

Original Article

# Comparison of the Oncological Outcomes between Laparoscopic and Open Colectomy in T4 Colon Cancer

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## Key Words

Colon cancer;

T4;

Laparoscopic surgery;

Minimally invasive surgery;

Outcomes

**Purpose.** To compare the outcomes of laparoscopic and open colectomy for T4 colon cancer at Taipei Veterans General Hospital.

**Methods.** This retrospective study reviewed medical charts of 4403 patients who underwent surgical procedures for colon cancer from September 2014 to December 2019. After applying exclusion criteria, 310 T4 colon cancer cases were included and matched by various factors, resulting in 48 patients each in the laparoscopic and open colectomy groups. Primary outcomes were the 3-year overall survival (OS) rate and disease-free survival rate.

**Results.** Post propensity score matching, patient demographics were comparable between groups. The laparoscopic group had smaller tumor size and higher lymphovascular invasion rates. The laparoscopic group exhibited less blood loss but similar operation times, hospital stays, and lymph node harvests compared to the open group. Postoperative complications were lower in the laparoscopic group but not significantly different. The 3-year overall survival rates were 80.7% and 70.2%, and the 3-year disease-free survival rates were 65.7% and 64% for the laparoscopic and open groups, respectively, with no significant differences. Multivariate analysis identified differentiation and adjuvant chemotherapy as significant factors for overall survival, and differentiation, perineural invasion, and margin for disease-free survival.

**Conclusions.** Laparoscopic colectomy for T4 colon cancer demonstrated safety with comparable clinical and oncological outcomes to open colectomy. Larger studies are necessary to confirm these findings.

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In 2020, colorectal cancer was the second most prevalent cancer (including pTis) in Taiwan, with an incidence rate of 104.45 and 75.17, and mortality rate of 31.15 and 24.00 per 100,000 males and females, respectively.<sup>1</sup> Approximately 15% of colon cancer cases present with locally advanced disease.<sup>2</sup> The AJCC 8th

edition defined T4a as penetrating the surface of the visceral peritoneum and T4b as directly invading (or adhering to) organs and structures.<sup>3</sup> T4 cancers are associated with significantly worse outcomes and often require en bloc resection of the invaded structures (R0 resection). Several large randomized trials, such as the

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CLASICC, COLOR, and Barcelona trials, have shown that laparoscopic surgery improves postoperative outcomes without negatively affecting oncological outcomes.<sup>4-6</sup> However, these trials typically excluded patients with locally advanced T4 tumors. Indeed, few studies have specifically focused on the outcomes of laparoscopic management of T4 colorectal cancer;<sup>7-12</sup> however, the benefits and safety of laparoscopic compared to open approaches have shown improved perioperative outcomes and comparable long-term outcomes.<sup>3</sup> However, most of these studies had limitations, such as a small number of included patients and a short median follow-up. Thus, the safety of laparoscopic surgery for T4 colon cancer remains unclear. Therefore, the aim of this study was to compare the outcomes between laparoscopic and open colectomy for T4 colon cancer at Taipei Veterans General Hospital.

## Materials and Methods

This study was a retrospective review of all pa-

tients who underwent surgical procedures for colon cancer at a single institution from September 2014 to December 2019. The medical charts of a total of 4403 patients were reviewed. Patients with rectal cancer (n = 1574), pathologies other than adenocarcinoma (n = 100), metastasis (n = 716), and T stages other than T4 (n = 1612) were excluded, as were those with emergent operations (n = 39), mortality within 30 days (n = 6), loss of follow-up or data errors (n = 16), or conversion to open surgery (n = 29). Finally, 310 T4 colon cancer cases were included, with 282 cases classified as pT4a and 28 as pT4b. After matching for age, sex, location, pathological stage, pathological T stage, pathological N stage, CEA, and ASA, 96 patients were assigned to each group: open colectomy (n = 48) and laparoscopic colectomy (n = 48) (Fig. 1). The primary outcomes were the 3-year overall survival (OS) rate and disease-free survival rate. Categorical data are presented as numbers and percentages and were analyzed using the chi-square test, while continuous data are described by median and range and were analyzed using Student's t-test. Nonparametric analyses were

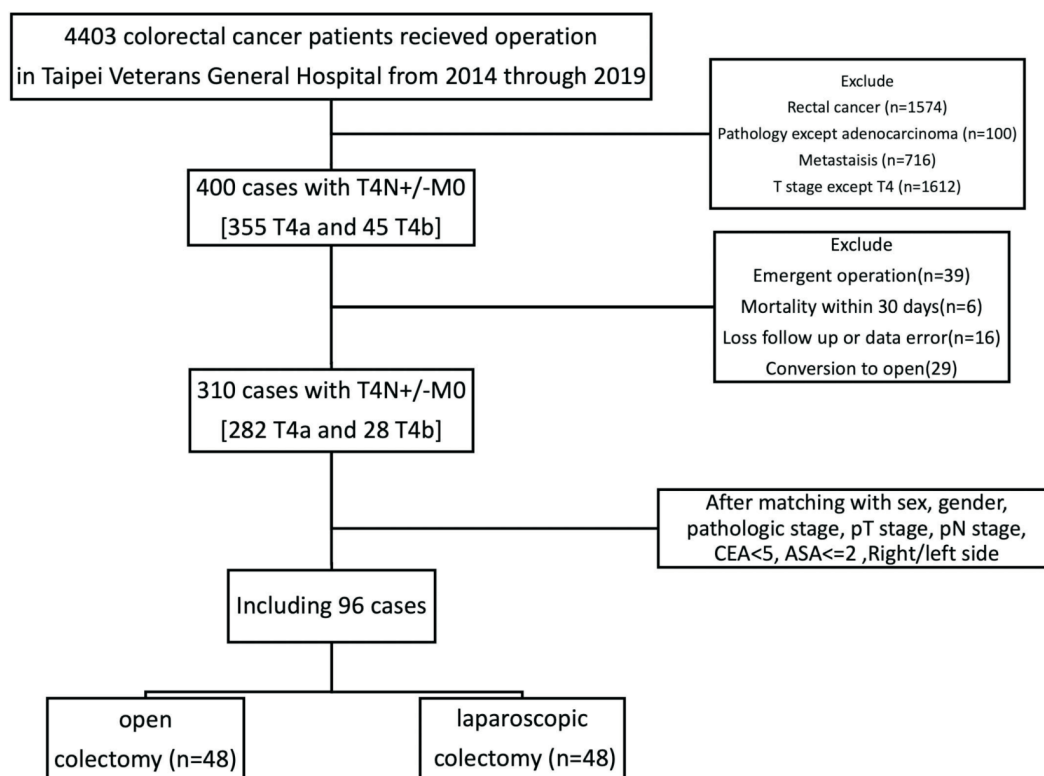


Fig. 1. Study flowchart.

performed using the  $\chi^2$  or Fisher's exact test as appropriate. The Kaplan-Meier method was used to analyze OS and recurrence. Cox proportional hazard models were used to assess the impact of the factors on OS. Statistical analysis was performed using SPSS version 26 software.

## Result

After propensity matching, the patient demographics, including age, body mass index (BMI), sex, tumor location, CEA, ASA, and underlying diseases, showed no significant differences between the two groups (Table 1). The mean age of the patients was 70.03 and 69.35 years in the laparoscopic and open group, respectively. In terms of age, 78% and 66.7% were male in the laparoscopic and open group, respectively. The mean BMI was 23.74 and 22.95 in the laparoscopic and open group, respectively. Right-sided colon cancer was found in 43.8% and 37.5% of patients in the laparoscopic and open group, respectively. CEA levels  $\geq 5$  were observed in 54.2% and 41.7% of patients in the laparoscopic and open group, respectively. Moreover, 81% and 68.8% of the patients received chemotherapy in the laparoscopic and open group, respectively. Pathological demographics showed

no significant differences in pathological stage, T stage, N stage, or lateral margin between the two groups, whereas the laparoscopic group demonstrated smaller tumor size and higher rates of lymphovascular (Table 2). Furthermore, lymphovascular invasion was present in 45.8% and 25% of the laparoscopic and open group, respectively ( $p = 0.033$ ), whereas perineural invasion was observed in 22.9% and 16.7% of the laparoscopic and open group, respectively. The positive lateral margin rate was similar between the two groups, with rates of 6.3% and 4.2% in the laparoscopic and open group, respectively. Poor differentiation was observed in 4.2% and 14.6% of the laparoscopic and open group, respectively, with no significant difference. The mean tumor size was 4.62 cm and 5.94 cm in the laparoscopic and open group, respectively ( $p = 0.008$ ). The two groups showed no significant difference in the number of invaded organs ( $p = 0.264$ ), but did show differences in organ invasion, as shown in Table 2-1.

Perioperative outcomes, the laparoscopic group showed less blood loss, but no significant differences in operation time, hospital stay, or harvested lymph node numbers (Table 3). The median operation time was 232 min and 218 min in the laparoscopic and open group, respectively. The median blood loss was 30 cc and 50 cc in the laparoscopic and open group, respec-

**Table 1.** Baseline characteristics

	Overall cohort			Matched cohort		
	Laparoscopic (n = 245)	Open (n = 65)	<i>p</i> value	Laparoscopic (n = 48)	Open (n = 48)	<i>p</i> value
Male, n (%)	137 (55.9)	44 (67.7)	0.087	34 (70.8)	32 (66.7)	0.660
Age (years), mean $\pm$ SD	69.69 $\pm$ 14.49	68.40 $\pm$ 13.53	0.799	70.03 $\pm$ 15.11	69.35 $\pm$ 14.18	0.819
BMI, mean $\pm$ SD	23.90 $\pm$ 5.442	22.32 $\pm$ 4.600	0.041	23.74 $\pm$ 3.44	22.95 $\pm$ 5.30	0.395
ASA			0.909			0.214
1, 2	183 (74.7)	49 (75.4)		23 (47.9)	17 (35.4)	
3, 4	62 (25.3)	16 (24.6)		25 (52.1)	31 (64.6)	
Location			0.623			0.533
Right	91 (37.1)	22 (33.8)		21 (43.8)	18 (37.5)	
Left	154 (62.9)	43 (66.2)		27 (56.3)	30 (62.5)	
CEA			0.065			0.220
< 5	135 (55.1)	27 (42.2)		26 (54.2)	20 (41.7)	
$\geq 5$	110 (44.9)	37 (57.8)		22 (45.8)	28 (58.3)	
Previous OP history	48 (19.6)	18 (27.7)	0.156	10 (20.8)	9 (18.8)	0.798
Adjuvant chemotherapy+, n (%)	203 (82.9)	45 (60.2)	0.027	39 (81.3)	33 (68.8)	0.157

tively ( $p < 0.0001$ ). The mean hospital stay was 12 days in both groups, while the median number of harvested lymph nodes was 21 in both groups. Postoperative complications, as shown in Table 3-1, occurred in 18.8% and 27.1% of the laparoscopic and open group, respectively ( $p = 0.331$ ). The rate of wound complications was higher in the open group (14.6%) than in the laparoscopic group (4.2%), albeit with no significant differences ( $p = 0.08$ ).

In terms of the primary outcomes, the two groups showed no significant difference in 3-year OS rate, with rates of 80.7% and 70.2% in the laparoscopic and open group, respectively ( $p = 0.748$ ) (Fig. 2), or 3-year disease-free survival, with rates of 65.7% and 64% in the laparoscopic and open group, respectively ( $p = 0.944$ ) (Fig. 3).

Univariate Cox regression analysis showed that neither open nor laparoscopic surgery influenced the

**Table 2-1.** Invaded organ

	Matched cohort		<i>p</i> value
	Laparoscopic (n = 48)	Open (n = 48)	
Abdominal wall	1	0	
Small intestine	1	1	
Ileum	0	3	
Bladder	1	1	
Uterus	1	0	
Adnexa	0	1	
Invaded organ numbers (cases)			0.264
0	44	44	
1	4	2	
2	0	2	

**Table 2.** Pathology characteristics

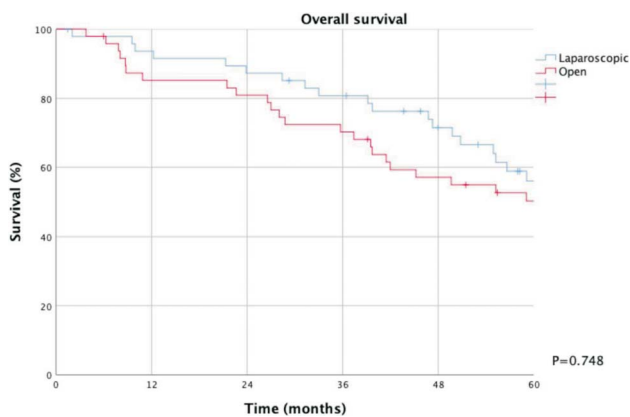
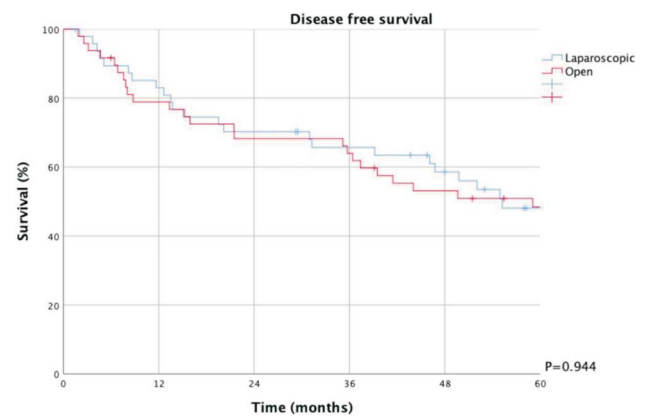
	Overall cohort			Matched cohort		
	Laparoscopic (n = 245)	Open (n = 65)	<i>p</i> value	Laparoscopic (n = 48)	Open (n = 48)	<i>p</i> value
p stage			0.122			0.837
II	91 (37.1)	31 (47.7)		21 (43.8)	22 (45.8)	
III	154 (62.9)	34 (52.3)		27 (56.3)	26 (54.2)	
pT stage			0.000			1.000
T4a	235 (95.9)	47 (72.3)		44 (91.7)	44 (91.7)	
T4b	10 (4.1)	18 (27.7)		4 (8.3)	4 (8.3)	
pN stage			0.122			0.837
N0	91 (37.1)	31 (47.7)		21 (43.8)	22 (45.8)	
N+	154 (62.9)	34 (52.3)		27 (56.3)	26 (54.2)	
LVI+	98 (40)	17 (26.2)	0.040	22 (45.8)	12 (25)	0.033
PNI+	48 (19.6)	13 (20)	0.150	11 (22.9)	8 (16.7)	0.442
Lateral margin			0.461			0.749
0	202 (82.5)	56 (86.2)		43 (89.6)	45 (93.8)	
1	20 (8.2)	6 (9.2)		3 (6.3)	2 (4.2)	
x	23 (9.3)	3 (4.6)		2 (4.2)	1 (2.1)	
Poor, Un-differentiation	18 (7.3)	7 (10.8)	0.368	2 (4.2)	7 (14.6)	0.08
Timor size (cm), mean ± SD	4.02 ± 2.294	5.41 ± 3.404	0.000	4.62 ± 2.17	5.94 ± 2.56	0.008

**Table 3.** Clinical outcome

	Overall cohort			Matched cohort		
	Laparoscopic (n = 245)	Open (n = 65)	<i>p</i> value	Laparoscopic (n = 48)	Open (n = 48)	<i>p</i> value
OP time (min), median (range)	210 (102-425)	209 (96-595)	0.848	232 (115-415)	218 (100-585)	0.755
Blood loss (cc), median (range)	30 (10-1300)	50 (30-3110)	0.000	30 (30-300)	50 (30-1100)	0.000
Hospital (day), median (range)	11 (8-71)	14 (6-67)	0.000	12 (8-29)	14 (6-59)	0.093
Number of harvested LN, median (range)	22 (6-51)	23 (9-59)	0.871	21 (6-51)	21 (9-101)	0.823

**Table 3-1.** Post OP complication

	Laparoscopic (n = 48)		Open (n = 48)		p value	
	Number	Percentage	Number	Percentage		
Wound	2	4.2%	7	14.6%	0.08	
Ileus	4	8.3%	1	2.1%		
Pneumonia	0	0.0%	2	4.2%		
UTI	1	2.1%	2	4.2%		
Chyle leakage	2	4.2%	0	0.0%		
Diarrhea	0	0.0%	1	2.1%		
Sepsis	1	2.1%	2	4.2%		
Bladder leakage	0	0.0%	1	2.1%		
Bloody stool	1	2.1%	0	0.0%		
Post OP complication (cases)	9	18.8%	13	27.1%		0.331

**Fig. 2.** Primary outcome: overall survival.**Fig. 3.** Primary outcome: disease free survival.

OS rate, but factors such as pN stage, differentiation, perineural invasion, adjuvant chemotherapy, and margin did ( $p < 0.2$ ). Moreover, factors such as differentiation, perineural invasion, adjuvant chemotherapy, and margin appeared to influence the disease free survival rate ( $p < 0.2$ ). Multivariate Cox regression analysis showed that differentiation and adjuvant chemotherapy were significant factors in the 3-year OS rate, whereas differentiation, perineural invasion, and margin were significant in the 3-year disease-free survival rate (Table 4).

## Discussion

Approximately 10-20% of colon cancer cases present with locally advanced disease.<sup>14</sup> Several large randomized trials comparing laparoscopic and open colectomy excluded T4 tumors. In this study, we com-

pared the outcomes between laparoscopic and open colectomy in patients with T4 colon cancer at Taipei Veterans General Hospital.

A meta-analysis by Mauro et al. in 2022, including 21 retrospective cohort studies and 3 prospective cohort studies, comprising a total of 29,191 patients, with 11,170 who underwent laparoscopic colectomy and 18,021 who underwent open surgery, showed that laparoscopic colectomy for pT4 colon cancer improved clinical outcomes without compromising oncological outcomes. Additionally, their clinical outcomes demonstrated lower estimated intraoperative blood loss, equivalent results in terms of operation duration, a decrease in the mean length of hospital stay, lower rates of mortality and postoperative morbidity, and a lower complication rate with a higher rate of Clavien-Dindo grade III-IV complications after open surgery. Moreover, there was no significant difference in the radicality (R0) of surgical resection between laparoscopic

**Table 4.** Cox regression

Factors	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	3 years overall survival	<i>p</i> value	HR (95%)	<i>p</i> value	3 years disease free survival	<i>p</i> value	HR (95%)	<i>p</i> value
Colectomy		0.748				0.944		
Laparoscopic	80.7%				65.7%			
Open	70.2%				64.0%			
pT stage		0.468				0.328		
4a	74.7%				63.1%			
4b	85.7%				85.7%			
pN stage		0.169		0.114		0.414		
-	81.0%		1 (Reference)		69.2%			
+	71.1%		1.642 (0.888-3.037)		61.2%			
Side		0.820				0.415		
Right	76.8%				69.1%			
Left	74.6%				61.8%			
CEA		0.298				0.349		
< 5	75.6%				64.4%			
≥ 5	75.5%				65.2%			
Differentiation		<b>0.004</b>		<b>0.001</b>		<b>0.044</b>		0.022
Well, Moderate	77.6%		<b>1 (Reference)</b>		67.0%		<b>1 (Reference)</b>	
Poor, un-	55.6%		<b>4.384 (1.853-10.371)</b>		44.4%		<b>2.614 (1.148-5.592)</b>	
LVI		0.440				0.344		
-	83.4%				71.8%			
+	61.4%				52.3%			
PNI		<b>0.104</b>		0.050		<b>0.053</b>		0.034
-	78.7%		1 (Reference)		69.4%		<b>1 (Reference)</b>	
+	63.2%		1.959 (0.948-3.755)		46.3%		<b>1.967 (1.051-3.681)</b>	
Adjuvant chemotherapy		<b>0.018</b>		<b>0.005</b>		<b>0.094</b>		0.076
+	83.1%		<b>1 (Reference)</b>		68.8%		1 (Reference)	
-	52.3%		<b>2.451 (1.308-4.594)</b>		52.5%		1.720 (0.945-3.133)	
Margin		<b>0.131</b>		0.056		<b>0.014</b>		0.025
-	77.6%		1 (Reference)		68.2%		<b>1 (Reference)</b>	
+/x	50%		2.367 (0.977-5.735)		25%		<b>2.514 (1.120-5.642)</b>	

and open surgery, and no significant difference in the recurrence rate. Furthermore, a lower rate of margin positivity was observed in the laparoscopic group, and a higher proportion of patients in the laparoscopic group had more than 12 lymph nodes retrieved. However, the laparoscopic group demonstrated a smaller mean tumor size and a higher rate of pT4a tumors, whereas the open group had a higher frequency of pT4b tumors.

Our primary outcomes are consistent with the findings of the meta-analysis conducted by Mauro et al. After 1:1 propensity matching, the baseline characteristics of the two groups showed no significant differ-

ences, with the exception of smaller tumor size and higher rates of lymphovascular invasion in the laparoscopic group. Laparoscopic colectomy had comparable clinical and oncological outcomes to open colectomy, with less blood loss and potentially shorter hospital stays. Moreover, the oncological outcomes, including OS, disease-free survival, and number of harvested lymph nodes, between the two groups showed no significant differences.

However, the technical challenges of laparoscopic surgery in the context of T4 colon cancer cannot be overlooked. Tumors with extensive invasion into adjacent structures may necessitate meticulous dissec-

tion and advanced laparoscopic skills, which may lead to longer operative times and increased conversion rates to open surgery, particularly in T4b colon cancer. A retrospective study conducted by Thinh H. Nguyen showed that laparoscopic radical colectomy for patients with T4b colon cancer was both safe and feasible in selected patients, except for those requiring major and complicated reconstruction.<sup>15</sup> In our study, we did not perform subgroup analysis due to the small number of T4b colon cancer cases. Patients with T4b colon cancer had variable organ invasion and require careful patient selection, and it is essential to consider tumor characteristics to optimize surgical outcomes.

The limitations of this study include its single-center, retrospective design, and potential selection bias although propensity matching was used to reduce selection bias. The small sample sizes also decreased the statistical power.

## Conclusion

In our study, laparoscopic colectomy may be safer than open colectomy for T4 colon cancer, with comparable clinical and oncological outcomes. However, larger cohort studies or RCTs are needed to confirm the safety and efficacy of laparoscopic colectomy in T4 colon cancer.

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原 著

## 腹腔鏡及傳統開腹手術在 T4 大腸癌的預後比較

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**目的** 比較台北榮民總醫院腹腔鏡與開放性結腸切除術在 T4 期結腸癌病人的預後。

**方法** 這篇回顧性研究包含從 2014 年 9 月到 2019 年 12 月進行結腸癌手術的 4403 名病患。在排除後，310 例 T4 期結腸癌病人被納入研究，並進行傾向性評分匹配，最終腹腔鏡和開放手術組各有 48 例病人。主要結果包括 3 年整體存活率和無病存活率。

**結果** 傾向性評分匹配後，兩組病人的人口統計學特徵相當。腹腔鏡組的腫瘤大小較小，且淋巴血管侵犯率較高。相比開放組，腹腔鏡組的失血量較少，但手術時間、住院時間和淋巴結數量相似。腹腔鏡組的術後併發症較少，但沒有顯著差異。腹腔鏡和開放手術組的 3 年整體存活率分別為 80.7% 和 70.2%，而 3 年無病存活率分別為 65.7% 和 64%，均無統計學上顯著差異。多變量分析發現分化程度和輔助化療是整體存活的重要因素，而分化程度、神經周圍侵犯和手術邊緣是無病存活的重要因素。

**結論** 腹腔鏡結腸切除術對於 T4 期結腸病人是具有安全性，並且其臨床結果及預後與開放手術相當。需要更大規模的研究來確認。

**關鍵詞** 大腸癌、T4 期、腹腔鏡手術、微創手術、預後。