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ORIGINAL RESEARCH

Safety and Efficacy of Partial Omentectomy in Laparoscopic Distal Gastrectomy for pT3-T4a Stage Gastric Cancer

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Purpose: Partial omentectomy (PO) has been gradually applied in laparoscopic gastrectomy for gastric cancer (GC); however, its efficacy remains unclear. The purpose of this study was to assess the safety and efficacy of PO in laparoscopic distal gastrectomy for pT3-T4a stage GC.

Patients and Methods: From June 2019 to May 2021, 108 patients with pT3 or pT4a stage GC who underwent laparoscopic distal gastrectomy were retrospectively included and divided into the PO (n=58) and total omentectomy (TO, n=50) groups. The surgical outcomes, recurrence patterns and postoperative 2-year overall survival (OS) rates were compared between the PO and TO groups.

Results: The PO group showed a shorter operation time than the TO group (183.9±21.6 vs 197.6±22.7 min, p=0.002). Less intraoperative blood loss (155.3±113.0 vs 178.8±154.4 mL, p=0.336) and intraoperative complications (5.1% vs 12.0%, p=0.298) were also observed in the PO group than in the TO group, but the difference was not significant. The numbers of retrieved lymph nodes (LNs) and metastatic LNs, postoperative hospital stays and postoperative complications in the two groups were comparable (p>0.05). Moreover, the postoperative overall recurrence rates (25.9% vs 26.0%, p=0.987) and the 2-year OS rates (63.8% vs 65.4%, p=0.437) in the PO and TO groups were also comparable. TO was not an independent prognostic factor for GC patients (HR=0.806, p=0.443).

Conclusion: In laparoscopic distal gastrectomy, PO could provide better surgical outcomes and comparable oncological outcomes compared to TO for patients with pT3-T4a stage GC, suggesting that PO may be an acceptable surgical procedure for these patients.

Keywords: partial omentectomy, total omentectomy, gastric cancer, laparoscopic distal gastrectomy, surgical outcomes, oncological outcomes

Introduction

In 2018, a large-scale randomized controlled trial (JCOG1001) carried out by 57 hospitals in Japan confirmed that bursectomy did not provide a survival advantage over non-bursectomy, and D2 lymphadenectomy with total omentectomy (TO) should be regarded as a standard procedure for resectable gastric cancer (GC).[1] Henceforth, bursectomy is not recommended for GC surgery in the Japanese Gastric Cancer Treatment Guidelines (5th and 6th editions).[2,3] According to the current Japanese Gastric Cancer Treatment Guidelines 2021 (6th edition), partial omentectomy (PO), in which the greater omentum is dissected 3 cm away from the gastroepiploic vascular arcade, and the residual greater omentum on the side of the transverse colon is preserved, is recommended for T1-T2 stage GC, but TO is still recommended for T3 stage or deeper tumors.[3] Nevertheless, the clinical benefit of TO for T3 stage or deeper GC remains unclear because of the lack of large-scale randomized controlled trials.

Intra-abdominal seeding is the most common recurrent pattern after curative gastrectomy for GC, so TO is usually recommended in traditional radical gastrectomy in order to eliminate the microscopic cancer seeds.[4,5] However, as intra-abdominal organs and the abdominal wall are extensively covered with peritoneum, complete removal of the peritoneum from the abdominal cavity is theoretically impossible and operationally impractical. So the efficacy of TO on the

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prevention of peritoneal recurrence may be very limited.[6] In recent years, some retrospective studies have reported that TO not only increases operation time, intraoperative blood loss, and intraoperative or postoperative complications, but also provides no survival advantage over PO for patients with GC.[7–9] Especially for laparoscopic GC surgery, TO is time-consuming and can easily lead to intraoperative complications such as hemorrhage and spleen or colon injury.[10] Therefore, some surgeons choose PO instead of TO as a common surgical procedure in laparoscopic radical gastrectomy.[10–12] Nevertheless, the efficacy of PO in laparoscopic gastrectomy for GC remains unclear. In the light of the above consideration, we designed this study to assess the safety and efficacy of PO in laparoscopic distal gastrectomy for pT3-T4a stage GC.

Materials and Methods

Patients

A total of 185 patients underwent laparoscopic distal gastrectomy at The Affiliated Hospital of Southwest Medical University between June 2019 and May 2021 were retrospectively included. This retrospective study was approved by the Clinical Ethics Committee of The Affiliated Hospital of Southwest Medical University and complied with the Declaration of Helsinki, and written informed consent was obtained from all the patients. The inclusion criteria were as follows: (1) patients had a clear postoperative pathological diagnosis of primary GC, (2) patients belonged to pT3 or pT4a stage GC, and (3) patients received laparoscopic distal gastrectomy with D2 lymphadenectomy. The exclusion criteria were as follows: (1) patients belonged to pT1 or pT2 stage GC by postoperative pathologic diagnosis, (2) combined with other primary malignancies, (3) distant metastases or peritoneal dissemination, (4) pre-operative chemotherapy or radiotherapy, and (5) patients without complete clinicopathological data. Finally, 108 patients (58 patients with PO and 50 patients with TO) were included in this study after applying the aforementioned criteria. The flowchart of the patients included in this study is shown in Figure 1.

Surgical Management

All patients were diagnosed using preoperative gastroscopy and pathological biopsy, and preoperative contrast-enhanced computed tomography was performed to evaluate the clinical stage of the tumors. All patients underwent laparoscopic distal gastrectomy with D2 lymphadenectomy according to the Japanese Gastric Cancer Treatment Guidelines 2018 (5th edition).[2] Generally, for PO, the greater omentum was dissected 3 cm away from the gastroepiploic vascular arcade and the residual greater omentum on the side of the transverse colon was preserved (Figure 2A). In order to maintain the blood supply to the remnant omentum, the omental branches of the left gastroepiploic artery were preserved, but the right gastroepiploic vessels were divided at their roots. While for TO, the gastrocolic ligament was dissected from the transverse colon along the avascular plane (Figure 2B). The left and right gastroepiploic vessels were both divided at their roots. All operations were performed by an experienced GC surgeon, and as many perigastric lymph nodes (LNs) as possible were removed from the excised specimens after the operation. Postoperative chemotherapy (generally oxaliplatin with capecitabine) was recommended for all patients, and 89 (82.4%) patients completed postoperative chemotherapy at last.

Follow-Up

All patients were periodically followed up by outpatient visits or telephone interviews after surgery. Follow-up was performed every three months during the first two postoperative years and every six months during the subsequent two years. Tumor markers such as carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) were tested every three months, abdominal computed tomography was performed every six months, and endoscopic examination was performed annually. Tumor recurrence patterns were classified into four groups as follows: (1) local recurrence, defined as tumors in the remnant stomach or adjacent organs; (2) intra-abdominal seeding, including malignant ascites, recurrence of the peritoneum or omentum or mesentery, and Krukenberg's tumors; (3) hematogenous spread, defined as metastasis to a distant organ, such as the liver, lung, and bone; and (4) lymphatic spread, including tumors in the aortocaval area or in extra-abdominal LNs. Survival time was defined as the period from the date of surgery to the last contact time (June 2023) or the date of death. Among the 108 patients, 103 (95.4%) underwent complete follow-up.

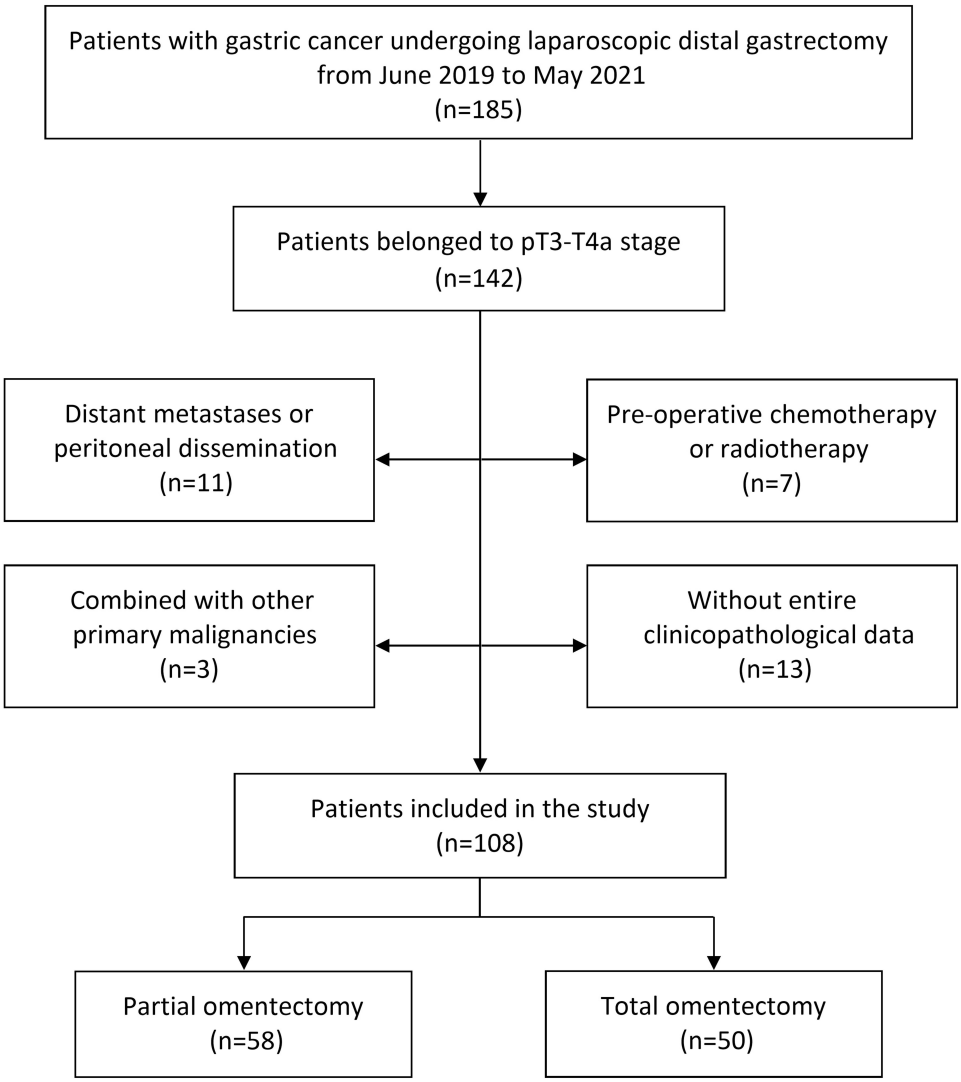

Figure 1 The flowchart of patients with gastric cancer included in this study.

Statistical Analysis

Data are expressed as the mean ± standard deviation for parametric continuous variables and as frequencies with percentages for nominal variables. All statistical analyses were performed using the SPSS software version 26.0. The Chi-square test or Fisher's exact test was used to analyze unordered categorical variables. Overall survival (OS) rates were calculated using the Kaplan-Meier method, and differences between groups were compared using the Log rank test. Univariate and multivariate survival analyses were performed using the Cox's proportional hazards regression model with conditional backward stepwise regression. A p value of <0.05 (2-sided) was defined to be statistically significant.

Results

Patients and Clinicopathological Features

Out of the entire study cohort (n=185), 77 patients were excluded for the following reasons: patients belonged to pT1 or pT2 stage GC (n=43), combined with other primary malignancies (n=3), pre-operative chemotherapy or radiotherapy (n=7), distant metastases or peritoneal dissemination (n=11), and incomplete clinicopathological data (n=13). Consequently, 108 patients (58 patients with PO and 50 patients with TO) were included in the analysis. As shown in Table 1, the clinicopathological factors, including gender, age, body mass index (BMI), American Society of

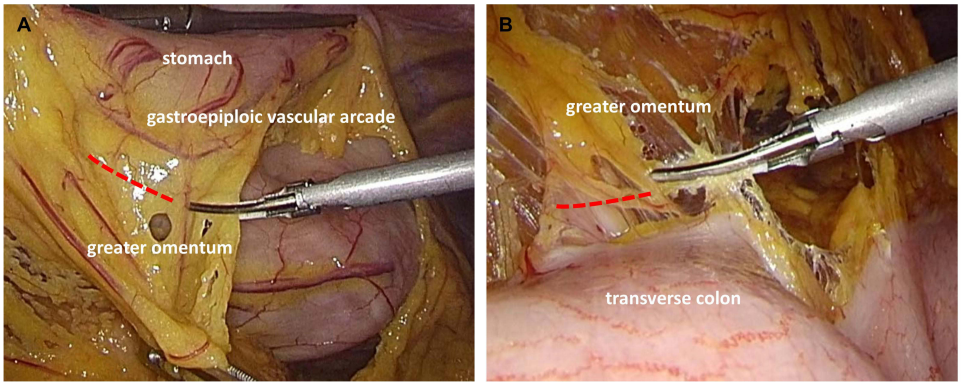

Figure 2 PO and TO in laparoscopic distal gastrectomy for gastric cancer. (**A**) PO, the greater omentum is dissected 3 cm away from the gastroepiploic vascular arcade and the residual greater omentum on the side of the transverse colon is preserved; (**B**) TO, the gastrocolic ligament is dissected from the transverse colon along the avascular plane.
Abbreviations: PO, partial omentectomy; TO, total omentectomy.

Anesthesiologists (ASA) score, CEA level, tumor size, macroscopic type, tumor differentiation, pT stage, pN stage, vascular invasion, nerve invasion, and postoperative chemotherapy, were all balanced between the PO and TO groups ($p>0.05$).

Table 1 Comparison of Clinicopathological Features Between PO and to Groups for GC Patients

	PO Patients (n=58)	TO Patients (n=50)	*P* value
Gender			0.406
Male	29 (50.0%)	29 (58.0%)	
Female	29 (50.0%)	21 (42.0%)	
Age (year)			0.252
≤60	26 (44.8%)	17 (34.0%)	
>60	32 (55.2%)	33 (66.0%)	
BMI			0.108
≤24	31 (53.4%)	19 (38.0%)	
>24	27 (46.6%)	31 (62.0%)	
ASA			0.553
I / II	28 (48.3%)	27 (54.0%)	
III / IV	30 (51.7%)	23 (46.0%)	
CEA (ng/mL)			0.333
≤6	25 (43.1%)	17 (34.0%)	
>6	33 (56.9%)	33 (66.0%)	
Tumor size (cm)			0.954
≤5	27 (46.6%)	23 (46.0%)	
>5	31 (53.4%)	27 (54.0%)	

(*Continued*)

Table 1 (Continued).

	PO Patients (n=58)	TO Patients (n=50)	*P* value
Macroscopic type			0.313
Bormmann I / II	28 (48.3%)	29 (58.0%)	
Bormmann III / IV	30 (51.7%)	21 (42.0%)	
Tumor differentiation			0.836
Well / moderately	29 (50.0%)	24 (48.0%)	
Poorly / undifferentiated	29 (50.0%)	26 (52.0%)	
pT stage			0.925
T3	25 (43.1%)	22 (44.0%)	
T4a	33 (56.9%)	28 (56.0%)	
pN stage			0.869
N0-1	20 (34.5%)	18 (36.0%)	
N2-3	38 (65.5%)	32 (64.0%)	
Vascular invasion			0.409
No	37 (63.8%)	28 (56.0%)	
Yes	21 (36.2%)	22 (44.0%)	
Nerve invasion			0.422
No	38 (65.5%)	29 (58.0%)	
Yes	20 (34.5%)	21 (42.0%)	
Postoperative chemotherapy			0.918
No	10 (17.2%)	9 (18.0%)	
Yes	48 (82.8%)	41 (82.0%)	

Abbreviations: PO, partial omentectomy; TO, total omentectomy; GC, gastric cancer; BMI, body mass index; ASA, American society of anesthesiologists; CEA, carcinoembryonic antigen.

Surgical Outcomes

As shown in Table 2, the PO group showed a shorter operation time than the TO group (183.9±21.6 vs 197.6±22.7 min, p=0.002). Less intraoperative blood loss (155.3±113.0 vs 178.8±154.4 mL, p=0.336) was also observed in the PO group than in the TO group, but without statistical difference. However, in terms of lymphadenectomy, the numbers of retrieved LNs (36.0±9.4 vs 34.2±8.9, p=0.327) and metastatic LNs (3.8±2.6 vs 4.1±2.8, p=0.531) were comparable between the two groups. There was no difference in postoperative hospital stays (10.2±1.6 vs 10.4±1.7 days, p=0.503) between the two groups. The intraoperative complications, including hemorrhage (3.4% vs 6.0%, p=0.661), spleen injury (1.7% vs 4.0%, p=0.595), and colon injury (0.0% vs 2.0%, p=0.463) were all comparable, but there was indeed a trend that the overall intraoperative complications in the PO group were lower than that in the TO group (5.1% vs 12.0%, p=0.298). The postoperative complications, including pulmonary complications (5.1% vs.10.0%, p=0.467), intra-abdominal hemorrhage (3.4% vs 2.0%, p=1.000), duodenal stump or anastomotic leakage (1.7% vs 4.0%, p=0.595), pancreatic fistula (1.7% vs 0.0%, p=1.000), intestinal obstruction (5.1% vs 2.0%, p=0.622), intra-abdominal infection (3.4% vs 2.0%, p=1.000), and the overall postoperative complications (20.6% vs 20.0%, p=0.929), were all comparable between the two groups.

Table 2 Comparison of Surgical Outcomes Between PO and to Groups for GC Patients

Surgical Outcomes	PO Patients (n=58)	TO Patients (n=50)	*P* value
Operation time (min)	183.9±21.6	197.6±22.7	0.002
Intraoperative blood loss (mL)	155.3±113.0	178.8±154.4	0.366
Number of retrieved LNs	36.0±9.4	34.2±8.9	0.327
Number of metastatic LNs	3.8±2.6	4.1±2.8	0.531
Postoperative hospital stay (days)	10.2±1.6	10.4±1.7	0.503
Intraoperative complications	3 (5.1%)	6 (12.0%)	0.298
Hemorrhage	2 (3.4%)	3 (6.0%)	0.661
Spleen injury	1 (1.7%)	2 (4.0%)	0.595
Colon injury	0 (0.0%)	1 (2.0%)	0.463
Postoperative complications	12 (20.6%)	10 (20.0%)	0.929
Pulmonary complications	3 (5.1%)	5 (10.0%)	0.467
Intraperitoneal hemorrhage	2 (3.4%)	1 (2.0%)	1.000
Duodenal stump or anastomotic leakage	1 (1.7%)	2 (4.0%)	0.595
Pancreatic fistula	1 (1.7%)	0 (0.0%)	1.000
Intestinal obstruction	3 (5.1%)	1 (2.0%)	0.622
Intra-abdominal infection	2 (3.4%)	1 (2.0%)	1.000

Abbreviations: PO, partial omentectomy; TO, total omentectomy; GC, gastric cancer; LNs, lymph nodes.

Tumor Recurrence Outcomes

As shown in Table 3, tumor recurrence was recorded in 15 (25.9%) patients in the PO group and 13 (26.0%) patients in the TO group, and there was no difference between the two groups (p=0.987). The recurrence patterns in the two groups

Table 3 Comparison of Recurrence Patterns Between PO and to Groups for GC Patients

Recurrence Patterns	PO Patients (n=58)	TO Patients (n=50)	*P* value
Overall recurrence	15 (25.9%)	13 (26.0%)	0.987
Local recurrence	0 (0.0%)	1 (2.0%)	0.463
Intra-abdominal seeding	4 (6.9%)	5 (10.0%)	0.730
Ascites	1 (1.7%)	0 (0.0%)	1.000
Peritoneum or omentum or mesentery	3 (5.2%)	4 (8.0%)	0.702
Ovary	0 (0.0%)	1 (2.0%)	0.463
Hematogenous spread	9 (15.5%)	6 (12.0%)	0.781
Liver	6 (10.3%)	3 (6.0%)	0.500
Lung	2 (3.4%)	3 (6.0%)	0.661
Bone	1 (1.7%)	0 (0.0%)	1.000
Lymphatic spread	2 (3.4%)	1 (2.0%)	1.000

Abbreviations: PO, partial omentectomy; TO, total omentectomy; GC, gastric cancer.

were also similar, including local recurrence (0.0% vs 2.0%, p=0.463), intra-abdominal seeding (6.9% vs 10.0%, p=0.730), hematogenous spread (15.5% vs.12.0%, p=0.781), and lymphatic spread (3.4% vs 2.0%, p=1.000), and they were all comparable between the two groups.

Survival Outcomes

Overall, the median follow-up time was 27.0 months (range 7.0 to 48.0 months), and 103 (95.4%) patients had complete follow-up. According to the Kaplan-Meier method and Log rank test, the 2-year OS rates of the PO and TO groups were comparable (37/58 vs 32/50, 63.8% vs 65.4%, p=0.437), with the median survival time 32.8 and 35.1 months, respectively. In the subgroup analysis, the 2-year OS rates of the PO and TO groups for pT3 (17/25 vs.15/22, 68.0% vs 68.2%, p=0.737) and pT4 (20/33 vs 17/28, 60.6% vs 63.1%, p=0.425) stage patients were comparable, as shown in Figure 3.

Moreover, the Cox proportional hazards model was used to evaluate the prognostic significance of omentectomy for GC patients. As shown in Table 4, the Cox proportional hazards model for multivariate analysis revealed that tumor differentiation (well and moderately vs poorly and undifferentiated, HR=2.009, p=0.043) and pN stage (pN0-1 vs pN2-3, HR=3.781, p=0.003) were independent prognostic factors for GC patients. However, omentectomy (PO vs TO, HR=0.806, p=0.443) combined with clinicopathological factors, such as gender, age, BMI, ASA, CEA, tumor size, macroscopic type, pT stage, vascular invasion, nerve invasion, and postoperative chemotherapy, were not significant independent prognostic factors for GC according to the multivariate Cox regression analysis (p>0.05), although some of them were closely associated with OS in the univariate analysis.

Discussion

According to the latest Japanese Gastric Cancer Treatment Guidelines 2021 (6th edition), TO with D2 lymphadenectomy is essential in standard gastrectomy for T3 or deeper tumors.[3] However, until now, there is still a lack of large-scale randomized controlled trials to verify the survival benefit of TO for GC patients. Some retrospective studies have reported that TO increases operation time, intraoperative blood loss, and intraoperative or postoperative complications, but provides no oncological advantage over PO for GC patients.[7–10] Therefore, PO is becoming a common surgical procedure for surgeons in managing GC, particularly in laparoscopic GC surgery.

The greater omentum is an important intra-abdominal organ with the largest peritoneal fold and occupies an important position in peritoneal defense mechanisms. This is achieved through its innate immune function, high absorptive ability, and capacity to adhere to adjacent structures to seal off intra-abdominal lesions.[13,14] Therefore, in managing patients with intra-abdominal malignancies, omentectomy should be performed cautiously, which indicates whether there is an exact benefit of omentectomy and the amount of omentum that needs to be removed. Radical gastrectomy for GC requires a proper extent of lymphadenectomy and a negative resection margin. The PO does not violate the principle of radical surgery because LNs on the greater omentum are mainly distributed around the gastroepiploic vascular arcade, and LNs

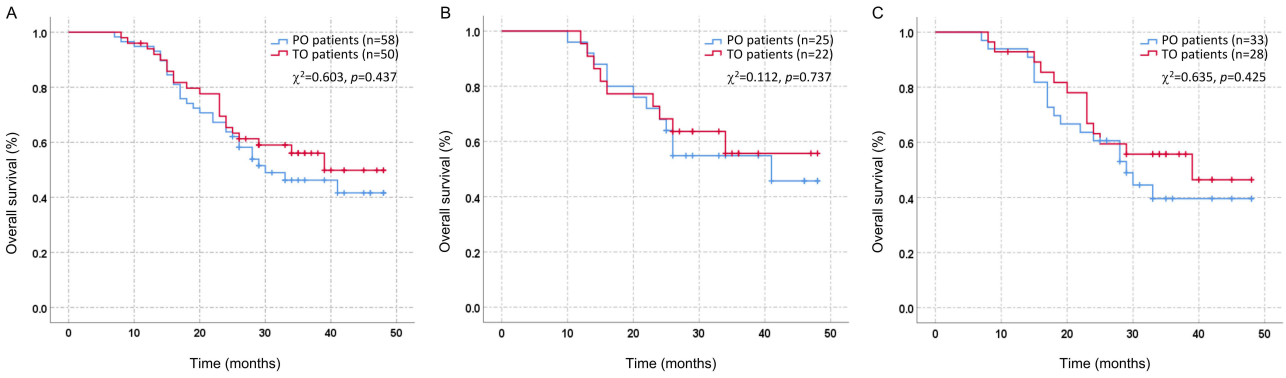

Figure 3 Comparison of over survival between PO and TO patients by Kaplan-Meier method and Log rank test. (**A**) pT3 and pT4a stage patients; (**B**) pT3 stage patients; (**C**) pT4a stage patients.
Abbreviations: PO, partial omentectomy; TO, total omentectomy.

Table 4 Univariate and Multivariate Analyses of the Clinicopathologic Factors by Cox Regression Model for the Survival of GC Patients

Factors	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Gender (Male / Female)	0.906 (0.524–1.566)	0.723	–	–
Age (≤60 years />60 years)	0.926 (0.532–1.612)	0.787	–	–
BMI (≤24 />24)	0.819 (0.475–1.413)	0.474	–	–
ASA (I–II / III–IV)	0.635 (0.366–1.103)	0.107	–	–
CEA (≤6 ng/mL />6 ng/mL)	0.890 (0.510–1.552)	0.680	–	–
Tumor size (≤5 cm />5 cm)	2.049 (1.155–3.633)	0.014	1.138 (0.586–2.211)	0.703
Macroscopic type (Bormmann I–II / III–IV)	1.349 (0.782–2.327)	0.282	–	–
Tumor differentiation (Well, moderately/Poorly, undifferentiated)	2.299 (1.297–4.076)	0.004	2.009 (1.023–3.946)	0.043
pT stage (T3/T4a)	1.186 (0.681–2.064)	0.547	–	–
pN stage (N0-1/N2-3)	5.465 (2.453–12.174)	<0.001	3.781 (1.571–9.097)	0.003
Vascular invasion (No/Yes)	0.958 (0.550–1.670)	0.881	–	–
Nerve invasion (No/Yes)	1.085 (0.623–1.889)	0.773	–	–
Chemotherapy (No/Yes)	0.473 (0.251–0.892)	0.021	0.509 (0.244–1.060)	0.071
Omentectomy (PO/TO)	0.806 (0.464–1.399)	0.443	–	–

Note: –: not enter the regression model.
Abbreviations: PO, partial omentectomy; TO, total omentectomy; GC, gastric cancer; BMI, body mass index; ASA, American society of anesthesiologists; CEA, carcinoembryonic antigen; HR, hazard ratio; CI, confidence interval.

along the arcade can be completely removed by dissecting 3 cm away from the gastroepiploic vascular arcade in the PO. Thus, as shown in our study, the number of retrieved or metastatic LNs were comparable between the PO and TO groups (p>0.05), which was consistent with a previous report.[8] Considering the assumption that TO can reduce intra-abdominal recurrence, we believe that its efficacy is very limited. Because if there are cancer seeds in the great omentum, that means the tumor is classified as stage IV, and non-surgical treatments, such as systemic chemotherapy, targeted therapy, or hyperthermic intraperitoneal chemotherapy, should be selected for these patients.[15–17] Moreover, complete removal of the peritoneum from the abdominal cavity is theoretically impossible and operationally impractical because of the widely distributed peritoneum. Jongerius et al pointed out that metastatic carcinoma in the greater omentum was associated with non-radical features, and surgery was futile for such patients.[18] A large-scale randomized controlled trial also indicated that surgery should be eliminated for GC patients who had micrometastatic seeds in abdominal cavity, and these patients should treated by systemic chemotherapy rather than surgical intervention.[19]

Recently, several clinical studies on laparoscopic gastrectomy for GC have been reported, and two well-designed randomized control trials (CLASS-01 and KLASS-02) have demonstrated that laparoscopic distal gastrectomy could lead to fewer surgical complications and non-inferiority in patients' survival compared to open surgery in advanced GC.[20,21] So laparoscopic surgery has become one of the most popular surgical procedures for GC surgery. Nevertheless, TO in laparoscopic GC surgery is technically a more demanding procedure than PO, calling for a wider extent of resection, resulting in longer operation time and a higher risk of intraoperative complications, such as hemorrhage and spleen or colon injury. Particularly for overweight patients, manipulating the bulky greater omentum during laparoscopic surgery is even more challenging for surgeons. Murakami et al pointed out that PO can reduce operation time and intraoperative blood loss compared to TO.[22] Lee et al reported that PO was associated with fewer intraoperative and postoperative complications.[11] Indeed, just as the results of our study, the PO group showed significantly shorter operation time than

the TO group ($p<0.05$) and less intraoperative blood loss as well as intraoperative complications were also observed in the PO group.

In terms of oncological outcomes, Lee et al reported that no significant difference in relapse-free survival and peritoneal seeding-free survival was observed between the PO and TO groups.[12] Seo et al maintained that the tumor recurrence rates and patterns were similar, and the 5-year OS rates and relapse-free survival rates were comparable between the PO and TO groups.[8] In our study, as shown in Table 3, tumor recurrence rates and patterns for the two groups were also similar ($p>0.05$), and the 2-year OS rates of the PO and TO groups were comparable (63.8% vs 65.4%, $p>0.05$). Moreover, the Cox proportional hazards model for multivariate analysis revealed that tumor differentiation (well and moderately vs poorly and undifferentiated) and pN stage (pN0-1 vs pN2-3), but not omentectomy (PO vs TO), were independent prognostic factors for GC patients. These results were consistent with the results of our previously published meta-analysis and suggested that PO might be an oncologically safe procedure for GC patients.[23]

Our study had limitations. Firstly, the retrospective nature of our single-center study may have limited the efficacy of the results. Secondly, due to the shorter follow-up time, only 2-year OS rates were analyzed, and the survival outcome over a longer period still needs to be observed. Therefore, large-scale prospective multicenter studies are required to address this issue. Expectantly, a large-scale randomized controlled Phase III trial to evaluate PO for patients with advanced GC (JCOG1711) is ongoing in Japan, and the results of this study may confirm PO as a new standard for GC surgery in the future.[24]

Conclusion

Despite these limitations, this study indicates that PO could provide better surgical outcomes and comparable oncological outcomes compared to TO for patients with pT3-T4a stage GC in laparoscopic distal gastrectomy, suggesting that PO may be an acceptable surgical procedure for these patients.

Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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