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ORIGINAL ARTICLE

Outcomes of laparoscopic surgery for pathological T4 colon cancer

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Abstract

Purpose The surgical indication of laparoscopic surgery for pT4 colon cancer remains to be established because only a few studies have investigated the short- and long-term outcomes of laparoscopic surgery for them to date. Therefore, we aimed to elucidate the validity of laparoscopic surgery for them.

Methods We retrospectively analyzed 81 patients with pT4 colon cancer who underwent surgical resection with a curative intent at Kobe University Hospital from January 2007 to December 2015. The short- and long-term outcomes were compared between the propensity score–matched patients who underwent laparoscopic colectomy (LAP group, $n = 25$) and those who underwent open colectomy (OP group, $n = 25$).

Results Intraoperative blood loss was significantly less in the LAP group than in the OP group ($p = 0.029$). Operative time, R0 resection rate, and morbidity did not significantly differ between the two groups. The 5-year overall survival (OS) and the 5-year recurrence-free survival (RFS) did not significantly differ between the propensity score–matched groups. Univariate and multivariate analyses of the entire cohort showed the surgical approach (LAP vs OP) selected was not a significant prognostic factor for OS or RFS.

Conclusions The short and the long-term outcomes were similar between the LAP and OP groups. Laparoscopic surgery might be a safe and feasible option for pT4 colon cancer patients.

Keywords Pathological T4 · Colon cancer · Laparoscopic surgery · Colectomy

Introduction

Colorectal cancer is a malignant tumor with a high prevalence worldwide. In fact, it is the third most diagnosed cancer in the world [1]. Although several treatment options for colorectal cancer, including chemotherapy, molecular targeted therapy, and radiotherapy, have emerged, surgical resection remains the only approach to achieve complete cure. Since the 1990s, when Jacobs for the first time reported the use of laparoscopic colectomy for colon cancer, laparoscopic surgery has become widespread [2]. Numerous studies had reported the safety and validity of laparoscopic surgery for colorectal cancer, with the same outcomes as those of open surgery. Additionally, in the majority of randomized trials, the short-term outcomes of laparoscopic surgery were better than those of open surgery [3, 4]. However, only a limited number of studies have reported the short- and long-term outcomes of laparoscopic surgery for pathological T4 (pT4) colorectal cancer. Therefore, no consensus exists regarding the surgical indication of laparoscopic surgery for pT4a/pT4b colorectal cancer [5–15]. In the present study, we aimed to elucidate the validity of laparoscopic surgery for pT4a/pT4b colon cancer by comparing the short- and long-term outcomes of patients with pT4 colon cancer who underwent laparoscopic or open surgery.

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Materials and methods

Patients

Patients with pT4a/pT4b colon cancer who underwent surgery at Kobe University Hospital from January 2007 to December 2015 were enrolled in this study. The study patients were staged according to the American Joint Committee on Cancer (AJCC) TNM classification system [16].

Between January 2007 and December 2015, 114 patients with pT4 colorectal cancer underwent colorectal resection. Of these, 5 patients who underwent recurrent tumor resection, 6 patients who presented with other concomitant cancers, 9 patients who underwent palliative surgery, and 13 patients who underwent proctectomy were excluded from the study. Then, 81 patients, including 46 patients who underwent laparoscopy surgery (LAP group) and 35 patients who underwent open surgery (OP group), remained. For adjusting heterogeneity between the treatment groups, propensity analyses were conducted. Propensity scores (i.e., predicted probability of receiving laparoscopic surgery) were generated based on confounding covariates including sex, age, BMI, tumor size, and cStage. After propensity score matching, 25 matched pairs of patients were selected and analyzed by retrospective chart review.

Written informed consent for this publication was obtained from all patients. All procedures and subsequent analyses were performed with the approval of the Clinical & Translational Research Center of Kobe University Hospital in Japan. The study was conducted in accordance with the guidelines of the 1975 Declaration of Helsinki, as revised in 2000 (5), concerning Human and Animal Rights.

Surgical procedure

All patients underwent surgical resection in conformity with the Japanese Society for Cancer of the Colon and Rectum guidelines [17]. Depending on the tumor site, the following methods of resection were adopted as required: ileocecal resection, right colectomy, transverse colectomy, left colectomy, descending colectomy, sigmoid colectomy, anterior resection, Hartmann's operation, and multivisceral resection. Ileocecal resection, right colectomy, and transverse colectomy were considered as right hemicolectomy (RHC), whereas left colectomy, descending colectomy, and sigmoid colectomy were considered as left hemicolectomy (LHC). Surgical approach whether laparoscopy or open was selected according to surgeon's preference. Open approach tended to be selected at the beginning of the cohort, whereas laparoscopic approach gradually increased later in the cohort. Conversion cases were analyzed as the LAP group.

Follow-up

All patients with high-risk stage II, III, or IV disease were recommended to receive adjuvant chemotherapy. If the patients agreed with chemotherapy, medical oncologists managed their chemotherapeutic regimen. The patients were followed up every 3 months for the first 2 years and at every 6 months thereafter. The follow-up program comprised physical examinations and blood tests, including tests for tumor markers, carcinoembryonic antigen, and carbohydrate antigen 19-9 (CA19-9), at each visit; thoracic and abdominal computed tomography at every 6 months; and total colonoscopy at every 2 years.

Table 1 Demographic and tumor characteristics of the entire cohort and propensity score–matched patients

Parameter		Entire cohort ($n = 81$)			Propensity score–matched pairs ($n = 50$)		
		LAP ($n = 46$) *N* (%)	OP ($n = 35$) *N* (%)	*p* value	LAP ($n = 25$) *N* (%)	OP ($n = 25$) *N* (%)	*p* value
Sex	Male	18 (39.1)	13 (37.1)	0.855	8 (32.0)	9 (36.0)	0.765
	Female	28 (60.9)	22 (62.9)		17 (68.0)	16 (64.0)	
Age (years)	Median (range)	71.5 (34–93)	73 (44–86)	0.787	74 (34–93)	72 (44–83)	0.625
BMI (kg/m^2)	Median (range)	20.7 (12.2–27.0)	21.3 (14.7–28.8)	0.142	21.4 (17.6–27.0)	20.8 (14.7–28.8)	0.389
Tumor size (mm)	Median (range)	44 (23–118)	58 (30–223)	0.001*	45 (24–118)	55 (30–110)	0.273
cStage	I	3 (6.5)	0	0.068	0	0	0.839
	II	15 (32.6)	6 (17.1)		7 (28.0)	6 (24.0)	
	III	16 (34.8)	14 (40.0)		8 (32.0)	10 (40.0)	
	IV	12 (26.1)	15 (42.9)		10 (40.0)	9 (36.0)	

LAP, laparoscopic colectomy; *OP*, open colectomy; *BMI*, body mass index

* $p < 0.05$ in all variables

Table 2 Clinical data and operative outcomes of propensity score–matched patients

Parameter		Propensity score–matched pairs ($n = 50$)		
		LAP ($n = 25$) *N* (%)	OP ($n = 25$) *N* (%)	*p* value
ASA grade	I	11 (44.0)	15 (60.0)	0.394
	II	11 (44.0)	9 (36.0)	
	III	3 (12.0)	1 (4.0)	
Comorbidity		13 (52.0)	9 (36.0)	0.253
Prior abdominal surgery		9 (36.0)	9 (36.0)	1.000
CEA (ng/ml)	Median (range)	5.2 (0.8–7382.3)	22.3 (1.3–4350.5)	0.574
CA19-9 (U/ml)	Median (range)	17 (1–31,815)	33.5 (2–39,225)	0.785
Tumor location	Right side	13 (52.0)	8 (32.0)	0.150
	Left side	12 (48.0)	17 (68.0)	
pT	T4a	22 (88.0)	18 (72.0)	0.153
	T4b	3 (12.0)	7 (28.0)	
pN	N0	7 (28.0)	12 (48.0)	0.339
	N1	12 (48.0)	9 (36.0)	
	N2	6 (24.0)	4 (16.0)	
pStage	IIB + IIC	7 (28.0)	9 (36.0)	0.608
	IIIB + IIIC	8 (32.0)	5 (20.0)	
	IV	10 (40.0)	11 (44.0)	
Preoperative treatment	Chemotherapy	1 (4.0)	0	0.236
	Nothing	24 (96.0)	25 (100.0)	
Adjuvant therapy	Chemotherapy	14 (73.7)	10 (55.6)	0.247
	Nothing	5 (26.3)	8 (44.4)	
Surgical procedure	RHC	13 (52.0)	8 (32.0)	0.093
	LHC	6 (24.0)	14 (56.0)	
	AR	4 (16.0)	1 (4.0)	
	Hartmann's	2 (8.0)	2 (8.0)	
Multivisceral resection	Any	2 (8.0)	8 (32.0)	0.029*
	Ileum	1 (4.0)	2 (8.0)	
	Bladder	0	1 (4.0)	
	Uterus	0	2 (8.0)	
	Ovary	0	3 (12.0)	
	Peritoneum	1 (4.0)	3 (12.0)	
Conversion laparotomy		2 (8.0)	–	
Operative time (min)	Median (range)	255 (126, 441)	209 (90, 530)	0.169
Blood loss (ml)	Median (range)	50 (0, 2210)	280 (26, 2660)	0.029*
Transfusion		7 (28.0)	8 (32.0)	0.758
R0, 1, 2	0	17 (68.0)	16 (48.0)	0.493
	1	0	1 (4.0)	
	2	8 (32.0)	8 (32.0)	
Postoperative hospital stay	Median (range)	13 (7–100)	19 (10–38)	0.715
Morbidity (CD ≥ Grade II)		3 (12.0)	7 (28.0)	0.153
	Bleeding	0	0	
	SSI	0	2 (8.0)	
	Abscess	1 (4.0)	2 (8.0)	
	Anastomotic leakage	0	1 (4.0)	
	Ileus	0	2 (8.0)	
	Others	3 (12.0)	1 (4.0)	
Mortality		0	0	–

LAP, laparoscopic colectomy; *OP*, open colectomy; *ASA*, American Society of Anesthesiologists; *CEA*, carcinoembryonic antigen; *CA19-9*, carbohydrate antigen 19-9; *CD*, Clavien–Dindo classification; *RHC*, right hemicolectomy; *LHC*, left hemicolectomy; *AR*, anterior resection; *SSI*, surgical site infection

* $p < 0.05$ in all variables

Statistical analysis

The data on clinicopathological characteristics were obtained by retrospective chart review. OS and RFS were derived from the Kaplan–Meier estimates. Additionally, univariate and multivariate analyses of the clinical factors were performed to predict the long-term outcomes, OS, and RFS.

Statistical analyses were performed using JMP 11.2.0 (SAS Institute Inc., Cary, NC, USA). Quantitative data were expressed as the median and range. Categorical data were compared by χ^2 test or Fisher's exact test. The OS and RFS rates

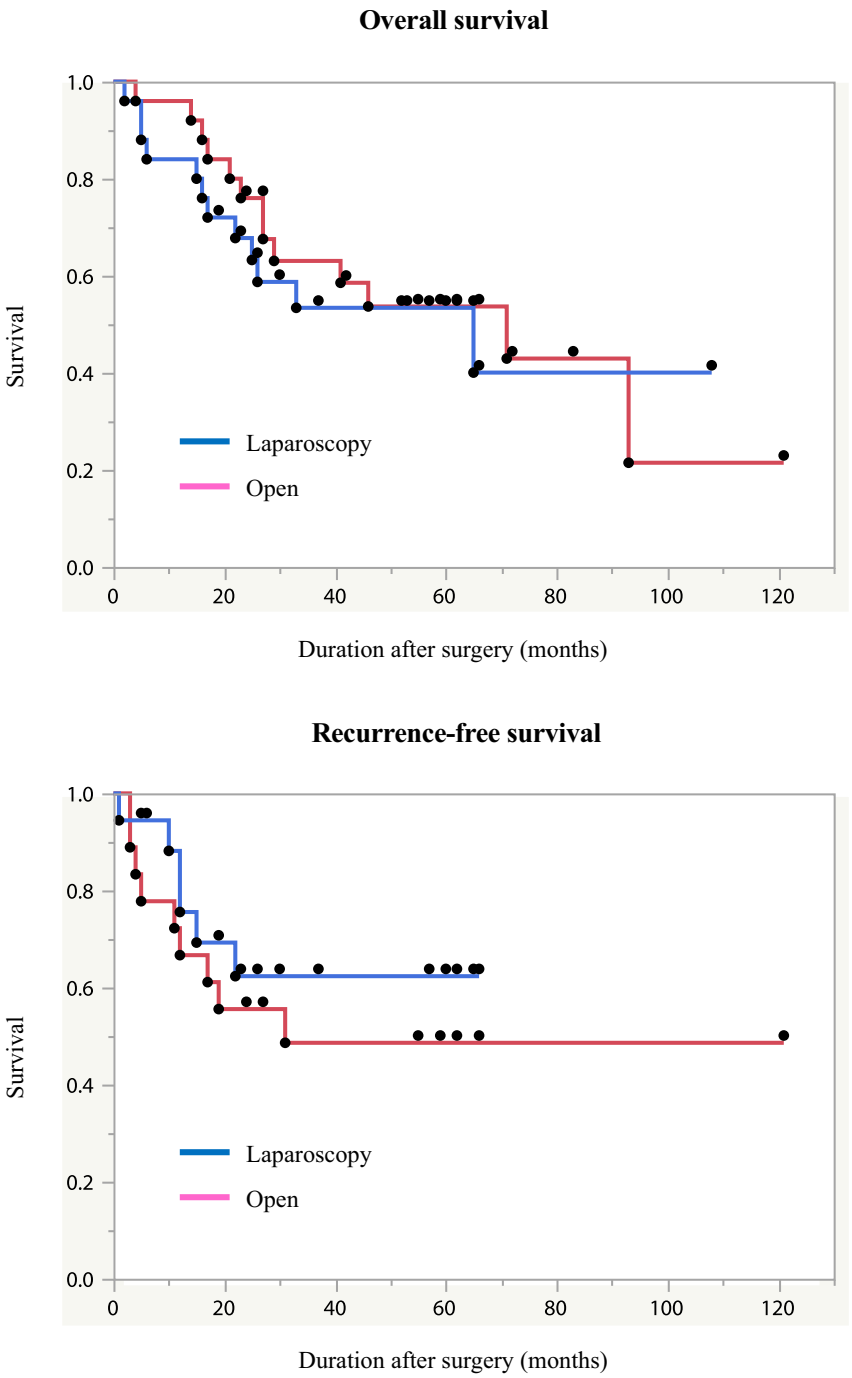

Fig. 1 Kaplan–Meier curves for the overall survival (OS) rates and the recurrence-free survival (RFS) rates of the laparoscopic (LAP) and open colectomy (OP) groups. No apparent difference was noted between the two groups. The 5-year OS rate was 53.4% in the LAP group and 53.7% in the OP group ($p = 0.658$). The 5-year RFS rate was 62.3% in the LAP group and 48.6% in the OP group ($p = 0.434$)

were compared by log-rank test. Multivariate Cox proportional hazards regression analyses for predicting prognostic factors were reported as a hazard ratio with 95% confidence interval. $p < 0.05$ was considered statistically significant.

Results

Table 1 summarizes demographic and tumor characteristics of the entire cohort patients and propensity score–matched patients. The mean tumor size was significantly larger ($p < 0.001$) and cStage tended to be advanced ($p = 0.068$) in the OP group before propensity score matching. After propensity score matching, this heterogeneity was balanced.

Table 2 presents the clinical data and the operative outcomes of propensity score–matched patients. Although the operative time did not differ between the groups, the estimated blood loss was significantly higher in the OP group. The number of patients who underwent multivisceral resection was greater in the OP group. In the LAP group, only 2 patients

Table 3 Recurrence pattern of propensity score–matched patients

Parameter		Propensity score–matched pairs ($n = 50$)		
		LAP ($n = 25$) *N* (%)	OP ($n = 25$) *N* (%)	*p* value
Recurrence rate		7/19 (36.8)	9/18 (50.0)	0.419
Recurrence site	Local or peritoneum	4 (21.1)	2 (11.1)	0.408
	Liver or lung	2 (10.5)	6 (33.3)	0.087
	Lymph	0	2 (11.1)	0.083
	Others	1 (5.3)	2 (11.1)	0.512

LAP, laparoscopic colectomy; *OP*, open colectomy

(8.0%) required conversion to open surgery. R0 resection was achieved in 68.0% and 48.0% of the patients in the LAP and OP groups, respectively.

The 5-year OS rate was 53.4% in the LAP group and 53.7% in the OP group ($p = 0.658$). The 5-year RFS rate was 62.3% in the LAP group and 48.6% in the OP group ($p = 0.434$) (Fig. 1).

Table 3 indicates the patterns of recurrence. The recurrence rates of propensity score–matched patients in the LAP and OP groups were 36.8% (7/19) and 50.0% (9/18), respectively, albeit with no significant difference ($p = 0.419$). The recurrence of liver, lung, or lymph node tended to develop more often in the OP group, while the local or peritoneal recurrence was more frequent in the LAP group, although these differences did not reach significance.

In univariate and multivariate analyses of the entire cohort, the factors of age, CA 19-9, tumor location, and R0 resection were significant predictors of OS and the factors of age, CAl9-9, tumor location, and pT were significant predictors of RFS. pT4a was a significant independent predictor of poorer RFS compared with pT4b. The surgical approach (LAP vs OP) selected was not a significant prognostic factor for OS or RFS (Table 4).

Table 4 Univariate and multivariate analyses of clinical factors predicting long-term outcomes

Parameter	Overall survival ($n = 81$)		Recurrence-free survival ($n = 61$)	
	Univariate *p* value	Multivariate *p* value, HR (95% CI)	Univariate *p* value	Multivariate *p* value, HR (95% CI)
Sex	0.558		0.909	
Age (years) > 65	0.083	0.028*; 2.326 [1.091–5.346]	0.034*	0.042*; 2.999 [1.040–11.023]
BMI (kg/m^2) > 25	0.508		0.259	
ASA grade I vs II/III	0.369		0.305	
Comorbidity	0.427		0.671	
CEA (ng/ml) > 5	0.048*	0.737; 1.144 [0.532–2.637]	0.366	
CA19-9 (U/ml) > 37	0.002*	0.001*; 3.502 [1.743–7.161]	0.010*	<0.001*; 5.535 [2.229–13.616]
Tumor location (right side vs left side)	0.039*	0.003*; 3.108 [1.486–6.777]	0.008*	0.007*; 3.373 [1.394–8.794]
Tumor size (mm) > 50	0.923		0.560	
pT stage T4a vs T4b (T4a/T4b)	0.867		0.040*	0.018*; 4.386 [1.269–20.590]
pN stage N0 vs N1/2/3	0.314		0.022*	0.119; 2.067 [0.834–5.708]
Adjuvant therapy	0.142		0.101	
Approach (laparoscopy vs open colectomy)	0.396		0.926	
Multivisceral resection	0.730		0.062	0.784; 1.192 [0.300–3.790]
Conversion laparotomy	0.334		0.505	
Operative time (min) > 240	0.611		0.177	
Blood loss (ml) > 100	0.299		0.514	
Transfusion	0.364		0.137	
R0 vs R1/2	0.024*	0.005*; 2.905 [1.389–6.073]	0.474	

BMI, body mass index; *ASA*, American Society of Anesthesiologists; *vs*, versus; *CEA*, carcinoembryonic antigen; *CA19-9*, carbohydrate antigen 19-9; *HR*, hazard ratio; *CI*, confidence interval

* $p < 0.05$ in all variables

Discussion

Since several large clinical trials have reported the safety and favorable long-term outcomes of laparoscopic surgery for colorectal cancer compared with those of open surgery, laparoscopic surgery has become the standard procedure for colorectal cancer [18–20]. However, reports regarding the outcomes of laparoscopic surgery for pT4 colon cancer remain scarce [10, 11, 15]. As with previous reports, in terms of the short-term outcomes, laparoscopic surgery was not inferior to open surgery in this study. Intraoperative blood loss in the LAP group was significantly less than that in the OP group, with no difference in the operative time. Because major blood loss has been demonstrated to be an independent prognostic factor for survival, less intraoperative blood loss in the LAP group should be a favorable result in terms of the long-term outcomes [21]. The conversion rate of surgery in this study was 8.0% (2 of the 25 patients in the LAP group), which was comparable with the conversion rate of 3.8 to 23% reported in previous studies [5–15]. The requirement of multivisceral resection (ileum or peritoneum) is the reason for the conversion.

Notably, no significant differences were noted between the groups in terms of postoperative complications.

Although the 5-year OS and 5-year RFS did not significantly differ between the propensity score–matched groups, the entire cohort showed the local recurrence rate was significantly higher in the LAP group (10/36, 27.8%) than in the OP group (2/25, 8.0%) ($p = 0.045$). Multivariate analysis of clinical factors predicting local recurrence detected no independent prognostic factors including surgical approach; however, all 10 patients who had local/peritoneal recurrence in the LAP group showed pT4a. Fujii et al. compared the laparoscopic colectomy group and the open colectomy group of pStage II/III colon cancer, and revealed that the peritoneal recurrences of pT4 were higher in the laparoscopic colectomy group than the open colectomy group, which was presented at the annual meeting of the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) in 2016. Similarly, a large-scale phase 3 randomized controlled trial JCOG0404, in which survival outcomes following laparoscopic versus open colectomy for stage II or III colon cancer were investigated, revealed that patients with clinical T4 disease in the laparoscopic surgery group tended to show worse survival compared with those in the open surgery group [22]. Importantly, it is presumed that most of the T4 patients were likely to be with T4a staging because only patients with T4 disease without involvement of other organs were eligible in JCOG0404. Therefore, surgeons might be better to have caution for the indication of laparoscopic surgery for pT4a colon cancer. Large-scale analysis is warranted to investigate this in the future.

To date, only three studies have examined the prognostic factors for the outcomes of curative resection for pT4 colorectal cancer [11, 13, 15]. On the basis of the findings of these studies, we identified CA19-9 and tumor location as significant independent predictors for both OS and RFS, pN for RFS, and R0 resection for OS. Right-sided tumor was a significant independent predictor related to poor prognosis compared with left-sided tumor, which is consistent with the reports of previous studies on whole or metastatic colorectal cancers [23, 24]. Ishihara et al. [25] have reported that stage IV right-sided colon cancer showed a worse prognosis than left-sided colon cancer, suggesting that stage IV right-sided colon cancer is biologically more aggressive than left-sided colon cancer. Right-sided colon cancer is characterized by a high frequency of BRAF mutation, which is correlated with worse prognosis [26–28]. Such biological characteristics may have resulted in the worse prognosis of the right-sided pT4 colon cancer in this study.

Interestingly, we identified pT4a as a significant independent predictor of poorer RFS compared with pT4b. Similarly, Kyang et al. [29] have reported that T4a tumors were prognostically worse in terms of peritoneal metastasis than T4b tumors. Thus, we ascertained that tumor cell spillage might develop more frequently in T4a tumor than in T4b tumor. However, further studies are warranted to arrive at a definitive conclusion.

In conclusion, this study revealed favorable short-term and long-term outcomes of laparoscopic surgery for patients with pT4 colon cancer. However, recurrence pattern might differ between the open and laparoscopic approaches for pT4 colon cancer, and further analysis was essential for more definitive conclusions.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F (2015) Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 136:E359–E386

2. Jacobs M, Verdeja JC, Goldstein HS (1991) Minimally invasive colon resection (laparoscopic colectomy). Surg Laparosc Endosc 1:144–150
3. Fazio VW, López-Kostner F (2000) Role of laparoscopic surgery for treatment of early colorectal carcinoma. World J Surg 24:1056–1060
4. Kienle P, Weitz J, Koch M, Buchler MW (2006) Laparoscopic surgery for colorectal cancer. Color Dis 8:33–36
5. Ng DC, Co CS, Cheung HY et al (2011) The outcome of laparoscopic colorectal resection in T4 cancer. Color Dis 13:e349–e352
6. Shukla PJ, Trencheva K, Merchant C, Maggiori L, Michelassi F, Sonoda T, Lee SW, Milsom JW (2015) Laparoscopic resection of t4 colon cancers: is it feasible? Dis Colon Rectum 58:25–31
7. Kim IY, Kim BR, Kim YW (2016) The short-term and oncologic outcomes of laparoscopic versus open surgery for T4 colon cancer. Surg Endosc 30:1508–1518
8. Bretagnol F, Leroy J (2016) Laparoscopic resection for T4 colon cancer: perioperative and long-term outcomes. Updat Surg 68:59–62
9. Chan DK, Tan KK (2017) Laparoscopic surgery should be considered in T4 colon cancer. Int J Color Dis 32:517–520
10. Kang J, Baik SH, Lee KY, Sohn SK (2017) Outcomes of laparoscopic surgery in pathologic T4 colon cancers compared to those of open surgery. Int J Color Dis 32:531–538
11. de'Angelis N, Landi F, Vitali GC et al (2017) Multicentre propensity score-matched analysis of laparoscopic versus open surgery for T4 rectal cancer. Surg Endosc 31:3106–3121
12. Kumamoto T, Toda S, Matoba S, Moriyama J, Hanaoka Y, Tomizawa K, Sawada T, Kuroyanagi H (2017) Short- and long-term outcomes of laparoscopic multivisceral resection for clinically suspected T4 colon cancer. World J Surg 41:2153–2159
13. Yamanashi T, Nakamura T, Sato T, Naito M, Miura H, Tsutsui A, Shimazu M, Watanabe M (2018) Laparoscopic surgery for locally advanced T4 colon cancer: the long-term outcomes and prognostic factors. Surg Today 48:534–544
14. Leon P, Iovino MG, Giudici F, Sciuto A, de Manzini N, Cuccurullo D, Corcione F (2018) Oncologic outcomes following laparoscopic colon cancer resection for T4 lesions: a case-control analysis of 7-years' experience. Surg Endosc 32:1133–1140
15. Yang ZF, Wu DQ, Wang JJ, Lv ZJ, Li Y (2018) 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 24:76–86
16. Edge SB, Compton CC (2010) The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol 17:1471–1474
17. Watanabe T, Muro K, Ajioka Y, Japanese Society for Cancer of the Colon and Rectum et al (2018) Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2016 for the treatment of colorectal cancer. Int J Clin Oncol 23:1–34
18. Guillou PJ, Quirke P, Thorpe H, MRC CLASICC trial group et al (2005) Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. Lancet 365:1718–1726
19. Jayne DG, Guillou PJ, Thorpe H, UK MRC CLASICC Trial Group et al (2007) Randomized trial of laparoscopic-assisted resection of colorectal carcinoma: 3-year results of the UK MRC CLASICC Trial Group. J Clin Oncol 25:3061–3068
20. Colon Cancer Laparoscopic or Open Resection Study Group, Buunen M, Veldkamp R, Hop WC, et al (2009) Survival after laparoscopic surgery versus open surgery for colon cancer: long-term outcome of a randomised clinical trial. Lancet Oncol 10:44–52
21. Lehnert T, Methner M, Pollok A, Schaible A, Hinz U, Herfarth C (2002) Multivisceral resection for locally advanced primary colon and rectal cancer: an analysis of prognostic factors in 201 patients. Ann Surg 235:217–225
22. Kitano S, Inomata M, Mizusawa J, Katayama H, Watanabe M, Yamamoto S, Ito M, Saito S, Fujii S, Konishi F, Saida Y, Hasegawa H, Akagi T, Sugihara K, Yamaguchi T, Masaki T, Fukunaga Y, Murata K, Okajima M, Moriya Y, Shimada Y (2017) Survival outcomes following laparoscopic versus open D3 dissection for stage II or III colon cancer (JCOG0404): a phase 3, randomised controlled trial. Lancet Gastroenterol Hepatol 2:261–268
23. O'Connell JB, Maggard MA, Ko CY (2004) Colon cancer survival rates with the new American Joint Committee on Cancer sixth edition staging. J Natl Cancer Inst 96:1420–1425
24. Golan T, Urban D, Berger R, Lawrence YR (2013) Changing prognosis of metastatic colorectal adenocarcinoma: differential improvement by age and tumor location. Cancer 119:3084–3091
25. Ishihara S, Nishikawa T, Tanaka T, Tanaka J, Kiyomatsu T, Kawai K, Hata K, Nozawa H, Kanazawa T, Kazama S, Yamaguchi H, Sunami E, Kitayama J, Hashiguchi Y, Sugihara K, Watanabe T (2014) Prognostic impact of tumor location in stage IV colon cancer: a propensity score analysis in a multicenter study. Int J Surg 12:925–930
26. Kalady MF, Dejulius KL, Sanchez JA et al (2012) BRAF mutations in colorectal cancer are associated with distinct clinical characteristics and worse prognosis. Dis Colon Rectum 55:128–133
27. Pai RK, Jayachandran P, Koong AC, Chang DT, Kwok S, Ma L, Arber DA, Balise RR, Tubbs RR, Shadrach B, Pai RK (2012) BRAF-mutated, microsatellite-stable adenocarcinoma of the proximal colon: an aggressive adenocarcinoma with poor survival, mucinous differentiation, and adverse morphologic features. Am J Surg Pathol 36:744–752
28. Tran B, Kopetz S, Tie J, Gibbs P, Jiang ZQ, Lieu CH, Agarwal A, Maru DM, Sieber O, Desai J (2011) Impact of BRAF mutation and microsatellite instability on the pattern of metastatic spread and prognosis in metastatic colorectal cancer. Cancer 117:4623–4632
29. Kyang LS, Valle SJ, Alzahrani NA, Morris DL (2018) Prevention of peritoneal recurrence in high-risk colorectal cancer and evidence of T4 status as a potential risk factor. ANZ J Surg 88:975–981