Original Article

The exploration of surgery and survival prediction in patients with peritoneal metastasis from gastric adenocarcinoma based on the SEER database

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Background: As one of the most common diseases in terms of cancer-related mortality worldwide, gastric adenocarcinoma (GA) frequently develops peritoneal metastases (PMs) in advanced stages. Systemic therapy or optimal supportive care are recommended for advanced GA; however, patients frequently develop drug resistance. Surgical resection is not recommended for stage IV patients, and there have been some controversies regarding the role of it in GA patients with PMs. The aim of the study was to preliminarily evaluate the possible effect of surgical treatments on patients with only PMs from GA.

Methods: Data were collected from the Surveillance, Epidemiology and End Results (SEER) database (year 2000–2022). A propensity score matching (PSM) was performed to reduce the influence of selection bias and confounding variables on comparisons. Then Cox proportional hazard regression, Kaplan-Meier analysis, and log-rank test were performed to assess the efficacy of surgical treatment in patients with PMs from GA.

Results: A total of 399 patients diagnosed with PMs from GA were enrolled for our analysis, of which, 180 (45.1%) patients did not receive surgery and 219 (54.9%) patients received surgery. Multivariate Cox regression analysis before PSM indicated higher rates of overall survival (OS) outcome for patients who had received surgery [hazard ratio (HR) =0.4342, 95% confidence interval (CI): 0.3283–0.5742, P<0.001]. After PSM, a total of 172 patients were enrolled, with 86 in each group. Multivariate Cox analysis showed that surgery was the independent factor reflecting patients' survival (HR =0.4382, 95% CI: 0.3037–0.6324, P<0.001). Subgroup survival analysis revealed that surgery may bring advantages to patients with grades I–IV, stages T1–T4, stage N0, and tumor size less than 71 mm (P<0.05). We also found that the OS of chemotherapy patients who had undergone surgery was better than that of chemotherapy patients who had not undergone surgery (P<0.01).

Conclusions: Based on the SEER database, surgery has better OS for patients only with PMs from GA. Patients without lymph node metastasis and those who received chemotherapy before may benefit from surgery. These specific groups of patients may have surgery as an option to improve the prognosis.

Keywords: Gastric adenocarcinoma (GA); peritoneal metastasis (PM); Surveillance, Epidemiology and End Results (SEER); propensity score matching (PSM); surgery

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Introduction

With more than one million new cases each year, gastric cancer (GC) is the fifth most common malignancy all over the world (1). There are three main types of stomach cancer: gastric adenocarcinoma (GA), non-Hodgkin lymphoma, and gastrointestinal stromal tumors. Among all of them, about 95% are GAs (2). Peritoneal metastasis (PM) is a common form of rapidly progressing GA (3), accounting for about 30% of the diseased population (4). PMs are strongly associated with treatment failure and surgical recurrence of GC. The prognosis of patients with PMs from GA remains dismal, with a median survival of less than 1 year (5).

For GA patients with PMs, systemic chemotherapy or optimal supportive care is recommended by current National Comprehensive Cancer Network (NCCN) guidelines (6). However, although chemotherapy can achieve remission, resistance usually develops within 6 months because of the plasma-peritoneal barrier between mesothelial cells and mesangial capillaries (7,8). Surgery is usually not the first option for these patients because of the poor prognosis. Whether surgery can bring benefits to GA patients with PMs remains unknown. Several prior studies have documented that palliative gastric gastrectomy plays a positive role in improving survival in patients with PMs from GC (9). Another study shows that for GC patients with PMs whose abdominal cytology is negative after translational therapy, radical surgery can be beneficial (10,11). GC patients with PMs who have good efficacy of preoperative treatment and negative abdominal cytology may benefit from radical surgery on an elective basis (12). A previous study also suggested that chemotherapy plus surgery may have a positive effect on the overall survival (OS) of GC patients undergoing PMs (13). However, in a clinical study by Mezhir *et al.*, no survival benefit was found in patients with negative cytology who underwent gastrectomy compared to those who did not (median OS 2.5 *vs.* 2.3 years, P=0.76) (14).

These studies suggest that the significance and indications for surgery in GC patients with PMs remain controversial. The surgical efficacy of different lymph node staging, concomitant therapeutic modalities such as chemo-radiotherapy, age group, and clinical stage has not been fully established. High-quality registered large-sample surgical data analysis based on modern radiologic staging and up-to-date pathologic classifications is needed to determine the therapeutic efficacy of surgical resection in different GA patients with PMs. Thus, in this study, we preliminarily evaluated the possible treatment efficacy of surgical resection in patients with PMs of GA by using propensity score matching (PSM) analysis to explore the data from the Surveillance, Epidemiology and End Results (SEER) database. We present this article in accordance with the STROBE reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-886/rc).

Highlight box

Key findings

- Our findings based on the Surveillance, Epidemiology and End Results (SEER) database suggest that surgery has better overall survival in patients with gastric adenocarcinoma (GA) who develop only peritoneal metastasis (PMs); and is associated with better survival in patients without lymph node metastasis and those who received chemotherapy before.

What is known and what is new?

- The use of surgery for stage IV patients is currently not widely agreed upon by experts and is clinically controversial.
- GA patients with only PMs probably have the option to have surgery at the primary site to improve survival.

What is the implication, and what should change now?

- Based on the SEER data, this research was conducted to focus on the special group of GA patients who had only PMs without liver, brain, bone and lung metastases. Although surgery is still not recommended for patients who develop PMs, the study initially found the possible benefits of surgical treatment for this special group of patients, providing some reference data for clinicians to make decisions on the treatment of this group of patients.

Methods

Cohort selection

The patients in our study were sourced from the SEER database, which includes cancer incidence information from 17 registries in the United States. The following selection criteria were used to obtain patients with PMs from GA: (I) the primary site of the malignant tumor was limited to "stomach"; (II) evidence of PMs (identified through code 40 of the variable "CS Mets at Dx"); (III) no evidence of liver, lungs, bone, or brain metastases; (IV) the pathological subtype was GA, including 8,140/3 [adenocarcinoma, no otherwise specific (NOS)], 8,144/3 (adenocarcinoma, intestinal type), 8,211/3 (tubular adenocarcinoma), 8,255/3 (adenocarcinoma, mixed subtype), 8,480/3 (mucinous adenocarcinoma), 8,481/3 (secretory mucinous adenocarcinoma), 8,490/3 (signet

ring cell carcinoma), and 8,574/3 (adenocarcinoma with neuroendocrine differentiation); (V) the primary site of surgery was "stomach", including types: "Radical gastrectomy, in continuity with the resection of other organs", "Gastrectomy, NOS", "Antrectomy, lower (distal-less than 40% of stomach)", "Lower (distal) gastrectomy (partial, subtotal, hemi-)", "Upper (proximal) gastrectomy (partial, subtotal, hemi-)", "Total gastrectomy", "Partial or subtotal gastrectomy", "Gastrectomy with a resection in continuity with the resection of other organs", "Partial or subtotal gastrectomy, in continuity with the resection of other organs", "Near total or total gastrectomy, in continuity with the resection of other organs", "Radical gastrectomy, in continuity with the resection of other organs", "Surgery, NOS". The exclusion criteria were: (I) diagnosed age <20 years; (II) 'surgery to primary cite' code=22, 23, 27 (see Table S1 for the specific modalities of the surgery corresponding to code); (III) unknown features; (IV) survival months =0 months; and (V) non-malignant primary indicators. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Since publicly available data were used, ethical approval was not required in our study.

Data collection

We used SEER*Stat software version 8.4.1 to retrieve data (SEER Study Data, 17 registry, November 2022 sub-2000-2022) for our study. The collected data for all included patients covered: age, sex, race, year of diagnosis, primary tumor site, histological type, T stage, N stage, tumor size, surgery to the primary site, radiation, chemotherapy, and survival outcome. In this study, we used X-tile software to group patients with different tumor sizes and determine the optimal cutoff values. All data in our research were transferred into binary or categorical variables to comply with the specifications. Age was categorized into five age groups: 20–39, 40–59, 60–79, and ≥80 years; sex into male and female; race into White, Black, and others; year of diagnosis into 2010–2012, 2013–2014, and 2015 up to now; tumor size into 2–43, 44–70, and 71–245 mm; grade into grades I–II and grades III–IV; histological type into eight categories: adenocarcinoma NOS, adenocarcinoma intestinal type, tubular adenocarcinoma, adenocarcinoma with mixed subtypes, mucinous adenocarcinoma, mucin-producing adenocarcinoma, signet ring cell carcinoma, adenocarcinoma with neuroendocrine differentiation; T stage into T1–T2 and T3–T4; N stage into four categories: N0, N1, N2, and N3; surgery, radiation, and chemotherapy were divided into "No" or "Yes" group.

Statistical analysis

This study employed *t*-test or Chi-square test as thresholds to determine the significance of differences. Single-factor and multiple-factor Cox regression analyses were conducted to examine the relationships between variables with survival by hazard ratio (HR) and 95% confidence interval (CI). Kaplan-Meier method was used to plot survival curves, and the log-rank test was performed to compare survival outcomes. A 1:1 PSM was employed to match patients in the surgical and non-surgical groups, in order to reduce the impact of baseline differences in demographics and clinical characteristics on outcomes. The principle of PSM is to balance confounding factors in non-randomized studies in a similar manner to randomization, thereby reducing selection bias. Matching factors included sex, age, race, stage, T stage, N stage, grade, chemotherapy, and radiation. A ratio of 1 and a caliper value of 0.05 were used. All analyses were performed via R software (version 4.2.2) using "survival", "survminer", "Matching", "tableone", and "ggplot2" R-packages. A two-sided P value <0.05 was considered statistically significant.

Results

Patient characteristics

We retrieved data from "SEER study Data, 17 registry, November 2022 sub-2000-2022", and after going through the inclusion and exclusion criteria mentioned in the methods section, we finally included 399 patients with GA who developed PMs in a total of 6 years from 2010–2015 (*Figure 1*, Figure S1), without evidence of brain, liver, lungs, distant lymph nodes, or bone metastases. There were 219 patients in the surgery group and 180 patients in the non-surgery group (*Table 1*). Differences between the two groups (surgery and non-surgery), including T stage, N stage, chemotherapy, and tumor size were significant. Patients in the non-surgery group had a higher proportion of receiving chemotherapy (77.2% *vs.* 65.8%). Meanwhile, patients in this group tended to have lower T stage (T1–T2 stage, 29.4% *vs.* 6.4%; T3–T4 stage, 70.6% *vs.* 93.6%), N stage (N0 stage, 48.9% *vs.* 16.0%; N3 stage, 4.4% *vs.* 46.6%) and smaller tumor size (2–43 mm, 52.2% *vs.* 27.4%; 71–245 mm, 18.9% *vs.* 36.5%). This suggests that surgery is

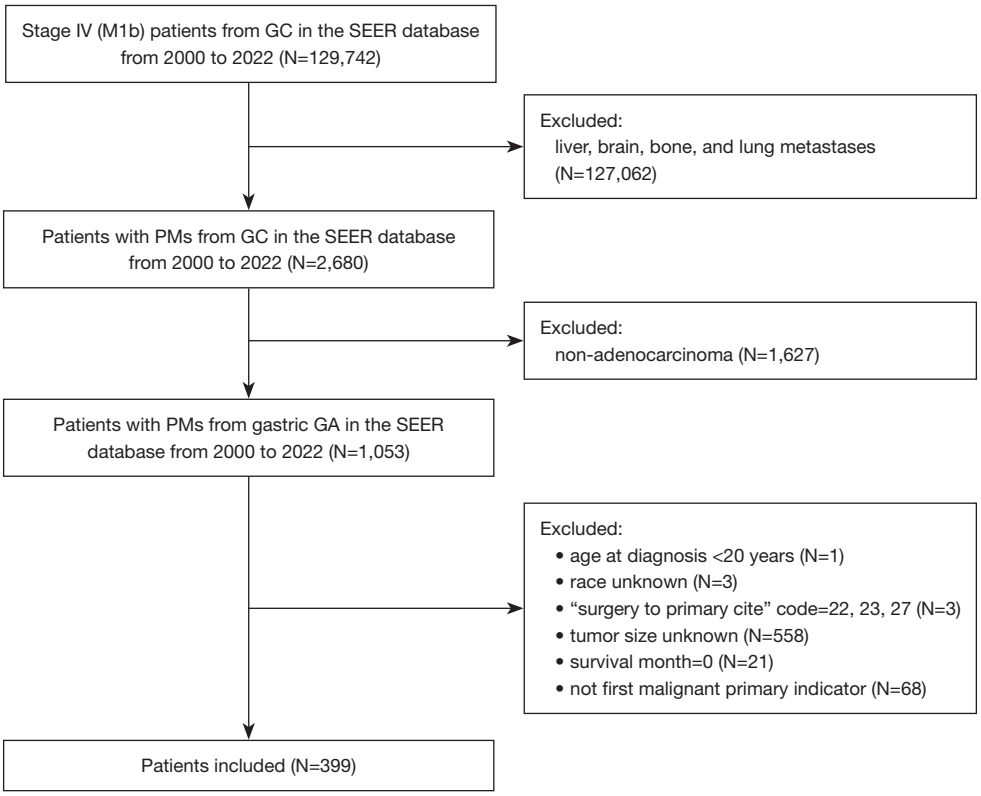


Figure 1 Flowchart of the study. GC, gastric cancer; SEER, Surveillance, Epidemiology and End Results; PM, peritoneal metastasis; GA, gastric adenocarcinoma.

typically used in clinical practice for patients with higher T and N stages.

Impact of different factors on patient survival

From the univariate Kaplan-Meier (K-M) survival curve and log-rank test, age (P<0.001), radiation (P=0.03), chemotherapy (P<0.001), and surgery (P<0.001) can be defined as risk factors influencing the prognosis of GA with PMs. The K-M survival curve was established and the log-rank test results reflected that the factors of age ≥80 years, no radiation, no chemotherapy, and no surgery were relevant to poor survival time (*Figure 2*).

Univariate and multivariate Cox regression results

Consistent with the K-M analysis, the univariate Cox regression analysis showed that the age ≥80 years, N2 stage, surgery, radiation, and chemotherapy were relevant to the patients' prognosis and survival. Furthermore, multivariate Cox regression analysis revealed that radiation, chemotherapy, and surgery were independent factors reflecting patient survival (*Table 2*).

Group

Considering the clinical controversy surrounding the benefits of surgery, a PSM analysis was conducted between the non-surgical and surgical patient groups to mitigate the impact of bias. The matched patients, as shown in *Table 3*, included 192 individuals who underwent evaluation, with 86 in each group. Baseline characteristics, except for the N stage, showed no significant differences. In the matched population, a multivariate Cox regression analysis was employed to assess factors influencing patient survival, revealing a substantial benefit for patients from surgery (HR =0.4382, 95% CI: 0.3037–0.6324, P<0.001, *Table 4*). While radiation and chemotherapy also showed associations with survival, what is noteworthy is that the analysis after PSM was performed to mitigate the impact of selection bias. Therefore, the focus was on the significant factors of surgery in relation to patient survival.

Table 1 Characteristics of 399 patients in surgery and non-surgery groups before PSM

Items	Non-surgery (N=180)	Surgery (N=219)	P value
Age (years)			0.055
20–39	15 (8.3%)	16 (7.3%)	
40–59	71 (39.4%)	78 (35.6%)	
60–79	67 (37.2%)	107 (48.9%)	
≥80	27 (15.0%)	18 (8.2%)	
Sex			0.48
Male	101 (56.1%)	114 (52.1%)	
Female	79 (43.9%)	105 (47.9%)	
Race			0.13
White	129 (71.7%)	147 (67.1%)	
Black	22 (12.2%)	20 (9.1%)	
Others	29 (16.1%)	52 (23.7%)	
Grade			0.94
I–II	31 (17.2%)	36 (16.4%)	
III–IV	149 (82.8%)	183 (83.6%)	
T stage			<0.001***
T1–T2	53 (29.4%)	14 (6.4%)	
T3–T4	127 (70.6%)	205 (93.6%)	
N stage			<0.001***
N0	88 (48.9%)	35 (16.0%)	
N1	76 (42.2%)	38 (17.4%)	
N2	8 (4.4%)	44 (20.1%)	
N3	8 (4.4%)	102 (46.6%)	
Radiation			0.49
No	150 (83.3%)	189 (86.3%)	
Yes	30 (16.7%)	30 (13.7%)	
Chemotherapy			0.02*
No	41 (22.8%)	75 (34.2%)	
Yes	139 (77.2%)	144 (65.8%)	
Tumor size (mm)			<0.001***
2–43	94 (52.2%)	60 (27.4%)	
44–70	52 (28.9%)	79 (36.1%)	
71–245	34 (18.9%)	80 (36.5%)	

*, P<0.05, ***, P<0.001, Student's *t*-test. PSM, propensity score matching.

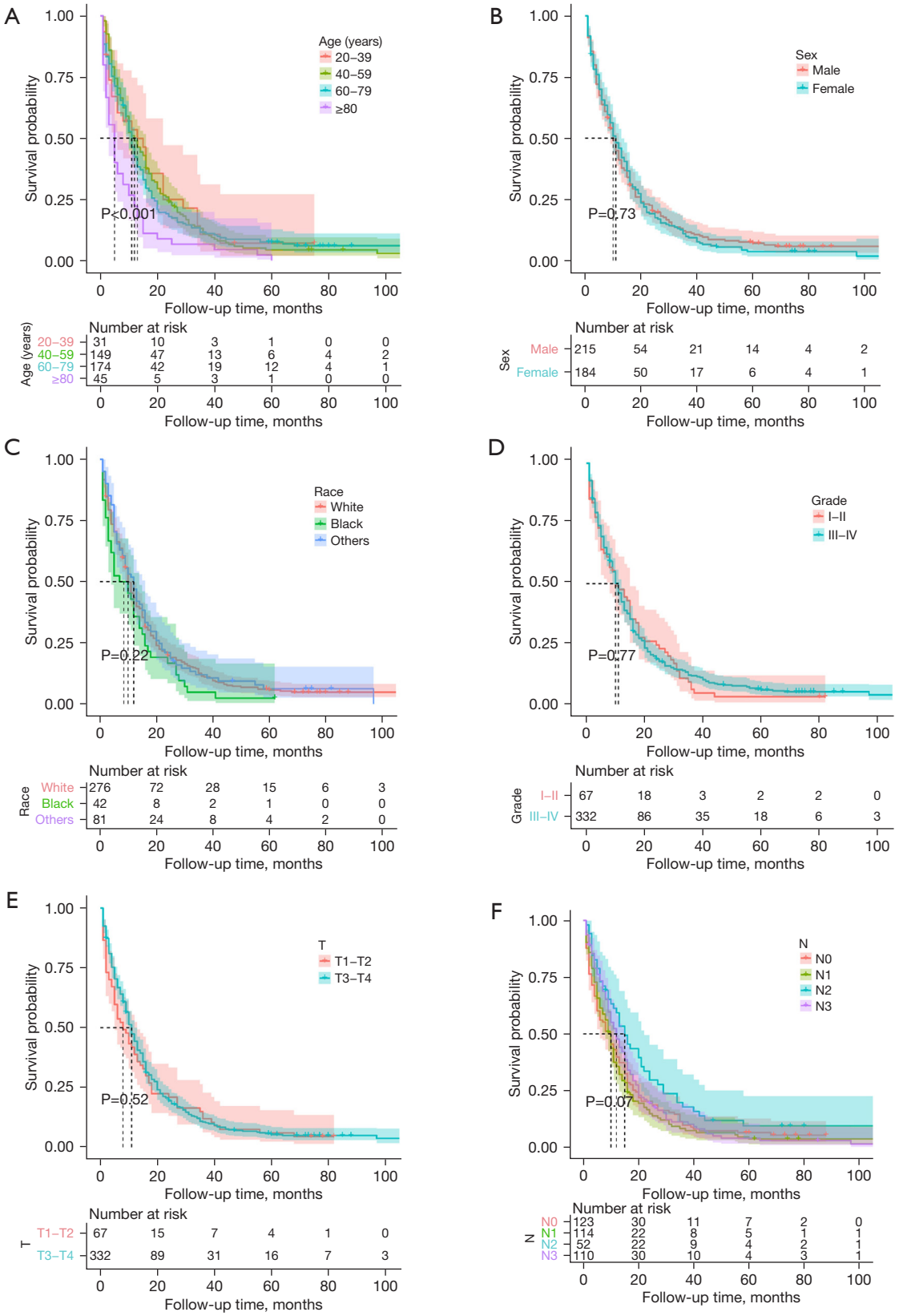
Subgroup analysis after PSM

To assess the effect of surgery on different grades or stages of patients, we categorized the patients into grades I–II, grades III–IV, as well as T1–T2, T2–T3 stages (*Figure 3*), and N0, N1, N2, and N3 stages (*Figure 4*) for subgroup analysis. The K-M curves showed that surgery was associated with longer survival in patients with PMs of GA in grades I–II (HR =0.393, 95% CI: 0.183–0.847, P=0.002), grades III–IV (HR =0.579, 95% CI: 0.404–0.829, P=0.002), T1–T2 (HR =0.482, 95% CI: 0.228–1.019, P=0.04), T3–T4 (HR =0.541, 95% CI: 0.378–0.775, P<0.001), and N0 (HR =0.411, 95% CI: 0.229–0.739, P<0.001) stages, whereas surgery was not an independent factor associated with survival in patients with N1 (HR =0.692, 95% CI: 0.431–1.111, P=0.12), N2 (HR =0.576, 95% CI: 0.206–1.607, P=0.21) and N3 (HR =0.557, 95% CI: 0.185–1.801, P=0.33) stages. Also, in patients who received chemotherapy (HR =0.574, 95% CI: 0.392–0.840, P=0.003), surgery was a factor associated with better survival. In contrast, in patients who received radiotherapy (HR =0.848, 95% CI: 0.381–1.887, P=0.67), surgery was not significantly associated with survival. Finally, we found that surgery was also associated with better survival in patients with tumor size 2–43 mm (HR =0.544, 95% CI: 0.351–0.844, P=0.003) and 44–70 mm (HR =0.458, 95% CI: 0.239–0.875, P=0.005), except 71–245 mm (HR =0.524, 95% CI: 0.251–1.094, P=0.07) mm groups (*Figure 5*). For patients without lymph node metastasis, surgical resection may bring a certain benefit to survival. It is worth noting that surgery is not a recommended treatment option for patients with tumor sizes larger than 71 mm.

Discussion

Our findings preliminarily suggest that surgery may have a role in improving the survival of patients with GA who develop only PMs and is associated with better survival in patients with different grades, T stages, N0 stages, and tumor sizes less than 71 mm. Particularly, patients without lymph node metastasis could have a certain benefit from surgery, and patients who received chemotherapy before also could benefit from surgery.

The former studies have shown that surgery has negative effects on systemic therapy, such as discontinuing systemic therapy, lowering immune function, and impairing tolerance to postoperative chemotherapy (15), and surgery is not recommended as first-line treatment for patients



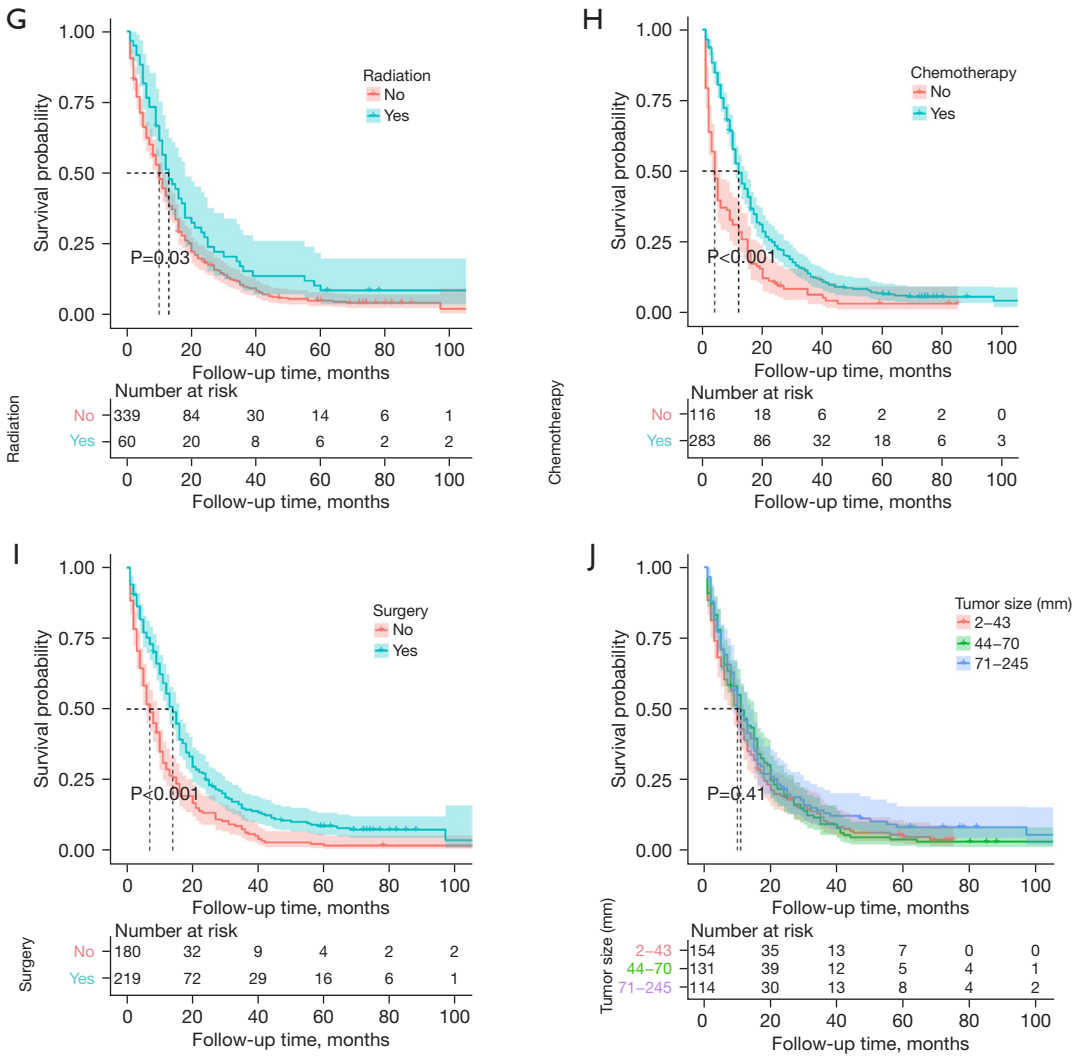


Figure 2 Kaplan Meier survival curve in GA patients with PMs. (A) Age; (B) sex; (C) race; (D) grade; (E) T stage; (F) N stage; (G) radiation; (H) chemotherapy; (I) surgery; (J) tumor size. GA, gastric adenocarcinoma; PM, peritoneal metastasis.

with metastases. However, based on our findings, surgery is probably a beneficial option for GA patients who only developed PMs. The possible explanation is that, surgery can lower the burden of the tumor and reduce the risk of metastasis and recurrence (16). Additionally, as shown in the other study, PMs' symptoms including ascites, bloating, and abdominal pain can be treated with surgery (17).

There are several uncertainties in the surgical benefits among GC patients with different baseline characteristics in the former studies (18). When it comes to lymph node metastases, a previous study indicated that GC with lymph node metastasis is typically considered unresectable and carries a high risk of recurrence (19). Studies also indicated that for PMs of GA with extensive lymph node metastasis, surgery combined with lymph node dissection or resection is clinically recommended (20,21). In our study, patients without lymph node metastasis may benefit from surgery. Furthermore, large tumors tend to have lymph node metastasis, as previously reported (22), and our study suggests that surgery is suitable for PMs of GA with a tumor size less than 71 mm. By altering miRNA expression, studies have found that surgery also increases survival in individuals with advanced PMs who have undergone chemotherapy (23), which is in line with our findings. These findings initially give these subgroups of the population support for a possible option for surgery.

Table 2 Univariate and multivariate Cox regression analysis of GA patients with PMs

Characteristics	Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value
Age (years)				
20–39	Reference		Reference	
40–59	1.024 (0.6783, 1.546)	0.91	0.7639 (0.4879, 1.1961)	0.24
60–79	1.100 (0.7316, 1.654)	0.65	0.8720 (0.5621, 1.3526)	0.54
≥80	2.033 (1.2593.3.281)	0.004**	1.3946 (0.8302, 2.3428)	0.20
Sex				
Male	Reference		Reference	
Female	1.036 (0.8454, 1.296)	0.74	0.9597 (0.7738, 1.1903)	0.71
Race				
White	Reference		Reference	
Black	1.3141 (0.9444, 1.829)	0.11	1.3756 (0.9726, 1.9456)	0.07
Others	0.9593 (0.7427, 1.239)	0.75	1.1074 (0.8399, 1.4601)	0.47
Grade				
I–II	Reference		Reference	
III–IV	0.9613 (0.734, 1.259)	0.77	0.9989 (0.7543, 1.3228)	>0.99
T stage				
T1–T2	Reference		Reference	
T3–T4	0.9417 (0.6986, 1.198)	0.52	1.0755 (0.7876, 1.4687)	0.65
N stage				
N0	Reference		Reference	
N1	1.0773 (0.8242, 1.4009)	0.58	1.1037 (0.8267, 1.4736)	0.50
N2	0.6816 (0.4842, 0.9594)	0.03*	1.0709 (0.7262, 1.5793)	0.73
N3	0.9194 (0.7056, 1.1980)	0.53	1.2779 (0.9166, 1.7817)	0.15
Surgery				
No	Reference		Reference	
Yes	0.5948 (0.4846, 0.7302)	<0.001***	0.4342 (0.3283, 0.5742)	<0.001***
Radiation				
No	Reference		Reference	
Yes	0.7276 (0.545, 0.9715)	0.03*	0.6989 (0.5126, 0.9528)	0.02*
Chemotherapy				
No	Reference		Reference	
Yes	0.5434 (0.4347, 0.6793)	<0.001***	0.4372 (0.3382, 0.5651)	<0.001***
Tumor size (mm)				
2–43	Reference		Reference	
44–70	0.9235 (0.7275, 1.172)	0.51	0.9348 (0.7273, 1.2014)	0.60
71–245	0.8409 (0.6531, 1.083)	0.18	0.9682 (0.7347, 1.2760)	0.82

*, P<0.05, **, P<0.01, ***, P<0.001, univariate and multivariate Cox regression. GA, gastric adenocarcinoma; PM, peritoneal metastasis; HR, hazard ratio; CI, confidence interval.

Table 3 Characteristics of 132 patients in surgery and non-surgery groups after PSM

Items	Non-surgery (N=86)	Surgery (N=86)	P value
Age (years)			0.07
20–39	4 (4.7%)	5 (5.8%)	
40–59	36 (41.9%)	28 (32.6%)	
60–79	32 (37.2%)	47 (54.7%)	
80+	14 (16.3%)	6 (7.0%)	
Sex			0.76
Male	49 (57.0%)	46 (53.5%)	
Female	37 (43.0%)	40 (46.5%)	
Race			0.742
White	63 (73.3%)	65 (75.6%)	
Black	10 (11.6%)	7 (8.1%)	
Others	13 (15.1%)	14 (16.3%)	
Grade			0.57
I–II	16 (18.6%)	20 (23.3%)	
III–IV	70 (81.4%)	66 (76.7%)	
T stage			0.43
T1–T2	18 (20.9%)	13 (15.1%)	
T3–T4	68 (79.1%)	73 (84.9%)	
N stage			0.03*
N0	27 (31.4%)	35 (40.7%)	
N1	44 (51.2%)	29 (33.7%)	
N2	7 (8.1%)	17 (19.8%)	
N3	8 (9.3%)	5 (5.8%)	
Radiation			0.84
No	72 (83.7%)	70 (81.4%)	
Yes	14 (16.3%)	16 (18.6%)	
Chemotherapy			0.74
No	23 (26.7%)	26 (30.2%)	
Yes	63 (73.3%)	60 (69.8%)	
Tumor size (mm)			0.54
2–43	45 (52.3%)	45 (52.3%)	
44–70	21 (24.4%)	26 (30.2%)	
71–245	20 (23.3%)	15 (17.4%)	

*, P<0.05, Student's *t*-test. PSM, propensity score matching.

Table 4 Multivariate Cox regression analysis for patient survival after PSM

Characteristics	HR (95% CI)	P value
Age (years)		
20–39	Reference	
40–59	0.8252 (0.3588, 1.8977)	0.65
60–79	0.7020 (0.3084, 1.5979)	0.40
≥80	1.1708 (0.4685, 2.9261)	0.74
Sex		
Male	Reference	
Female	0.8709 (0.6114, 1.2404)	0.44
Race		
White	Reference	
Black	0.9495 (0.5329, 1.6916)	0.86
Others	1.2767 (0.7712, 2.1137)	0.34
Grade		
I–II	Reference	
III–IV	0.9957 (0.6538, 1.5165)	0.98
T stage		
T1–T2	Reference	
T3–T4	0.9389 (0.5986, 1.4728)	0.78
N stage		
N0	Reference	
N1	1.4114 (0.9319, 2.1375)	0.10
N2	1.3273 (0.7547, 2.3341)	0.33
N3	1.0959 (0.5423, 2.2143)	0.80
Surgery		
No	Reference	
Yes	0.4382 (0.3037, 0.6324)	<0.001***
Radiation		
No	Reference	
Yes	0.5463 (0.3355, 0.8896)	0.02*
Chemotherapy		
No	Reference	
Yes	0.3782 (0.2514, 0.5689)	<0.001***
Tumor size (mm)		
2–43	Reference	
44–70	1.0131 (0.6915, 1.4843)	0.95
71–245	0.8655 (0.5417, 1.3829)	0.55

*, P<0.05, ***, P<0.001, multivariate Cox regression. PSM, propensity score matching; HR, hazard ratio; CI, confidence interval.

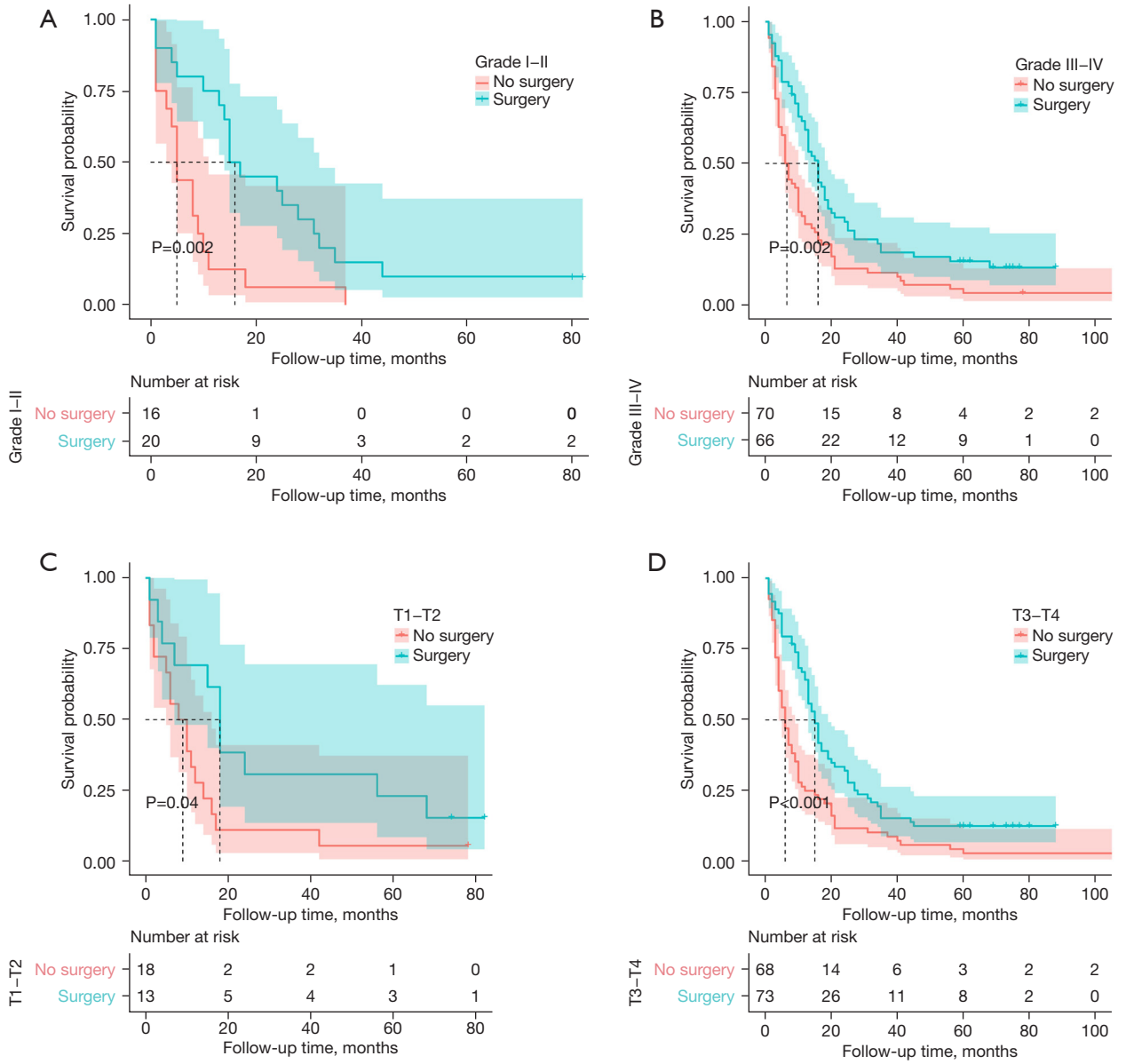


Figure 3 Kaplan-Meier survival curve of GA with PMs in different grades and T stages after PSM. (A) Grades I–II; (B) grades III–IV; (C) T1–T2 stages; (D) T3–T4 stages. GA, gastric adenocarcinoma; PM, peritoneal metastasis; PSM, propensity score matching.

The interesting thing is that, in *Table 1*, patients in the surgery group had higher T and N stages. In our opinion, the possible reason is that, when the T-stage and N-stage are higher, the tumor is larger, and this kind of gastric local tumor loading is higher, and even the possibility of local bleeding and obstruction symptoms is also higher. That explains why patients in *Table 1* with higher T and N stages tended to accept surgery because the urgency of the gastric palliative surgery for these patients is higher than that of patients with lower T and N stages, which is closer to the clinical reality. Our finding suggests that patients without lymph node metastasis and tumor size less than 71 mm will probably benefit more from surgery, but in clinical practice, it is the patients with higher T and N stages who have a more urgent need for palliative surgery to alleviate their symptoms, which reflects the difference in emphasis in the application of this conclusion to the clinic.

The advantages of our study are that, as far as we know,

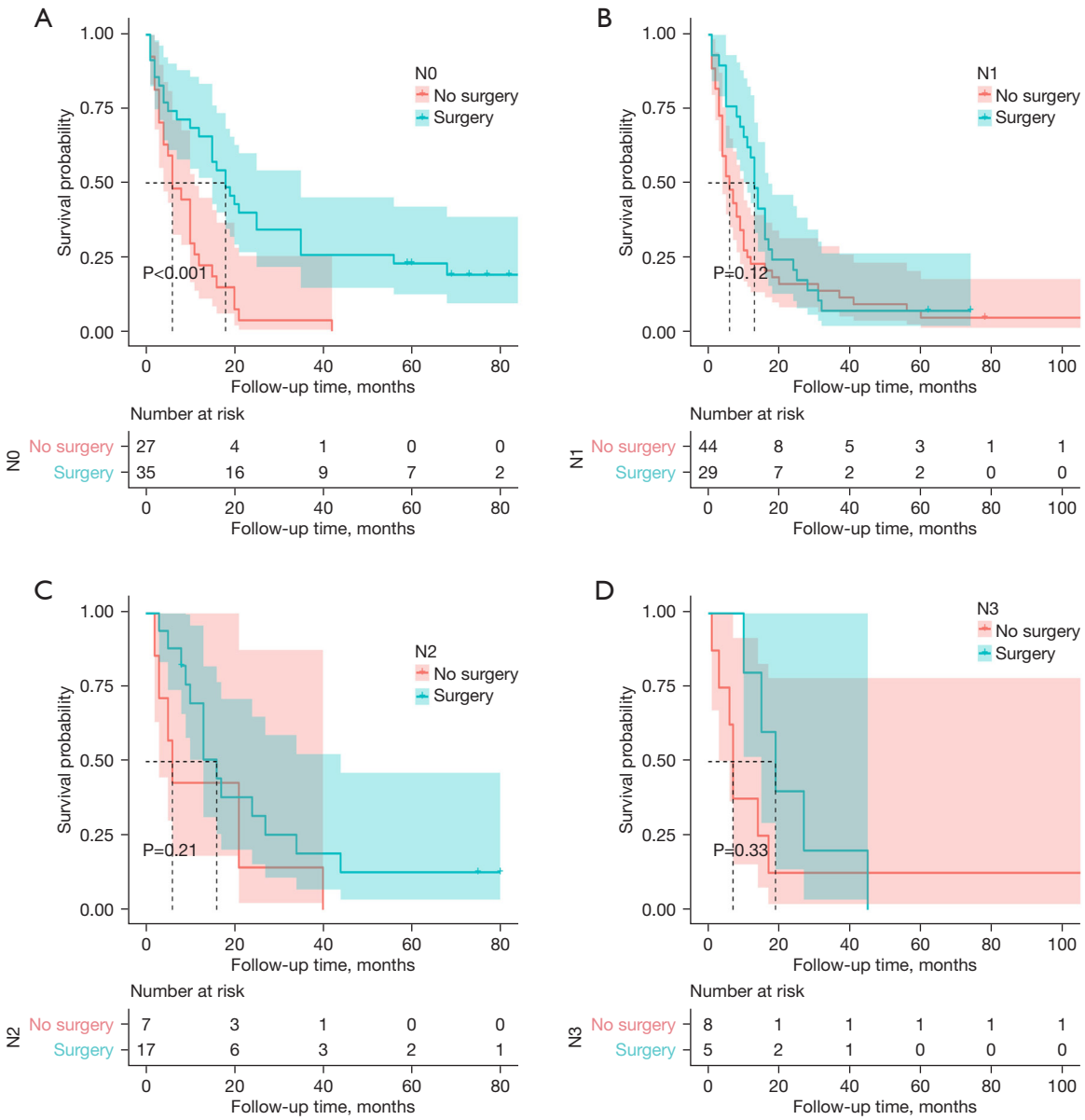


Figure 4 Kaplan-Meier survival curve of GA patients with PMs in different N stages after PSM. (A) N0 stage; (B) N1 stage; (C) N2 stage; (D) N3 stage. GA, gastric adenocarcinoma; PM, peritoneal metastasis; PSM, propensity score matching.

our study is probably the first study focusing on the role of surgery in GA patients happening metastases only to peritoneal and providing preliminary information for clinical practice. Subgroup analysis was used to accurately identify the patients who would benefit from surgery. The PSM method was also used to reduce bias to obtain robust results. This study still has certain limitations, such as our study is observational and not experimental and therefore the conclusions drawn are limited; and we use samples from a single cohort, the number of the patients included is small, it still requires a larger sample size, and validation with multicenter data. Under different treatment conditions, the effect of surgery on GA patients with PMs may be reversed (19,23). However, due to the limitations of publicly available data, the effects of prior treatments could not be balanced in this study. In addition, some important variables, such as the extent of PM, mismatch repair deficiency, Epstein-Barr virus (EBV) positivity, use of immune checkpoint

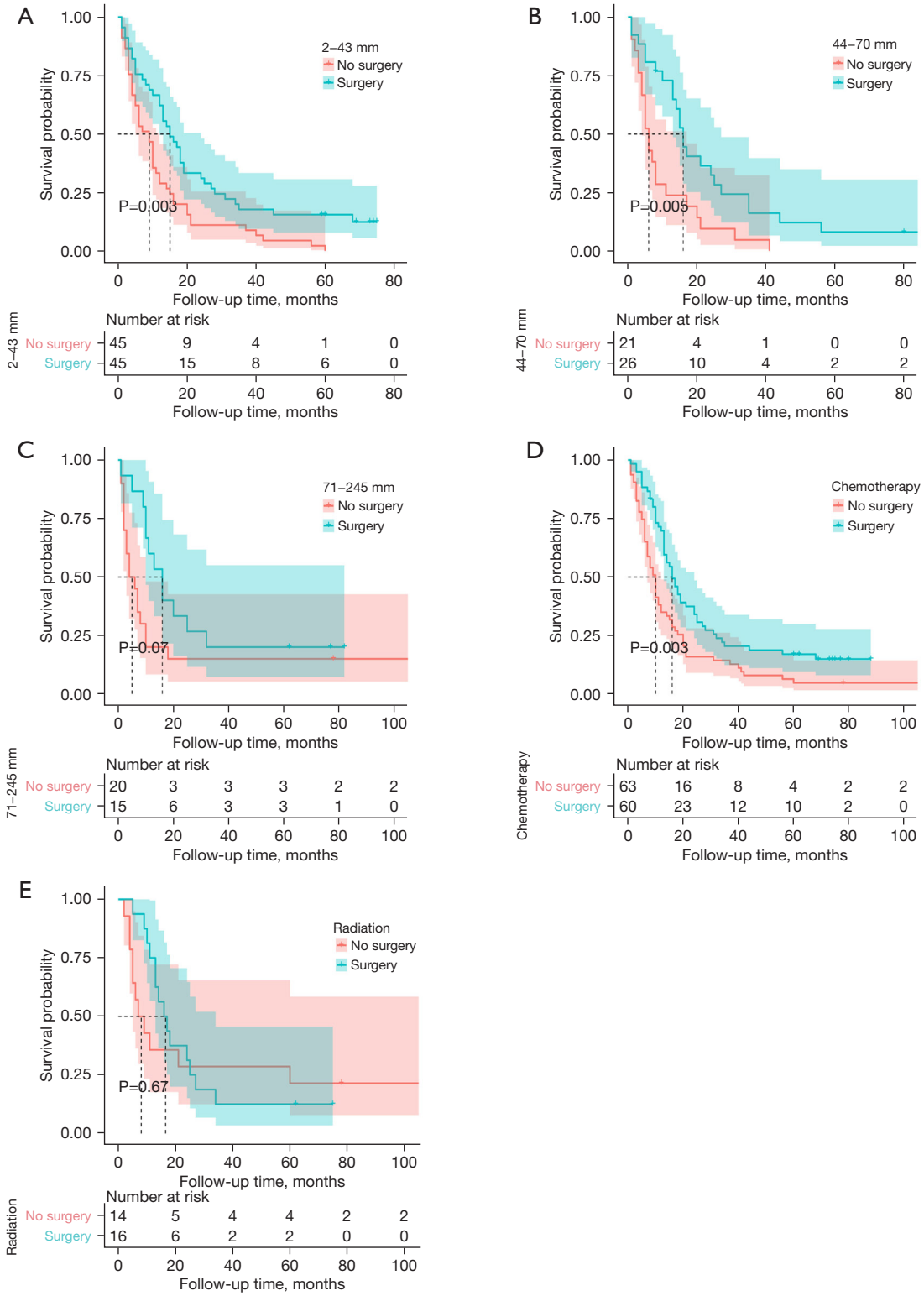


Figure 5 Kaplan-Meier survival curve of GA with PMs in different tumor sizes, chemotherapy, and radiation subgroup after PSM. (A) Tumor size 2–43 mm; (B) tumor size 44–70 mm; (C) tumor size 71–245 mm; (D) chemotherapy; (E) radiation. GA, gastric adenocarcinoma; PM, peritoneal metastasis; PSM, propensity score matching.

blockades were not included in the PSM due to the inherent shortcomings of the SEER database.

Moreover, surgery is indeed not the standard treatment for stage IV peritoneal disease, and the use of surgery for stage IV patients is currently not widely agreed upon by experts and is clinically controversial. Whether patients with PMs should be treated with surgery will be strictly screened and limited by clinicians, such as the physical status score, whether they are combined with serious medical disorders, and whether they are combined with critical symptoms such as gastric bleeding and obstruction. Based on the SEER data, this research was conducted to focus on the special group of GA patients who had only PMs, to initially explore the possible benefits of surgical treatment for this special group of patients, providing some reference data for clinicians to make decisions on the treatment of this group of patients. According to the fact that it is not strongly recommended, clinicians should still be very cautious about whether to use surgery for this group of patients or not. surgery in these patients.

The treatment of PMs of GA remains an urgent challenge. Multiple studies of new and combined strategies are emerging to further improve the prognosis of these patients. A meta-analysis showed that surgery combined with intraoperative peritoneal chemotherapy (IPC) improved 2- and 5-year OS [risk ratio (RR) =1.62, RR =3.10] and reduced the risk of recurrence [odds ratio (OR) =0.45] compared with surgery alone, whereas IPC combined with intraoperative extensive intraperitoneal lavage (EIPL) further improved 2- and 5-year OS and reduced recurrence (RR =2.33, RR =6.19, OR =0.13) (24). In addition, another meta-analysis reported that in selected patients with GC, complete cytoreduction, gastrectomy, and heat-packed intense chemotherapy (HIPEC) with or without systemic chemotherapy can achieve prolonged patient survival (24,25). In conclusion, for patients only PMs of GA, multidisciplinary integrated treatment modalities may be a new trend to improve prognosis. It is hoped that effective treatment strategies for patients with PMs of GA will be available in the future and that patients will be able to maximize the benefits of the integrated treatment modalities.

Conclusions

Based on the SEER database, surgery has better OS for patients only with PMs from GA. Patients without lymph node metastasis and those who received chemotherapy before may benefit from surgery. These specific groups of patients may have surgery as an option to improve the prognosis.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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