

Long-term outcomes after complete mesocolic excision for colon cancer at a tertiary care center in Saudi Arabia

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BACKGROUND: Data on long-term survival and recurrence of cancer after complete mesocolic excision (CME) for colon cancer has not been reported from our center and related to international data.

OBJECTIVE: Describe overall and disease-free survival, survival by surgery site and stage, and recurrence rates after curative surgery.

DESIGN: Retrospective chart review.

SETTING: Academic tertiary care center.

PATIENTS AND METHODS: The study included all patients who underwent either laparoscopic or open surgery for colon cancer with curative intent between 2001 and 2011. The colorectal database was reviewed for the following: demographic data, comorbidities, radiologic investigations, clinical stage, type of operation, complications, pathologic assessment, adjuvant treatment, recurrence and survival. Survival and recurrence rates were calculated, and survival curves were generated.

MAIN OUTCOME MEASURES: 5-year overall survival, secondary endpoints were 5-year disease-free survival, survival by surgery site and stage, and recurrence rates.

SAMPLE SIZE: 220.

RESULTS: The mean (SD) age at diagnosis was 57 (13) years (CI 95%: 55-59 years). There were 112 males. Mean (SD) body mass index was 27.6 (5.7) kg/m² (CI 95%: 27-28). Pathological assessment revealed R0 (microscopically margin-negative) resection in 207 (94%). The overall 5-year survival and disease-free survival was 77.9% and 70%, respectively. The 5-year disease-free survival was 69% for the sigmoid/left colon and 69% for the right colon (difference statistically nonsignificant). Stages at the time of resection were stage 0 for 2 (0.01%) patients, stage I for 18 (8%), stage II for 92 (42%), stage III for 100 (46%), and stage IV for 6 (3%). The 5-year overall survival by stages I, II, III and IV was 94%, 80%, 75% and 50%, respectively (difference statistically nonsignificant). The overall 5-year recurrence rate was 23.4%.

CONCLUSION: The outcomes of surgical treatment for colon cancer at our institution are equivalent to international sites. No difference was noted between left and right colon in terms of survival after CME.

LIMITATIONS: Single center, retrospective, small sample size.

CONFLICT OF INTEREST: None.

Worldwide, the incidence of colorectal cancer is the third highest cancer in males after lung and prostate cancer and the second highest in females after breast cancer.¹ In Saudi Arabia, colorectal cancer is the highest in incidence in males and third highest in females.² There is global variation in incidence and the survival rate,³ which depends on the stage at diagnosis along with the expertise of the surgeon.⁴ The primary determinant of survival is nodal involvement.⁵⁻⁷ The presence of perforation and/or obstruction lowers the survival rate.⁷⁻⁹ Tumor deposits are also associated with reduced disease-free and overall survival.¹⁰⁻¹² Surgery for rectal cancer has been standardized using the total mesorectal excision (TME) technique, which has resulted in lower local recurrence rates and improved survival.¹³ Following the same concept, complete mesocolic excision (CME) has been proposed to improve survival and lower recurrence in patients with colon cancer.¹⁴ This approach has been championed recently by dedicated colorectal units in Europe and China.¹⁵⁻¹⁷ The aim of this study was to assess survival after curative treatment by CME for colon cancer at a tertiary care center in Saudi Arabia.

PATIENTS AND METHODS

This retrospective study included all patients who underwent CME according to the technique described by Hohenberger et al¹⁴ for colon cancer with curative intent between 2001 and 2011 by a dedicated colorectal surgical team at King Faisal Specialist Hospital and Research Center in Riyadh, Saudi Arabia. Although Hohenberger et al described the technique in 2009,¹⁴ his technique was widely practiced by surgeons from his generation and this was the standard at our unit. The mesocolon was completely excised along the fascia plan of Toldt's fascia with central ligation of the feeding vessels. The central vascular ligation is as important as the total mesocolic excision. Patients who had unresectable colon cancer were excluded. The colorectal database was reviewed for demographic data, comorbidities, radiologic investigations, clinical stage, type of operation, pathologic assessment for completeness of mesocolic excision, complications, adjuvant treatment, recurrence and survival. Right disease site is right hemicolectomy; left disease site is left hemicolectomy and total colectomy. Survival and recurrence rates were calculated using IBM SPSS version 21. Kaplan-Meier survival curves with statistical comparisons of grouped data were generated using the R statistical software version 3.6.1 and the ggplot2 package. Statistical comparisons were by the log-rank test. Data are summarized as mean (standard deviation) for

continuous variables and number (percentage) for categorical data.

RESULTS

The mean (standard deviation) age at diagnosis of 220 patients was 57 (13) years (CI 95%: 55-59) (**Table 1**). There were 112 males (51%). Mean (SD) body mass index was 27.6 (5.7) kg/m² (CI 95%: 27-28). Only 16 patients were non-Saudis. Eighty-six patients (39.1%) had diabetes and 68 (31.7%) were hypertensive. **Table 2** shows clinical signs and symptoms at presentation. Cancer was located in the left and right side in 137 (62.8%) and 81 (37%) patients, respectively. Surgeries performed were sigmoid/left colectomy, right hemicolectomy and total colectomy in 128 (59%), 77 (35%), 13 (6%) patients, respectively. Open and laparoscopic surgery was performed in 174 (80%) and 44 (20%) patients, respectively. Postoperative complications by Clavien-Dindo grades are shown in **Table 3**.

The overall 5-year survival and disease-free survival was 77.9% and 70%, respectively, but these values are underestimated compared with Kaplan-Meier survival curves shown in **Figures 1 and 2**. The 5-year disease-free survival for sigmoid/left (left hemicolectomy and total colectomy) and right hemicolectomy was 69% and 72%, respectively. The two groups are contrasted in **Figure 3** by showing survival curves only for patients who died (differences statistically nonsignificant).

Colon cancer stages at resection were I, II, III and IV in 18 (8%), 92 (42%), 100 (46%) and 6 (3%) patients, respectively. The 5-year overall survival by stages I, II, III and IV were: 94%, 80%, 75% and 50%. The 5-year disease-free survival by stages I, II, III and IV were: 94%, 80%, 59.6% and 33.3%, respectively. **Figures 4A and B** show overall and disease-free survival by stage for patients who died (differences statistically nonsignificant).

The overall 5-year recurrence rate was 23.4%. **Figure 5** is a Kaplan-Meier survival curve for 48 patients who had recurrences (date of recurrence missing for 4 patients). After two years, about 60 percent of patients had not had a recurrence among those who eventually had a recurrence. It is important to mention that a comparison between the colorectal surgeons with regard to the 5-year overall and disease free survival did not yield a significant difference, ($P=.14$).

DISCUSSION

While the mean age at diagnosis of colon cancer in Saudi Arabia is 57 years (59 years for men and 55 years for women),¹⁸ in the US it is 68 years for men and 72 years for women.¹⁹ This younger age at the time of diagnosis poses a difficult question for it implies that

screening may need to be conducted at an age lower than 50 years, which is the international standard. The Saudi guidelines for screening recommend screening at the age of 45 years.²

At our center, few cases of stage 1 disease are diagnosed, as might be expected as there is no screening program in Saudi Arabia. The clinical practice guidelines for screening for colorectal cancer, produced using the GRADE methodology,²⁰ were published in 2011 but national implementation has stalled. It is imperative to popularize screening to diagnose colon cancer at an early stage and improve survival, or even prevent colon cancer through polypectomy of adenomas.

Overweight and obesity is a huge issue in Saudi Arabia with a prevalence is 71.1% in females and 69.7% in males in 2016.^{21,22} Diabetes is also a public issue that has attracted huge attention. In a national study, the prevalence of diabetes in Saudi Arabia was estimated at 25.4%,²³ In our study population, overweight and diabetes were present in 31.8% and 39.4%, respectively. This poses a risk for perioperative complications, which in our study occurred in 22.9% of patients and were mainly septic complications of Clavien-Dindo class I and II.²⁴

The 5-year overall and disease-free survival in this study were 77.9% and 70%, respectively. This is comparable to the 5-year overall survival reported from Scotland in the United Kingdom at 72.2%,²⁵ the National Registry in Denmark at 66%,²⁶ and the CONCORD-2 study in the US at 64.6%.²⁷ However, the survival rate reported in this study is much lower than that reported from the University Hospital in Erlangen, Germany at 89.1% where a total mesocolic excision technique has been used since 1995; an accomplishment achieved only at that center. Notably, a systematic review published in 2015 refuted any survival benefit for CME.²⁸ One must consider factors like the case-mix and the stage as possible causes for the improved survival in the Erlangen study. In our sample stage I-II is 50% while in Hohenberger et al¹⁴ they comprise 62% of the case-mix.

The reason behind the move to perform CME is the decreased survival after right hemicolectomy for colon cancer.¹⁷ However, we did not find a significant difference between the survival of right or left colon cancer in our study, which is probably related to all surgeries being performed by a certified consultant colorectal surgeons who used CME as the preferred technique to resect right and left colonic cancer. Evidence of this is the high R0 resection, which was reported at 95%.

In conclusion, the quality of surgical treatment at King Faisal Specialist Hospital and Research Center is comparable to that at international centers with dedicated colon and rectal surgery units. However, most

Table 1. Demographic and clinical data by sex.

	Male (n=112)	Female (n=108)
Age (years)	59.0 (13.7)	54.8 (13.1)
Body mass index	26.1 (5.0)	29.1 (5.9)
Diabetes		
Yes	44 (36.4)	42 (40.0)
No	68 (60.7)	63 (60.0)
Hypertension		
Yes	40 (36.4)	28 (26.4)
No	70 (63.6)	78 (73.6)
Colon cancer stage		
0	1 (1.0)	1 (1.0)
1	10 (9.0)	8 (7.5)
2	48 (43.2)	44 (41.1)
3	49 (44.1)	51 (47.7)
4	3 (2.7)	3 (2.8)

Data are n (%) or mean (SD). A few observations are missing for some variables.

Table 2. Symptoms at presentation.

	Number of cases (%)
Fresh bleeding per rectum	85 (40.2)
Bowel obstruction	45 (21.3)
Abdominal pain	45 (21.3)
Anemia	25 (11.8)
Bowel perforation	1 (0.5)
Incidental findings on screening colonoscopy	1 (0.5)

Table 3. The Clavien-Dindo Classification in 50 patients (22.7%).

Clavien-Dindo Grade	
I	37 (17)
II	7 (7)
III	3 (1.4)
IV	3 (1.4)

Data are number (percentage).

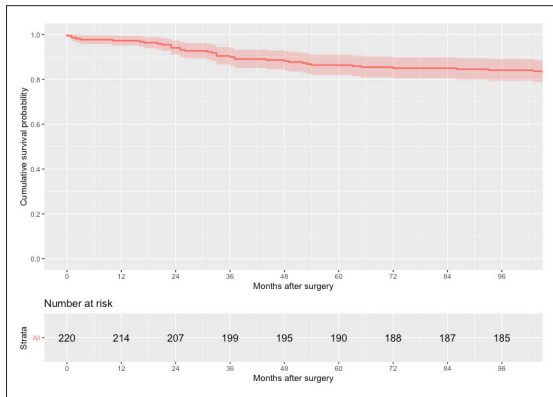


Figure 1. Kaplan-Meier survival curve for all patients (n=183 survivors).

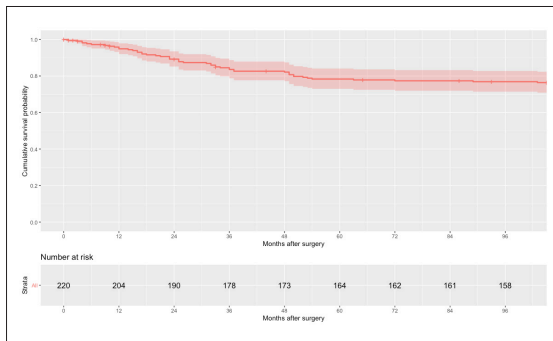


Figure 2. Kaplan-Meier survival curve for disease-free patients (n=169). DFS excludes all patients with recurrence date but not recurrence without a recurrence date because time is unknown (6 cases, 2 no data on recurrence event or date).

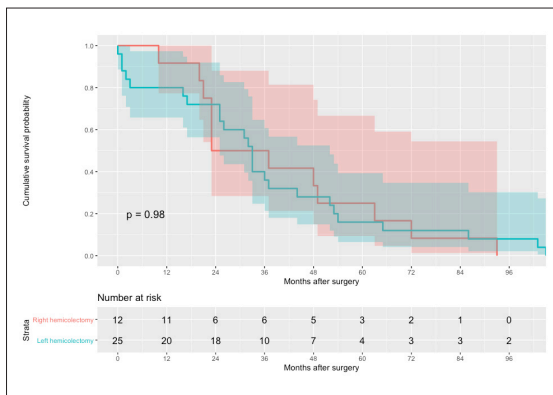


Figure 3. Kaplan-Meier survival curves for patients who died (n=37) by disease site.

Saudi patients present with advanced disease due to lack of screening and have a high rate of comorbidities. One of the limitations of the study is the small sample size, which is mainly because we treat rectal cancer. A

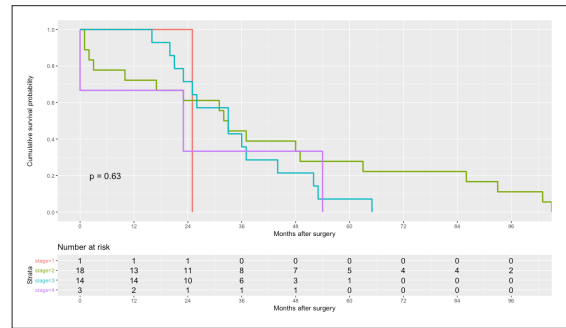


Figure 4A. Kaplan-Meier survival curves for patients who died by stage (n=36).

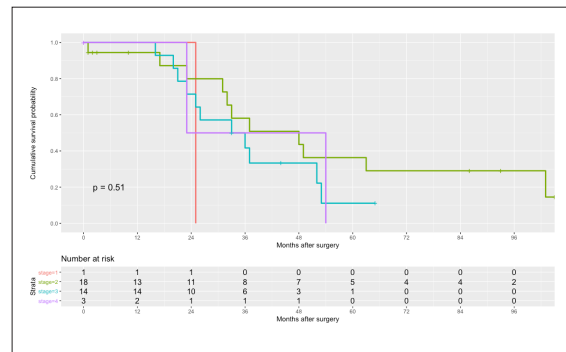


Figure 4B. Kaplan-Meier survival curves for disease-free survival for patients who died by stage.

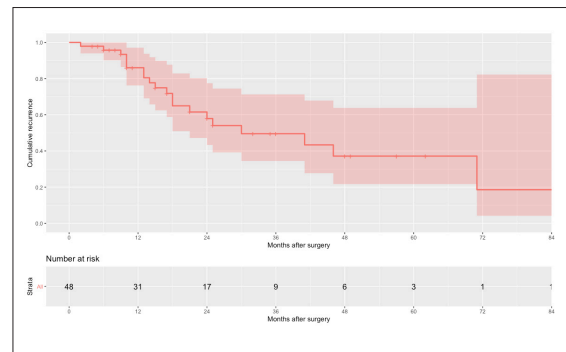


Figure 5. Kaplan-Meier survival curve for patients with recurrence.

huge proportion of the cases were operated on using an open technique as only those who cannot be treated outside our institution with large and locally advanced colon cancers were accepted. Our sample was skewed to stage III, which affected the case-mix and the survival data, and is a limitation of the study.

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