original article

Survival and outcomes after laparoscopic versus open curative resection for colon cancer

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BACKGROUND: Many studies have shown that open and laparoscopic surgery for resection of colonic cancers produce similar short- and long-term results, but no data have been reported from Saudi Arabia.

OBJECTIVE: Compare 3-year disease-free and overall survival after laparoscopic versus open curative resection for potentially curable colon cancer.

DESIGN: Multicenter retrospective cohort study.

SETTING: Tertiary academic hospital.

PATIENTS AND METHODS: We analyzed data of patients who underwent curative resection for potentially curable colon cancer using the laparoscopic or open approach at three tertiary care centers during the period 2000-2015.

MAIN OUTCOME MEASURES: Overall and disease-free 3-year survival were the primary endpoints. Secondary endpoints included conversion rate, duration of surgery, length of hospital stay, rate of wound infection, resumption of bowel function, number of lymph nodes retrieved, adequacy of resection and rate of recurrence. Risk factors for recurrence, including complete mesocolic excision, were assessed.

SAMPLE SIZE: 721.

RESULTS: Patient and tumor characteristics were similar in the two groups except for ASA class ($P<.01$), weight ($P<.05$) and tumor stage ($P<.05$). Over a median follow-up of 46 months, the 3-year overall survival was 76.7% for open resection and 90.3% for laparoscopic colon resection ($P<.05$). The 3-year disease-free survival was 55.3% for open colon resection and 64.9% for laparoscopic colon resection ($P=.0714$).

CONCLUSION: Overall and disease-free survival after the laparoscopic approach for curative resection of colon cancer is comparable to the open approach.

LIMITATIONS: Retrospective design and the possibility of selection bias.

CONFLICT OF INTEREST: None.

Data collected since 2002 indicate that colon cancer is the commonest malignancy among men and the third most common among women in Saudi Arabia.[1] Traditionally, open resection was favored for potentially curable cancer, but laparoscopic resection has became accepted as equivalent to the open approach in the last decade. Upon the start of laparoscopic surgery in 2003 for the treatment of colon cancer, concerns arose about the technique and its comparability with the open approach in terms of disease recurrence and survival rate. In the COLOR trial (2017), investigators were unable to rule out a difference in the 3-year disease-free survival in favor of open colonic resections because the upper limit of the 95% CI for the difference just exceeded the predetermined non-inferiority boundary of 7%.[2] Moreover, the authors believed that the difference in disease-free survival between the laparoscopic and open approaches was small and clinically acceptable, justifying the implementation of laparoscopic surgery into daily practice. Five-year analyses of the CLASICC trial revealed that the laparoscopic approach for resection of both colon and rectal cancers is safe from an oncological standpoint.[3] Implementation of the laparoscopic technique in an attempt to improve short-term outcomes did not jeopardize the long-term oncologic outcomes.[4] Lacey et al analyzed the long-term survival outcomes for patients that underwent laparoscopic-assisted colon cancer resection, and concluded that laparoscopic-assisted resection was more effective than open resection.[5] Also, Storli et al suggested that complete laparoscopic mesocolic excision might be the preferred approach for right colon cancer because of its benefits in short-term morbidity, length of stay and oncological outcome.[6]

Laparoscopic resection of colon cancer has been shown to be oncologically safe with numerous short-term advantages in comparison to the open method.[2,3] Multiple studies have analyzed outcomes of laparoscopic resection that included length of hospital stay, local recurrence, cancer-related survival, decreases of stay, perioperative complications, overall morbidity and reduction in the cost of care.[5,7,8]

There have been no analyses of data from Saudi Arabia on the oncologic safety and efficacy of laparoscopic colon cancer resection, there also has been no comparative analysis with open resection. Therefore, we compared data on the short- and long-term outcomes of the two surgical approaches using databases of three tertiary care centers in Saudi Arabia.

PATIENTS AND METHODS

Data was collected from the databases of three tertiary care centers, King Faisal Specialist Hospital and Research Center (KFSHRC), King Khalid University Hospital (KKUH) and Prince Sultan Military Medical City (PSMMC). After obtaining approval from the Institutional Review Board, patient data was collected and analyzed. All patients with non-metastatic colon cancer during the period from 2000 to 2015 who underwent curative resection were included in the study. Exclusion criteria included metastatic colon cancers and disease requiring multiorgan resections. All patients had undergone a full colonoscopy and CT scan of the chest, abdomen and pelvis for metastasis. Baseline blood investigations were requested for all patients preoperatively including a carcinoembryonic antigen (CEA) level. Results were discussed in multidisciplinary meetings to determine the appropriate management plan. Certified colorectal surgeons assisted by colorectal fellows performed all operations.

Patients included in this study underwent resections with curative intent. For the laparoscopic approach, a medial-to-lateral mobilization is undertaken followed by proximal ligation of the respective vessels. Medial dissection continues while providing attention to vital retroperitoneal structures including the ureters and the duodenum and a complete mesocolic excision is achieved. Lateral mobilization of the colon is then undertaken, and finally, the colonic segment is resected and an anastomosis is created. Ultrasonic or bipolar devices were used in the majority of cases. A small skin incision is made and a wound protector is applied to extract the specimen. Ileocolic anastomosis were created either intra- or extracorporeally. Distal, or colorectal anastomoses were performed transanally using a circular stapler.

For colonic resections with an open approach, a midline incision is made. Dissection is performed in a lateral-to-medial approach. The majority of patients undergo a complete mesocolic excision. For resections of the right colon, a side-to-side ileocolic anastomosis is created. For left-sided colonic resections, an end-to-end colorectal anastomosis is performed using a circular stapler. In both the laparoscopic and open approaches, tumors in the transverse colon are resected through an extended right hemicolectomy, except for tumors of the distal transverse colon, which are resected through an extended left hemicolectomy, and anastomosis of the hepatic flexure of the colon to the rectum. A proximal and distal margin of at least 5 cm of healthy colon from the edges of the tumors is obtained prior to creating an anastomosis. Patient follow-up after discharge was based on local and international guidelines and included colonoscopy, CEA

determination and CT scans at predetermined intervals.[9,11]

The 3-year overall and disease-free survivals were the primary endpoints. Secondary endpoints were conversion rate, duration of surgery, length of hospital stay, rate of wound infection, resumption of gut function, number of lymph nodes retrieved, adequacy of resection and rate of recurrence. The study assessed risk factors for recurrence including mesocolic excision.

The *t* test and chi-square test was used for univariate analysis of continuous and categorical data, respectively. The Kaplan-Meier method was used for survival analysis. A *P* value <.05 was considered statistically significant.

RESULTS

Table 1 summarizes the patient and tumor characteristics. Operative details and tumor location are shown in **Table 2.** Patients were followed for a median of 46 months.Wound infections and dehiscence were found to be slightly higher in the open group, although the findings were not statistically significant (**Table 3**). Intra- and postoperative bleeding occurred in a higher percentage of patients in the laparoscopic group, but the difference was not statistically significant. A statistically significant difference was found between the two groups for intra-abdominal fluid collections. Collections were found in 7.8% of patients in the open group in comparison to 4.3% of patients in the laparoscopic group (P=.0003). Anastomotic leaks were found in 1.6% of patients in the open group and 0.97% of patients in the laparoscopic group, however these values failed to reach statistical significance. Recurrences were very similar in both groups. Local recurrences were higher in the open group whereas distal recurrences were higher in the laparoscopic group. These observations did not reach statistical significance. No 30-day mortalities were observed in either group. The 3-year overall survival for open and laparoscopic colon resection was 76.7% and 90.3% (*P*<.05), respectively. The 3-year disease-free survival was 55.3% for open colon resection and 64.9% for laparoscopic colon resection (*P*=.0714). **Figures 1 and 2** depict the overall and disease-free survival curves.

DISCUSSION

In our study, the laparoscopic approach for resection of colon cancer yielded significantly higher rates of overall survival, but statistical significance was not achieved for disease-free survival. The higher rates for laparoscopy may have been in part due to selection bias; however, patients in the laparoscopic group had a significantly higher proportion of stage III tumors while the open group had a significantly higher number of patients with diversion colostomy preoperatively. Reasons for preoperative diversion included complete obstruction and peritumoral inflammation with the possibility of microperforation. Moreover, perioperative blood transfusion was significantly more common in patients in the open group. These factors may have contributed to the observed lower overall and disease-free survival rates in the open group in comparison to the laparoscopic group.[10]

Analysis of operative complications revealed a higher rate of septic complications in the open group. Although most variables did not reach statistical significance, intra-abdominal collections and anastomotic leaks were significantly more frequent in the open group. Tumor recurrence was similar; local recurrence rates were higher in the open group while distant recurrences were higher in the laparoscopic groups, but none of the differences were statistically significant. In comparison to international trials, median opera-

Table 1. Patient and tumor characteristics (n=721).

	Open	Laparoscopic	*P*
Number of patients	333 (46.2)	388 (53.8)	
Age (years)	57.8	57.3	.654
Male	179 (53.7)	199 (51.3)	
ASA			.010
I	77 (10.7)	56 (7.7)	
II	170 (23.6)	226 (31.3)	
III	86 (11.9)	106 (14.7)	
Patient weight (kg)	70.9 (15.3)	74.4 (16.9)	.005
Tumor stage			.005
I	43 (5.96)	62 (8.60)	
II	109 (15.1)	82 (11.4)	
III	181 (25.1)	244 (33.8)	
Neoadjuvant chemotherapy	9 (1.25)	5 (0.69)	.170
Adjuvant chemotherapy	174 (24.1)	219 (30.4)	.259
Preoperative CEA level (ng/mL)	12.2	6.6	.001
Postoperative CEA level (ng/mL)	18.8	28.6	.249

Data are mean (standard deviation) or number (percentage). ASA: American Society of Anesthesiologists

Table 2. Operative characteristics (n=721).

	Open	Laparoscopic	*P*
Number of patients	333 (46.2)	388 (53.8%)	
Resection site			
Right colon	119 (16.5)	106 (14.7)	.015
Transverse colon	3 (0.42)	1 (0.14)	.246
Left colon	47 (6.5)	57 (7.9)	.826
Sigmoid	144 (20.0)	208 (28.9)	.005
Total colectomy	21 (2.9)	16 (2.2)	.185
Blood transfusion (units)	1.2	0.6	.0001
Duration of surgery (min)	208.3	224.8	.0079
Lymph node	19.5	19.4	.839
Diversion	85 (11.8)	34 (4.7)	.001
Preoperative stent	6 (0.83)	7 (0.97)	.998
Positive margin			
Proximal	-	-	-
Distal	2 (0.28)	3 (0.42)	.780

Data are mean (standard deviation) or number (percentage).

Table 3. Complications (n=721).

	Open	Laparoscopic	*P*
Number of patients	333 (46.2)	388 (53.8)	
Wound infection	49 (6.8)	43 (5.9)	.145
Wound dehiscence	5 (0.69)	2 (0.28)	.178
Intra-abdominal fluid collections	56 (7.8)	31 (4.3)	.0003
Bleeding	11 (1.5)	16 (2.2)	.563
Hematoma	5 (0.69)	3 (0.42)	.352
Anastomotic leak	12 (1.6)	7 (0.97)	.0427
Stenosis	13 (1.8)	6 (0.83)	
Recurrence	73 (10.1)	76 (10.5)	.440
Local	12 (2.2)	7 (1.3)	
Distal	41 (7.7)	48 (8.9)	
Both	20 (3.6)	21 (3.9)	
30-day mortality	0 (0)	0 (0)	

Data are mean (standard deviation) or number (percentage).

Table 4. Comparison of operative times (median) with international studies.

	Present study	COLOR[2]	CLASICC[5]
Laparoscopic	225 (81.9)	202	172.3
Open	208.0 (83.3)	170	118.2

Time in minutes.

Table 5. Comparison of 3-year outcomes in international trials.

	Laparoscopic				Open			
	OS	DFS	LR	DR	OS	DFS	LR	DR
Present study	90.3	64.9	1.3	8.9	76.7	55.3	2.2	7.7
COLOR[2]	81.8	74.2	10.8	21.0	84.2	76.2	8.7	20.6
CLASICC[5]	68.4	66.3	7.3	11.3	66.7	67.7	6.0	12.5

Data are percentage. OS: overall survival, DFS: disease-free survival, LR: local recurrence, DR: distal recurrence.

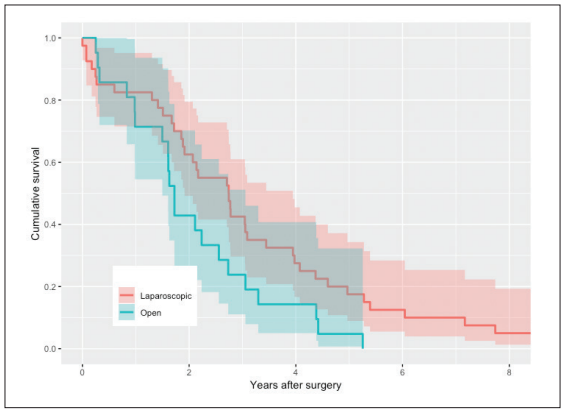

Figure 1. Overall survival laparoscopic vs. open surgery (95% confidence interval).

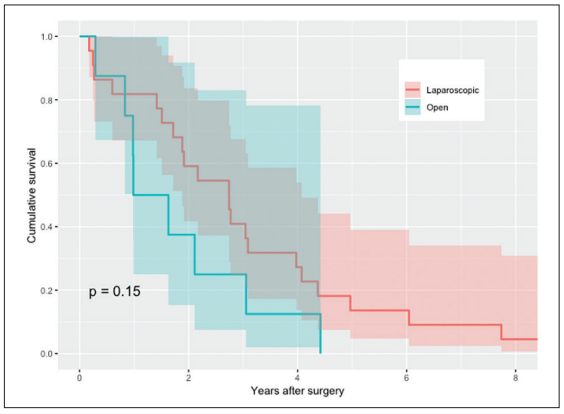

Figure 2. Disease-free survival laparoscopic vs open surgery (95% confidence interval).

tive durations for both approaches were longer, more than 200 minutes (**Table 4**), possibly because the participating centers are training centers for fellowships in colorectal surgery and residencies in general surgery.

The 3-year overall survival for the laparoscopic and open approaches in our study was similar to the results of the COLOR trial. In our study, the 3-year disease free survival for the laparoscopic group was also similar to the survival rates in the COLOR and CLASICC trials, but the disease-free survival in the open group in our study was lower, possibly because of a selection bias towards advanced cases. In our study, local and distant recurrences were lower in comparison to the COLOR and CLASICC trials. This may be related to underestimation of recurrences. Recurrences may have been missed on postoperative imaging, resulting in an overestimation of survival. **Table 5** summarizes the main outcome measures in comparison to international trials. In conclusion, overall and disease-free survival with the laparoscopic approach for resection of colon cancer is comparable to the open approach. Limitations of the study include its retrospective design and selection bias.

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