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Should be a locally advanced colon cancer still considered a contraindication to laparoscopic resection?

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Abstract

Background

The role of elective laparoscopic resection (LR) for the treatment of locally advanced colon cancer (LACC) is unclear. Most studies have retrospectively investigated the outcomes of LR for pT4 cancers, while clinical T4 (cT4) cancers are excluded in the large randomized controlled trials comparing LR and open resection (OR). The aim of this study was to investigate the outcomes in patients undergoing elective LR for LACC.

Methods

A prospective single-institution database including consecutive patients undergoing elective LR for clinical LACC (high-risk T3 or T4 N0-2) between March 1996 and March 2017 was retrospectively reviewed. A multivariate analysis was performed to identify predictors of conversion to OR and risk factors for adverse oncologic outcomes.

Results

A total of 300 patients undergoing LR for LACC were included. A multi-visceral resection was needed in 17 (5.7%) patients. A total of 63 (21%) LRs were converted to OR, mainly due to suspected adjacent organ invasion (82.5%) or obesity (9.5%). Overall postoperative Clavien-

Dindo 3–4 complication rate was 4.7%, with no significant differences between completed and converted LRs. Final pathology showed 18 (6%) pT2, 215 (71.7%) pT3, 54 (18%) pT4a, and 13 (4.3%) pT4b cancers. A R0 resection was achieved in 98.3% of patients. On multivariate analysis, tumor size ≥ 7 cm and tumor site (splenic flexure) were the independent risk factors for conversion to OR. A pT4 colon cancer and LNR of 0.25 or greater, but not conversion to OR, were independently associated with both poorer OS and DFS.

Conclusion(s)

Clinical LACC should not be considered a contraindication to LR itself. Bulky tumors ≥ 7 cm and splenic flexure cancers are at higher risk of conversion to OR; however, there is no increased postoperative morbidity or adverse oncologic outcomes in converted patients.

Colon cancer is one of the most common malignancies worldwide. Even though the wide spread of population-based screening programs has led to a significant increase in the diagnosis of early cancers, almost 15% of colon cancers are still diagnosed as locally advanced colon cancers (LACC) [1, 2].

Surgery followed by adjuvant chemotherapy is the recommended treatment for LACC [3,4,5,6]. Open resection (OR) is the current standard of care, while there are several concerns regarding the laparoscopic approach to LACC. LACC is commonly regarded as a relative contraindication to laparoscopic resection (LR), mainly due to the high rates of conversion to OR and concerns about the oncologic adequacy of LR [7, 8]. However, only a few small and retrospective studies have investigated the long-term outcomes of LR for LACC, reporting conflicting results [9, 10]. In addition, clinical T4 (cT4) cancers were exclusion criteria in the largest randomized controlled trials that have compared LR and OR for colon cancer [11,12,13].

Recently, some evidence has become available showing that LR might reduce postoperative morbidity and increase the chance of receiving adjuvant chemotherapy in LACC patients, with subsequent better oncologic outcomes [14]. Even though these data seem to support the laparoscopic approach to LACC, the selection criteria for LR for the treatment of LACC are still unclear.

The aim of this study was to evaluate the outcomes of LR in a large prospective series of patients with clinical LACC, focusing on predictors of conversion to OR and risk factors for adverse oncologic outcomes, in order to better define the subgroup of LACC patients that still should be considered a contraindication to the minimally invasive approach.

Materials and methods

This study is a retrospective analysis of a prospective database including all patients undergoing resection for colorectal cancer at our Institution, between March 1, 1996 and March 31, 2017. All patients who underwent an elective resection for LACC, defined as cT3 with extramural cancer spread of more than 5 mm beyond the colon wall or cT4 N0-2 at staging CT scan [15,16,17], were included in the study. Exclusion criteria were cT1–T2 colon cancer, tumors different from adenocarcinoma, adenomas, rectal cancer, previous history of colon surgery, and acute obstruction or colon perforation requiring emergent surgery. All patients were preoperatively informed about the surgical procedure and gave written consent. No IRB approval was needed due to the retrospective nature of the study. Each patient undergoing LR for LACC was matched by age (± 5 years), ASA score, tumor size (± 0.5 cm), and tumor site in a 1:1 fashion with a patient undergoing OR for LACC.

The following variables were prospectively collected for each LACC patients in the database: patient's characteristics (age, gender, body mass index, ASA score, comorbidities), operative outcomes (type of resection, operative time, need for blood transfusions, complications, conversion to OR), pathology (tumor diameter, tumor grading, radicality of resection, number of lymph nodes harvested, lymph node ratio—LNR, presence of lymph and/or blood vessels invasion, TNM stage), early postoperative outcomes (time to resume oral feeding, time to recovery of bowel function, length of hospital stay, complications according to Clavien-Dindo classification [18]), and long-term oncologic outcomes [recurrence rate, disease-free survival (DFS), overall survival (OS)]. Electronic medical charts were reviewed when data were missing in the database.

Preoperative work-up included clinical examination, total colonoscopy with biopsy, a CT scan of chest and abdomen, and serum carcinoembryonic antigen (CEA) assay.

All LRs were performed by attending surgeons with extensive experience in both colorectal and advanced minimally invasive surgeries. Conversion from LR to OR was defined as completion of the operation through an enlarged incision or an incision performed earlier than planned. Patients were divided in LAP group, if the resection was completed laparoscopically, and in CONV group, in case of converted LR.

A clinical oncologic evaluation was performed within 8 weeks after surgery: adjuvant chemotherapy was offered to the patients with a postoperative confirmed diagnosis of high-risk stage 2 colon cancer and to those patients with a stage 3 colon cancer.

Oncologic follow-up protocol included clinical examination, serum CEA levels every 3 months, and an abdominal ultrasound every 6 months for the first 3 years and then annually thereafter. A CT scan of the chest and abdomen was performed annually. A total colonoscopy was obtained at one year after LR and then every 3 years.

Statistical analysis

Quantitative data are provided as mean and standard deviation, while categorical data are given as percentages. Proportions were compared using the $\chi 2$ test or the Fisher's exact test, where appropriate. Student's t test was used to compare normally distributed variables. Univariable OS and DFS rate analyses were performed using the Kaplan–Meier method, and the differences between the groups were assessed with the log rank test. OS and DFS were calculated from the date of surgery to the date of death from any cause or to the date of recurrence, respectively. Patients alive with or without recurrence were censored at the date of last examination. Time to local recurrence or distant metastases was calculated from the time of surgery to date of evidence of relapse. A multivariable Cox regression analysis was also performed to identify independent predictors of conversion to OR. The included variables were age, gender, body mass index (BMI), ASA score, previous abdominal surgery, tumor location, and tumor size. A multivariable Cox regression analysis was also performed to identify independent predictors of survival. The included variables were age, gender, tumor location, conversion to OR, pT staging, tumor grading, number of lymph nodes harvested, LNR, lymphovascular invasion, postoperative anastomotic leak, and use of adjuvant chemotherapy. Explanatory variables with univariable $P \leq 0.200$ were included in the multivariable analyses in order to evaluate all potential predictors in the final modeling process. A level of 5% was set as the criterion for statistical significance. Data were collected in an Excel spreadsheet. The statistical analysis was performed using SYSTAT version 10 (Copyright © SPSS Inc., 2000).

Results

Between March 1996 and March 2017, 2237 elective colorectal LRs have been performed in our Institution. A total of 978 patients had colon cancer: of them, 300 had a preoperatively clinically suspected LACC. Table 1 summarizes baseline patients' characteristics. Mean age was 68.3 years. Most common tumor site was right colon, followed by sigmoid colon.

Intraoperative results

Surgical operations are summarized in Table 2. Conversion rate to OR was 21% (63 patients); it did not change significantly over time. In most cases (N = 60, 95.2%), conversion was preemptive due to suspected invasion of adjacent organs, obesity, or adhesions. Among the 52 patients who had LR converted to OR due to suspected adjacent organ invasion, a multivisceral resection was performed in 8 (15.4%) cases: 3 ileal resections, 2 wedge gastric

resections, 2 partial cystectomies, and 1 left nephrectomy. Nine multivisceral resections were performed in the LAP group (3.8%): an en-bloc right ovariectomy in 3 patients with right-sided LACC, an ileal resection in 3 patients with sigmoid LACC cancer, an en-bloc left ovariectomy was performed in 2 patients with sigmoid LACC, while a distal splenopancreatectomy was performed in a patient with a LACC of the splenic flexure.

Mean operative time was 132 min in the LAP group, and 184 min in the CONV group ($P < 0.001$). There were no significant differences in the need for blood transfusions between LAP and CONV patients. Intraoperative complication rate was 2.5% (N = 6) in the LAP group and 3.2% (N = 2) in the CONV group ($P = 0.874$); 2 anastomotic twists requiring to redo the anastomosis, 2 anastomotic leaks detected at the air bubble test, 1 bleeding from the inferior mesenteric vein, and 1 ileal injury occurred in the LAP group, while 1 bleeding from the inferior mesenteric artery and 1 ureteral lesion was registered in the CONV group.

The multivariate analysis showed that tumor site (splenic flexure; OR 3.11, 95% CI 2.10–5.13, $P < 0.001$) and tumor size (≥ 7 cm; OR 2.78, 95% CI 2.19–4.15, $P < 0.001$) were the independent risk factors for conversion to OR (Table 3).

Postoperative results

Return to bowel function occurred one day earlier in the LAP than CONV patients ($P < 0.001$). Resumption of solid diet was on postoperative day 4 and 5, respectively ($P = 0.001$). Postoperative complication rates were similar: 17.7% in the LAP group and 22.2% in the CONV group ($P = 0.467$). A reoperation was needed in 10 (4.2%) patients of the LAP group and 1 (1.6%) in the CONV group ($P = 0.461$). There was no mortality. Complications according to the Clavien-Dindo classification are resumed in Table 4. Mean length of postoperative hospital stay was 8 days in the LAP group and 8.8 days in the CONV group ($P = 0.348$).

Pathology results

Mean tumor size was significantly greater in the CONV group than in the LAP group (7.8 cm vs. 6.1 cm). The number of lymph nodes harvested, the number of patients with 12 or more lymph nodes harvested in the specimen, positive radial margin rates, and tumor budding did not significantly differ between the two groups.

Overall, final pathology reports showed a pT2 cancer in 18 patients (6%), a pT3 in 215 patients (71.7%), a pT4a in 54 patients (18%), and a pT4b in 13 patients (4.3%), with no significant differences between the two groups (Table 5).

Long-term oncologic results

Overall mean follow-up was 56.6 ± 46.3 months. After excluding the 22 metastatic LACC patients and 26 patients lost to follow-up, 252 (84%) patients were available for the long-term oncologic outcomes analysis: 200 in the LAP group and 52 in the CONV group.

Adjuvant chemotherapy was more likely administered in the LAP group than in the CONV group: 124 (62%) versus 24 (46.2%) (P = 0.042).

Local recurrence rate was 7.9% in the LAP group, while it was 23.8% in the CONV group (P = 0.005). Distant metastases rate was 15.2% in the LAP group and 12.7% in the CONV group (P = 0.767).

Five-year OS rate was 90.4% in the LAP group and 78.2% in the CONV group (P = 0.013). Five-year DFS rate was 76.6% and 65.6% in the LAP and CONV group, respectively (P = 0.017).

At multivariate analysis, pT4 colon cancer and LNR of 0.25 or greater were independently associated with both poorer OS (Table 6) and DFS (Table 7).

Case-matched analysis: OR vs. LR

During the study period, 50 patients underwent OR and were matched to 50 patients who were treated by LR (Table 8).

Intraoperative results

The type of procedure performed was similar between the groups, as reported in Table 8. An en-bloc multi-visceral resection was performed in 6 (12%) OR patients (2 partial cystectomies, 2 distal splenopancreatectomies, 1 ileal resection, and 1 sleeve gastric resection) and in 4 (8%) LR patients (2 ileal resections, 2 partial cystectomies). A total of 12 (24%) LR patients were converted to OR. Mean operative time was significantly shorter in the OR group (112.5 ± 35.6 min) than in the LR group (141.2 ± 45.9 min; P < 0.001). Mean estimated blood loss was 115.7 ml (SD, 49.7) in the OR group and 87.9 ml (SD, 50.3) in the LR group (P = 0.007).

Short-term postoperative results

Mean postoperative length of hospital stay was 14.4 days (9.8) in the OR group, and 8.3 (9.5) in the LR group (P = 0.002). Overall morbidity rate was 34% in the OR group and 16% in the LR group (P = 0.063). The severity of complications according to the Dindo classification was similar between the groups. Mortality rate was 4% among OR patients (2 cases of acute respiratory failure). No death occurred among LR patients.

Pathology results

There were no significant differences in positive margins rates, number of lymph nodes harvested in the specimen, and tumor staging between the two groups. A significantly higher proportion of converted patients had a tumor larger than 7 cm than patients who had a laparoscopically completed colon resection (75% vs. 28.9%, P = 0.007).

Long-term oncologic results

Mean duration of follow-up was 56.3 ± 38.6 months for OR patients and 47.5 ± 34.5 months for LR patients. The percentage of patients who underwent adjuvant CT was similar: 83.3% of OR patients and 76% of LR patients (P = 0.455).

The 5-year OS and DFS rate for all patients on an “intention-to-treat” basis did not differ significantly between OR and LR patients: 66.7% versus 65.8% (P = 0.828) and 59.7% versus 58.6% (P = 0.634).

Discussion

The last two decades have witnessed significant changes in the surgical treatment of colon cancer, with several large multicenter RCTs showing that LR for colon cancer is associated with better short-term outcomes than OR, without adverse long-term oncologic outcomes [11,12,13]. However, patients with LACC were excluded in most RCTs. Only the COLOR trial [19] included T4 colon cancers: a conversion rate close to 50% was reported in these patients. Based on these data and on the lack of evidence about feasibility and safety of LR, most guidelines published in the following years have recommended against the use of LR for the treatment of LACC, favoring OR [7, 8].

Since 2012, a growing number of studies assessing both short-term and long-term oncologic outcomes after elective LR or OR for LACC have been published [20,21,22,23,24,25,26,27,28,29,30,31,32]. Two recent meta-analyses [33, 34] of these comparative studies have shown that the pooled postoperative complication rate was

significantly lower after LR than OR. Rates of conversion to OR ranged between 7 and 28%. No significant differences were observed in terms of radical resection rates, number of lymph nodes harvested, 3- and 5-year DFS, and 3- and 5-year OS rates. These results seem to suggest that LR is feasible and safe, with better short-term outcomes and similar survival when compared with OR. However, these findings need to be interpreted with caution due to the non-randomized and heterogeneous nature of the studies, the higher proportions of multivisceral resections in the OR than LR groups, and inclusion of patients according to the pathologic and not the clinical stage of the colon cancer in most studies.

Since the current evidence does not allow to define if LR should be actually contraindicated in all LACC patients, we reviewed a consecutive series of 300 patients with clinical LACC, focusing on possible predictors of conversion to OR and risk factors for adverse oncologic outcomes. We found that 63 (21%) LRs were converted to OR, mainly due to the large tumor size (82.5%) or obesity (9.5%). Overall postoperative Clavien-Dindo type 3–4 complication rate was 4.7%, with no significant differences between LAP and CONV patients. On multivariate analysis, tumor size ≥ 7 cm and tumor site (splenic flexure) were the only independent risk factors for conversion to OR. Our conversion rate is comparable to those reported in several LACC studies. It has been suggested that conversion rates change according to the surgeon's experience: a learning curve ranging between 20 and 60 cases has been identified to lower the conversion rate [35, 36]. We excluded from our analysis the first 87 patients undergoing LR between April 1992 (when the laparoscopic approach was first used in colon cancer patients in our Institution) and February 1996 in order to avoid the effects related to the learning curve on the outcomes. Interestingly, we did not observe significant changes in the conversion rate over time in LACC patients, suggesting that tumor-related characteristics, rather than the experience of the surgeon, are more likely the main factors that lead to conversion to OR in these patients.

We observed in our series of LACC patients that converted LRs were associated with prolonged operative times, while there were no differences in intraoperative complications and needs for perioperative blood transfusions. Early postoperative outcomes reported in our study are consistent with those published in the literature, with quicker resumption of gastrointestinal function after completed LR than converted LR, while no significant differences were observed in postoperative complications. We confirm that mean length of hospital stay is longer in the CONV group, even though the difference did not reach the statistical significance (difference: 0.8 days, P = 0.348).

The oncologic outcomes after LR in LACC patients are unclear, since only a few studies have follow-up periods longer than 3 years. In addition, recent studies have reported controversial results. For instance, Wasmann et al. [14] included 424 patients with a pT4 N0-2 M0 colon cancer in a multicenter propensity score analysis. They found that LR was associated with higher rates of negative margins, lower postoperative complications, and increased use of adjuvant chemotherapy than OR. This reflected in both significantly longer 5-year DFS e 5-

year OS than OR. The authors argued that LR, by lowering postoperative morbidity, increased the probability for patients to receive adjuvant chemotherapy. It has also been speculated that postoperative complications might have a negative impact on survival leading to upregulation of proinflammatory cytokines that promote cancer growth [37, 38]. On the contrary, a recent retrospective analysis by Nagata et al. [10] of 272 patients undergoing LR for pT4a colon cancer without distant metastases showed that LR was an independent risk factor for peritoneal cancer relapse: 28% versus 12% (P = 0.003) at 5 years, when compared with OR. Some mechanisms have been proposed, including the dehumidification of the peritoneum by dry CO2, injury to the peritoneal lining, and aerosolization of cancer cells [39, 40]. Conversion to OR is also associated with poorer oncologic outcomes in colon cancer patients [41]. We observed both significantly lower OS and DFS in CONV patients than in LAP patients; however, the multivariate analysis showed that pT4 cancer staging and a LNR ≥ 0.25, but not conversion to OR, were the independent risk factors for poorer survival.

One of the major concerns that still limit the adoption of laparoscopy for LACC is the increased risk of R1 resections, with subsequent poorer oncologic long-term outcomes. A R0 resection was achieved in 98.3% of our patients. Overall mean number of lymph nodes harvested was 17.6; 12 or more lymph nodes were retrieved in the specimen in 83.7% of patients, with no significant differences between completed and converted LRs. Overall, a multivisceral resection was necessary in 17 (5.7%) patients. Interestingly, a multivisceral resection was not an independent risk factor for conversion to OR. This finding might be due to the tumor site and the type of organ involved by the LACC. In our series, none of the 4 patients with preoperative suspected infiltration of the duodenum or the body of the pancreas, that are considered main contraindications to the laparoscopic approach [42, 43], underwent elective LR for LACC.

Recently, some studies have shown that neoadjuvant chemotherapy may increase the rate of R0 resections, without adding significant toxicity [44]. However, the supposed reduction of the number of multivisceral resections has not been demonstrated, and the absence of studies with long follow-up does not allow to draw any definitive conclusion about the oncologic impact of this strategy in LACC.

We acknowledge that this study has some limitations. First, it is a retrospective study. Second, it has been conducted in a single institution and, therefore, the findings may not be generalized. However, some recent data have shown that patients with LACC might benefit from centralization of care in referral centers. It has been speculated that centralization of these patients with implementation of multidisciplinary team discussions might be associated with better outcomes and increased use of the minimally invasive approach [45]. In addition, it is the first study that is focused on a large series of patients with clinically diagnosed LACC, aiming at identifying those patients who may not benefit from LR. As a consequence, we feel that the results of this large study will contribute to fuel the discussion and shed more light on the role of LR in the management of LACC patients.

In conclusion, the results of this study show that clinical LACC should not be considered a contraindication to LR itself. A proper preoperative evaluation is crucial to better select LACC patients for LR. Bulky tumors ≥ 7 cm and splenic flexure cancers are at higher risk of conversion to OR; however, there is no increased postoperative morbidity or adverse oncologic outcomes in converted patients.

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	Total ($n=300$)	LAP ($n=237$)	CONV ($n=63$)	*P* value
Male, *n* (%)	173 (57.7)	138 (58.2)	35 (55.5)	0.775
Age (years)	68.3 ± 11.2	67.9 ± 11.4	69.8 ± 10.2	0.549
BMI (Kg/m^2)	25.3 ± 4.6	25 ± 4.7	26.2 ± 4.3	0.081
ASA score, *n* (%)				
1–2	174 (58)	142 (59.9)	32 (50.8)	0.199
3–4	126 (42)	95 (40.1)	31 (49.2)	
Tumor site, *n* (%)				
Right colon	138 (46)	109 (46)	29 (46)	1
Transverse colon	8 (2.7)	6 (2.5)	2 (3.2)	0.676
Splenic flexure	24 (8)	12 (5.1)	12 (19)	<0.001
Descending colon	8 (2.7)	6 (2.5)	2 (3.2)	0.676
Sigmoid colon	103 (34.3)	89 (37.6)	14 (22.2)	0.025
Rectosigmoid junction	19 (6.3)	15 (6.3)	4 (6.4)	0.996
Comorbidities, *n* (%)				
Diabetes	29 (9.7)	24 (10.1)	5 (7.9)	0.881
Cardiovascular diseases	30 (10)	22 (9.3)	8 (12.7)	0.478
Respiratory diseases	14 (4.7)	9 (3.8)	5 (7.9)	0.181
Previous abdominal surgery, *n* (%)	92 (30.7)	66 (27.8)	26 (41.3)	0.046
Synchronous metastases, *n* (%)	20 (6.7)	12 (5.1)	8 (12.7)	0.044

LAP laparoscopically completed, *CONV* converted, *BMI* body mass index

Table 1 Baseline patient's characteristics

	Total ($n=300$)	LAP ($n=237$)	CONV ($n=63$)	*P* value
Surgical procedure, *n* (%)				
Right colectomy	138 (46)	109 (46)	29 (46)	0.997
Extended right colectomy	5 (1.7)	3 (1.3)	2 (3.2)	0.283
Transverse colon resection	5 (1.7)	3 (1.3)	2 (3.2)	0.283
Splenic flexure resection	9 (3)	6 (2.5)	3 (4.8)	0.403
Left colectomy	57 (19)	46 (19.4)	11 (17.5)	0.857
Sigmoidectomy	59 (19.7)	54 (22.8)	5 (7.9)	0.007
Subtotal colectomy	5 (1.7)	2 (0.8)	3 (4.8)	0.064
Anterior resection	18 (6)	13 (5.5)	5 (7.9)	0.549
Hartmann procedure	4 (1.2)	1 (0.4)	3 (4.8)	0.030
Operative time (min)	142.8 ± 56	132.1 ± 48.7	183.8 ± 63.3	< 0.001
Reasons for conversion, *n* (%)	63 (21)			
Suspected adjacent organ invasion	52 (82.5)			
Obesity	6 (9.5)			
Adhesions	2 (3.2)			
Ureteral injury	2 (3.2)			
Uncontrollable bleeding	1 (1.6)			
Multivisceral resection, *n* (%)	17 (5.7)	9 (3.8)	8 (12.7)	0.012
Complications, *n* (%)	8 (2.7)	6 (2.5)	2 (3.2)	0.676
Peri-operative transfusion, *n* (%)	31 (10.3)	23 (9.7)	8 (12.7)	0.488

LAP laparoscopically completed, *CONV* converted

Table 2 Intraoperative results

	Univariate analysis		Multivariate analysis	
	Odds Ratio (95% CI)	*P* value	Odds Ratio (95% CI)	*P* value
BMI (Kg/m^2)				
<25	1	0.081	1	0.611
≥25	2.11 (0.95–3.17)		1.58 (0.76–2.16)	
Tumor site				
Others	1		1	
Splenic flexure	3.71 (2.12–6.16)	<0.001	3.11 (2.10–5.13)	<0.001
Tumor size (cm)				
<7	1	<0.001	1	<0.001
≥7	3.02 (1.94–6.08)		2.78 (2.19–4.15)	
Previous abdominal surgery				
No	1		1	
Yes	3.34 (1.88–5.04)	0.012	1.87 (0.77–3.46)	0.244
Multivisceral resection				
No	1		1	
Yes	1.48 (1.03–2.89)	0.046	1.25 (0.67–1.65)	0.834

BMI body mass index

Table 3 Univariate and multivariate analysis of risk factors for conversion to open surgery

	Total (n=300)	LAP (n=237)	CONV (n=63)	*P* value
Flatus (days)	2.7±1.1	2.5±0.9	3.6±1.3	<0.001
Stools (days)	4.2±1.9	4.1±2	4.9±1.7	<0.001
Oral intake (days)	4.3±1.9	4.1±1.9	5±1.4	0.001
Length of hospital stay (days)	8.1±5.7	8±6.1	8.8±3.4	0.348
Complications, n (%)				
Overall	56 (18.7)	42 (17.7)	14 (22.2)	0.467
Grade 2	42 (14)	29 (12.2)	13 (20.6)	
Grade 3a	1 (0.3)	1 (0.4)	0	
Grade 3b	11 (3.7)	10 (4.2)	1 (1.6)	
Grade 4	2 (0.7)	2 (0.8)	0	

LAP laparoscopically completed, *CONV* converted

Table 4 Early postoperative results

	Total ($n=300$)	LAP ($n=237$)	CONV ($n=63$)	P value
Tumor size (cm)	6.5 ± 2.2	6.1 ± 1.9	7.8 ± 2.9	< 0.001
Grading, *n* (%)				
G1–G2	246 (82)	202 (85.2)	44 (69.8)	0.009
G3	54 (18)	35 (14.8)	19 (30.2)	
Tumor budding, *n* (%)				
Low	219 (73)	177 (74.7)	42 (66.7)	0.206
High	81 (27)	60 (25.3)	21 (33.3)	
Lymphovascular invasion, *n* (%)	74 (24.7)	52 (21.9)	22 (34.9)	0.048
Neural invasion, *n* (%)	42 (14)	30 (12.7)	12 (19)	0.220
Lymphocytic infiltration, *n* (%)	171 (57)	140 (59.1)	31 (49.2)	0.197
Positive radial margin, *n* (%)	5 (1.7)	2 (0.8)	3 (4.8)	0.064
Number of lymph nodes	17.6 ± 7.6	17.7 ± 7.5	17.2 ± 7.7	0.669
Lymph nodes ≥ 12, *n* (%)	251 (83.7)	200 (84.4)	51 (80.9)	0.565
Tumor stage, *n* (%)				
2	18 (6)	14 (5.9)	4 (6.3)	0.867
3	215 (71.7)	175 (73.8)	40 (63.5)	0.117
4a	54 (18)	41 (17.3)	13 (20.6)	0.581
4b	13 (4.3)	7 (2.9)	6 (9.5)	0.034
N stage, *n* (%)				
N0	172 (57.3)	141 (59.5)	31 (49.2)	0.154
N1	82 (27.3)	60 (25.3)	22 (34.9)	0.152
N2	46 (15.3)	36 (15.2)	10 (15.9)	0.847
TNM, *n* (%)				
1	15 (5)	12 (5.1)	3 (4.8)	0.820
2	149 (49.7)	121 (51)	28 (44.4)	0.396
3	114 (38)	91 (38.4)	23 (36.5)	0.884
4	22 (7.3)	13 (5.5)	9 (14.3)	0.027

LAP laparoscopically completed; *CONV* converted

Table 5 Pathology results

	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	*P* value	Hazard ratio (95% CI)	*P* value
Conversion to OR				
No	1	0.015	1	0.432
Yes	2.14 (1.15–4.29)		1.51 (0.80–2.58)	
pT staging				
T2-T3	1		1	
T4	4.08 (2.11–10.01)	<0.001	3.19 (1.88–8.02)	<0.001
Lymph node ratio				
0	1		1	
0.01–0.24	1.61 (0.88–3.77)	0.116	1.26 (0.48–1.52)	0.655
≥0.25	5.17 (2.77–9.46)	<0.001	3.15 (1.56–7.19)	0.031
Adjuvant chemotherapy				
Yes	1		1	
No	1.95 (0.81–2.98)	0.122	1.11 (0.59–2.54)	0.781

OR open resection

Table 6 Univariate and multivariate analysis of risk factors for overall survival

	Univariate analysis		Multivariate analysis	
	Hazard Ratio (95% CI)	*P* value	Hazard Ratio (95% CI)	*P* value
Conversion to OR				
No	1		1	
Yes	2.10 (1.17–4.47)	0.017	1.58 (0.83–2.37)	0.507
pT staging				
T2–T3	1		1	
T4	3.81 (2.31–11.46)	<0.001	3.31 (2.10–9.13)	<0.001
Lymph node ratio				
0	1		1	
0.01–0.24	1.88 (0.78–3.59)	0.158	1.24 (0.51–1.66)	0.544
≥0.25	4.77 (2.34–9.37)	<0.001	2.75 (1.46–8.05)	0.038
Adjuvant Chemotherapy				
Yes	1		1	
No	1.81 (0.86–3.21)	0.118	1.41 (0.69–2.74)	0.687

OR open resection

Table 7 Univariate and multivariate analysis of risk factors for disease-free surviva

	OR ($n=50$)	LR ($n=50$)	*P* value
Gender, *n* (%)			
Male	31 (62)	29 (58)	0.838
Age (years)	68.1 ± 10.4	68.5 ± 10.7	0.850
ASA score, *n* (%)			
1–2	40 (80)	40 (80)	1
3–4	10 (20)	10 (20)	
Tumor location, *n* (%)			
Right colon	18 (36)	20 (40)	0.837
Transverse colon	4 (8)	3 (6)	1
Left colon	28 (56)	27 (54)	1
Surgical procedure, *n* (%)			
Right colectomy	20 (40)	20 (40)	1
Transverse colon resection	2 (4)	3 (6)	1
Left colectomy	22 (44)	20 (40)	0.839
Sigmoidectomy	6 (12)	7 (14)	1
Multivisceral resection, *n* (%)	6 (12)	4 (8)	0.741
Diverting stoma	1 (2)	0	1
Postoperative complications Overall	17 (34)	8 (16)	0.063
Grade 1	1 (2)	1 (2)	1
Grade 2	7 (14)	4 (8)	0.525
Grade 3	6 (12)	3 (6)	0.487
Grade 4	1 (2)	0	1
Grade 5	2 (4)	0	0.495
Positive margins, *n* (%)	1 (2)	0	1
Tumor size (cm)	5.9 ± 2.5	6.1 ± 1.5	0.690
Number of lymph nodes	17 ± 6.2	16.8 ± 6.9	0.879
Tumor stage, *n* (%)			0.308
4a	38 (76)	43 (86)	
4b	12 (24)	7 (14)	
TNM, *n* (%)			0.422
2	25 (50)	20 (40)	
3	25 (50)	30 (60)	

OR open resection, *LR* laparoscopic resection

Table 8 Open versus laparoscopic resection for locally advanced colon cancer