DOI: 10.4274/tjcd.galenos.2020.2020-8-4
Turk J Colorectal Dis 2020;30:301-310

RESEARCH ARTICLE

Is Complete Mesocolic Excision Technique Superior to Conventional Hemicolectomy Technique for Patients with Right-Sided Colon Cancer? Preliminary Findings from a Single-Center Retrospective Analysis

Sağ Kolon Kanserinde Tam Mezokolik Eksizyon Tekniği Standart Hemikolektomi Tekniğinden Üstün Müdür? Tek Merkez Erken Dönem Retrospektif Analiz Sonuçları

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ABSTRACT

Aim: To evaluate the surgical and oncological outcomes of complete mesocolic excision versus conventional hemicolectomy in patients with right-sided colon cancer.

Method: A total of 87 patients with stage I-III cancer disease who underwent conventional hemicolectomy (n=39) or complete mesocolic excision (n=48) in a tertiary center were included. Data on patient demographics, tumor characteristics, treatment, and outcomes were assessed and compared between groups.

Results: No significant difference was noted between conventional hemicolectomy and complete mesocolic excision groups in terms of patient and tumor characteristics, chemotherapy, surgical morbidity, recurrence rates and apical node metastasis rates. The median total (58.0 vs 31.0, p<0.001) and apical lymph node yield (3.0 vs 2.0, p=0.034) were significantly higher with complete mesocolic excision than with conventional hemicolectomy, while there was a non-significant tendency toward a higher apical lymph node metastasis rate in the conventional hemicolectomy group (7.7% vs 2.1%). No significant difference was noted between the conventional hemicolectomy and complete mesocolic excision groups in terms of morbidity, length of hospital stay, recurrence, overall survival (66.7 vs 93.8% and 113.1 vs 74.9 months, respectively) and disease-free survival (64.1% vs 85.4% and 107.9 vs 68.7 months, respectively) at a median of 87.3 months and 25.1 months of follow-up, respectively.

Conclusion: Complete mesocolic excision was not associated with an increased risk of surgical morbidity or mortality compared to conventional hemicolectomy. Our findings emphasise the likelihood of residual metastatic apical lymph nodes in nearly 5.6% of cases in which complete mesocolic excision is not used. There may also be a potential longer term survival benefit for complete mesocolic excision vs conventional hemicolectomy.

Keywords: Colon cancer, morbidity, complete mesocolic excision, conventional hemicolectomy, lymph node yield, recurrence

ÖZ

Amaç: Sağ kolon kanserinde tam mezokolik eksizyon ile standart hemikolektomi tekniklerinin cerrahi ve onkolojik sonuçlarını karşılaştırmak.

Yöntem: Tam mezokolik eksizyon (n=48) ve standart teknik ile (n=39) sağ hemikolektomi yapılan toplam 87 evre 1-3 sağ kolon kanseri olgusu çalışmaya dahil edildi. Hastaların demografik yapıları, tümor özellikleri, yapılan tedaviler ve sonuçları gruplar arasında karşılaştırıldı.

Bulgular: Gruplar arasında hasta, tümör ve kemoterapi tedavi özellikleri, cerrahi morbidite, nüks oranları ve apikal lenf nodu metastaz oranları açısından farklılık saptanmadı. Tam mezokolik eksizyon grubunda ortalama total lenf nodu sayısı (58,0 vs 31,0, p<0,001) ve apikal lenf nodu sayısı (3,0 vs 2,0, p=0,034) anlamlı olarak yüksek saptandı. Standart teknik grubunda apikal lenf nodu metastaz oranının anlamlı fark oluşturmasa da

This paper was presented orally at 4th Congress of Cukurova Gastrointestinal Surgery Diseases, which was held on Feb 28-Mar 01, 2020 in Adana, Turkey

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Received/Geliş Tarihi: 01.09.2020 **Accepted/Kabul Tarihi:** 27.10.2020

yüksek olduğu gözlendi (%7,7 vs %2,1). Tam mezokolik eksizyon ve standart teknik grupları arasında ortalama 25,1 ve 87,3 ay takip süresinde morbidite, hastanede kalış süresi, nüks, genel sağkalım oranları (%93,8 vs %66,7) ve süreleri (74,9 vs 113,1 ay) ile hastalıksız sağkalım oranları (%85,4 vs %64,1) ve süreleri (68,7 vs 107,9 ay) açısından anlamlı farklılık saptanmadı.

Sonuç: Standart teknik ile karşılaştırıldığında tam mezokolik eksizyon tekniğinin cerrahi morbidite veya mortalite riskini arttırmadığı ve standart hemikolektomi yapılan olgularda %5,6 oranında rezidüel metastazik apikal lenf nodu kalabileceği gözlenmiştir. Bulgularımız erken dönemde tam mezokolik eksizyon tekniğinin sağkalım açısından anlamlı bir faydasını ortaya koyamasa da uzun dönemde potansiyel olarak faydalı olabileceğini düşündürmektedir.

Anahtar Kelimeler: Kolon kanseri, morbidite, tam mezokolik eksizyon, standart hemikolektomi, lenf nodu sayısı, nüks

Introduction

Complete mesocolic excision (CME) is a surgical technique first described by Hohenberger in 2009 which includes sharp dissection along embryological planes involving an intact envelope of mesentery together with high vascular ligation and resection of a sufficient length of bowel.[1,2] This technique adopts similar principles to that for total mesorectal excision in order to reach similar favorable outcomes in treating patients with rectal cancer.[1,2,3] Thus, CME may become the standard method for right-sided colon cancer resection, as promising oncological outcomes have reported previous reports and comparative studies.[2,3,4]

CME, however, is a more technically demanding procedure than conventional resections, especially when considering the complex vascular anatomy of the right colon and the poorer oncological outcomes for patients with right-sided vs left-sided colon cancers.[5] The utility of CME also presents a challenge in terms of continuously improving minimally invasive surgery and new adjuvant chemotherapies. Some of its other challenges include lack of level 1 evidence, the paucity of long-term results demonstrating improved oncological outcome to justify the higher risk of potentially catastrophic complications and the efforts required to overcome the extensive learning curve.[2,3,6,7]

The present study was therefore designed to comparatively evaluate the surgical and oncological outcomes of patients with right-sided colon cancer operated on with CME vs conventional hemicolectomy (CON) in terms of lymph node yield, surgical morbidity, survival and recurrence.

Material and Methods

This study has been conducted in accordance with the principles set forth in the Helsinki Declaration and current legislation. Permission was obtained from our institute for the use of patient data for publication purposes (date of approval: 05/12/2019, reference number/protocol number: 2019-19/23).

Study Population

A total of 87 patients [mean standard deviation (SD) age: 63.8 (14.3) years, 57.5% female] with stage I-III right-sided colon cancer were enrolled in this retrospective comparative study. The patients were divided into two groups according to surgical technique and timeline, including patients who underwent CON (n=39, February 2006-December 2012) and those who underwent CME (n=48, January 2013-June 2019). The CON group served as the historical comparison group for patients who underwent CME following the implementation of this technique in our clinic in 2013. Patients lost to follow-up as well as those with stage IV cancer or synchronous tumors were excluded from the study.

Study Parameters

Data were recorded for each patient on criteria such as patient demographics (age, gender), ASA Physical Status Classification System score (Class I-IV), surgery type and chemotherapy use. Tumor characteristics were also included, such as pathological stage (pT, pTNM), histological differentiation, tumor invasion (perineural, venous, lymphatic and extra-nodal) and the presence of mucinous components or signet-ring cells. Tumor staging was performed according to the American Joint Committee on Cancer-TNM (AJCC-8th) staging system.[8] Surgical morbidity, recurrence rate, presence of apical node metastasis, lymph node yield (total, metastatic, apical), length of hospital stay (LOS, day) and duration of follow-up (month) were also recorded. Complications that developed within the postoperative 30 days or during the entire postoperative LOS in patients with prolonged periods of hospitalization were considered as surgical morbidity and scored using the Clavien-Dindo Classification.[9] Overall survival (OS) and disease-free survival (DFS) for the study population were compared between the CON vs CME groups.

Histopathological Examination

Following the fixation of surgical samples in 10% neutral buffered formalin for a minimum of 36 hours, only the tumors were stained with Indian ink, while the mesenteric regions were not stained to allow for superior identification of lymph nodes. Tissue sections were taken from different regions of the tumors along with additional sections for assessment of the radial borders if necessary. Lymph node retrieval was conducted based on inspections and manual

identification, which was followed by the histological assessment. The lymph node sections were cut at 4 µm and stained with hematoxylin-eosin (H-E) for routine histology. Pathological evaluation was performed by the same team who carried out the study, composed of a gastrointestinal subspecialized pathologist and two pathology assistants. Local recurrence was defined as identification of the clinical or pathological disease evidence at lymphatic drainage site of the tumor or intestinal wall anastomosis line. DFS was considered the time (months) from R0 resection to identification of clinical or pathological local recurrence or distant metastasis. Survival status, survival time and follow up duration were calculated based on June 2019.

Surgery

The surgical procedures included right hemicolectomy, extended right hemicolectomy and laparoscopic right hemicolectomy. Mechanical bowel preparation was not performed; however, preoperative enemas were performed twice. Parenteral cefazolin 2x1 g and metronidazole 3x500 mg were initiated intraoperatively and continued 48 hours postoperatively. Conventional right hemicolectomy and extended right hemicolectomy were performed for tumors located up to or at the level of the hepatic flexure, respectively by colorectal surgeons. For both techniques, 10 cm of uninvolved surgical margins proximal and distal to the tumor with a wide resection were targeted. For patients at the T4 stage, invaded tissue was removed to enable R0 resection; this was one of the steps implemented as an additional intervention as shown in Table 2. Anastomoses were performed using the stapler or were done manually. For the CON technique, vascular ligation ensuring no observable or palpable residual lymph nodes was performed. For the CME technique, as described by Hohenberger, dissections were done in conformity with embryological planes and avoidance of any visceral fascial layer breaches; the procedure also involved central vascular ligation (CVL).[1] The operations were performed by the senior surgeon in majority of cases, while a few operations were performed by two surgeons with EBSQ-CP (2016 , Milan) board certificate and under supervision of the senior surgeon.

Follow-up

In accordance with postoperative National Comprehensive Cancer Network (NCCN) guidelines, patients were followed up in 3-month intervals in the first 2 years and in 6 months intervals in the following 3 years.[10] Blood biochemistry and tumor markers (CEA and CA19-9) were analyzed at each visit, while thoracoabdominopelvic CT and colonoscopy were performed once yearly. PET CT was optional. For the purpose of this study, patients or relatives were contacted to confirm survival status.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY). Categorical data were analyzed using Pearson Chi-Square test, Fisher's exact test, Linear-by-Linear Association and Mantel Haenzsel test, while Mann-Whitney U test was used for analysis of the numeric variables. Survival analysis was performed via Kaplan-Meier analysis and comparisons were made via Log-Rank test. Data were expressed as means (and SD), medians (minimum-maximum), 95% confidence intervals (CI) and percentages (%) where appropriate.

Results

Baseline Patient and Tumor Characteristics

Overall, mean patient age was 63.8 (SD 14.3, range 23 to 103) years and females composed 57.5% of the study population. Most of patients were American Society of Anesthesiologists (ASA) Class I-II (78.2%) status. The tumor histology revealed poor-moderate differentiation in 88.5% of tumors. Mucinous and signet-ring cell components were noted in 47.1% (pure mucinous in 18.4%) and 9.2% (pure signet-ring in 4.6%) of tumors. Perineural, venous, lymphatic and extra-nodal tumor invasion was noted in 39.1%, 20.7%, 34.5% and 29.9% of patients, respectively (Table 1). No significant difference was noted between CON and CME groups in terms of patient and tumor characteristics (Table 1).

Surgery, Chemotherapy and Staging

Chemotherapy was not administered in 43.7% of patients, while 56.3% did receive adjuvant chemotherapy. Locally advanced disease was noted in 75 (86.2%) patients, while additional interventions were performed in 12 (13.85%) patients at pT4b stage including small intestinal resection (n=7), partial abdominal wall resection (n=4) and cholecystectomy (n=1). In comparing the two surgery techniques, the laparoscopic approach was preferred in CON surgery (33.3 vs 2.1%, p<0.001) (Table 2).

Lymph Node Yield, Surgical Morbidity and Recurrence

Overall, postoperative complications were noted in 29 (33.3%) patients with a Clavien-Dindo Score (CDS) of ≥3 in 10 (11.5%) patients. Median total (58.0 vs 31.0, p<0.001) and apical (3.0 vs 2.0, p=0.034) lymph node yield were significantly higher in those who underwent CME compared to those who underwent CON, while there was a non-significant tendency for a higher rate of apical lymph node metastasis in the CON group (7.7 vs 2.1%) (Table 3). Median overall duration of follow up was 37.5 months (range: 3.5 to 156.3), and 87.3 months (range: 3.5 to 156.3) and 25.1 months (6.7 to 84.8) in the CON and

Table 1. Baseline patient and tumor characteristics

		Total (n=87)	Conventional hemicolectomy (n=39)	Complete mesocolic excision (n=48)	p value
Patient characteristics					
Age (year)	Mean (SD)	63.8 (14.3)	65.4 (12.5)	62.6 (15.6)	0.374[1]
	Median (min-max)	66.0 (23.0-103.0)	67.0 (41.0-87.0)	63.0 (23.0-103.0)	
Gender, n (%)					
Female		50 (57.5)	22 (56.4)	28 (58.3)	0.857[2]
Male		37 (42.5)	17 (43.6)	20 (41.7)	
ASA class, n (%)					
1		48 (55.2)	22 (56.4)	26 (54.2)	0.961[3]
2		20 (23.0)	9 (23.1)	11 (22.9)	
3		15 (17.2)	5 (12.8)	10 (20.8)	
4		4 (4.6)	3 (7.7)	1 (2.1)	
Tumor characteristics					
Mucinous component, n (%)					
None		46 (52.9)	25 (64.1)	21 (43.8)	0.205[3]
<50%		25 (28.7)	7 (17.9)	18 (37.5)	
>50%		16 (18.4)	7 (17.9)	9 (18.8)	
Signet-ring cell component, n (%)					
None		79 (90.8)	36 (92.3)	43 (89.6)	0.520[3]
<50%		4 (4.6)	2 (5.1)	2 (4.2)	
>50%		4 (4.6)	1 (2.6)	3 (6.3)	
Differentiation, n (%)					
Poor		34 (39.1)	17 (43.6)	17 (35.4)	0.532[2]
Moderate		43 (49.4)	19 (48.7)	24 (50.0)	
Well		10 (11.5)	3 (7.7)	7 (14.6)	
Tumor invasion, n (%)					
Perineural	Yes	34 (39.1)	14 (35.9)	20 (41.7)	0.583[2]
	No	53 (60.9)	25 (64.1)	28 (58.3)	
Venous	Yes	18 (20.7)	8 (20.5)	10 (20.8)	0.971[2]
	No	69 (79.3)	31 (79.5)	38 (79.2)	
Lymphatic	Yes	30 (34.5)	11 (28.2)	19 (39.6)	0.267[2]
	No	57 (65.5)	28 (71.8)	29 (60.4)	
Extra-nodal	Yes	26 (29.9)	14 (35.9)	12 (25.0)	0.269[2]
	No	61 (70.1)	25 (64.1)	36 (75.0)	

[1]Mann-Whitney U test, [2]Pearson chi-square, [3]Linear-by-Linear Association, [4]Fisher's exact test, SD: Standard deviation

Table 2. Surgery, chemotherapy and stage distribution

	Total (n=87)	Conventional hemicolectomy (n=39)	Complete mesocolic excision (n=48)	p value
Surgery characteristics				
Type, n (%)				
Emergency	4 (4.6)	2 (5.1)	2 (4.2)	0.610[1]
Elective	83 (95.4)	37 (94.9)	46 (95.8)	
Procedure, n (%)				
Right hemicolectomy	68 (78.2)	25 (64.1)	43 (89.6)	
Extended right hemicolectomy	5 (5.7)	1 (2.6)	4 (8.3)	<0.001[2]
Laparoscopic right hemicolectomy	14 (16.1)	13 (33.3)	1 (2.1)	
Additional intervention, n (%)				
Yes	12 (13.8)	5 (12.8)	7 (14.6)	0.813[2]
No	75 (86.2)	34 (87.2)	41 (85.4)	
Treatment characteristics				
Chemotherapy, n (%)				
None	38 (43.7)	18 (46.2)	20 (41.7)	0.907[2]
Adjuvant	49 (56.3)	21 (53.8)	28 (58.3)	
Stage distribution				
T-Stage, n (%)				
1	6 (6.9)	2 (5.1)	4 (8.3)	
2	6 (6.9)	2 (5.1)	4 (8.3)	0.855[2]
3	42 (48.3)	20 (51.3)	22 (45.8)	
4	33 (37.9)	15 (38.5)	18 (37.6)	
TNM-Stage, n (%)				
1	12 (13.8)	4 (10.3)	8 (16.7)	
2	35 (40.2)	17 (43.6)	18 (37.5)	0.657[2]
3	40 (46.0)	18 (46.2)	22 (45.8)	

[1]Fisher's exact test, [2]Pearson chi-square

CME groups, respectively. Overall, recurrence was noted in 16 (18.4%) of patients including systemic recurrence in 11 (12.6%) patients and local recurrence in 5 (5.7%) patients. Total, systemic and local recurrences occurred in 7 (14.6%), 6 (12.5%) and 1 (2.1%) patients in the CME group and in 9 (23.1%), 5 (12.8%) and 4 (10.3%) patients in the CON group, respectively. Local recurrence was seen in 1 patient with pT4b stage cancer in the CME group, while 3 patients with pT4a stage and 1 patient with pT4b stage were observed in the CON group. Median time to recurrence development was 6.0 months (range: 2.2 to 18.5 months) in the CME group and 13.2 months (range: 4.7 to 43.0 months) in the CON group (Table 3). Peritonitis carcinomatosa was evident in 4 overall, including 3 patients with pT4a stage and 1 with pT3c stage. No significant difference was noted between the CON and CME groups in terms of CDS, LOS, or recurrence (Table 3).

Survival Data

In total, OS and DFS rates were 81.6% and 75.9%, respectively with average OS and DFS of 119.0 months and 112.5 months duration, respectively (Table 4). No significant difference was noted between the CON and CME groups in terms of OS (66.7 vs 93.8% and 113.1 vs 74.9 months, respectively, log rank p=0.216) (Figure 1) and DFS (64.1% vs 85.4% and 107.9 vs 68.7 months, respectively, log rank p=0.446) (Figure 2) at a median 87.3 months and 25.1 months of follow up, respectively (Table 4).

Table 3. Lymph node yield, surgical morbidity and recurrence

		Total (n=87)	Conventional hemicolectomy (n=39)	Complete mesocolic excision (n=48)	p value
Clavien–Dindo Score, n (%)					
1		5 (5.7)	1 (2.6)	4 (8.3)	0.388[3]
2		14 (15.7)	8 (20.5)	6 (12.5)	
3		8 (9.2)	5 (12.8)	3 (6.3)	
4		2 (2.3)	0 (0.0)	2 (4.2)	
Recurrence, n (%)					
Yes		16 (18.4)	9 (23.1)	7 (14.6)	0.194[2]
No		71 (81.6)	30 (76.9)	41 (85.4)	
Apical node metastasis, n (%)					
Yes		4 (4.6)	3 (7.7)	1 (2.1)	0.321[1]
No		83 (95.4)	36 (92.3)	47 (97.9)	
Follow up (month)	Median(min-max)	37.5 (3.5-156.3)	87.3 (3.5-156.3)	25.1 (6.7-84.8)	<0.001[4]
	Mean (SD)	55.4 (42.8)	84.4 (45.4)	31.8 (20.2)	
Time to recurrence (month)	Median (min-max)	10.4 (2.2-43.0)	13.2 (4.7-43.0)	6.0 (2.2-18.5)	0.071[4]
	Mean (SD)	12.1 (9.6)	15.3 (11.0)	7.9 (5.9)	
Lymph node yield (count)					
Total	Mean (SD)		33.6(16.7)	57.9 (24.5)	<0.001[4]
	Median (min-max)		31.0(4.0-74.0)	58.0 (14.0-118.0)	
Metastatic	Mean (SD)		3.7(9.5)	1.8 (4.2)	0.561[4]
	Median (min-max)		0.0(0.0-49.0)	0.0 (0.0-23.0)	
Apical	Mean (SD)		2.4(1.7)	3.3 (2.0)	0.034[4]
	Median (min-max)		2.0(1.0-9.0)	3.0 (1.0-10.0)	
Length of hospital stay (day), Median (min-max)			6.0(4.0-38.0)	7.0 (5.0-41.0)	0.526[4]

[1]Fisher's exact test, [2]Pearson chi-square, [3]Mantel Haenzsel test, [4]Mann-Whitney U test, min: Minimum, max: Maximum, SD: Standard deviation

Table 4. Survival data for each group

	Total (n=87)	Conventional hemicolectomy (n=39)	Complete mesocolic excision (n=48)	p value
Overall survival				
Rate, %	81.6	66.7	93.8	0.216
Time (months), mean (SE, 95% CI LB-UB)	119.0 (8.1, 103.2-134.8)	113.1 (9.7, 94.1-132.1)	74.9 (3.5,68.1-81.8)	
Disease-free survival				
Rate, %	75.9	64.1	85.4	0.446
Time (months), mean (SE, 95% CI LB-UB)	112.5 (8.2, 96.5-128.5)	107.9 (10.3, 87.6-128.2)	68.7 (4.4, 60.1-77.2)	

CI: Confidence interval, LB: lower bound; UB: upper bound. Log Rank (Mantel cox)

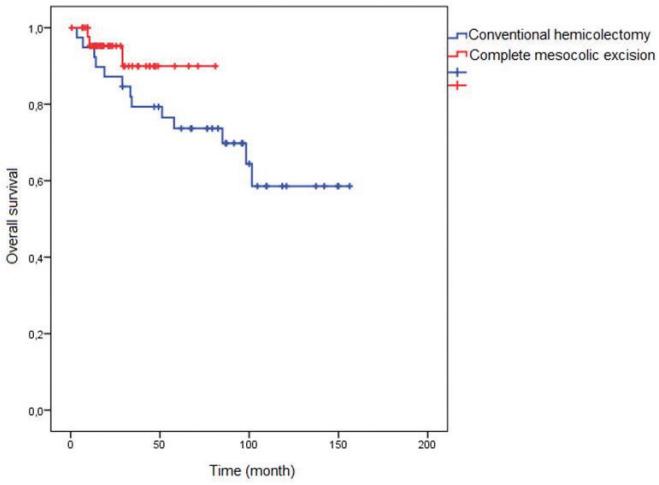

Figure 1. Kaplan-Meier analysis for overall survival according to surgery technique

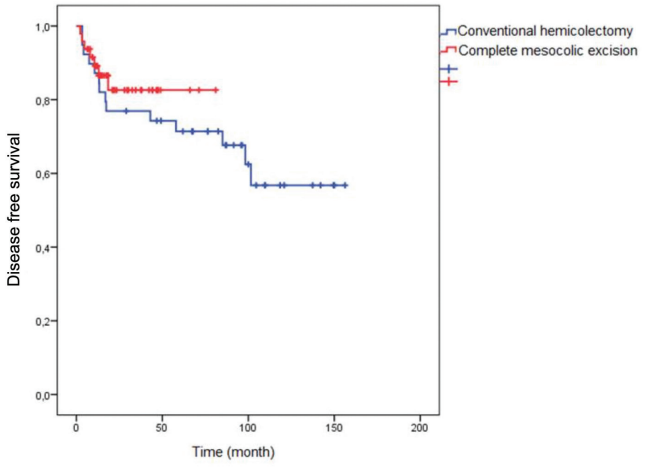

Figure 2. Kaplan-Meier analysis for disease-free survival according to surgery technique

Discussion

The current study revealed superiority of CME over the CON technique in terms of providing a more radical dissection of apical lymph nodes for patients with right-sided colon cancer. However, this was not associated with a significant survival advantage for CME-operated patients during a median follow up of 37.5 (range: 3.5 to 156.3) months. While CME is technically more difficult than CON, no significant increase was noted in surgical morbidity.

CME differs from conventional surgery in two major ways: it achieves a more radical excision of the lymphovascular pedicle and the mesocolon and achieves resection with an intact visceral peritoneum along with near and distal resection margins of at least 10 cm. Bertelsen and colleagues have generated strong evidence that improving colonic surgery can potentially improve survival to an equivalent or greater extent than adjuvant chemotherapy.[11] Quirke and West commented in their article that the findings of Bertelsen et al.[12] cannot be ignored and must be explored further.

In the current study, CON and CME groups were homogenous in terms of patient demographics, tumor characteristics, chemotherapy administration and surgical morbidity. This is important given the heterogeneity of historical comparison in terms of factors with the potential to influence on the outcome to change between the two periods may potentially cause bias in the interpretation of results.[7,13]

Patients with apical lymph node involvement were reported to have a poor prognosis similar to those with metastatic disease.[14] The authors also emphasized the likelihood of incomplete resection risk in many patients with occult apical lymph node metastasis. This pre-cognition is in fact refers to the rationale behind the CME technique development. The increased total (median: 58.0 vs 31.0) and apical (3.0 vs 2.0) lymph node yield for CME vs. CON in our study supports the reported benefits of CME for increasing lymph node yield.[2] This appears to be in accordance with CVL or "high-tie" that is often performed with CME to ensure apical lymph node resection (for more accurate lymph node staging), minimize the risk of leaving residual disease and to reduce the risk of future metastasis.[2,15,16,17] In our series, the apical lymph node yield (2.0 vs 3.0) was lower in the CON vs the CME groups, respectively, despite the higher apical lymph node metastasis rate (7.7 vs 2.1%). This higher rate reflects the likelihood of residual metastatic apical lymph nodes seen in approximately 5.6% of patients without radical clearance. In addition, given the association between a lymph node yield ≥22 with an improved 5-year OS[18,19,20] and a lymph node yield ≥28 with an improved 5-year cancer related survival[1], the lymph node yield advantage of CME in our cohort appears to demonstrate the beneficial implications for local disease control and survival.[2]

CME is a technically more challenging procedure compared to CON with a potentially higher risk of damaging critical structures during dissection due to greater anatomical variability in the right colon than that in the left colon or rectum.[2,4,21] Notably, in a meta-analysis of 12 studies with 8586 patients that compared the safety, quality and effect of CME vs non-CME in patients with colon cancer, CME was reported to be associated with greater intraoperative blood loss, more postoperative surgical complications, longer large bowel resection, larger area of mesentery and higher rate of lymph nodes resection. In addition, CME has positive effects on 5-year survival [hazard ratio (HR)

0.33], 3-year OS (HR 0.58) and 3-year survival for Stage III disease (HR 0.69) as compared with survival rates for those in the non-CME group.[4] Use of a standardized assessment method proposed by Dindo et al.[9] in assessing the surgical morbidity in our patients was also important given that this approach can assess morbidity in a more objective manner.[3] In our series, surgical morbidity was evident in one-third of patients with a CDC score ≥3 which represented 10% of patients; furthermore there were no surgical mortalities. Hence, CME appears to offer benefits without adversely affecting the surgical morbidity in patients with right-sided colon cancer.

In a past study among 779 patients with colon cancer who underwent CME between 1996 and 2007, the authors reported that CME was associated with a median lymph node count of 15 (range: 0-113), few complications, a low recurrence rate (10.2%), high 5-year OS (76.2%) and 5-year cancer-specific survival (89.8%).[6] Other studies also reported favorable oncological outcomes in terms of 5-year survival rates (range, 63.7 to 76.2%)[6,15,22], cancer-specific survival rates (range: 76.6% to 89.9%)[1,6,22] and median lymph node count (range: 14.7 to 32.0).[1,6,15] In the current study, after a median follow up of 25.1 months (range: 6.7 to 84.8 months), OS and DFS rates were 93.8% and 85.4%, respectively in the CME group.

Data from comparative studies on non-CME vs CME resection studies revealed lower local 5-year recurrence rates[3,5,23] as well as improved 3-year survival rates (79.0% vs 88.1%), 5-year OS (by 16%)[3,23,24], DFS (75.9 vs 85.8%, 74.3 vs 82.1% and 82 vs 89%)[11,25,26] and cancer-specific survival (90.5% vs 95.2%).[25] In a systematic review of 22 studies, CME was found to be advantageous in terms of OS rate (58.7% vs 53.5%), DFS rate (77.4% vs 66.7%) and local recurrence rate (4.5% vs 7.8%).[27] Notably, in a retrospective study comparing oncological outcomes for CME (n=364) vs non-CME (n=1031) colectomies, no significant difference was noted between the two groups in terms of OS rates, despite higher 4-year DFS rates in the CME group.[11] To explain the lack of difference in OS, the authors considered the possible role of the short follow-up, improved surgical outcomes for recurrent disease resection, or advances in chemotherapy for patients with non-resectable recurrent disease.[11]

In the current study, total, systemic and local recurrence rates were 23.1%, 12.8% and 10.3% within a median occurrence time of 13.2 months in the CON group and 14.6%, 12.5% and 2.1% within median 6.0 months in the CME group, respectively with no significant difference between study groups. Notably, pT4 stage was evident in 8 of 16 patients who experienced disease, which suggests that the potential benefit of CME may be limited or unrecognized for those at this stage. The incidence of the T4 colorectal cancer among the advanced resected cases has been reported to be up to 21%-43%.[28,29,30] In this regard, the observed rate for locoregional recurrence in the current study seems to be associated with presence of T4 stage tumor, considered as a risk factor for locoregional recurrence, in 37.9% of our cases.[31,32] In fact, none of our patients received neoadjuvant chemotherapy, while much higher rates for local recurrence (15.7%) was reported in a study among patients with T4 stage locally advanced disease without neoadjuvant chemotherapy.[33]

Our findings suggest right-sided CME is not associated with increased short-term mortality or morbidity.[1,5,11,25] Although our preliminary data on the CME technique (used in our clinic since 2013), indicates no survival benefit of CME over CON, this finding should be interpreted considering the shorter follow up duration in the CME group. Nonetheless, CME appears to be associated with an increased lymph node yield without adversely affecting LOS or surgical morbidity. In addition, the Kaplan-Meier analysis appears to indicate a tendency in favor of a survival benefit when using CME for patients with colon cancer.

Study Limitations

Certain limitations to this study should be considered. First, due to the retrospective, single center design, establishing a cause and effect temporality as well as generalizing our findings to the overall colon cancer population may not be possible. Second, there was discordance between follow up duration among the studies. Third, while heterogeneity in the small patient group in terms of laparoscopic technique, number of surgeons, type of surgeries may be considered amongst the limitations of the study, their effect on outcomes seems minimal given a) proven similar oncological outcomes of open and laparoscopic techniques, b) the limited use of laparoscopic technique (only in 1 case with CME) ruling out the potential negative impact of learning curve on oncological outcome and c) implementation of majority of the operations by the same senior surgeon. Finally, the possibility that the number of lymph nodes harvested is higher in the extended right hemicolectomy vs right hemicolectomy can be criticized. Since dissection plans are the same, their effect on oncological outcomes will be minimal and their effect on the average of the lymph nodes removed will be limited due to the small number of cases. Nevertheless, despite these limitations, given the restricted amount of data available on utility of CME in patients with colon cancer, our findings represent a valuable contribution to the literature.

Conclusion

In conclusion, our findings suggest that CME is safe when performed by experienced surgeons and there appears to be no risk of increased morbidity. CME has potential to improve oncological outcomes and may offer a survival benefit. Although CME appears to offer no significant survival benefit over CON in terms of OS and DFS, the potential survival benefit seems likely based on the longer term follow up. Nonetheless there is a need for further statistically and clinically significant evidence on long-term benefits of CME in order for it to be adopted as a standard of care for patients with colon cancer.

Ethics

Ethics Committee Approval: ATADEK date of approval: 05/12/2019, reference number/protocol number: 2019-19/23

Informed Consent: Due to the retrospective design of the study, informed consent was waived

Peer-review: Internally peer reviewed.

Availability of data and material (data transparency): The dataset supporting the conclusions of this article will be public available after publication with the DOI: 10.6084/m9.figshare.12298856

Authorship Contributions

Surgical and Medical Practices: L.V.T., O.S.G., A.Z., Concept: L.V.T., O.S.G., İ.B.B., A.Z., Design: L.V.T., A.Z., Data Collection or Processing: L.V.T., İ.B.B., Analysis or Interpretation: L.V.T., O.S.G., A.Z., Literature Search: L.V.T., İ.B.B., Writing: L.V.T., O.S.G.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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