The American Journal of Surgery 217 (2019) 491–495

Contents lists available at ScienceDirect

The American Journal of Surgery

journal homepage: www.americanjournalofsurgery.com

Conversion to open from laparoscopic colon resection is a marker for worse oncologic outcomes in colon cancer

Leonardo de Castro Duraes, Scott R. Steele, Mariane Gouvêa Monteiro de Camargo, Emre Gorgun, Matthew F. Kalady, Michael Valente, Anuradha Bhama, Conor Patrick Delaney*

Department of Colorectal Surgery, Cleveland Clinic Foundation, Crile Building, 2049 East 100th Street, Cleveland, OH, 44195, USA

ARTICLE INFO

Article history:
Received 28 July 2018
Received in revised form
25 October 2018
Accepted 26 October 2018

ABSTRACT

Background: This study aimed to evaluate the oncological outcomes of conversion in patients undergoing resection for colon cancer.

Methods: Patients with stages I-III colon adenocarcinoma operated on between 2000 and 2012 were included. Oncologic outcomes were assessed by surgical approach (laparoscopy vs. open). A secondary analysis compared patients who required conversion to open vs. laparoscopic only.

Results: We identified 1196 patients that met inclusion criteria (28% laparoscopic, 72% open). Overall, 13% of laparoscopic cases were converted to open. There were no differences in 5-year overall survival (OS) ($p = 0.258$), disease-free survival, (DFS) ($p = 0.070$), cancer-specific survival (CSS) ($p = 0.207$), or recurrence ($p = 0.216$) between laparoscopy and open surgery. However, patients with conversion had a worse OS ($p = 0.010$) and DFS ($p = 0.006$) when compared to laparoscopic only.

Conclusion: Conversion from laparoscopic to open surgery is a marker for worse survival outcomes. Further investigation is needed to define the underlying cause of these differences.

Introduction

The use of laparoscopy for colon cancer resection is widely accepted. Large multicenter randomized clinical trials have reported several short-term benefits when compared with open resection, such as reduced blood loss, less post-operative pain and shorter length of hospital stay.[1,2] Long-term results of these trials have confirmed that laparoscopic colon cancer resection is similar to open resection regarding survival and locoregional recurrence.[3]

These trials have reported that conversion to open surgery range from 0% to 42%,[4] and may be due to factors including body mass index (BMI), gender, American Society of Anesthesiologists (ASA) grade, previous abdominal surgery, and tumor-related factors such as location, T-stage and node status. However, the effects of conversion to open surgery on oncologic outcomes remain controversial, mainly because the majority of these studies only included a limited number of patients, did not analyze colon and rectal cancer patients separately, or did not analyze the cause for conversion.[5–8]

As such, we wanted to evaluate a cohort of colon cancer patients in a high-volume tertiary center undergoing colectomy. The aim of this study was to evaluate the oncological outcomes of conversion in patients undergoing resection for colon cancer. We hypothesized that conversion was associated with worse oncological outcomes.

Methods

Patients with stages I-III colon adenocarcinoma undergoing laparoscopic colectomy with curative intent between January 2000 and December 2012 were identified through a prospectively maintained, institutional review board (IRB) - approved departmental database. The database includes demographic characteristics, patient comorbidities, intraoperative variables, and postoperative and long-term oncologic outcomes.

The exclusion criteria included stage IV disease, urgent or palliative surgery, concurrent inflammatory bowel disease, or hereditary cancer. Patients were initially stratified by surgical

* Corresponding author.
E-mail addresses: duraesl@ccf.org (L.C. Duraes), steeles3@ccf.org (S.R. Steele), camargm@ccf.org (M.G.M. Camargo), gorgune@ccf.org (E. Gorgun), kaladym@ccf.org (M.F. Kalady), valentm2@ccf.org (M. Valente), bhamaa@ccf.org (A. Bhama), delanec@ccf.org (C.P. Delaney).

https://doi.org/10.1016/j.amjsurg.2018.10.042
0002-9610/

approach (laparoscopy vs. open). A secondary analysis was performed comparing patients who required conversion to open against laparoscopic only. Hand-assisted and single-port approaches were included in the laparoscopy group. Conversion was defined as the use or extension of any incision to perform any part of the operation other than specimen extraction or port placement. Extracorporeal anastomosis, however, was not considered as a conversion. Reasons for conversion were grouped as: technical difficulties (e.g., conversion due unclear anatomy or dense adhesions), tumor stage (e.g., bulky tumors with suspicious or proved invasion to other organs), early conversion (e.g., bowel dilation, severe adhesions from previous surgeries upon establishment of pneumoperitoneum, and one case of intestinal malrotation), and intraoperative complications (e.g., bleeding, enterotomy, hemodynamic instability, or technical problems with the anastomosis).

Both laparoscopic and open colorectal resections were performed according to the oncologic surgical principles of lymphovascular ligation at the origin of the main vessels. Anastomotic techniques and use of proximal diverting ileostomy depended on the type of resection and the individual surgeon's discretion. An R0 resection was defined as a resection with a distal margin clearance greater than 1 cm and a radial margin clearance exceeding 2 mm. Follow-up assessment at our institution included a combination of physical examination, serial evaluation of biochemical tumor markers, colonoscopy, and computed tomography (CT) scans in line with national colorectal cancer surveillance guidelines. For the patients who continued postoperative cancer surveillance elsewhere, the oncologic follow-up assessment was performed by phone interviews and through the request for clinical documentation.

Categorical variables were analyzed using chi-square, or Fisher's exact test as appropriate, and the Wilcoxon rank sum test was used for quantitative and ordinal variables. Comparisons of overall, disease-free, cancer-specific survival and distant recurrence rates were performed using Kaplan–Meier curves. A p value of less than 0.05 was considered statistically significant.

Results

We identified 1196 patients meeting the inclusion criteria, from which 340 (28%) patients underwent a laparoscopic approach (including 51 hand-assisted and 25 single-port), and 856 (72%) underwent open surgery. Overall, 43 (13%) laparoscopic cases were converted to an open approach. Patient and disease characteristics are summarized in Table 1.

When we analyzed by surgical approach (laparoscopy vs. open), no difference was observed in patient characteristics. However, the open group had a higher pathological stage and worse pathological differentiation. (Table 1). Higher morbidity was seen in the laparoscopic surgery, potentially reflecting the surgeons' collective learning curve at the beginning of our experience, but this group had shorter hospital stay when compared to open. No differences were observed in adjuvant chemotherapy.

After a median follow-up of 4 years, we observed no difference in 5-year overall survival (OS) (71% vs. 69%, $p = 0.258$), disease-free survival (DFS) (65% vs. 63%, $p = 0.070$), cancer-specific survival (CSS) (90% vs. 88%, $p = 0.207$) or recurrence (16% vs. 17%, $p = 0.216$) between laparoscopy and open, respectively (Table 1, Fig. 1).

A secondary analysis was performed comparing patients who required conversion to open against laparoscopic only. The groups were comparable regarding ASA score, tumor differentiation, pathological stage, postoperative morbidity and mortality, and adjuvant chemotherapy. Of note, patients in the conversion group were older than patients in the laparoscopic group ($p = 0.013$) (Table 1).

Patients with conversion had a worse OS (53% vs. 75%, $p = 0.010$) and DFS (42% vs. 69%, $p = 0.006$) when compared to the laparoscopic cohort only (Fig. 1). No difference was observed on CSS (90% vs. 94%, $p = 0.693$) or recurrence (15% vs. 18%, $p = 0.567$).

When we evaluated patients by final pathologic stage, conversion was associated with worse survival outcomes in stage II (OS 50% vs. 79%, $p = 0.041$; DFS 40% vs. 72%, $p = 0.066$), and stage III (OS 32% vs. 65%, $p = 0.033$; DFS 22% vs. 59, $p = 0.017$) disease.

The reasons for conversion included: conversion due to technical difficulties (53%), tumor stage (19%), early conversion (16%), and intraoperative complications (12%). None of the reasons for conversion were associated with OS ($p = 0.937$), DFS ($p = 0.621$), CSS ($p = 0.219$), or recurrence ($p = 0.437$).

Discussion

In our study, no difference was observed in oncologic outcomes between open and laparoscopic surgery; however, patients who required conversion to an open approach had worse OS and DFS when compared to patients who had their operations completed by laparoscopy. Conversion was also associated with worse survival outcomes when patients were stratified by pathological stages II and III.

We also compared the reasons for conversion, considering that tumor location or size could make laparoscopic dissection more difficult and lead to a higher conversion rate and potentially worsen oncologic outcomes. However, the reasons for conversion (technical difficulties, tumor stage, early conversion, and intraoperative complications) were not associated with worse OS, DFS, CSS or recurrence.

Previous reports are consistent with our findings. In a meta-analysis, Clancy and colleagues[8] concluded that unsuccessful laparoscopic surgery might further worsen the outcome, despite many confounding factors such as advanced tumor stage and elevated BMI were present. Chan and associates[5] reported a higher chance to develop local recurrence in the patient with conversion compared to open surgeries. Unique to our series, we included only patients with colon cancer, while those studies included colon and rectal cancer patients.

Other series did not find differences in oncologic outcomes between conversion and laparoscopy. Martínek et al.,[9] showed a tendency toward a longer survival (OS and DFS) period in the laparoscopic group compared to conversion, but no statistically significant difference was confirmed. This may be due to the small number of patients in their series. Li et al.,[10] used a prospective database to identify consecutive operations for non-metastatic colon cancer and found no differences in the 5-year OS between laparoscopic, open and conversion group. In multivariate analysis, pT3–4 cancer and poor differentiation were independent predictors of both lower OS and lower DFS, whereas leakage and lack of adjuvant chemotherapy were independent risk factors only of lower DFS. Most of the studies that do not support our results found a tendency toward worse outcomes in converted patients but did not reach statistical significance.[9,10]

Conversion has been previously associated with demographic and perioperative factors such as gender, comorbidities, tumor size and location, patient selection, intraoperative complications, and surgeon experience.[4,11] Rottoli et al.,[12] in a well-designed case-match study with colorectal cancer patients, included variables as age, ASA score, surgery period, tumor location and pathologic stage in the case-match analysis. Like our study, they reported decreased OS and DFS in the converted patients.

Many factors could be associated with worse survival in converted patients. This includes tumor stage, more inflammatory response due to conversion and possibly more postoperative

Table 1
Patient and disease characteristics, and long-term survival by use of laparoscopy vs. open surgery, and by laparoscopic completed surgeries vs. conversion.

	Laparoscopy (n = 340)	Open (n = 856)	*p* value	Laparoscopic Only (n = 297)	Conversion (n = 43)	*p* value
Age	66.6 ± 13.9	68.1 ± 13.2	0.051	66.0 ± 13.9	71.0 ± 12.9	0.013
Male Gender	199 (58.5)	472 (55.1)	0.287	173 (58.2)	26 (60.5)	0.783
BMI	28.6 ± 6.0	28.1 ± 5.8	0.161	28.4 ± 6.0	29.6 ± 6.3	0.348
ASA[a]			0.528			0.229
I − II	107 (32.6)	254 (30.7)		97 (33.8)	10 (24.4)	
III − IV	221 (67.4)	573 (69.3)		190 (66.2)	31 (75.6)	
Pathological stage			0.002			0.762
I	115 (33.8)	205 (23.9)		102 (34.3)	13 (30.2)	
II	122 (35.9)	357 (41.7)		107 (36.0)	15 (34.9)	
III	103 (30.3)	294 (34.3)		88 (29.6)	15 (34.9)	
Pathological differentiation[a]			<0.001			0.845
Well	28 (8.4)	50 (5.9)		24 (8.3)	4 (9.3)	
Moderately	259 (77.8)	588 (69.3)		227 (78.3)	32 (74.4)	
Poorly	46 (13.8)	210 (24.8)		39 (13.4)	7 (16.3)	
Procedure			0.003			0.124
Right Hemicolectomy	199 (58.5)	495 (57.8)		175 (58.9)	24 (55.8)	
Anterior/low anterior resection	85 (25)	175 (20.4)		74 (24.9)	11 (25.6)	
Sigmoid Colectomy	43 (12.6)	116 (13.6)		37 (12.5)	6 (14.0)	
Total Abdominal Colectomy	12 (3.5)	30 (3.5)		11 (3.7)	1 (2.3)	
Other	1 (0.3)	40 (4.7)	–	1 (2.3)		
Postoperative morbidity	106 (31.2)	207 (24.2)	0.013	92 (31.0)	14 (32.6)	0.834
Clavien-Dindo		0.617				0.930
I	42 (39.6)	71 (34.3)		36 (39.1)	6 (42.9)	
II	26 (24.5)	64 (30.9)		23 (25.0)	3 (21.4)	
III	27 (25.5)	48 (23.2)		24 (26.1)	3 (21.4)	
IV	11 (10.4)	24 (11.6)		9 (9.8)	2 (14.3)	
Reoperation	22 (6.5)	29 (3.4)	0.017	21 (7.1)	1 (2.3)	0.237
Postoperative mortality	4 (1.2)	21 (2.5)	0.164	3 (1.0)	1 (2.3)	0.455
Length of hospital stay	7.1 ± 7.3	8.8 ± 7.6	<0.001	6.8 ± 7.2	9.5 ± 7.9	<0.001
Postoperative chemotherapy[a]	60 (31.6)	204 (33.8)	0.566	54 (3.6)	6 (22.2)	0.259
5 y Overall Survival	71%	69%	0.258	75%	53%	0.010
5 y Disease Free Survival	65%	63%	0.070	69%	42%	0.006
5 y Cancer Specific Survival	90%	88%	0.207	94%	90%	0.693
5 y Overall Recurrence	16%	17%	0.216	18%	15%	0.567

Data reported as mean ± SD or number (%).
BMI = body mass index; ASA = American Society of Anesthesiologists; y = year.
Other procedures: Hartmann's Procedure, Transverse colectomy.
[a] Data not available for all subjects. Missing values: ASA: 41, Pathological differentiation: 15, Postoperative chemotherapy: 403.

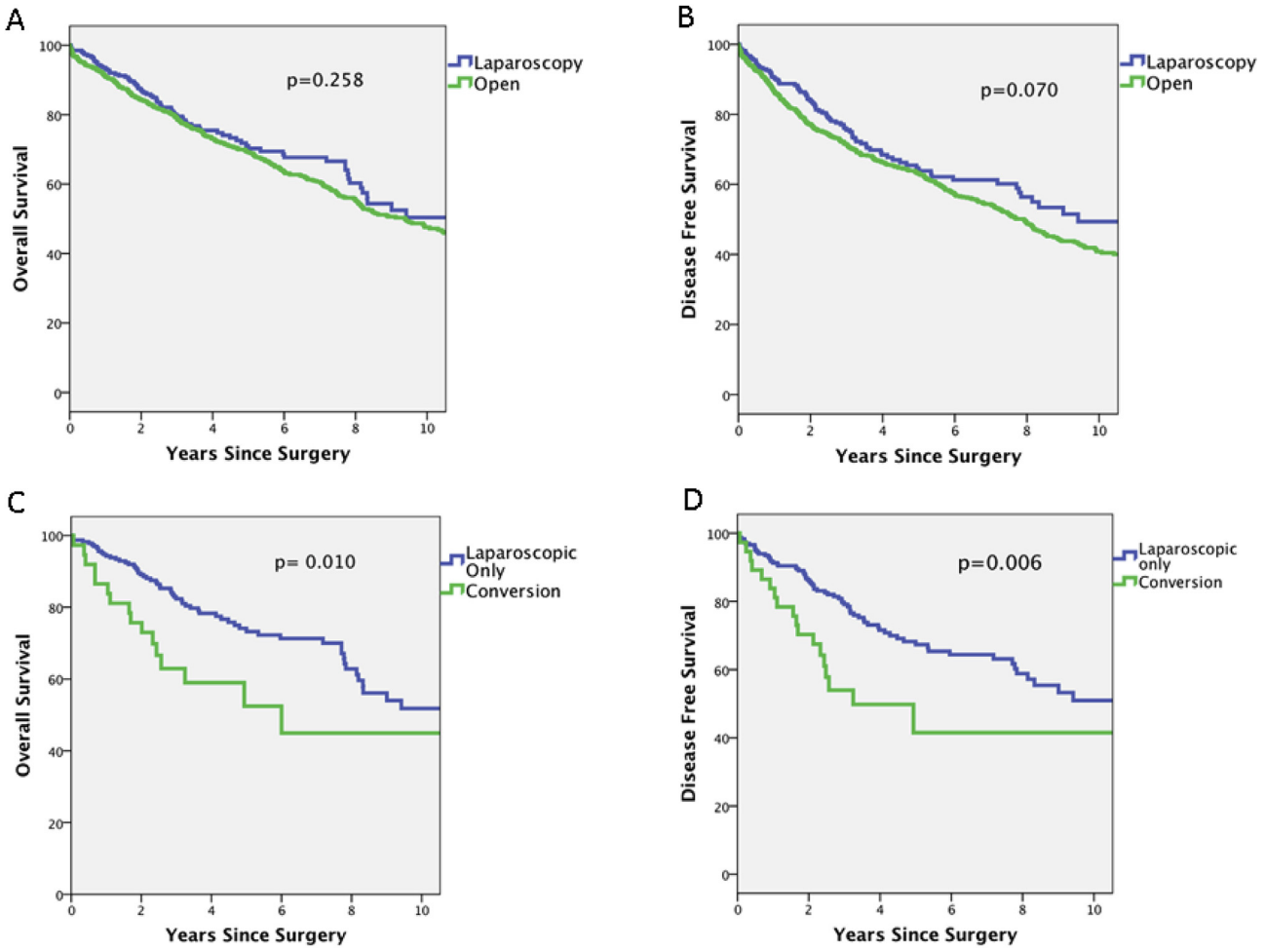

Fig. 1. Overall survival and disease-free survival Kaplan-Meyer curves.
Overall Survival and Disease Free Survival by use of laparoscopy vs. open surgery (A, B), and for patients who had operation completed by laparoscopy vs. conversion (C,D).

complications. In our study, we could not identify any of those factors. Conversion can delay the beginning of adjuvant treatment with chemotherapy, which can lead to worse survival. In our study, we did not evaluate the timing of chemotherapy. Further studies are needed to clarify if any of those factors are the reasons for worsening survival outcomes.

Limitations of our results include its non-randomized design and retrospective nature.

Also, a selection bias can occur for patients who had conversion. However, as the impact of conversion on the long-term outcomes of colon cancer is still subject of controversy, it was valuable to report our results. Deducting that conversion has isolated influence upon worsen long-term outcomes, may oversee all the other factors that must contribute to worse survival.

In conclusion, in a retrospective analysis of prospectively collected data for colon cancer patients, our results suggest that conversion from laparoscopic to open surgery is a marker for a worse overall and disease-free survival. Further work is needed to define the exact reason for worse outcomes.

Disclosure

The authors have no disclosures. This study did not have any financial support.

References

1. Guillou PJ, Quirke P, Thorpe H, et al. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. *Lancet (London, England)*. 2005;365:1718–1726. https://doi.org/10.1016/S0140-6736(05)66545-2.
2. Lacy AM, García-Valdecasas JC, Delgado S, et al. Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial. *Lancet*. 2002;359:2224–2229. https://doi.org/10.1016/S0140-6736(02)09290-5.
3. Colon Cancer Laparoscopic or Open Resection Study Group, Buunen M, Veldkamp R, et al. Survival after laparoscopic surgery versus open surgery for colon cancer: long-term outcome of a randomised clinical trial. *Lancet Oncol*. 2009;10:44–52. https://doi.org/10.1016/S1470-2045(08)70310-3.
4. Thorpe H, Jayne DG, Guillou PJ, et al. Patient factors influencing conversion from laparoscopically assisted to open surgery for colorectal cancer. *Br J Surg*. 2008;95:199–205. https://doi.org/10.1002/bjs.5907.
5. Chan ACY, Poon JTC, Fan JKM, et al. Impact of conversion on the long-term outcome in laparoscopic resection of colorectal cancer. *Surg Endosc*. 2008;22:2625–2630. https://doi.org/10.1007/s00464-008-9813-3.
6. Allaix ME, Degiuli M, Arezzo A, et al. Does conversion affect short-term and oncologic outcomes after laparoscopy for colorectal cancer? *Surg Endosc Other Interv Tech*. 2013;27:4596–4607. https://doi.org/10.1007/s00464-013-3072-7.
7. Allaix ME, Furnée EJB, Mistrangelo M, et al. Conversion of laparoscopic colorectal resection for cancer: what is the impact on short-term outcomes and survival? *World J Gastroenterol*. 2016;22:8304. https://doi.org/10.3748/wjg.v22.i37.8304.
8. Clancy C, O'Leary DP, Burke JP, et al. A meta-analysis to determine the oncological implications of conversion in laparoscopic colorectal cancer surgery. *Colorectal Dis*. 2015;17:482–490. https://doi.org/10.1111/codi.12875.
9. Martínek L, Dostalík J, Guòková P, et al. Impact of conversion on outcome in laparoscopic colorectal cancer surgery. *Videosurg Other Miniinvasive Tech*.

2012;2:74–81. https://doi.org/10.5114/wiitm.2011.25799.
10. Li J, Guo H, Guan XD, et al. The impact of laparoscopic converted to open colectomy on short-term and oncologic outcomes for colon cancer. *J Gastrointest Surg*. 2015;19:335–343. https://doi.org/10.1007/s11605-014-2685-z.
11. Tekkis PP, Senagore AJ, Delaney CP. Conversion rates in laparoscopic colorectal surgery: a predictive model with 1253 patients. *Surg Endosc Other Interv Tech*. 2005;19:47–54. https://doi.org/10.1007/s00464-004-8904-z.
12. Rottoli M, Stocchi L, Geisler DP, Kiran RP. Laparoscopic colorectal resection for cancer: effects of conversion on long-term oncologic outcomes. *Surg Endosc Other Interv Tech*. 2012;26:1971. https://doi.org/10.1007/s00464-011-2137-8.