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# Favorable short-term oncologic outcomes following laparoscopic surgery for small T4 colon cancer: a multicenter comparative study

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## Abstract

**Background:** Laparoscopic surgery for T4 colon cancer may be safe in selected patients. We hypothesized that small tumor size might preoperatively predict a good laparoscopic surgery outcome. Herein, we compared the clinicopathologic and oncologic outcomes of laparoscopic and open surgery in small T4 colon cancer.

**Methods:** In a retrospective multicenter study, we reviewed the data of 449 patients, including 117 patients with tumors  $\leq 4.0$  cm who underwent surgery for T4 colon cancer between January 2014 and December 2017. We compared the clinicopathologic and 3-year oncologic outcomes between the laparoscopic and open groups. Survival curves were estimated using the Kaplan–Meier method and compared using the log-rank test. Univariate and multivariate analyses were performed using the Cox proportional hazards model. A  $p < 0.05$  was considered statistically significant.

**Results:** Blood loss, length of hospital stay, and postoperative morbidity were lower in the laparoscopic group than in the open group (median [range], 50 [0–700] vs. 100 [0–4000] mL,  $p < 0.001$ ; 8 vs. 10 days,  $p < 0.001$ ; and 18.0 vs. 29.5%,  $p = 0.005$ , respectively). There were no intergroup differences in 3-year overall survival or disease-free survival (86.6 vs. 83.2%,  $p = 0.180$ , and 71.7 vs. 75.1%,  $p = 0.720$ , respectively). Among patients with tumor size  $\leq 4.0$  cm, blood loss was significantly lower in the laparoscopic group than in the open group (median [range], 50 [0–530] vs. 50 [0–1000] mL,  $p = 0.003$ ). Despite no statistical difference observed in the 3-year overall survival rate (83.3 vs. 78.7%,  $p = 0.538$ ), the laparoscopic group had a significantly higher 3-year disease-free survival rate (79.2 vs. 53.2%,  $p = 0.012$ ).

**Conclusions:** Laparoscopic surgery showed similar outcomes to open surgery in T4 colon cancer patients and may have favorable short-term oncologic outcomes in patients with tumors  $\leq 4.0$  cm.

**Keywords:** Colon cancer, Laparoscopy, Open surgery, T4 cancer, Tumor size

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## Background

Approximately 10–20% of patients with colon cancer are diagnosed with T4 colon cancer [1–3]. R0 resection is essential for curative surgery in T4 colon cancer, although R0 resection is not easily achieved in case of tumor invasion into the adjacent organs or structures. Several meta-analyses and randomized controlled trials [4–7] have reported that laparoscopic surgery is non-inferior to open surgery for colon cancer. However, in T4 colon cancer, the feasibility of laparoscopic surgery with regard to oncologic outcomes remains debatable. In addition, treatment guidelines recommend an open approach for pathological T4 colon cancer.

Several recent studies [8–10] have reported that laparoscopic surgery for T4 colon cancer had better short-term outcomes (e.g., less intraoperative blood loss and shorter hospital stay) than open surgery, as well as non-inferiority in oncologic outcomes. However, the exact clinical conditions wherein laparoscopic surgery for T4 colon cancer is feasible or harmful, with regard to oncologic outcomes, need to be ascertained. Studies [11, 12] have reported that a technical difficulty during laparoscopic surgery could threaten oncological safety, while tumor size is a factor that is known to influence the technical difficulty associated with tumor resection.

In T4 colon cancer, a laparoscopic approach seems to be superior in regard to clinical outcomes in cases where the tumor is easy to access or handle, such as with a small invasive tumor. However, large-sized tumors are more difficult to resect laparoscopically, which may increase the risk of tumor spillage. However, there is scant evidence of the comparative outcomes of laparoscopic and open surgery with respect to the tumor size in T4 colon cancer.

In this study, we investigated the hypothesis that tumor size may influence the preoperative prediction of a favorable outcome following a laparoscopic approach and evaluated the clinicopathologic and oncologic outcomes of laparoscopic and open surgery in patients with small T4 colon cancer.

## Methods

### Patient characteristics

A retrospective chart review and analysis of multicenter data were undertaken, including data from patients diagnosed with pathological T4 colon cancer who underwent curative surgery at three institutions between January 2014 and December 2017. Rectal cancer was defined as cancer in which the lower margin of the tumor was located within 15.0 cm above the anal verge, and patients with rectal cancer were excluded from this study. Moreover, patients with T1–3 colon cancer, a histological diagnosis indicating cancer other than adenocarcinoma,

palliative surgery, inflammatory bowel disease, or hereditary colon cancer were excluded.

The patient characteristics and perioperative outcomes were analyzed, including age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) score, preoperative carcinoembryonic antigen level, tumor location, operative time, blood loss, intraoperative transfusion, length of hospital stay, and postoperative morbidity. The pathologic features that were analyzed included tumor size, T stage, nodal status, angiolymphatic invasion, venous invasion, perineural invasion, adjacent organ resection, and R0 resection. The tumor size was measured on the basis of the long diameter of the tumor in the pathologic specimen. Patients with ASA scores of 1–2 and 3–4 were included in the same group for analysis. The tumor location was divided into the right (from the cecum to the transverse colon) and left (from the splenic flexure to the sigmoid colon) sides. The nodal status was classified as the absence (N0) or presence (N+) of metastatic regional lymph node(s).

All surgeons who participated in the study were experts who had performed laparoscopic or open colorectal surgery for >10 years. Laparoscopic or open surgery was performed according to each surgeon's preference.

### Outcomes

The primary outcome of this study was the comparison of oncologic outcomes, including 3-year overall survival (OS) and 3-year disease-free survival (DFS), between the laparoscopic and open groups. With regard to DFS, we additionally analyzed locoregional recurrence-free survival (LRFS) and distant recurrence-free survival (DRFS) in the entire cohort and in patients with tumor size  $\leq$  4.0 cm. The secondary outcome was the R0 resection rate. Small T4 colon cancer was defined as tumor size  $\leq$  4.0 cm, which may be advantageous in laparoscopic surgery with small incisions.

OS was defined as the time from surgery to death, and DFS was defined as the time from surgery to any recurrence, secondary cancer, or death. R0 resection was defined as a microscopically margin-negative resection in which no gross or microscopic tumor remains in the primary tumor bed. A negative margin was defined as a margin of normal tissue >1.0 mm from the edge of the tumor.

### Statistical analyses

Data are reported as mean  $\pm$  standard deviation or median (range) for continuous variables and as number (percentage) for categorical variables. The comparison of the variables between the laparoscopic and open groups was performed using the independent *t*

test or Wilcoxon rank sum test and chi-square test or Fisher's exact test. Survival curves were analyzed using the Kaplan–Meier method, and the intergroup differences were compared using the log-rank test. The univariate Cox proportional hazards model was used to determine prognostic factors for OS and DFS. Variables with  $p < 0.05$  in the univariate analysis were included in the multivariate analysis. The backward elimination method, with  $p > 0.05$  as the criterion for removal, was performed for the multivariate analysis. After significant clinical variables were adjusted, the prognosis of the surgical procedure was evaluated. A  $p$  value  $< 0.05$  was considered statistically significant. Statistical analyses were performed using R (version 3.6.2; The R Foundation for Statistical Computing, Vienna, Austria) and SAS (version 9.4; SAS Institute Inc., Cary, NC, USA).

## Results

### Patient characteristics

A total of 449 patients were included and classified according to tumor size; 117 and 332 patients had tumors of  $\leq 4.0$  and  $> 4.0$  cm, respectively. In the  $\leq 4.0$ -cm group, 88 and 29 patients underwent laparoscopic and open surgery, respectively. In the  $> 4.0$ -cm group, 194 and 138 patients underwent laparoscopic and open surgery, respectively (Fig. 1). Twenty-one patients who converted from laparoscopic to open surgery were included in the open group.

Patients in the laparoscopic group had a higher BMI (23.7 vs. 22.0 kg/m<sup>2</sup>,  $p < 0.001$ ) and a lower proportion of patients in this group had an ASA score of  $> 2$  (4 vs. 14.1%,  $p < 0.001$ ) than in the open group. The proportions of blood loss and postoperative transfusion were lower in the laparoscopic group than in the open group (50 vs. 100 mL,  $p < 0.001$ , and 0.7 vs. 12.8%,  $p < 0.001$ , respectively). Patients in the laparoscopic group had a shorter hospital stay (8 vs. 10

days,  $p < 0.001$ ) and a lower postoperative morbidity (18 vs. 29.5%,  $p = 0.005$ ) than those in the open group (Table 1).

### Pathologic and oncologic outcomes

Patients in the laparoscopic group had smaller tumors (5.2 vs. 6 cm,  $p < 0.001$ ) and a lower T4b rate (17.3 vs. 43.0%,  $p < 0.001$ ) than those in the open group. Angiolymphatic, venous, and perineural invasion were more common in the laparoscopic group than in the open group (74 vs. 43.0%,  $p < 0.001$ ; 50 vs. 34.9%,  $p = 0.003$ ; and 78 vs. 62.4%,  $p = 0.001$ , respectively). Similarly, the adjacent organ resection rate was lower in the laparoscopic group than in the open group (6 vs. 28.2%,  $p < 0.001$ ).

The R0 resection rate did not differ significantly between the two groups (94.0 vs. 97.3%,  $p = 0.078$ ; Table 2). The median follow-up period was 34 months. There were no significant intergroup differences with regard to the 3-year OS and DFS rates (83.2 vs. 86.6%,  $p = 0.180$  and 75.1 vs. 71.7%,  $p = 0.720$ , respectively; Fig. 2). The 3-year LRFS and DRFS rates also did not differ significantly between the two groups (92.4 vs. 90.5%,  $p = 0.587$  and 79.4 vs. 76.8%,  $p = 0.826$ , respectively; Fig. 3).

### Outcomes of small T4 colon cancer

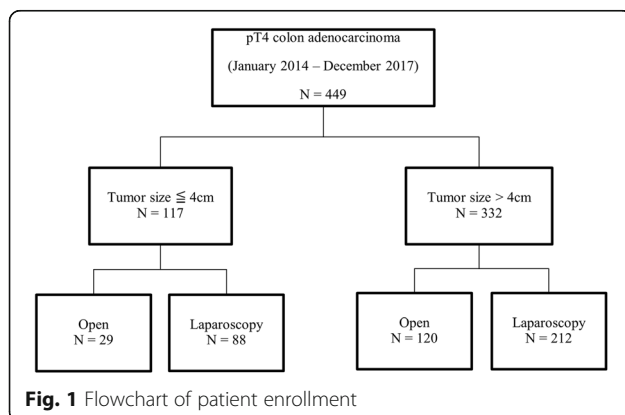
Table 3 shows the clinical characteristics and perioperative outcomes of patients with tumor size  $\leq 4.0$  cm. The laparoscopic group had a higher BMI (23.9 vs. 22.3 kg/m<sup>2</sup>,  $p = 0.026$ ) and less blood loss (50 [0–1000] vs. 50 [0–530] mL,  $p = 0.03$ ) than the open group. Other variables did not differ significantly between the two groups.

Table 4 presents the pathologic features and oncologic outcomes of patients with tumor size  $\leq 4.0$  cm. Patients in the laparoscopic group were more likely to have angiolymphatic invasion than those in the open group (77.3 vs. 37.9%,  $p < 0.001$ ).

R0 resection was performed in all patients in both groups. In patients with tumor size  $\leq 4.0$  cm, the 3-year OS rate did not differ significantly between the two groups (78.7 vs. 83.3%,  $p = 0.538$ ). However, the 3-year DFS rate was higher in the laparoscopic group than in the open group (79.2 vs. 53.2%,  $p = 0.012$ ; Fig. 4). The 3-year LRFS rate did not differ significantly between the two groups (92.7 vs. 91.5%,  $p = 0.948$ ). In contrast, the DRFS rate was higher in the laparoscopic group than in the open group (83.8 vs. 55.3%,  $p = 0.007$ ; Fig. 5).

## Discussion

Although the safety of laparoscopic surgery for colon cancer had been demonstrated in several studies [4–7], the safety of this surgical approach is controversial



**Table 1** Patient characteristics and perioperative outcomes

| Variable                            |                         | Open (N = 149) | Laparoscopy (N = 300) | p value             |
|-------------------------------------|-------------------------|----------------|-----------------------|---------------------|
| Age (years)                         |                         | 64.9 ± 12.8    | 63.6 ± 12.6           | 0.298 <sup>a</sup>  |
| Gender                              | Male                    | 82 (55.0)      | 172 (57.3)            | 0.643 <sup>c</sup>  |
|                                     | Female                  | 67 (45.0)      | 128 (42.7)            |                     |
| BMI (kg/m <sup>2</sup> )            |                         | 22.0 ± 3.3     | 23.7 ± 3.5            | < .001 <sup>a</sup> |
| ASA score                           | 1, 2                    | 128 (85.9)     | 288 (96)              | < .001 <sup>c</sup> |
|                                     | 3, 4                    | 21 (14.1)      | 12 (4)                |                     |
| Preoperative CEA (ng/ml)            |                         | 3.3 (0.5–338)  | 4.3 (0.4–543)         | 0.126 <sup>b</sup>  |
| Location                            | Right                   | 64 (43.0)      | 142 (47.3)            | 0.380 <sup>c</sup>  |
|                                     | Left                    | 85 (57.0)      | 158 (52.7)            |                     |
| Operative time (min)                |                         | 141 (43–520)   | 160 (50–460)          | 0.007 <sup>b</sup>  |
| Blood loss (ml)                     |                         | 100 (0–4000)   | 50 (0–700)            | < .001 <sup>b</sup> |
| Transfusion                         | No                      | 130 (87.3)     | 298 (99.3)            | < .001 <sup>d</sup> |
|                                     | Yes                     | 19 (12.8)      | 2 (0.7)               |                     |
| Hospital stay (days)                |                         | 10 (5–45)      | 8 (4–158)             | < .001 <sup>b</sup> |
| Postoperative morbidity             | No                      | 105 (70.5)     | 246 (82.0)            | 0.005 <sup>c</sup>  |
|                                     | Yes                     | 44 (29.5)      | 54 (18.0)             |                     |
| Postoperative morbidity type        | Ileus                   | 7 (15.9)       | 15 (27.8)             |                     |
|                                     | Urinary retention       | 2 (4.6)        | 5 (9.3)               |                     |
|                                     | Anastomotic leakage     | 0 (0)          | 3 (5.6)               |                     |
|                                     | Surgical site infection | 17 (38.6)      | 15 (27.8)             |                     |
|                                     | Pneumonia               | 5 (11.4)       | 2 (3.7)               |                     |
|                                     | Sepsis                  | 3 (6.8)        | 3 (5.6)               |                     |
|                                     | Others                  | 10 (22.7)      | 11 (20.4)             |                     |
| <b>Clavien–Dindo classification</b> | 1, 2                    | 34 (77.3)      | 42 (77.8)             | 0.953 <sup>c</sup>  |
|                                     | 3                       | 10 (22.7)      | 12 (22.2)             |                     |
| Adjuvant chemotherapy (N = 329)     | No                      | 20 (28.6)      | 39 (15.1)             | 0.009 <sup>c</sup>  |
|                                     | Yes                     | 50 (71.4)      | 220 (78.7)            |                     |

<sup>a</sup>Two-sample t test<sup>b</sup>Wilcoxon rank sum test<sup>c</sup>Chi-square test<sup>d</sup>Fisher's exact testData are expressed as mean ± standard deviation or median (range) for continuous variables and as number (percentage) for categorical variables  
ASA American Society of Anesthesiologists, BMI body mass index, CEA carcinoembryonic antigen

in T4 colon cancer. Several studies have suggested that a laparoscopic approach in T4 colon cancer may be feasible in some patients. Few studies have provided useful indications for laparoscopic surgery in T4 colon cancer. Klaver et al. [2] reported that laparoscopic surgery for T4a tumors might be safe. However, the pathologic features would not be helpful in determining the indication of laparoscopic surgery preoperatively. Park et al. [13] found the laparoscopic approach to be feasible for left-sided T4 colon cancer. Nevertheless, a useful predictor is still necessary to preoperatively determine the safety of laparoscopic surgery for T4 cancer.

In this study, the clinicopathologic and oncologic outcomes of laparoscopic surgery for T4 colon cancer were generally comparable to those of open surgery. The laparoscopic approach, especially for small T4 tumors, had better 3-year DFS rates than open surgery. To adjust for confounding variables, we analyzed the Cox proportional hazards regression model for OS and DFS in the entire cohort and in patients with tumor size ≤ 4.0 cm. Laparoscopic surgery had better DFS rates in patients with tumor size ≤ 4.0 cm ( $p = 0.020$ ) (Additional files 1 and 2).

A previous study [14] has reported that malignant cells are intraoperatively exfoliated from the tumor

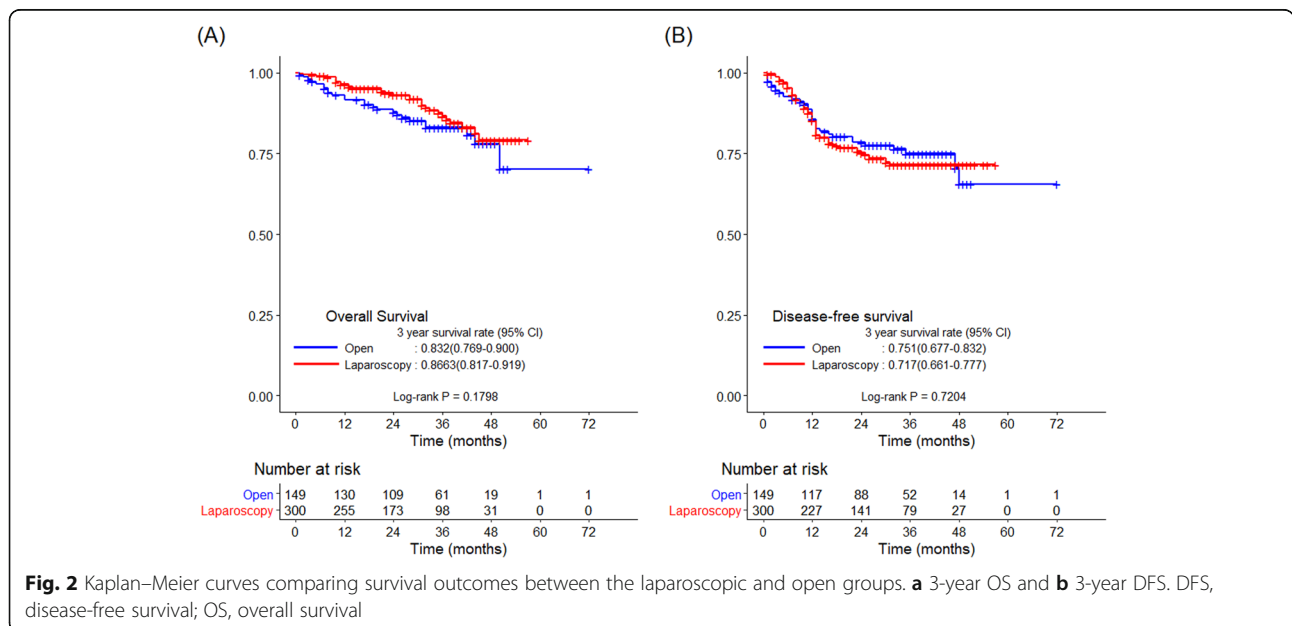
**Table 2** Pathologic features and oncologic outcomes

| Variable                |                | Open (N = 149) | Laparoscopy (N = 300) | p value            |
|-------------------------|----------------|----------------|-----------------------|--------------------|
| Tumor size (cm)         |                | 6 (2–30)       | 5.2 (0.9–14.5)        | <.001 <sup>a</sup> |
| Node state              | N0             | 53 (35.6)      | 85 (28.3)             | 0.118 <sup>b</sup> |
|                         | N+             | 96 (64.4)      | 215 (71.7)            |                    |
| T stage                 | T4a            | 85 (57.0)      | 248 (82.7)            | <.001 <sup>b</sup> |
|                         | T4b            | 64 (43.0)      | 52 (17.3)             |                    |
| Angiolymphatic invasion | Not identified | 85 (57.0)      | 78 (26.0)             | <.001 <sup>b</sup> |
|                         | Present        | 64 (43.0)      | 222 (74.0)            |                    |
| Venous invasion         | Not identified | 97 (65.1)      | 150 (50.0)            | 0.003 <sup>b</sup> |
|                         | Present        | 52 (34.9)      | 150 (50.0)            |                    |
| Perineural invasion     | Not identified | 56 (37.6)      | 66 (22.0)             | 0.001 <sup>b</sup> |
|                         | Present        | 93 (62.4)      | 234 (78.0)            |                    |
| Combined resection      | No             | 107 (71.8)     | 282 (94.0)            | <.001 <sup>b</sup> |
|                         | Yes            | 42 (28.2)      | 18 (6.0)              |                    |
| R0 resection rate       |                | 140 (94)       | 292 (97.3)            | 0.078 <sup>b</sup> |
| Harvested lymph nodes   | N = 298        | 29 (5–117)     | 29 (7–244)            | 0.677 <sup>a</sup> |
| Proximal margin         | N = 447        | 14 (0.5–174)   | 10.7 (1.5–119.8)      | 0.004 <sup>a</sup> |
| Distal margin           |                | 8 (0–125.5)    | 8.3 (0.4–101)         | 0.532 <sup>a</sup> |
| Radial margin           | N = 100        | 0.4 (0–8.5)    | 0.4 (0–4)             | 0.895 <sup>a</sup> |

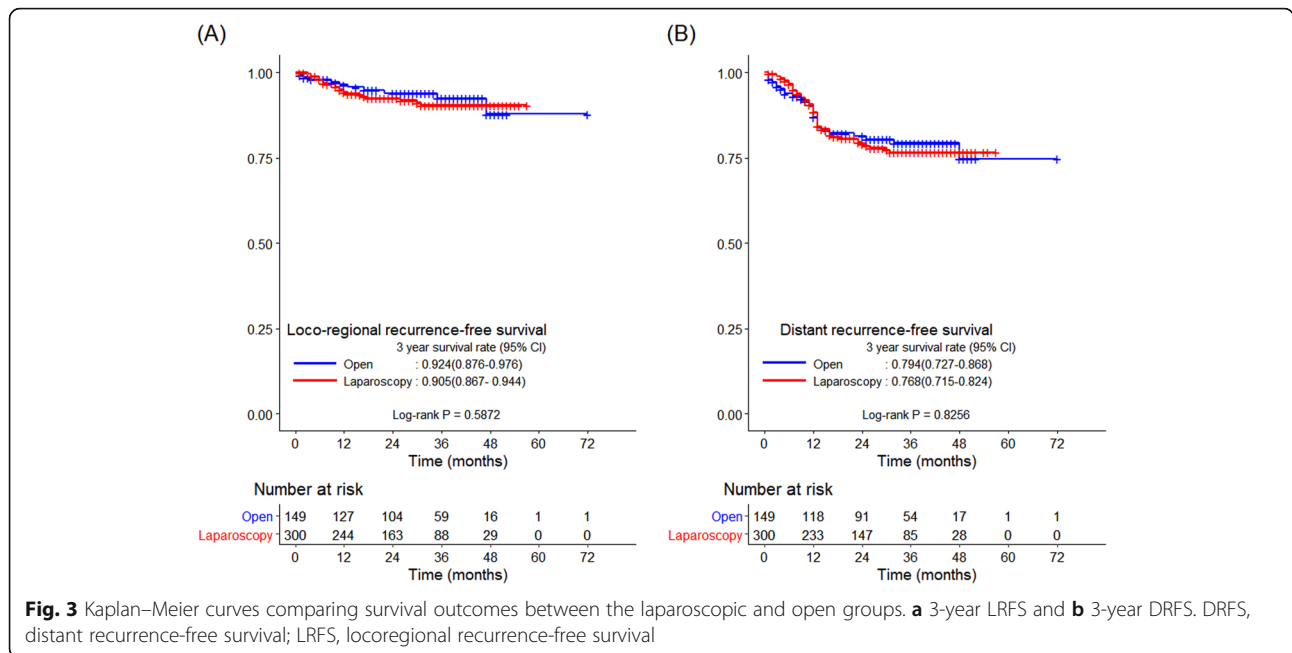
<sup>a</sup>Wilcoxon rank sum test

<sup>b</sup>Chi-square test

Data are expressed as median (range) for continuous variables and as number (percentage) for categorical variables



**Fig. 2** Kaplan–Meier curves comparing survival outcomes between the laparoscopic and open groups. **a** 3-year OS and **b** 3-year DFS. DFS, disease-free survival; OS, overall survival



during resection and spread to the peritoneal surface and portal vein system. This can be prevented by minimizing tumor manipulation, e.g., through laparoscopic surgery. Lacy et al. [15] showed better cancer-related survival with laparoscopic colectomy than open surgery for non-metastatic colon cancer in a randomized clinical trial, as did our study. When laparoscopic surgery is conducted by an experienced surgeon, tumor spillage, and spread may be prevented in some patients.

As tumor size increases, some technical challenges arise with regard to laparoscopic surgery, because it reduces the working space, narrows the operative visual field, increases bleeding, and makes the tumor difficult to remove. Moreover, larger tumors increase the risk of tumor spillage, thereby increasing peritoneal seeding or trocar-site recurrence. Our data show that the 3-year OS and DFS rates in patients with tumor size >4.0 cm are not significantly different between the two groups (84.4 vs. 87.8%,  $p = 0.22$  and 80.6 vs. 68.7%,  $p = 0.091$ , respectively), suggesting that the laparoscopic approach is more feasible in patients with small tumors than in those with larger tumors.

Laparoscopic surgery is better than open surgery in regard to perioperative outcomes. In previous studies [1, 16, 17] comparing laparoscopic and open surgery in T4 colon cancer, laparoscopic surgery was associated with less intraoperative blood loss, which has been proven to be a predictor of long-term

survival [18, 19]. Some studies [20, 21] have shown that hospital stays are shorter in patients who undergo laparoscopic surgery. In this study, patients in the laparoscopic group had less intraoperative blood loss and shorter hospital stays than those in the open group.

In a previous study [3] of T4 colon cancer, the conversion rate from laparoscopic to open surgery was reported to be in the range of 7.1–28.2%. Converted patients have high postoperative morbidity and adverse effects on long-term oncologic outcomes [22]. In the present study, the overall conversion rate was 7%, and the conversion rate for patients with tumor size  $\leq 4.0$  cm was 2.3%. The low conversion rate might be responsible for the better oncologic outcomes of laparoscopic surgery.

In this study, the 3-year DFS rate of patients in the open group with tumor size  $\leq 4.0$  cm was 53.2%, which was much lower than the 75.1% for all patients in the open group. This result is similar to that of the study by Huang et al. [23], which reported that a smaller tumor size was associated with a decreased survival in the T4b subset of colon cancer patients. Huang et al. [23] suggested that small tumors in T4b patients may reflect a more biologically aggressive phenotype. Another plausible explanation is that surgeons may have conducted more aggressive surgery for larger tumors. In the present study, the rate of multi-visceral resection was 28.2% in the entire open group, but only 6.9% in the small

**Table 3** Patient characteristics and perioperative outcomes in patients with tumor size  $\leq 4.0$  cm

| Variable                       |                         | Open (N = 29)   | Laparoscopy (N = 88) | p value             |
|--------------------------------|-------------------------|-----------------|----------------------|---------------------|
| Age (years)                    |                         | 62.2 $\pm$ 12.0 | 65.1 $\pm$ 12.8      | 0.287 <sup>a</sup>  |
| Gender                         | Male                    | 14 (48.3)       | 46 (52.3)            | 0.709 <sup>c</sup>  |
|                                | Female                  | 15 (51.7)       | 42 (47.7)            |                     |
| BMI (kg/m <sup>2</sup> )       |                         | 22.3 $\pm$ 3.2  | 23.9 $\pm$ 3.2       | 0.026 <sup>a</sup>  |
| ASA score                      | 1, 2                    | 28 (96.6)       | 87 (98.9)            | 0.436 <sup>d</sup>  |
|                                | 3, 4                    | 1 (3.5)         | 1 (1.1)              |                     |
| Preoperative CEA (ng/ml)       |                         | 2.4 (0.6–54.9)  | 3.3 (0.4–138)        | 0.270 <sup>b</sup>  |
| Location                       | Right                   | 12 (41.4)       | 40 (45.5)            | 0.702 <sup>c</sup>  |
|                                | Left                    | 17 (58.6)       | 48 (54.6)            |                     |
| Operative time (min)           |                         | 75 (45–505)     | 148 (85–460)         | < .001 <sup>b</sup> |
| Blood loss (ml)                |                         | 50 (0–1000)     | 50 (0–530)           | 0.003 <sup>b</sup>  |
| Transfusion                    | No                      | 27 (93.1)       | 88 (100)             | 0.060 <sup>d</sup>  |
|                                | Yes                     | 2 (6.9)         | 0 (0)                |                     |
| Hospital stay (days)           |                         | 8 (5–36)        | 8 (4–31)             | 0.942 <sup>b</sup>  |
| Postoperative morbidity        | No                      | 23 (79.3)       | 70 (79.6)            | 0.978 <sup>c</sup>  |
|                                | Yes                     | 6 (20.7)        | 18 (20.5)            |                     |
| Postoperative morbidity type   | Ileus                   | 1 (16.7)        | 6 (33.3)             | 0.539 <sup>d</sup>  |
|                                | Urinary retention       | 0 (0)           | 2 (11.1)             |                     |
|                                | Anastomotic leakage     | 0 (0)           | 1 (5.6)              |                     |
|                                | Surgical site infection | 3 (50)          | 4 (22.2)             |                     |
|                                | Sepsis                  | 0 (0)           | 1 (5.6)              |                     |
|                                | Others                  | 2 (33.3)        | 4 (22.2)             |                     |
| Clavien–Dindo classification   | 1, 2                    | 6 (100)         | 14 (77.8)            | 0.539 <sup>d</sup>  |
|                                | 3                       | 0 (0)           | 4 (22.2)             |                     |
|                                |                         |                 |                      |                     |
| Adjuvant chemotherapy (N = 77) | No                      | 1 (20.0)        | 18 (22.9)            | 1.000 <sup>c</sup>  |
|                                | Yes                     | 4 (80.0)        | 54 (77.1)            |                     |

<sup>a</sup>Two-sample t test<sup>b</sup>Wilcoxon rank sum test<sup>c</sup>Chi-square test<sup>d</sup>Fisher's exact test

Data are expressed as mean  $\pm$  standard deviation or median (range) for continuous variables and as number (percentage) for categorical variables  
 ASA American Society of Anesthesiologists, BMI body mass index, CEA carcinoembryonic antigen

tumor group. Although R0 resection was accomplished in all patients with small tumors, it is possible that disseminated lesions remained in adjacent organs. These may have contributed to the worse 3-year DFS rate in patients with tumor size  $\leq 4.0$  cm in the open group.

The limitations of this study are as follows. As this was a retrospective study, the choice of surgical approach may have been influenced by the patient's condition or tumor progression. First, this study was conducted on the basis of the pathological T4 instead of the clinical T4, although the former cannot be used to determine the surgical approach preoperatively. Engelmann et al. [24] reported that the

computed tomography accuracy of T4 staging in colon cancer was only 70–77%, although further studies are needed in patients with clinical T4 colon cancer. Second, more patients had higher ASA scores in the open group. This may have affected OS or DFS. However, in patients with tumor size  $\leq 4.0$  cm, there was no intergroup difference in ASA scores. Third, the T4b rate and number of adjacent organ resections were higher in the open group. Thus, it is apparent that open surgery was chosen for patients with more advanced tumors. However, there were no intergroup differences in the T4b rate and number of adjacent organ resections in patients with tumor size  $\leq 4.0$  cm.

**Table 4** Pathologic features and oncologic outcomes in patients with tumor size ≤ 4.0 cm

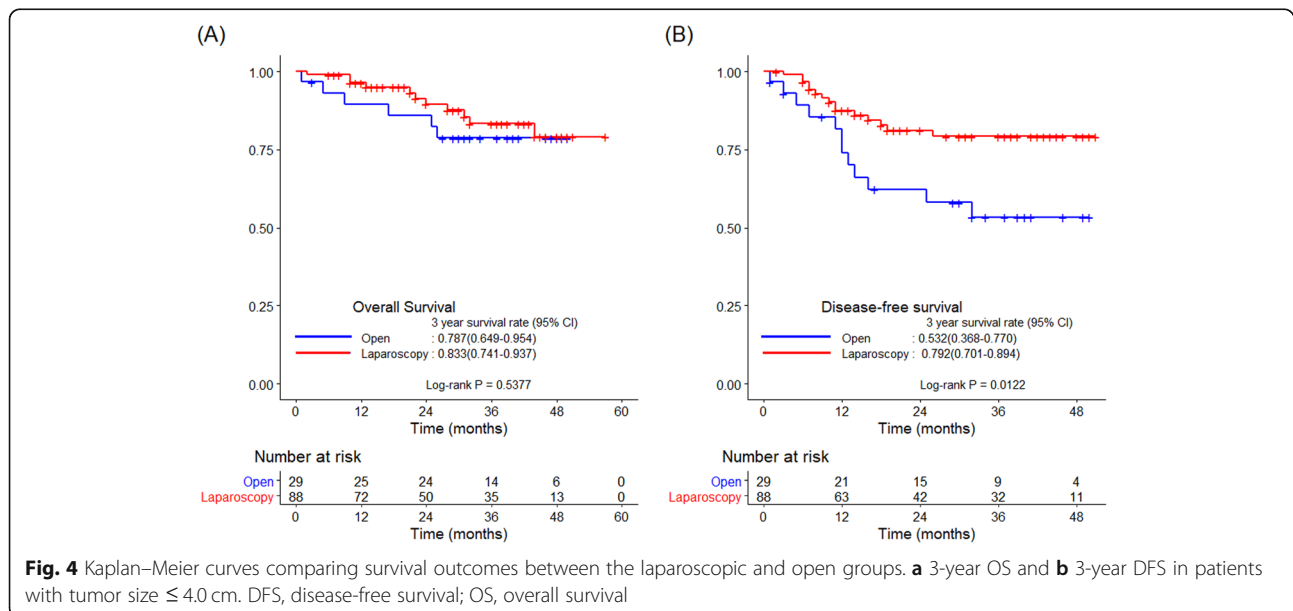
| Variable                |                | Open (N = 29) | Laparoscopy (N = 88) | p value             |
|-------------------------|----------------|---------------|----------------------|---------------------|
| Tumor size (cm)         |                | 3.5 (2–4)     | 3.4 (0.9–4)          | 0.208 <sup>a</sup>  |
| Node state              | N0             | 7 (24.1)      | 22 (25.0)            | 0.926 <sup>b</sup>  |
|                         | N+             | 22 (75.9)     | 66 (75.0)            |                     |
| T stage                 | T4a            | 26 (89.7)     | 85 (96.6)            | 0.161 <sup>c</sup>  |
|                         | T4b            | 3 (10.3)      | 3 (3.4)              |                     |
| Angiolymphatic invasion | Not identified | 18 (62.1)     | 20 (22.7)            | < .001 <sup>b</sup> |
|                         | Present        | 11 (37.9)     | 68 (77.3)            |                     |
| Venous invasion         | Not identified | 19 (65.5)     | 50 (56.8)            | 0.409 <sup>b</sup>  |
|                         | Present        | 10 (34.5)     | 38 (43.2)            |                     |
| Perineural invasion     | Not identified | 7 (24.1)      | 11 (12.5)            | 0.146 <sup>c</sup>  |
|                         | Present        | 22 (75.9)     | 77 (87.5)            |                     |
| Combined resection      | No             | 27 (93.1)     | 86 (97.7)            | 0.256 <sup>c</sup>  |
|                         | Yes            | 2 (6.9)       | 2 (2.3)              |                     |
| R0 resection rate       |                | 29 (100)      | 88 (100)             | -                   |
| Harvested lymph nodes   | N = 83         | 18 (8–60)     | 25 (7–107)           | 0.057 <sup>a</sup>  |
| Proximal margin         | N = 116        | 8.5 (2–43)    | 10.1 (1.5–48)        | 0.198 <sup>a</sup>  |
| Distal margin           |                | 5.5 (0–27.5)  | 7.5 (0.4–50)         | 0.241 <sup>a</sup>  |
| Radial margin           | N = 10         | 1.4 (0.4–2.3) | 1.1 (0.1–4)          | 0.896 <sup>a</sup>  |

<sup>a</sup>Wilcoxon rank sum test

<sup>b</sup>Chi-square test

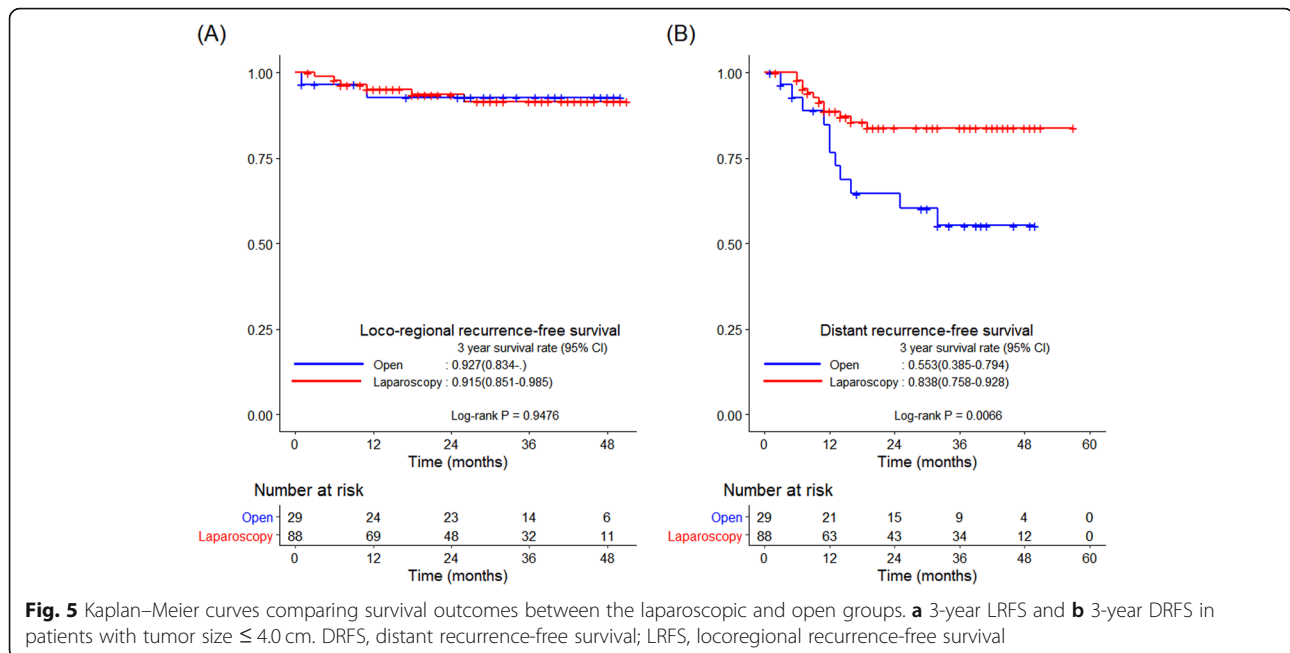
<sup>c</sup>Fisher’s exact test

Data are expressed as median (range) for continuous variables and as number (percentage) for categorical variables



**Fig. 4** Kaplan–Meier curves comparing survival outcomes between the laparoscopic and open groups. **a** 3-year OS and **b** 3-year DFS in patients with tumor size ≤ 4.0 cm. DFS, disease-free survival; OS, overall survival





## Conclusions

Although laparoscopic surgery showed similar outcomes in T4 colon cancer to open surgery, the former appears to have favorable short-term oncologic outcomes in patients with tumor size  $\leq 4.0$  cm. Prospective large-scale studies are needed to identify improved oncologic outcomes of laparoscopic surgery for small T4 colon cancer.

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12957-020-02074-5>.

**Additional file 1.** Univariate and multivariate analysis of OS and DFS.

**Additional file 2.** Univariate and multivariate analysis of OS and DFS in patients with tumor size  $\leq 4.0$  cm.

## Abbreviations

ASA: American Society of Anesthesiologists; BMI: Body mass index; DFS: Disease-free survival; DRFS: Distant recurrence-free survival; LRFS: Locoregional recurrence-free survival; OS: Overall survival

## Acknowledgements

We would like to thank Editage ([www.editage.com](http://www.editage.com)) for their writing support.

## Authors' contributions

Study concept and design (H-CP), acquisition of data (SSP, JSL), analysis and interpretation of data (SCP, DKS, JHO, KSH, D-WL, D-EL, S-BK, KJP, S-YJ), writing the manuscript (SSP, H-CP), critical revision of the manuscript (SSP, JSL, H-CP, D-EL), and approval of the final version of the manuscript (SSP, JSL, H-CP, SCP, DKS, JHO, KSH, D-WL, D-EL, S-BK, KJP, S-YJ).

## Funding

This work was supported by the Clinical Research Program of the National Cancer Center (grant number NCC 2011520-1).

## Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Ethics approval and consent to participate

This study was approved by the Institutional Review Board of the National Cancer Center, Korea (approval number NCC2020-0166). Research was conducted in accordance with the principles of the 1964 Declaration of Helsinki and its later amendments. The requirement for informed consent was waived owing to the retrospective nature of the study.

## Consent for publication

Not applicable.

## Competing interests

The authors declare that they have no competing interests.

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Received: 17 August 2020 Accepted: 29 October 2020

Published online: 13 November 2020

## References

- de'Angelis N, Vitali GC, Brunetti F, Wassmer C-H, Gagniere C, Puppa G, Tournigand C, Ris F. Laparoscopic vs. open surgery for T4 colon cancer: a propensity score analysis. *Int J Color Dis.* 2016;31:1785–97.
- Klaver CE, Kappen TM, Borstlap WA, Bemelman WA, Tanis PJ. Laparoscopic surgery for T4 colon cancer: a systematic review and meta-analysis. *Surg Endosc.* 2017;31:4902–12.
- Liu Z-H, Wang N, Wang F-Q, Dong Q, Ding J. Oncological outcomes of laparoscopic versus open surgery in pT4 colon cancers: a systematic review and meta-analysis. *Int J Surg.* 2018;56:221–33.
- Buunen M. Colon Cancer Laparoscopic or Open Resection Study Group. Survival after laparoscopic surgery versus open surgery for colon cancer: long-term outcomes of a randomised clinical trial. *Lancet Oncol.* 2009;10:44–52.

5. Jayne DG, Guillou PJ, Thorpe H, Quirke P, Copeland J, Smith AM, Heath RM, Brown JM. Randomized trial of laparoscopic-assisted resection of colorectal carcinoma: 3-year results of the UK MRC CLASICC Trial Group. *J Clin Oncol*. 2007;25:3061–8.
6. Kuhry E, Schwenk W, Gaupset R, Romild U, Bonjer J. Long-term outcome of laparoscopic surgery for colorectal cancer: a cochrane systematic review of randomised controlled trials. *Cancer Treat Rev*. 2008;34:498–504.
7. Ohtani H, Tamamori Y, Azuma T, Mori Y, Nishiguchi Y, Maeda K, Hirakawa K. A meta-analysis of the short-and long-term results of randomized controlled trials that compared laparoscopy-assisted and conventional open surgery for rectal cancer. *J Gastrointest Surg*. 2011;15:1375–85.
8. Chan DKH, Tan K-K. Laparoscopic surgery should be considered in T4 colon cancer. *Int J Color Dis*. 2017;32:517–20.
9. Lu J, Dong B, Yang Z, Song Y, Yang Y, Cao J, Li W. Clinical efficacy of laparoscopic surgery for T4 colon cancer compared with open surgery: a single center's experience. *J Laparoendosc Adv Surg Tech*. 2019;29:333–9.
10. Yamanashi T, Nakamura T, Sato T, Naito M, Miura H, Tsutsui A, Shimazu M, Watanabe M. Laparoscopic surgery for locally advanced T4 colon cancer: the long-term outcomes and prognostic factors. *Surg Today*. 2018;48:534–44.
11. Kang S-B, Park J-S, Kim D-W, Lee T-G. Intraoperative technical difficulty during laparoscopy-assisted surgery as a prognostic factor for colorectal cancer. *Dis Colon Rectum*. 2010;53:1400–8.
12. Targarona EM, Balague C, Pernas JC, Martinez C, Berindoague R, Gich I, Trias M. Can we predict immediate outcome after laparoscopic rectal surgery? Multivariate analysis of clinical, anatomic, and pathologic features after 3-dimensional reconstruction of the pelvic anatomy. *Ann Surg*. 2008;247:642–9.
13. Park JH, Park H-C, Park SC, Sohn DK, Oh JH, Kang S-B, Heo SC, Kim MJ, Park JW, Jeong S-Y. Laparoscopic approach for left-sided T4 colon cancer is a safe and feasible procedure, compared to open surgery. *Surg Endosc*. 2019;33:2843–9.
14. Bessa X, Castells A, Lacy AM, Elizalde JI, Delgado S, Boix L, Piñol V, Pellisé M, García-Valdecasas JC, Piqué JM. Laparoscopic-assisted vs. open colectomy for colorectal cancer: influence on neoplastic cell mobilization. *J Gastrointest Surg*. 2001;5:66–73.
15. Lacy AM, García-Valdecasas JC, Delgado S, Castells A, Taurá P, Piqué JM, Visa J. Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial. *Lancet*. 2002;359:2224–9.
16. Aoki T, Matsuda T, Hasegawa H, Yamashita K, Sumi Y, Ishida R, Yamamoto M, Kanaji S, Oshikiri T, Nakamura T. Outcomes of laparoscopic surgery for pathological T4 colon cancer. *Int J Color Dis*. 2019;34:1259–65.
17. Kang J, Baik SH, Lee KY, Sohn S-K. Outcomes of laparoscopic surgery in pathologic T4 colon cancers compared to those of open surgery. *Int J Color Dis*. 2017;32:531–8.
18. Lehnert T, Methner M, Pollok A, Schaible A, Hinz U, Herfarth C. Multivisceral resection for locally advanced primary colon and rectal cancer: an analysis of prognostic factors in 201 patients. *Ann Surg*. 2002;235:217.
19. Nakafusa Y, Tanaka T, Tanaka M, Kitajima Y, Sato S, Miyazaki K. Comparison of multivisceral resection and standard operation for locally advanced colorectal cancer: analysis of prognostic factors for short-term and long-term outcome. *Dis Colon Rectum*. 2004;47:2055–63.
20. Kim IY, Kim BR, Kim YW. The short-term and oncologic outcomes of laparoscopic versus open surgery for T4 colon cancer. *Surg Endosc*. 2016;30:1508–18.
21. Yang X, Zhong ME, Xiao Y, Gn Z, Xu L, Lu J, Lin G, Qiu H, Wu B. Laparoscopic vs open resection of pT 4 colon cancer: a propensity score analysis of 94 patients. *Color Dis*. 2018;20:O316–25.
22. Clancy C, O'Leary D, Burke J, Redmond H, Coffey J, Kerin M, Myers E. A meta-analysis to determine the oncological implications of conversion in laparoscopic colorectal cancer surgery. *Color Dis*. 2015;17:482–90.
23. Huang B, Feng Y, Mo S-B, Cai S-J, Huang L-Y. Smaller tumor size is associated with poor survival in T4b colon cancer. *World J Gastroenterol*. 2016;22:6726.
24. Engelmann BE, Loft A, Kjær A, Nielsen HJ, Berthelsen AK, Binderup T, Brinch K, Brünner N, Gerds TA, Høyer-Hansen G. Positron emission tomography/computed tomography for optimized colon cancer staging and follow up. *Scand J Gastroenterol*. 2014;49:191–201.

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