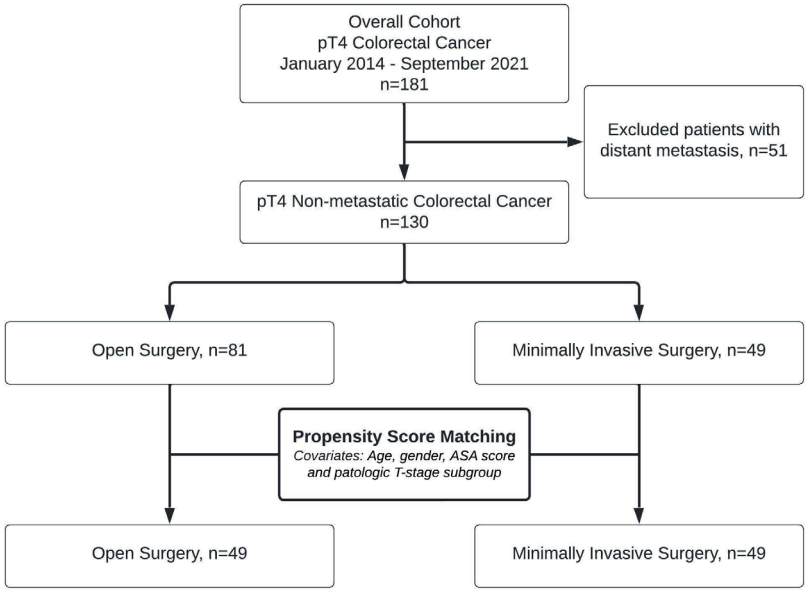

Chart 1. Flowchart

mean age, male proportion, and BMI of the patients were 65 (SD=16.8)/68 (SD=14.9), 59.2/57.1%, and 26.7 (SD=5.3)/22.7 (SD=5.2) for the MIS and OP groups, respectively (Table 1). The "T" stage based on histopathology of surgery specimen was T4a for 42 and 40 patients and T4b for the remaining 7 and 9 patients for the MIS and OP groups, respectively, and there was no significant difference in the pT and pN grades between the two surgical groups (p=0.59 and p=0.88, respectively) (Table 2). Seventy-nine (70.4%) of the patients were ASAI-II, and the remaining 29 (29.6%) were ASAIII-IV and were similar in both groups (p=0.83). Furthermore, there were no differences in tumor location or type of surgery (p=0.51 and p=0.27, respectively) (Tables 1, 3).

The median operation duration for the MIS group was significantly longer than for the OP group (167.65 and 132 minutes, respectively, p<0.01) (Table 3).

The conversion rate was 8.2% (Table 3). The main reasons for conversion were bleeding and technical difficulties.

The mean length of hospital stay and Clavien-Dindo scores of the patients were similar in both groups (p=0.28 and p=0.18). Nine patients in the MIS group and twelve patients in the OS group had additional surgery, and there was no significant difference (p=0.45). The postoperative surgical complication rate, reoperation rate, readmission, and mortality within 30 days were also similar between the two groups (p=0.16, p=0.28, p=0.39, p=1.0, respectively). Anastomotic leakage was observed in none of the patients in the MIS group and 3 patients in the OP group, and no statistically significant difference was found between the two groups (p=0.79) (Table 4).

Surgical margin positivity was not observed in the histopathological analysis of any surgically resected specimen in both groups. The number of harvested lymph nodes was >12 in both groups, which is the minimum required number for accurate staging, and the average numbers were 43.10 and 40.71 in the MIS and OP groups, respectively (p=0.17). Tumor size was higher in the OP group than in the MIS group, but the difference did not reach statistical significance (5.5 cm vs. 4.4 cm, respectively, p=0.08). There was no significant difference between the lymphovascular and perineural invasion rates (p=0.52 and p=0.7, respectively). Furthermore, the distance between the vascular tie and colon wall and between the vascular tie and tumor were similar in both groups (p=0.82 and p=0.33, respectively) (Table 2).

The overall 5-year survival rate was 85% in the MIS group and 88.5% in the OP group, and there was no significant difference (p=0.7) (Chart 2). Furthermore, the 5-year DFS rates were similar, at 62.5% for the MIS group and 70% for the OP group (p=0.33) (Chart 3). The local recurrence rate was comparable between the two groups (14.2% in the OP group vs. 31.1% in the MIS group, p=0.12).

Table 1. Patient charecteristics after matching

	MIS (n=49) n (%) or mean (SD)	OP (n=49) n (%) or mean (SD)	p-value
Age	65.35 (16.84)	68.16 (14.94)	0.19
Sex			0.84
Male	29 (59.2%)	28 (57.1%)	
Female	20 (40.8%)	21 (42.9%)	
BMI (kg/m^2)	26.65 (5.29)	22.66 (5.15)	0.82
ASA score			0.83
1-2	34 (69.4%)	35 (71.4%)	
≥3	15 (30.6%)	14 (28.6%)	
Tumor location			0.46
Cecum	3 (6.1%)	6 (12.2%)	
Ascending colon	11 (22.4%)	9 (18.4%)	
Hepatic flexure	2 (4.1%)	8 (16.3%)	
Transverse colon	6 (12.2%)	3 (6.1%)	
Splenic flexure	6 (12.2%)	4 (8.2%)	
Descending colon	2 (4.1%)	2 (4.1%)	
Sigmoid colon	12 (24.5%)	9 (18.4%)	
Rectosigmoid colon	7 (14.3%)	8 (16.3%)	
Previous abdominal surgery (+)	18 (36.7%)	20 (40.8%)	0.68

MIS: Minimally invasive surgery, SD: Standard deviation, OP: Open surgery, BMI: Body mass index, ASA: American Society of Anesthesiologists

Table 2. Pathological results after matching

	MIS (n=49) n (%) or mean (SD)	OP (n=49) n (%) or mean (SD)	p-value
pT			0.59
4a	42 (85.7%)	40 (81.6%)	
4b	7 (14.3%)	9 (18.4%)	
pN			0.78
0	16 (32.7%)	19 (38.8%)	
1a	7 (14.3%)	7 (14.3%)	
1b	12 (24.5%)	10 (20.4%)	
1c	1 (2%)	1 (2%)	
2a	5 (10.2%)	8 (16.3%)	
2b	8 (16.3%)	4 (8.2%)	
Harvested lymph node	43.10 (18.85)	40.71 (15.69)	0.17
Tumor size (largest cm) (min.-max.)	4.4 (2-13)	5.5 (3-17)	0.08
Surgical margin positivity	0 (0%)	0 (0%)	1
Lymphovascular invasion	32 (65.3%)	35 (71.4%)	0.52
Perineural invasion	27 (67.5%)	20 (47.6%)	0.07
Distance between vascular tie and colon wall	11.49 (3.3)	11.31 (3.59)	0.82
Distance between vascular tie and tumor	13.17 (4.14)	12.24 (4.11)	0.33

MIS: Minimally invasive surgery, SD: Standard deviation, OP: Open surgery, min.: Minimum, max.: Maximum

Table 3. Intraoperative results after matching

	MIS (n=49) n (%) or mean (SD)	OP (n=49) n (%) or mean (SD)	p-value
Type of surgery			0.27
Right hemicolectomy	16 (32.7%)	22 (44.9%)	
Left hemicolectomy	5 (10.2%)	5 (10.2%)	
Anterior resection	10 (20.4%)	13 (26.5)	
Extended right hemicolectomy	0 (0.0%)	1 (2.0%)	
Total hemicolectomy	2 (4.1%)	2 (4.1%)	
Subtotal colectomy	7 (14.3%)	4 (8.2%)	
Low anterior resection	9 (18.4%)	2 (4.1%)	
Conversion to open surgery	4 (8.2%)		
Operative time (minutes)	167.65 (64.41)	132 (41.29)	**<0.01**
Additional surgery	9 (18.4%)	12 (24.5%)	0.45
Cholecyctectomy	3 (6.1%)	3 (6.1%)	
Pulmonary wedge resection	0 (0%)	1 (2.0%)	
Splenectomy	1 (2.0%)	0 (0%)	
Gastrectomy	0 (0%)	1 (2.0%)	
Appendectomy	0 (0%)	1 (2.0%)	
Oopherectomy	1 (2.0%)	1 (2.0%)	
Small bowel resection	3 (6.1%)	4 (8.2%)	
Liver segmentectomy	1 (2.0%)	1 (2.0%)	

MIS: Minimally invasive surgery, SD: Standard deviation, OP: Open surgery

Table 4. Postoperative results after matching

	MIS (n=49) n (%) or mean (SD)	OP (n=49) n (%) or mean (SD)	p-value
Length of hospital stay (days)	7.20 (2.44)	7.71 (2.99)	0.28
Clavien-Dindo classification			0.18
<3	43 (87.8%)	38 (77.6%)	
≥3	6 (12.2%)	11 (22.4%)	
Complications within 30 days	9 (18.4%)	15 (30.6%)	0.16
Readmission within 30 days	0 (0.0%)	1 (2.0%)	0.39
Reoperation within 30 days	1 (2.0%)	4 (8.3%)	0.28
Mortality within 30 days	1 (2.0%)	1 (2.0%)	1
Anastomotic leak (+)	0 (0.0%)	3 (6.1%)	0.79

MIS: Minimally invasive surgery, SD: Standard deviation, OP: Open surgery

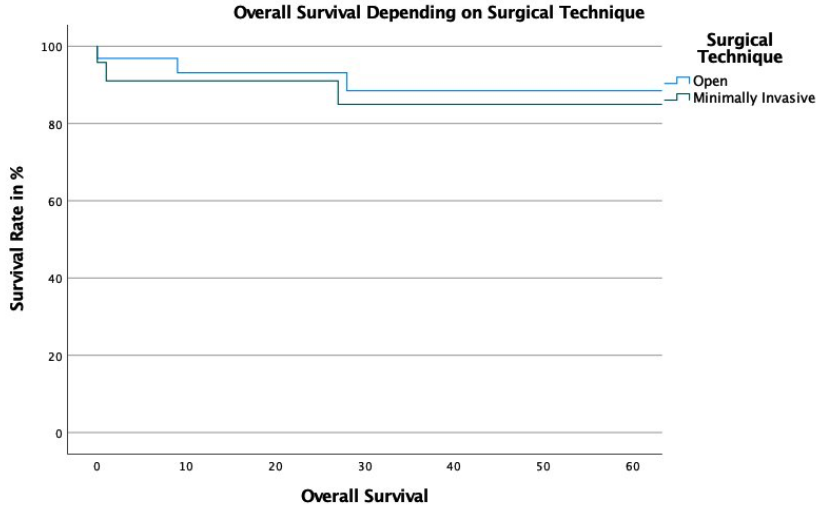

Chart 2. Overall survival depending on the surgical technique

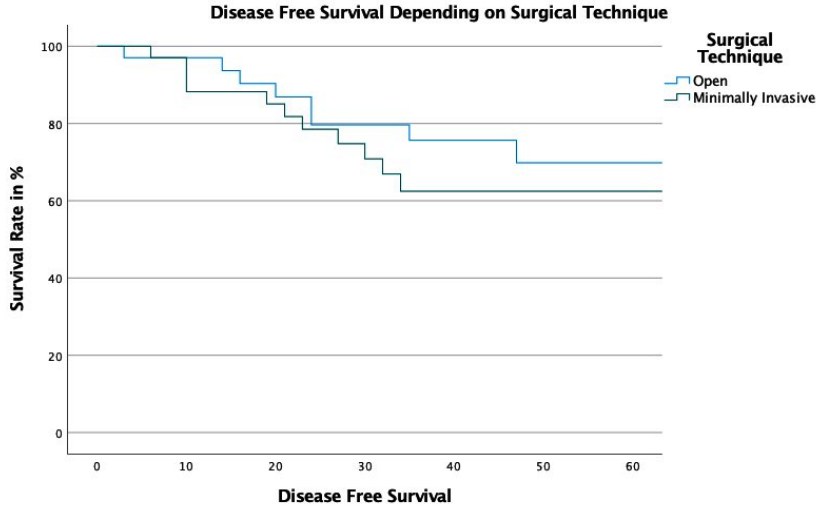

Chart 3. Disease-free survival depending on the surgical technique

Discussion

The surgical treatment of T4 colon cancer is challenging, regardless of whether the MIS or OP technique is deployed. Surgery for T4 colon cancer includes the en bloc resection of adjacent infiltrated structures. Surgeons with limited experience benefit from guidelines,[26] whereas more experienced colorectal surgeons have less trouble in decision-making during patient selection and changing the preoperative surgical strategy. Therefore, the practices of more experienced surgeons, such as those in this study, may deviate from the guideline-suggested paths. As a result, even though guidelines determine approximately similar clinical strategies, the approach can vary among different centers.

The crucial factor for conversion to OP is the degree of invasion into adjacent structures. Although there is no definitive written rule, its presence helps discriminate T4a tumor from T4b and is approached differently. Unfortunately, according to Feinberg et al.[27], the preoperative distinction between T3 and T4a tumors is complex, which makes the decision-making process of finding the optimal surgical strategy challenging.

Conversion to OP causes undesirable consequences. Conversion from MIS to OP methods offers several advantages, but it also carries the potential risk of conversion when opting for the laparoscopic method. Hence, we incorporated and examined these patients in the MIS group utilizing the intention-to-treat principle. Also, as stated by Klaver et al.[28], high conversion rates create a risk of disturbing outcomes in the case of intention-to-treat analysis, which was not the case in our sample. The conversion rate was 8.2%, which is in accordance with rates presented in the literature, which range from 7.6% to 18% (Liu et al.[29] 10.7%, Chan and Tan[30] 8.6%, Bretagnol and Leroy[31] 18%, Kang et al.[32] 7.6%, Kim et al.[33] 13.7%, COLOR Trial Group[34] 17%). Despite being in the normal range of the literature, the conversion rate is close to the lower border due to the high-level experience of our surgeons and surgical team and being a high-volume center. Preoperative preparation for conversion can be essential in the practice of MIS resection of T4 tumors. Informing operation room staff about possible conversion before the onset of surgery in cases with a higher risk of conversion is beneficial as it allows adequate surgical instrument preparation. In patients with a high risk of conversion, we routinely prepare to keep the surgical instruments for OP ready in the operating theatre during MIS, enabling prompt intervention in the case of an emergency.

Achieving high R0 resection rates is crucial in oncologic surgery, particularly for patients with T4 colorectal cancer, because R0 resection is considered one of the most critical factors affecting long-term survival.[35-38] In this study, the R0 resection rate was 100%, and the harvested lymph node number was ≥12, as suggested for appropriate staging in both the MIS and OP cases. These results are a measure of our surgical experience and our success in managing patients with colorectal cancer. Analyses of the intraoperative frozen section of all patients in our routine clinical practice are among the most critical factors in achieving a high R0 resection rate.

As a result of smaller incisions, laparoscopic surgery offers faster recovery and early mobilization, preventing complications of immobility, without any significant drawbacks. A shorter hospital stay is more comfortable for patients and may also decrease hospital-related complications. In this study, although the MIS group exhibited a shorter length of hospital stay compared with the OP group in patients with T4 colon tumors, the difference was not statistically significant after matching.

The distance from the vascular tie to the tumor epicenter is one of the parameters that can help to measure the quality of complete mesocolic excision.[39-44] This distance was found to be greater in the MIS group than in the OP group, without reaching statistical significance. This may indicate the quality of the MIS approach in reaching complete mesocolic excision, which is a crucial part of current oncologic colon surgery.

After MIS resection of T4 colon tumors, we found the 5-year OS and DFS rates to be 85% and 62.5%, respectively. This is in accordance with the data in the literature, where the 5-year OS and DFS rates range from 44.6% to 77.2% and 39.4% to 63.5%, respectively.[20,35,45,46] Our patients' survival rates are close to the upper limits presented in the literature, which demonstrates the high quality of care in our center. According to our study, MIS has comparable long-term oncologic outcomes and does not increase morbidity and mortality. As pivotal elements in evaluating the oncological outcome, OS and DFS are essential parameters. Our results show that MIS offers 5-year OS and DFS rates that are comparable with OP.

Study Limitations

Our study has some limitations. First, it is conducted in a single institution. Second, it is a retrospective study, and there is a lack of randomization in the selection procedure because of its retrospective nature. When extracting messages, we focused on the applicability of the MIS to patients with T4 colon cancer.

Conclusion

This study demonstrated that if the tumor's en bloc resection can be achieved, MIS should not be accepted as an absolute contraindication in T4 colon cancers, with its advantages of achieving oncologically acceptable results. The decision should be made individually based on patient characteristics and surgeons' experience.

Ethics

Ethics Committee Approval: This study was approved by Koç University Institutional Board of Review (approval code: 2020.491.IRB1.181, date: 04.03.2021).

Informed Consent: All participants agreed to a written informed consent before their participation.

Authorship Contributions

Surgical and Medical Practices: İ.H.Ö., D.S.U., İ.F.A., S.Z., D.B., E.B., Concept: İ.H.Ö., E.B., E.Ö., A.R., D.B., E.B., Design: İ.H.Ö., E.B., E.Ö., A.R., D.B., E.B., Data Collection or Processing: S.N.K., A.D.K., S.S., M.Y., E.Ö., D.S.U., İ.F.A., S.Z., Analysis or Interpretation: İ.H.Ö., S.N.K., A.D.K., S.S., M.Y., E.B., E.Ö., D.S.U., İ.F.A., S.Z., A.R., Literature Search: İ.H.Ö., S.N.K., A.D.K., M.Y., Writing: İ.H.Ö., S.N.K., A.D.K., S.S., M.Y., E.B., E.Ö., D.S.U., İ.F.A., S.Z., A.R., D.B., E.B.

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References

1. Brenner H, Kloor M, Pox CP. Colorectal cancer. Lancet 2014;383(9927):1490-1502.
2. Jacobs M, Verdeja JC, Goldstein HS. Minimally invasive colon resection (laparoscopic colectomy). Surg Laparosc Endosc 1991;1:144-150.
3. Laparoscopically assisted colectomy is as safe and effective as open colectomy in people with colon cancer Abstracted from: Nelson H, Sargent D, Wieand HS, et al; for the Clinical Outcomes of Surgical Therapy Study Group. A comparison of laparoscopically assisted and open colectomy for colon cancer. N Engl J Med 2004;350:2050-2059. Cancer Treat Rev 2004;30:707-709.
4. Chan DK, Chong CS, Lieske B, Tan KK. Laparoscopic resection for rectal cancer: what is the evidence? Biomed Res Int 2014;2014:347810.
5. Guillou PJ, Quirke P, Thorpe H, Walker J, Jayne DG, Smith AM, Heath RM, Brown JM; MRC CLASICC trial group. 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.
6. Lacy AM, García-Valdecasas JC, Delgado S, Castells A, Taurá P, Piqué JM, Visa J. Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial. Lancet 2002;359:2224-2229.
7. Veldkamp R, Kuhry E, Hop WC, Jeekel J, Kazemier G, Bonjer HJ, Haglind E, Påhlman L, Cuesta MA, Msika S, Morino M, Lacy AM; COlon cancer Laparoscopic or Open Resection Study Group (COLOR). Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial. Lancet Oncol 2005;6:477-484.
8. Berends FJ, Kazemier G, Bonjer HJ, Lange JF. Subcutaneous metastases after laparoscopic colectomy. Lancet 1994;344:58.
9. Kuhry E, Schwenk W, Gaupset R, Romild U, Bonjer J. Long-term outcome of laparoscopic surgery for colorectal cancer: a Cochrane systematic review of randomised controlled trials. Cancer Treat Rev 2008;34:498-504.
10. Lee JK, Delaney CP, Lipman JM. Current state of the art in laparoscopic colorectal surgery for cancer: Update on the multi-centric international trials. Ann Surg Innov Res 2012;6:5.
11. Lee SW. Laparoscopic procedures for colon and rectal cancer surgery. Clin Colon Rectal Surg 2009;22:218-224.
12. Veldkamp R, Gholghesaei M, Bonjer HJ, Meijer DW, Buunen M, Jeekel J, Anderberg B, Cuesta MA, Cuschierl A, Fingerhut A, Fleshman JW, Guillou PJ, Haglind E, Himpens J, Jacobi CA, Jakimowicz JJ, Koeckerling F, Lacy AM, Lezoche E, Monson JR, Morino M, Neugebauer E, Wexner SD, Whelan RL; European Association of Endoscopic Surgery (EAES). Laparoscopic resection of colon Cancer: consensus of the European Association of Endoscopic Surgery (EAES). Surg Endosc 2004;18:1163-1185.
13. Benson AB 3rd, Venook AP, Cederquist L, Chan E, Chen YJ, Cooper HS, Deming D, Engstrom PF, Enzinger PC, Fichera A, Grem JL, Grothey A, Hochster HS, Hoffe S, Hunt S, Kamel A, Kirilcuk N, Krishnamurthi S, Messersmith WA, Mulcahy MF, Murphy JD, Nurkin S, Saltz L, Sharma S, Shibata D, Skibber JM, Sofocleous CT, Stoffel EM, Stotsky-Himelfarb E, Willett CG, Wu CS, Gregory KM, Freedman-Cass D. Colon Cancer, Version 1.2017, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 2017;15:370-398.
14. Shukla PJ, Trencheva K, Merchant C, Maggiori L, Michelassi F, Sonoda T, Lee SW, Milsom JW. Laparoscopic resection of t4 colon cancers: is it feasible? Dis Colon Rectum 2015;58:25-31.
15. Bretagnol F, Dedieu A, Zappa M, Guedj N, Ferron M, Panis Y. T4 colorectal cancer: is laparoscopic resection contraindicated? Colorectal Dis 2011;13:138-143.
16. Kim KY, Hwang DW, Park YK, Lee HS. A single surgeon's experience with 54 consecutive cases of multivisceral resection for locally advanced primary colorectal cancer: can the laparoscopic approach be performed safely? Surg Endosc 2012;26:493-500.
17. Nagasue Y, Akiyoshi T, Ueno M, Fukunaga Y, Nagayama S, Fujimoto Y, Konishi T, Nagasaki T, Nagata J, Mukai T, Ikeda A, Ono R, Yamaguchi T. Laparoscopic versus open multivisceral resection for primary colorectal cancer: comparison of perioperative outcomes. J Gastrointest Surg 2013;17:1299-1305.
18. Vignali A, Ghirardelli L, Di Palo S, Orsenigo E, Staudacher C. Laparoscopic treatment of advanced colonic cancer: a case-matched control with open surgery. Colorectal Dis 2013;15:944-948.
19. Sammour T, Jones IT, Gibbs P, Chandra R, Steel MC, Shedda SM, Croxford M, Faragher I, Hayes IP, Hastie IA. Comparing oncological outcomes of laparoscopic versus open surgery for colon cancer: Analysis of a large prospective clinical database. J Surg Oncol 2015;111:891-898.
20. Yang ZF, Wu DQ, Wang JJ, Lv ZJ, Li Y. Short- and long-term outcomes following laparoscopic vs open surgery for pathological T4 colorectal cancer: 10 years of experience in a single center. World J Gastroenterol 2018;24:76-86.
21. Huh JW, Kim HR. The feasibility of laparoscopic resection compared to open surgery in clinically suspected T4 colorectal cancer. J Laparoendosc Adv Surg Tech A 2012;22:463-467.
22. Ng DC, Co CS, Cheung HY, Chung CC, Li MK. The outcome of laparoscopic colorectal resection in T4 cancer. Colorectal Dis 2011;13:e349-e352.
23. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-213.
24. Chiorean EG, Nandakumar G, Fadelu T, Temin S, Alarcon-Rozas AE, Bejarano S, Croitoru AE, Grover S, Lohar PV, Odhiambo A, Park SH, Garcia ER, Teh C, Rose A, Zaki B, Chamberlin MD. Treatment of Patients With Late-Stage Colorectal Cancer: ASCO Resource-Stratified Guideline. JCO Glob Oncol 2020;6:414-438.
25. Vogel JD, Eskicioglu C, Weiser MR, Feingold DL, Steele SR. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Treatment of Colon Cancer. Dis Colon Rectum 2017;60:999-1017.
26. Gunaratnam C, Bernstein M. Factors Affecting Surgical Decision-making-A Qualitative Study. Rambam Maimonides Med J 2018;9:e0003.

27. Feinberg AE, Chesney TR, Acuna SA, Sammour T, Quereshy FA. Oncologic Outcomes Following Laparoscopic versus Open Resection of pT4 Colon Cancer: A Systematic Review and Meta-analysis. Dis Colon Rectum 2017;60:116-125.
28. Klaver CEL, Kappen TM, Borstlap WAA, Bemelman WA, Tanis PJ. Laparoscopic surgery for T4 colon cancer: a systematic review and meta-analysis. Surg Endosc 2017;31:4902-4912.
29. Liu ZH, Wang N, Wang FQ, Dong Q, Ding J. Oncological outcomes of laparoscopic versus open surgery in pT4 colon cancers: A systematic review and meta-analysis. Int J Surg 2018;56:221-233.
30. Chan DK, Tan KK. Laparoscopic surgery should be considered in T4 colon cancer. Int J Colorectal Dis 2017;32:517-520.
31. Bretagnol F, Leroy J. Laparoscopic resection for T4 colon cancer: perioperative and long-term outcomes. Updates Surg 2016;68:59-62.
32. Kang J, Baik SH, Lee KY, Sohn SK. Outcomes of laparoscopic surgery in pathologic T4 colon cancers compared to those of open surgery. Int J Colorectal Dis 2017;32:531-538.
33. Kim IY, Kim BR, Kim YW. The short-term and oncologic outcomes of laparoscopic versus open surgery for T4 colon cancer. Surg Endosc 2016;30:1508-1518.
34. COLOR Study Group. COLOR: a randomized clinical trial comparing laparoscopic and open resection for colon cancer. Dig Surg 2000;17:617-622.
35. Yang X, Zhong ME, Xiao Y, Zhang GN, Xu L, Lu J, Lin G, Qiu H, Wu B. Laparoscopic vs open resection of pT4 colon cancer: a propensity score analysis of 94 patients. Colorectal Dis 2018;20:O316-o325.
36. de'Angelis N, Vitali GC, Brunetti F, Wassmer CH, Gagniere C, Puppa G, Tournigand C, Ris F. Laparoscopic vs. open surgery for T4 colon cancer: A propensity score analysis. Int J Colorectal Dis 2016;31:1785-1797.
37. Bae SY, Choi MS, Gwak GY, Paik YH, Lee JH, Koh KC, Paik SW, Yoo BC. Comparison of usefulness of clinical diagnostic criteria for hepatocellular carcinoma in a hepatitis B endemic area. Clin Mol Hepatol 2012;18:185-194.
38. Tilson L, Sharp L, Usher C, Walsh C, S W, O'Ceilleachair A, Stuart C, Mehigan B, John Kennedy M, Tappenden P, Chilcott J, Staines A, Comber H, Barry M. Cost of care for colorectal cancer in Ireland: a health care payer perspective. Eur J Health Econ 2012;13:511-524.
39. Wang C, Gao Z, Shen K, Shen Z, Jiang K, Liang B, Yin M, Yang X, Wang S, Ye Y. Safety, quality and effect of complete mesocolic excision vs non-complete mesocolic excision in patients with colon cancer: a systemic review and meta-analysis. Colorectal Dis 2017;19:962-972.
40. Merkel S, Weber K, Matzel KE, Agaimy A, Göhl J, Hohenberger W. Prognosis of patients with colonic carcinoma before, during and after implementation of complete mesocolic excision. Br J Surg 2016;103:1220-1229.
41. Feng H, Zhao XW, Zhang Z, Han DP, Mao ZH, Lu AG, Thasler WE. Laparoscopic Complete Mesocolic Excision for Stage II/III Left-Sided Colon Cancers: A Prospective Study and Comparison with D3 Lymph Node Dissection. J Laparoendosc Adv Surg Tech A 2016;26:606-613.
42. Galizia G, Lieto E, De Vita F, Ferraraccio F, Zamboli A, Mabilia A, Auricchio A, Castellano P, Napolitano V, Orditura M. Is complete mesocolic excision with central vascular ligation safe and effective in the surgical treatment of right-sided colon cancers? A prospective study. Int J Colorectal Dis 2014;29:89-97.
43. Storli KE, Søndenaa K, Furnes B, Nesvik I, Gudlaugsson E, Bukholm I, Eide GE. Short term results of complete (D3) vs. standard (D2) mesenteric excision in colon cancer shows improved outcome of complete mesenteric excision in patients with TNM stages I-II. Tech Coloproctol 2014;18:557-564.
44. Siani LM, Lucchi A, Berti P, Garulli G. Laparoscopic complete mesocolic excision with central vascular ligation in 600 right total mesocolectomies: Safety, prognostic factors and oncologic outcome. Am J Surg 2017;214:222-227.
45. Leon P, Iovino MG, Giudici F, Sciuto A, de Manzini N, Cuccurullo D, Corcione F. Oncologic outcomes following laparoscopic colon cancer resection for T4 lesions: a case-control analysis of 7-years' experience. Surg Endosc 2018;32:1133-1140.
46. Yamanashi T, Nakamura T, Sato T, Naito M, Miura H, Tsutsui A, Shimazu M, Watanabe M. Laparoscopic surgery for locally advanced T4 colon cancer: the long-term outcomes and prognostic factors. Surg Today 2018;48:534-544.