ISSN 1007-9327 (print)
ISSN 2219-2840 (online)

World Journal of *Gastroenterology*

World J Gastroenterol 2018 January 7; 24(1): 1-160

Published by Baishideng Publishing Group Inc

World Journal of Gastroenterology

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Weekly Volume 24 Number 1 January 7, 2018

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ABOUT COVER

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World Journal of Gastroenterology (*World J Gastroenterol*, *WJG*, print ISSN 1007-9327, online ISSN 2219-2840, DOI: 10.3748) is a peer-reviewed open access journal. *WJG* was established on October 1, 1995. It is published weekly on the 7th, 14th, 21st, and 28th each month. The *WJG* Editorial Board consists of 642 experts in gastroenterology and hepatology from 59 countries.

The primary task of *WJG* is to rapidly publish high-quality original articles, reviews, and commentaries in the fields of gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, hepatobiliary surgery, gastrointestinal oncology, gastrointestinal radiation oncology, gastrointestinal imaging, gastrointestinal interventional therapy, gastrointestinal infectious diseases, gastrointestinal pharmacology, gastrointestinal pathophysiology, gastrointestinal pathology, evidence-based medicine in gastroenterology, pancreatology, gastrointestinal laboratory medicine, gastrointestinal molecular biology, gastrointestinal immunology, gastrointestinal microbiology, gastrointestinal genetics, gastrointestinal translational medicine, gastrointestinal diagnostics, and gastrointestinal therapeutics. *WJG* is dedicated to become an influential and prestigious journal in gastroenterology and hepatology, to promote the development of above disciplines, and to improve the diagnostic and therapeutic skill and expertise of clinicians.

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World Journal of Gastroenterology (*WJG*) is now indexed in Current Contents®/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports®, Index Medicus, MEDLINE, PubMed, PubMed Central and Directory of Open Access Journals. The 2017 edition of Journal Citation Reports® cites the 2016 impact factor for *WJG* as 3.365 (5-year impact factor: 3.176), ranking *WJG* as 29th among 79 journals in gastroenterology and hepatology (quartile in category Q2).

NAME OF JOURNAL
World Journal of Gastroenterology

ISSN
ISSN 1007-9327 (print)
ISSN 2219-2840 (online)

LAUNCH DATE
October 1, 1995

FREQUENCY
Weekly

EDITORIAL OFFICE
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World Journal of Gastroenterology
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: editorialoffice@wjgnet.com
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http://www.wjgnet.com

PUBLISHER
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.f6publishing.com/helpdesk
http://www.wjgnet.com

PUBLICATION DATE
January 7, 2018

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World Journal of Gastroenterology

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World J Gastroenterol 2018 January 7; 24(1): 76-86

DOI: 10.3748/wjg.v24.i1.76

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

ORIGINAL ARTICLE

Retrospective Study

Short- and long-term outcomes following laparoscopic *vs* open surgery for pathological T4 colorectal cancer: 10 years of experience in a single center

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Author contributions: Yang ZF and Wu DQ contributed equally to this work and designed the research; Wang JJ and Lv ZJ acquired the data; Yang ZF and Wu DQ analyzed and interpreted the data; Lv ZJ drafted the manuscript; all authors made critical revisions related to important intellectual content of the manuscript, and have read and approved the final version to be published.

Supported by Natural Science Foundation of Guangdong Province, No. 2016A030310328 and No. 2016A030313762.

Institutional review board statement: This study was evaluated and approved by the ethics committee at our institution.

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Conflict-of-interest statement: All authors declare no conflict of interest.

Data sharing statement: No additional data are available.

Manuscript source: Unsolicited manuscript

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Received: October 26, 2017
Peer-review started: October 27, 2017
First decision: November 8, 2017
Revised: November 17, 2017
Accepted: November 21, 2017
Article in press: November 21, 2017
Published online: January 7, 2018

Abstract

AIM

To evaluate the short-term and long-term outcomes following laparoscopic *vs* open surgery for pathological T4 (pT4) colorectal cancer.

METHODS

We retrospectively analyzed the short- and long-term outcomes of proven pT4 colorectal cancer patients who underwent complete resection by laparoscopic or open surgery from 2006 to 2015 at Guangdong General Hospital.

RESULTS

A total of 211 pT4 colorectal cancer patients were included in this analysis, including 101 cases in the

laparoscopy (LAP) group and 110 cases in the open surgery (OPEN) group [including 15 (12.9%) cases of conversion to open surgery]. Clinical information (age, gender, body mass index, comorbidities, American Society of Anesthesiologists score, *etc.*) did not differ between the two groups. In terms of blood loss, postoperative complications and rate of recovery, the LAP group performed significantly more favorably ($P < 0.05$). With regard to pT4a/b and combined organ resection, there were significantly more cases in the OPEN group ($P < 0.05$). The 3- and 5-year overall survival rates were 74.9% and 60.5%, respectively, for the LAP group and 62.4% and 46.5%, respectively, for the OPEN group ($P = 0.060$). The 3- and 5-year disease-free survival rates were 68.0% and 57.3%, respectively, for the LAP group and 55.8% and 39.8%, respectively, for the OPEN group ($P = 0.053$). Multivariate analysis showed that ⅢB/ⅢC stage, lymph node status, and CA19-9 were significant predictors of overall survival. PT4a/b, ⅢC stage, histological subtypes, CA19-9, and adjuvant chemotherapy were independent factors affecting disease-free survival.

CONCLUSION

Laparoscopy is safely used in the treatment of pT4 colorectal cancer while offering advantages of minimal invasiveness and faster recovery. Laparoscopy is able to achieve good oncologic outcomes similar to those of open surgery. We recommend that laparoscopy be carried out in experienced centers. It is still required to screen the appropriate cases for laparoscopic surgery, optimize the preoperative diagnosis process, and reduce the conversion rate. Multi-center, prospective, and large-sample studies are required to assess these issues.

Key words: pT4 colorectal cancer; Laparoscopy; Open surgery

Core tip: Laparoscopy has been widely used in the treatment of colorectal cancer and has achieved a good radical effect in oncology. However, current clinical association guidelines do not recommend laparoscopic surgery for T4 colorectal cancer. This study retrospectively collected the data of pathological T4 (pT4) colorectal cancer patients at Guangdong General Hospital from 2006 to 2015, aiming to compare outcomes of laparoscopic *vs* open surgery. The conclusion is that laparoscopy is safely used in the treatment of pT4 colorectal cancer while offering advantages of faster recovery. Laparoscopy is able to achieve good oncologic outcomes similar to those of open surgery.

Yang ZF, Wu DQ, Wang JJ, Lv ZJ, Li Y. Short- and long-term outcomes following laparoscopic *vs* open surgery for pathological T4 colorectal cancer: 10 years of experience in a single center. *World J Gastroenterol* 2018; 24(1): 76-86 Available from: URL: http://www.wjgnet.com/1007-9327/full/v24/i1/76.htm DOI: http://dx.doi.org/10.3748/wjg.v24.i1.76

INTRODUCTION

Colorectal cancer is a common malignant tumor. It is the third most diagnosed cancer and the fourth leading cause of cancer-related deaths worldwide[1]. In China, the incidence and mortality of colorectal cancer are ranked among the top five of all cancers; thus, colorectal cancer is a very serious public health problem[2]. In promoting comprehensive, individualized, and precise treatments to date, surgical treatment is still the only way to cure colorectal cancer. Since 1991, when Jacobs first reported the technical feasibility of laparoscopic colectomy[3], a number of successful randomized controlled studies have been conducted around the world to compare laparoscopy and laparotomy, with encouraging results achieved. The laparoscopic treatment of colorectal cancer can not only achieve similar short- and long-term outcomes comparable to laparotomy, but its advantage of minimal invasiveness has gradually been recognized and promoted[4-7]. The American Joint Committee on Cancer (AJCC) classifies T4 colorectal cancers as those that invade into other organs and structures and/or perforate the visceral peritoneum; laparoscopic surgery in colorectal cancer at this stage is difficult as it is hard to reach and violates the "no touch" principle. Therefore, the AJCC and European Association of Endoscopic Surgery do not recommend laparoscopic treatment of pathological T4 (pT4) colorectal cancer[8]. This study retrospectively collected the data of pT4 colorectal cancer patients at Guangdong General Hospital from 2006 to 2015, aiming to compare the outcomes of laparoscopic *vs* open surgery.

MATERIALS AND METHODS

Patients

All pT4 colorectal cancer patients treated at Guangdong General Hospital from 2006 to 2015 were enrolled in this study. All patients were staged according to the AJCC 7th edition manual for colorectal cancer. The inclusion criteria included the following: (1) age of 18-75 years; (2) proven T4 pathology; and (3) radical surgery (D3 lymph node dissection). The exclusion criteria included the following: (1) low rectal cancer (peritoneal reflection as the boundary); (2) preoperative neoadjuvant treatment; (3) non-neoplastic deaths; and (4) palliative resection.

Surgical procedure

Preoperative computed tomography (CT) and magnetic resonance imaging were used to determine the

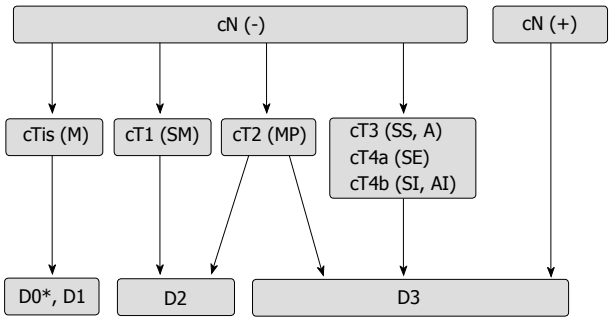

Figure 1 Flowchart for selection of the extent of lymph node dissection (from reference 9).

preoperative clinical stage. The decision to proceed with laparoscopy or open surgery was made for all subjects on a patient-by-patient basis following multidisciplinary discussions and meetings. All cases entailed surgical resection according to the Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines[9], which have the following requirements: D3 lymph node dissection (Figure 1) to ensure the appropriate resection length, and ensuring that the integrity of the mesorectum and intraoperative operations follow the principle of "no touch" (sharp separation, blood vessels first, tumor isolation, *etc.*). According to tumor location, the method of resection included the following: total colectomy, right colectomy, extended right colectomy, transverse colectomy, left colectomy, sigmoid colectomy, mid/upper anterior resection, and combined organ resection. Laparoscopic incision should not exceed 6 cm. The conversion cases were analyzed in the open surgery (OPEN) group.

Observation indexes

The preoperative indexes included age, gender, body mass index (BMI; kg/m^2), comorbidity, American Society of Anesthesiologists (ASA) score, tumor location, hemoglobin, and tumor markers (CA19-9 and CEA). The intraoperative indexes included surgical and pathological outcomes. Surgical outcomes included the conversion rate (conversion was defined as an open surgery performed during the laparoscopic procedure in order to ensure complete resection, reconstruction, or hemostasis and not just for the extraction of specimens), tumor size, resection length, operative time, blood loss, intraoperative complications, combined organ resection, postoperative complications and mortality. Pathological outcomes included the number of lymph nodes dissected, lymph node status, margin, pT stage, pN stage, pTNM stage, Dukes stage, histological subtype, and differentiation. The postoperative recovery indexes included time to flatus, diet, and ambulation and hospital stays.

Follow-up

All patients were postoperatively referred to the 7th AJCC/UICC TNM stage for adjuvant chemotherapy. All patients were followed through outpatient visits. According to the NCCN guidelines, patients were subjected to a 5-year surveillance program consisting of physical examinations and tumor marker (CEA and CA19-9) analysis every 3 mo up to 2 years. Every 6 mo, patients had complete colonoscopies at one and three years after surgery. Thoracic and abdominal CT scans were planned every year for five years of surveillance.

Statistical analysis

Statistical analyses were performed using SPSS 19.0. Quantitative data are reported as the mean ± SD or median. Categorical data were compared by χ^2 tests or Fisher's exact test. Survival curves [overall survival (OS) and disease-free survival (DFS)] were derived from Kaplan-Meier estimates, and the curves were compared by the log-rank test. Prognostic factors were identified by univariate analysis and further tested by multivariate analysis. The results are reported as a hazard ratio (HR) with 95%CI. A P-value < 0.05 was considered statistically significant.

RESULTS

During the period from 2006 to 2015, we collected a total of 211 pT4a/bN0-2M0 cases according to enrollment criteria from 2308 cases of colorectal cancer at the Department of General Surgery of Guangdong General Hospital. There were 101 cases in the laparoscopy (LAP) group and 111 cases in the OPEN group (Figure 2).

There were no significant differences in age, gender, BMI, ASA score, tumor location, hemoglobin, CA19-9, or CEA between the two groups (P > 0.05) (Table 1).

For surgical outcome, conversion to open surgery occurred in 15 (12.9%) patients, and all conversion cases were analyzed in the OPEN group. There was no significant difference between the two groups in terms of intraoperative complications and postoperative complications within 30 d (P > 0.05). Laparoscopic surgery was slightly slower than open surgery (210.8 ± 88.9 min *vs* 173.5 ± 72.7 min, P = 0.028); there was less blood loss (155.0 ± 75.9 mL *vs* 235.1 ± 120.5 mL, P = 0.033) in laparoscopic surgery, whereas open surgery showed better resection lengths (15.5 ± 7.3 cm *vs* 19.5 ± 10.4 cm, P = 0.046). In the case of combined organ resection, there were 21 (19.1%) patients in the OPEN group, including three cases of abdominal wall resection, five cases of small bowel (except duodenum) resection, three cases of duodenum resection, two cases of urinary organ resection, one case of stomach resection, four cases of gynecologic organ resection, and three cases of liver resection; in contrast, there were only five cases in the

Table 1 Clinical information of 211 colorectal cancer cases

Clinical information		LAP *n* = 101	OPEN *n* = 110	*P* value
Age	> 60 yr	55	58	0.270
	⩽ 60 yr	46	52	
Gender	Male	67	66	0.392
	Female	34	44	
BMI (kg/m^2)	< 24	67	73	0.348
	⩾ 24	34	37	
Comorbidities	Yes	39	42	1.000
	No	62	68	
ASA score	I	8	9	0.715
	II	63	72	
	III	30	29	
Tumor location	Mid/upper Rectum	33	35	0.989
	Left colon	43	47	
	Right colon	25	28	
HBG (g/L)	mean ± SD	124.0 ± 27.1	120.7 ± 22.9	0.263
CA19-9 (U/mL)	< 27	78	75	0.163
	⩾ 27	23	35	
CEA (ng/mL)	< 5	60	64	0.666
	⩾ 5	41	46	
Postoperative adjuvant chemotherapy	Yes	49	46	0.332
	No	52	64	
Recurrence	Yes	22	25	0.711
	No	79	85	

CRC: Colorectal cancer; LAP: Laparoscopic surgery group; OPEN: Open surgery group; BMI: Body mass index; ASA: American Society of Anesthesiology; HGB: Hemoglobin; CA19-9: Carbohydrate antigen 19-9; CEA: Caicinoembryonic antigen; SD: Standard deviation.

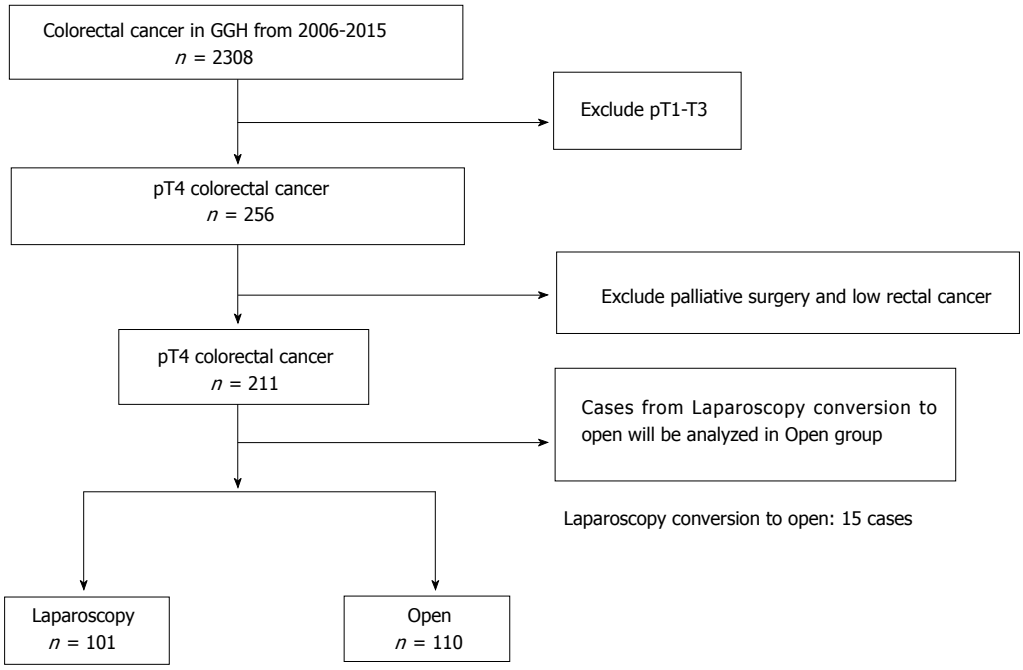

Figure 2 Study flowchart showing patient selection. GGH: Guangdong general hospital; pT4: Pathological proven T4.

LAP group (P = 0.001). For postoperative complications within 30 d, there were 12 (12.9%) cases in the LAP group, and there was a higher incidence in the OPEN group (31.8%, P = 0.006) (Table 2).

Regarding pathologic outcomes, no significant differences in the number of lymph nodes dissected, lymph node status, margin, pN stage, pTNM stage, Dukes stage, histological subtype, differentiation, or HER2 status were detected when comparing the two groups (P > 0.05). There were 21 pT4b cases in the OPEN group but only five cases in the LAP group; a comparison between the two groups in the pT stage revealed a statistically significant difference (P = 0.021) (Table 3).

Table 2 Surgical outcomes of 211 colorectal cancer cases

Surgical outcome		LAP *n* = 101	OPEN *n* = 110	*P* value
Conversion to open (*n*/%)		15 (12.9)	NR	/
Tumor size (cm)	mean ± SD	5.4 ± 1.9	5.2 ± 2.5	0.765
Resection length (cm)	mean ± SD	15.5 ± 7.3	19.5 ± 10.4	0.046
Operative time (min)	mean ± SD	210.8 ± 88.9	173.5 ± 72.7	0.028
Blood loss (mL)	mean ± SD	155.0 ± 75.9	235.1 ± 120.5	0.033
Intraoperative complications		3	8	0.117
Combined organ resection	Total (%)	5 (5.0)	21 (19.1)	0.001
	Abdominal wall	2	3	
	Small bowel (except duodenum)	1	5	
	Duodenum	0	3	
	Urinary organs	0	2	
	Stomach	1	1	
	Gynecologic organs	1	4	
	Liver	0	3	
Postoperative complications within 30 d	Total (%)	12 (12.9)	35 (31.8)	0.006
	Anastomotic Hemorrhage	1	2	
	Urinary injury	0	1	
	Intraabdominal bleeding	1	2	
	Leakage	1	4	
	Gastroplegia	2	4	
	Infection (incision and abdomen)	6	15	
	Disruption of incision	0	5	
	Obstruction	1	2	
Postoperative morbidity within 30 d		0	1	0.667

CRC: Colorectal cancer; LAP: Laparoscopic surgery group; OPEN: Open surgery group.

Table 3 Pathologic outcomes of 211 colorectal cancer cases

Pathologic outcome		LAP *n* = 101	OPEN *n* = 110	*P* value
Number of lymph nodes dissected	< 12	25	38	0.134
	⩾ 12	76	72	
Lymph node status	+	67	74	1.000
	-	34	36	
Margin	R1	2	3	0.779
	R0	99	107	
pT stage	T4a	96	89	0.021
	T4b	5	21	
pN stage	N0	36	35	0.841
	N1	28	32	
	N2	37	43	
pTNM stage	ⅡB + ⅡC	34	35	0.282
	ⅢB	30	24	
	ⅢC	37	51	
Dukes	B	34	35	0.883
	C	67	75	
Histological subtype	Adenocarcinoma	87	94	1.000
	Myxoadenocarcinoma	14	16	
Differentiation	Poor	20	25	0.719
	Median/high	81	85	
HER2	-/+	86	96	0.871
	++	10	10	
	+++	5	4	

CRC: Colorectal cancer; LAP: Laparoscopic surgery group; OPEN: Open surgery group; SD: Standard deviation; p: Pathological.

With regard to postoperative recovery indexes, the LAP group was significantly better than the OPEN group ($P < 0.05$) in time to flatus, diet, and ambulation. The median hospital stay was 7 (5-21) d for the LAP group and 15 (7-31) d for the OPEN group, which showed a statistically significant difference between the two groups ($P = 0.004$) (Table 4).

The mean overall follow-up time was 36 mo

Table 4 Postoperative recovery outcomes of 211 colorectal cancer cases

Recovery outcome		LAP *n* = 101	OPEN *n* = 110	*P* value
Time to flatus (d)	Median (range)	2 (1-9)	4 (3-15)	0.037
Time to diet (d)	Median (range)	3 (2-18)	7 (5-27)	0.003
Time to ambulation (d)	Median (range)	2 (1-5)	5 (3-9)	0.027
Hospital stays	Median (range)	7 (5-21)	15 (7-31)	0.004

LAP: Laparoscopic surgery group; OPEN: Open surgery group.

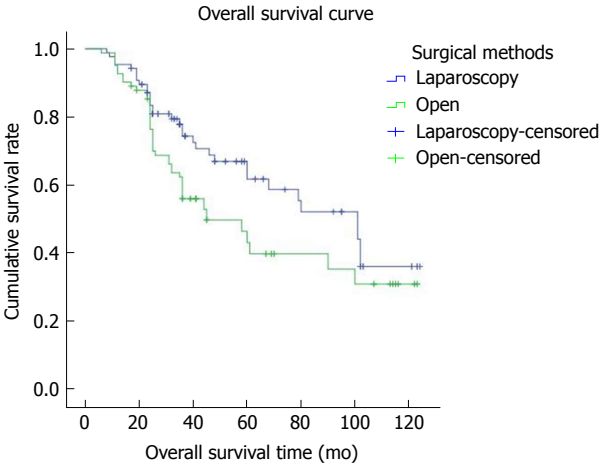

Figure 3 The overall survival curve shows that 3- and 5-year overall survival rates were 74.9% and 60.5%, respectively, in the LAP group and 62.4% and 46.5%, respectively, in the OPEN group. There was no significant difference between the LAP and OPEN groups (P = 0.060).

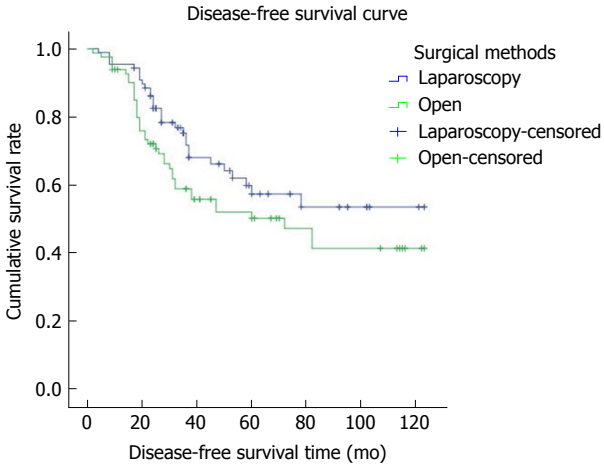

Figure 4 The disease-free survival curve shows that the 3- and 5-year disease-free survival rates were 68.0% and 57.3%, respectively, in the LAP group and 55.8% and 39.8%, respectively, in the OPEN group. There was no significant difference between the LAP and OPEN groups (P = 0.053).

(range, 2-24 mo); there was no difference between the LAP and OPEN groups in terms of OS and DFS. The 3- and 5-year OS rates were 74.9% and 60.5%, respectively, for the LAP group and 62.4% and 46.5%, respectively, for the OPEN group (P = 0.60) (Figure 3). The 3- and 5-year DFS rates were 68.0% and 57.3%, respectively, for the LAP group and 55.8 and 39.8%, respectively, for the OPEN group (P = 0.053) (Figure 4). Disease recurrence over the entire follow-up period was observed in 21.8% (n = 22) of patients in the LAP group and 22.7% (n = 25) of patients in the OPEN group (P = 0.711) (Table 1), without significant differences between the LAP and OPEN groups (P = 0.711). In the multivariate regression analysis, TNM stage (ⅢB, ⅢC), lymph node status (pN+), and CA19-9 were significant predictors of OS. TNM stage (ⅢC), histological subtype, CA19-9, and chemotherapy were predictive of DFS (Tables 5 and 6).

DISCUSSION

Since the first report of laparoscopic colorectal resection in 1991, some prospective clinical studies of laparoscopic resection for colorectal cancer have confirmed that laparoscopic techniques not only achieve minimally invasive and cosmetic effects but also achieve faster recovery and similar oncologic outcomes compared with open surgery[10-12]. However, due to the large tumor size of T4 colorectal cancer and more frequent invasion of peripheral tissues or nearby organs, laparoscopic complete resection is difficult and has high risks; the majority of clinical studies have fewer cases of T4 colorectal cancer[13,14], and some studies do not enroll any such cases[15,16]. Therefore, the evidence-based data that support the laparoscopic resection in T4 colorectal cancer are limited. Laparoscopic resection of T4 colorectal cancer is regarded a technique that demands precision, and its efficacy remains controversial. The relevant guidelines do not recommend laparoscopy in T4 colorectal cancer[8]. However, due to the maturity and progress of the laparoscopic platform, coupled with the popularity of and improvements in laparoscopic techniques, some surgeons in certain experienced centers have tried to use laparoscopic techniques in T4 colorectal cancer, achieving similar short- and long-term outcomes to open surgery[17-20].

This study decided whether laparoscopic or open surgery should be performed based on the results of preoperative imaging examination and the patient's condition; the main referenced indicators included the following: tumor location, tumor size, and the scope of invaded organ[21]. We found a statistically

Table 5 Univariate and multivariate analyses of 211 pathological T4 colorectal cancer patients for overall survival

	Univariate analysis		Multivariate analysis	
Variable	**HR (95%CI)**	***P* value**	**HR (95%CI)**	***P* value**
Age	1.217 (0.784-1.888)	0.381		
Gender	0.807 (0.508-1.281)	0.363		
Surgical method (LAP and OPEN)	1.528 (0.982-2.377)	0.060		
Tumor location				
Mid/upper rectum	Reference group	-		
Left colon	1.303 (0.813-2.091)	0.272		
Right colon	0.792 (0.409-1.533)	0.489		
Comorbidities	1.603 (1.007-2.552)	0.047	2.519 (1.436-4.419)	0.142
pT4a/b	0.790 (0.692-1.236)	0.445		
N stage				
N0	Reference group	-		
N1	1.328 (0.701-2.517)	0.384		
N2	2.079 (1.170-3.697)	0.013		
TNM stage				
ⅡB + ⅡC	Reference group	-	Reference group	-
ⅢB	1.229 (0.564-2.679)	0.604	1.324 (0.785-1.753)	0.019
ⅢC	3.092 (1.617-5.913)	0.001	1.104 (0.333-3.662)	0.001
Lymph node status	0.560 (0.324-0.968)	0.038	0.307 (0.103-0.919)	0.035
No. of lymph nodes resected	0.593 (0.385-0.915)	0.018	0.432 (0.264-0.708)	0.123
Histological subtype	0.369 (0.212-0.640)	0.000	0.433 (0.218-0.859)	0.247
Differentiation	0.326 (0.204-0.519)	0.000	0.460 (0.273-0.775)	0.087
CA19-9	1.868 (1.195-2.922)	0.006	1.662 (1.212-2.280)	0.002
CEA	1.089 (0.706-1.680)	0.013	0.608 (0.356-1.038)	0.068
Chemotherapy	1.611 (1.040-2.494)	0.033	2.225 (1.394-3.552)	0.181

CRC: Colorectal cancer; LAP: Laparoscopy surgery; OPEN: Open surgery; p: Pathological; CA19-9: Carbohydrate antigen 19-9; CEA: Carcinoembryonic antigen; HR: Hazard ratio.

Table 6 Univariate and multivariate analyses of 211 pathological T4 colorectal cancer patients for disease-free survival

	Univariate analysis		Multivariate analysis	
Variable	**HR (95%CI)**	***P* value**	**HR (95%CI)**	***P* value**
Age	1.621 (1.010-2.601)	0.045	1.892 (1.111-3.223)	0.419
Gender	1.328 (0.824-2.141)	0.243		
Surgical method (LAP and OPEN)	1.503 (0.933-2.422)	0.094		
Tumor location				
Mid/upper rectum	Reference group	-		
Left colon	1.010 (0.601-10697)	0.969		
Right colon	0.818 (0.411-1.629)	0.568		
Comorbidities	1.787 (1.058-3.019)	0.030	2.261 (1.235-4.139)	0.080
pT4a/b	0.818 (0.618-1.725)	0.013	1.214 (0.784-1.974)	0.001
N stage				
N0	Reference group	-		
N1	1.134 (0.594-2.167)	0.703		
N2	1.553 (0.861-2.801)	0.144		
TNM stage				
ⅡB + ⅡC	Reference group	-	Reference group	-
ⅢB	1.034 (0.471-2.269)	0.933	0.884 (0.393-1.989)	0.765
ⅢC	2.284 (1.202-4.337)	0.012	1.831 (0.935-3.584)	0.018
Lymph node status	0.710 (0.411-1.229)	0.221		
No. of lymph nodes resected	0.661 (0.411-1.061)	0.087		
Histological subtype	0.456 (0.243-0.854)	0.014	0.469 (0.225-0.974)	0.042
Differentiation	0.439 (0.266-0.725)	0.001	0.662 (0.374-1.170)	0.156
CA19-9	2.458 (1.526-3.960)	0.000	3.372 (1.968-5.778)	0.000
CEA	1.268 (0.790-2.036)	0.326	0.608 (0.356-1.038)	0.072
Chemotherapy	2.157 (1.323-3.514)	0.002	3.817 (2.194-6.639)	0.000

CRC: Colorectal cancer; LAP: Laparoscopic surgery; OPEN: Open surgery; p-Pathological; CA19-9: Carbohydrate antigen 19-9; CEA: Carcinoembryonic antigen; HR: Hazard ratio.

Table 7 Studies about laparoscopic surgery for pathological T4 colorectal cancer

Ref.	*n* (LAP:OPEN)	Study period	Study design	Country	Single/Multi center	Conversion rate	Location	Complication rate (LAP:OPEN)	Tumor stage	Combined resection (LAP:OPEN)	RI rate (LAP:OPEN)	5 years DFS (LAP:OPEN)	5 years OS (LAP:OPEN)
Park *et al*[22], 2016	93:18	2000-2010	RS	South Korea	Single	5.6%	Colon rectum	14.1%:31.5%	-	9.9%:32.5%	5.5%:4.5%	81.8%:73.9%	95.3%:86.5%
Shukla *et al*[20], 2015	61:22	2003-2011	RS	United States	Single	21%	Colon	28%:36%	Ⅱ:35 Ⅲ:48	23%:41%	0%:4%	75%:65% (3 yr)	82%:81% (3 yr)
Kang *et al*[29], 2016	52:57	2003-2013	RS	South Korea	Single	7.7%	Colon	13.5%:36.8%	Ⅱ:41 Ⅲ:68	13.5%:36.8%	-	53.6%:62.6%	60.7%:61.9%
de'Angelis *et al*[18], 2016	106:106	2005-2014	RPSM	France Switzerland	Multi	12.2%	Colon	29.1%:35.3%	Ⅱ:85 Ⅲ:127	14.2%:18.9%	5.7%:6.6%	58.6%:59.9%	57.6%:50.2%
de'Angelis *et al*[17], 2016	52:52	2005-2015	RPSM	France Switzerland Spain	Multi	21.2%	Rectum	30.8%:48.1%	Ⅱ:42 Ⅲ:33 Ⅳ:29	26.9%:30.8%	19.2%:17.3%	66.7%:64.1%	55.4%:53.3%
Chan *et al*[30], 2016	93:59	2008-2014	RS	Singapore	Single	8.6%	Colon	-	-	0%:3.4%	0%:0.7%	-	75%:80%
Leon *et al*[27], 2017	68:79	2008-2015	RS	Italy	Single	19%	Colon	7.4%:16.5%	Ⅱ:69 Ⅲ:78	-	11.8%:11.5%	40.3%:38.9%	44.6%:39.4%
Ahmad *et al*[25], 2015	455:406	2011-2012	RS	Canada	ACSNS QIP	24.7%	Colon	-	-	-	26.2%:24.3%	-	-

LAP: Laparoscopy; RS: Retrospective study; RPSM: Retrospective propensity score matching; ACSNS: American College of Surgeons National Surgical Quality Improvement Program; OS: Overall survival; DFS: Disease-free survival.

significant difference in the postoperative pT stage between the two groups (P = 0.021), with 21 cases of pT4b in the OPEN group. An examination of postoperative surgical outcomes (Table 2) revealed 21 cases of combined organ resection in the OPEN group, with the most commonly invaded organs including the small intestine, gynecological organs, and duodenum; in contrast, the LAP group had only five cases, and the number of cases of combined organ resection was thus significantly different for the two groups (P = 0.001), which is consistent with the results of previous studies[22,23]. These data also demonstrate that T4b stage may be an important consideration for surgeons to select laparoscopic or open surgery because it is very difficult to achieve the goal of complete resection using the "no touch" principle; therefore, guidelines do not recommend laparoscopic resection in T4 colorectal cancer[8]. However, such considerations lead to selective bias in the study, which is one of the limitations in both this study and a retrospective study.

Because of the larger tumor, a wide scope of invasion, combined with resection of other organs, especially due to the lack of laparoscopic experience in some centers, may lead to a high conversion rate. Previous studies of laparoscopic surgery in colorectal cancer (stage Ⅱ-Ⅲ)[11,15,24] reported that the conversion rate was 25% in the CLASSIC trial (for colon cancer), 17% in the COLOR trial, and 21% in the COSTSG trial, whereas a retrospective study of pT4 colorectal cancer showed that the conversion rate was 5.6%-24.7%[17,19,22,25-29]; this study showed a conversion rate of 12.9%, which is consistent with reports in the literature. The conversion rates reported by some studies of pT4 colorectal cancer in South Korea and Singapore were 5.6%, 7.7% and 8.6%[22,29,30], which are significantly lower than those from the US and Europe[17,18,25,27] (Table 7). We explain these differences as follows: (1) Laparoscopic technology and experience may differ between Asian and Western countries; (2) the conversion standard used was different; (3) there was a lack of preoperative imaging assessments to select appropriate laparoscopic surgery cases in Western countries; and (4) European populations had a higher BMI. All these factors increase the difficulty of surgery[17-25]. Thus, surgeons should choose the appropriate pT4 colorectal cases to perform laparoscopic surgery in order to reduce the conversion rate and ensure operation safety. We recommend laparoscopic surgery as an option in experienced centers and for T4a cases with tumor sizes < 5 cm and when only a single organ has been invaded by T4 colorectal cancer.

In this study, the LAP group had longer operative time (210.8 ± 88.9 min *vs* 173.5 ± 72.7 min, P = 0.028), which may be related to the lack of experience and

the difficulty of this surgery[19]. The resection length (19.5 ± 10.4 cm) obtained in the OPEN group was significantly better (P = 0.046). The literature shows that the incidence of postoperative complications associated with laparoscopic surgery was clearly lower than that associated with open surgery[31]. In this study, the rate of postoperative complication within 30 d in the LAP group was 12.9% (12/101), which was lower than 31.8% (35/110) in the OPEN group, and the most common complications in the OPEN group were infection (incision and abdomen) and disruption of incision, similar to a previous report in the literature[32]. Therefore, attention should be paid to intraoperative sterile principles and the suture of incision.

With regard to postoperative recovery outcomes, the LAP group had clear advantages in time to flatus (P = 0.037), diet (P = 0.003), and ambulation (P = 0.027) and hospital stays (P = 0.004) compared with the OPEN group (Table 4). Laparoscopy has the advantages of minimal invasion and fast recovery, which is in agreement with many earlier clinical studies[12,15,16].

In colorectal cancer surgery, lymph node dissection and R0 resection are important factors affecting long-term survival[33]. We performed D3 lymphadenectomy (parenteral lymph node -middle lymph node-central lymph node)[34] according to the guidelines recommended by the JSCCR. Previous studies have shown that laparoscopic treatment of colorectal cancer achieved an R0 resection rate between 80.8% and 98%[11,16,18]. In this study, the percentage of cases with the number of lymph nodes dissected greater than 12 was 75.2% (76/101) in the LAP group and 65.5% (72/110) in the OPEN group, and the difference was not significantly different (P = 0.134). Concurrently, the R0 resection rate in the LAP group was 98% (99/101), whereas in the OPEN group, it was 97.3% (107/110), which was not significantly different (P = 0.779). Thus, we believe that laparoscopic treatment in pT4 colorectal cancer can achieve similar oncological outcomes to open surgery. Finally, no differences in the 3- and 5-year OS rates (P = 0.060) and in 3- and 5-year DFS rates (P = 0.053) were observed when comparing the two groups, suggesting that laparoscopy may be a valid and effective tool to treat pT4 colorectal cancer without jeopardizing oncologic results, in accordance with the previously reported series. Multivariate analysis in our series detected ⅢB/ⅢC stage, lymph node status, and CA19-9 as independent predictors of OS, and pT4a/b, ⅢC stage, CA19-9, and adjuvant chemotherapy as independent predictors of DFS.

In conclusion, laparoscopic surgery may be safe and acceptable in the treatment of pathologic T4 colorectal cancer patients with fast recovery outcomes and oncologic outcomes compared with open surgery. Thus, laparoscopy should not be regarded as an absolute contraindication in the management of pT4 colorectal cancer. Finally, as this study is only a retrospective study in a single center with a small sample size, the results need to be confirmed by prospective, multi-center and large sample clinical studies.

ARTICLE HIGHLIGHTS

Research background

Laparoscopy has been widely used in the treatment of colorectal cancer and it has achieved a good radical effect in oncology. However, for the current clinical guidelines, laparoscopic surgery is not recommended in T4 colorectal cancer.

Research motivation

Due to the characteristics of T4 colorectal cancer, laparoscopic complete resection is difficult for the resection of this kind of tumor. The current colorectal studies about laparoscopy have fewer cases of T4 colorectal cancer, and some studies do not enroll any such cases. We tried to collect and analyze the data about laparoscopy in T4 colorectal cancer in order to add evidence-based clinical evidence.

Research objectives

We aimed to analyze the short- and long-term outcomes of proven pathological T4 colorectal cancer patients who underwent complete resection by laparoscopic or open surgery.

Research methods

We collected and analyzed the data of pT4 colorectal cancer cases at Guangdong General Hospital from 2006 to 2015. All patients were staged according to the AJCC 7th edition manual for colorectal cancer. We compared the laparoscopy (LAP) group and open (OPEN) group in clinical information, surgical and pathological outcomes, postoperative recovery outcomes, and survival.

Research results

There were 101 cases in the LAP group and 110 cases in the OPEN group [including15 (12.9%) cases of conversion to open surgery]. Clinical information did not differ between the two groups. In terms of blood loss, postoperative complications, and rate of recovery, the LAP group performed significantly more favorably (P < 0.05). With regard to pT4a/b and combined organ resection, there were significantly more cases in the OPEN group (P < 0.05). The 3- and 5-year overall survival rates were 74.9% and 60.5%, respectively, for the LAP group and 62.4% and 46.5%, respectively, for the OPEN group (P = 0.060). The 3- and 5-year disease-free survival rates were 68.0% and 57.3%, respectively, for the LAP group and 55.8% and 39.8%, respectively, for the OPEN group (P = 0.053). Multivariate analysis showed that ⅢB/ⅢC stage, lymph node status, and CA19-9 were significant predictors of overall survival. PT4a/b, ⅢC stage, histological subtype, CA19-9, and adjuvant chemotherapy were independent factors affecting disease-free survival.

Research conclusions

Laparoscopic surgery may be safe and acceptable in the treatment of pathologic T4 colorectal cancer patients with fast recovery outcomes and oncologic outcomes compared with open surgery. We recommend that it can be carried out in experienced centers. It is required to screen the appropriate cases for laparoscopic surgery, optimize the preoperative diagnosis process, and reduce the conversion rate.

Research perspectives

Although our study shows that laparoscopy is able to achieve good clinicopathological and oncologic outcomes similar to those of open surgery, this study is only a retrospective study in a single center with a small sample, and the results need to be confirmed by prospective, multi-center and large sample clinical studies.

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P- Reviewer: Kim SM, Sterpetti AV, Yokoyama S **S- Editor**: Chen K
L- Editor: Wang TQ **E- Editor**: Huang Y

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ISSN 1007-9327