# Long-term effects of total *vs.* partial pancreatectomy among patients with pancreatic cancer: a population-based study

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**Background:** Total pancreatectomy (TP) for pancreatic cancer (PC) has been limited historically for fear of elevated perioperative morbidity and mortality. With advances in perioperative care, TP may be an alternative option to partial pancreatectomy (PP). Limited evidence clarified the indication for these two procedures in PC patients, especially in patients with different tumor staging and location. Thus, this study aims to compare the outcomes after TP and PP for PCs of different T stages and locations.

**Methods:** The study identified 14,456 PC patients with potentially curable primary tumor (T1–3) who received TP or PP from the Surveillance, Epidemiology, and End Results (SEER) database during 2000 to 2016. Detailed clinical and tumor covariates were all collected. Overall survival (OS) and cancer-specific survival (CSS) were the primary endpoints of interest in this study. OS and CSS were compared between patients after TP and PP using log-rank analysis.

**Results:** For all patients, except for tumor location, TP group was comparable to the PP group. OS and CSS of the TP group were worse than of the PP group (median OS: 19 *vs.* 20 months, P=0.0058; median CSS: 24 *vs.* 26 months, P=0.00098, respectively). In stratifying analyses, TP was significantly related to worse OS and CSS than PP in pancreatic head and neck cancer patients with T2-stage tumors (median OS: 18 *vs.* 19 months, P=0.0016; median CSS: 22 *vs.* 24 months, P=0.00055, respectively), whereas for patients with T1- or T3-stage pancreatic head and neck cancer as well as T1- to T3-stage pancreatic body and tail cancer or overlapping location cancer, OS and CSS of the two groups were similar (all P>0.05).

**Conclusions:** Compared with PP, TP offered worse prognosis in pancreatic head and neck cancer patients with T2-stage tumors, furthermore, TP and PP achieved comparable prognosis in patients with T1- or T3-stage pancreatic head and neck cancer as well as T1- to T3-stage pancreatic body and tail cancer or overlapping location cancer.

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**Keywords:** Pancreatic cancer (PC); partial pancreatectomy (PP); Surveillance, Epidemiology, and End Results database (SEER database); survival; total pancreatectomy (TP)

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## Introduction

In the USA, pancreatic cancer (PC) ranks 10th in men and 9th in women among all new malignancies, and ranks 4th in malignancy-related mortality (1). As the sole potentially curative therapy, surgical resection is recommended for resectable tumors (2). Partial pancreatectomy (PP), including pancreaticoduodenectomy and distal pancreatectomy, is currently the primary surgical procedure depending on the tumor location. Pancreaticoduodenectomy is the surgery option for tumors of the head and neck, while distal pancreatectomy is applied to tumors of the body and tail (3). In clinical practice, total pancreatectomy (TP) has also been performed to avoid pancreatic fistula after PP depending on the pancreatic texture and risk profile and achieving negative margins to improve survival (4,5). Several indications for this procedure are as follows: large or locally advanced tumors requiring radical resection, multifocal or infiltrating tumors, and PP is technically impractical (6,7). However, the role of TP for PC is still controversial. Several previous studies showed similar overall survival (OS) of PC patients after PP and TP (5,8,9), and other reports presented encouraging results for TP (10,11). Variations in surgical proficiency and perioperative care techniques among surgeons at each center may contribute to this controversial effect. Furthermore, most of the published data on the effect of TP on PC are from single-center retrospective studies with small samples and generally focused on pancreatic head cancer including all T stages (12-14). Therefore, it is necessary to use large-scale, multicenter data to analyze the role of TP for PC of different stages and locations.

The American Joint Committee on Cancer (AJCC) published the 8th edition of TNM staging of PC, which has been use from January 2018 (15). In this edition for T-staging, a tumor size of 4 cm is applied as the cutoff for T2 and T3, which has been reported to be highly prognostic (16). To date, studies of TP for PC have failed to stratify patients according to the new T-stage combined with tumor location. Therefore, the influence of TP on survival of patients with PC at disparate locations and T-stages remains unclear.

Because PC is relatively rare, the Surveillance, Epidemiology, and End Results (SEER) database is a unique resource that overcomes the challenges of single- or multicenter analyses. We conducted a comparison of OS and cancer-specific survival (CSS) after TP *vs.* PP in patients with PC at disparate locations and T-stages using a large sample from SEER. We present the following article in accordance with the STROBE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-2217/rc).

## Methods

### *Ethics approval*

We retrieved all patient information used in our study from the SEER database, so the institutional review board approval could be waived. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

### *Patients and study design*

The SEER database compiles data on cancer incidence, prevalence and survival of approximately 34.6% of the American population (17). We identified PC patients from 2000 to 2016 using the dedicated software (SEER*Stat 8.3.9). Patients who met our inclusion criteria were entered into the study: (I) >18 years of age; (II) pathologically confirmed diagnosis of PC, including ductal adenocarcinoma, acinal cell carcinoma, pancreatoblastoma, and solid pseudopapillary neoplasm of pancreases; (III) no evidence of distant metastasis; (IV) potentially curable primary tumor (T1–3); (V) history of partial or TP. Exclusion criteria were: (I) incomplete information in key medical record; (II) tumor located in pancreatic ducts, islets of Langerhans, or unknown location.

We also collected the following patient-related data: age, race, sex, year of diagnosis, tumor location, pathologic grade, number and mode of regional lymph node resection,

 

tumor size, surgical type, other tumor history, insurance status, marital status, survival status and SEER cause-specific death classification. Patients were divided into TP and PP groups based on the method of pancreatic resection.

The vital status and follow-up information for all patients are updated regularly in each SEER registry. Survival time was calculated based on the time of surgery and the time of death or last follow-up visit. OS and CSS were the primary endpoints of interest in this study. We defined OS as the time between surgery and death from any cause or the last follow-up, and CSS as the time between surgery and death from PC or the last follow-up.

Patients were stratified by tumor location or tumor size. First, we stratified patients into a head and neck subgroup, body and tail subgroup, and overlapping subgroup based on tumor location. Next, patients were subclassified into T1 (≤2 cm), T2 (≤4 cm) and T3 (>4 cm) subgroups according to tumor size. Finally, we stratified the patients based on tumor location combined with T-stage, resulting in 9 subgroups: head and neck-T1, head and neck-T2, head and neck-T3, body and tail-T1, body and tail-T2, body and tail-T3, overlapping-T1, overlapping-T2 and overlapping-T3.

### *Statistical analysis*

Comparison of continuous variables was performed with Mann-Whitney U-test or Student's *t*-test. Comparison of categorical variables was conducted with Fisher's exact test or Chi-square test, and comparison of ordinal variables was performed with the Kruskal-Wallis test. P≥0.05 were considered comparable when the variables were compared between the two groups. Kaplan-Meier method was used to plot survival curves and the log-rank test was used to compare them. Continuous data were converted into categorical data by optimal cut points selected according to the judgments of clinical experts or clinical reference values. The survival hazard was calculated by a full Cox proportional hazard regression model, which included clinical factors and surgical treatment methods and adopted a forward stepwise procedure. Variables with P values less than 0.05 in the full Cox regression analysis were independent predictors of survival. All statistical analyses in this study were performed with R software (https://www.r-project.org/;version 4.0.4). P<0.05 was considered to be statistically significant for all statistical tests and two-sided tests were used to calculate P values.

## Results

### *All patients*

The baseline features of all patients in this study are shown in *Table 1*. In total, we extracted the data for 14,456 PC patients with potentially curable primary tumors (T1–3) from the SEER database, which were allocated to a PP (n=12,006) and TP (n=2,450) group. For the PP and TP groups, the median follow-up was 70 and 67 months respectively. Compared with pancreatic body and tail cancer, surgeons seemed to be more willing to try TP for pancreatic head and neck cancer. No significant difference was shown in race, sex, age, number and mode of regional lymph node resection, tumor size and tumor pathology grade between groups.

The results of survival analyses revealed that both the OS and CSS of the TP group were significantly worse than those of the PP group (median survival: 19 *vs.* 20 months, P=0.0058; median CSS: 24 *vs.* 26 months, P=0.00098, respectively) (*Figure 1A,1B*). In order to further investigate the association between TP and poorer survival, Cox proportional hazards regression was performed to control for potential confounders. Analyses showed that TP was still the independent risk factor for OS and CSS after adjusting all other variables [OS: hazard ratio (HR), 1.061; 95% confidence interval (CI), 1.010 to 1.114; P=0.020; CSS: HR, 1.063; 95% CI, 1.004 to 1.126; P=0.036] (*Table 2*).

### *Patients stratified by tumor location or tumor size*

Patients were stratified by tumor location or tumor size to additionally study the influence of TP on the survival of PC patients with tumors located in different locations or with tumors of different sizes. The clinicopathologic features of patients subclassified based on tumor location are listed in Table S1. We stratified patients into a head and neck subgroup, body and tail subgroup, and overlapping subgroup based on tumor location. Variables were distributed relatively uniformly in both the TP and PP groups of all three subgroups. In patients with tumors located in the head and neck of the pancreas, compared with PP, TP was significantly associated with poorer OS and CSS (median OS: 20 *vs.* 18 months, P=0.0096; median CSS: 25 *vs.* 23 months, P=0.0044, respectively; *Figure 2A,2B*). However, in the body and tail subgroup and the overlapping subgroup, the OS and CSS of the TP group resembled

**Table 1** Clinicopathologic characteristics of all patients

| Variables | PP (n=12,006) | TP (n=2,450) | P value |
|---|---|---|---|
| Race, n (%) | | | 0.905 |
| White | 9,917 (82.6) | 2,027 (82.7) | |
| Black | 1,164 (9.7) | 231 (9.4) | |
| Other | 925 (7.7) | 192 (7.8) | |
| Sex, n (%) | | | 0.107 |
| Female | 6,007 (50) | 1,182 (48.2) | |
| Male | 5,999 (50) | 1,268 (51.8) | |
| Year of diagnosis, n (%) | | | 0.278 |
| 2002–2007 | 3,197 (26.6) | 683 (27.9) | |
| 2008–2011 | 4,205 (35) | 866 (35.3) | |
| 2012–2015 | 4,604 (38.3) | 901 (36.8) | |
| Location of PC, n (%) | | | <0.001 |
| Head and neck | 8,848 (73.7) | 1,944 (79.3) | |
| Body and tail | 2,285 (19) | 251 (10.2) | |
| Overlapping | 520 (4.3) | 118 (4.8) | |
| Not specified | 353 (2.9) | 137 (5.6) | |
| Pathologic grade, n (%) | | | 0.197 |
| I | 1,401 (11.7) | 285 (11.6) | |
| II | 6,136 (51.1) | 1,212 (49.5) | |
| III | 4,263 (35.5) | 919 (37.5) | |
| IV | 206 (1.7) | 34 (1.4) | |
| LN resection, n (%) | | | 0.068 |
| 0 | 256 (2.1) | 45 (1.8) | |
| 1–3 | 762 (6.3) | 134 (5.5) | |
| >4 | 10,832 (90.2) | 2,227 (90.9) | |
| Biopsy | 56 (0.5) | 20 (0.8) | |
| Unknown | 100 (0.8) | 24 (1.0) | |
| Tumor size (cm), n (%) | | | 0.665 |
| ≤2 | 2,064 (17.2) | 403 (16.4) | |
| ≤4 | 6,855 (57.1) | 1,408 (57.5) | |
| >4 | 3,087 (25.7) | 639 (26.1) | |
| Other tumor history, n (%) | | | 0.015 |
| No | 9,098 (75.8) | 1,913 (78.1) | |
| Yes | 2,908 (24.2) | 537 (21.9) | |

**Table 1** (*continued*)

**Table 1** (*continued*)

| Variables | PP (n=12,006) | TP (n=2,450) | P value |
|---|---|---|---|
| Age (years), n (%) | | | 0.461 |
| ≤60 | 3,352 (27.9) | 702 (28.7) | |
| >60 | 8,654 (72.1) | 1,748 (71.3) | |
| Age (years), median [IQR] | 67 [59, 74] | 67 [59, 74] | 0.617 |
| Insurance, n (%) | | | <0.001 |
| Uninsured | 196 (1.6) | 51 (2.1) | |
| Insured | 8,561 (71.3) | 1,718 (70.1) | |
| Medicaid | 874 (7.3) | 134 (5.5) | |
| Unknown | 2,375 (19.8) | 547 (22.3) | |
| Marital status, n (%) | | | 0.614 |
| Unmarried | 1,326 (11.0) | 285 (11.6) | |
| Married | 7,528 (62.7) | 1,538 (62.8) | |
| Other[#] | 3,152 (26.3) | 627 (25.6) | |

[#], divorced, separated, widowed and unknown. PP, partial pancreatectomy; TP, total pancreatectomy; PC, pancreatic cancer; LN, lymph node; IQR, interquartile range.

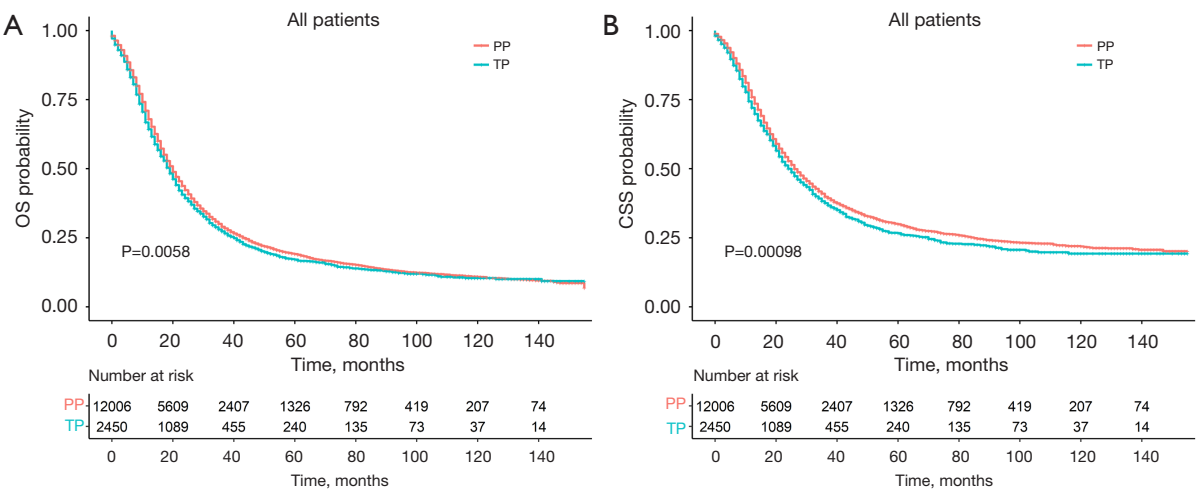


**Figure 1** Kaplan-Meier survival curves for all patients undergoing TP or PP. (A) Kaplan-Meier OS and (B) CSS curves for all patients. OS, overall survival; PP, partial pancreatectomy; TP, total pancreatectomy; CSS, cancer-specific survival.

those of the PP group (all P>0.05; *Figure 2C-2F*).

Next, patients were subclassified into T1 (≤2 cm), T2 (≤4 cm) and T3 (>4 cm) subgroups according to tumor size. Table S2 summarizes the features of the patients in the three subgroups. In all subgroups, PC patients with tumors located in the head and neck were more likely to undergo TP. The results of survival analyses are presented in *Figure 3*. Compared with PP, TP led to a lower OS and CSS of patients with T2-stage tumors (median OS: 20 *vs.* 18 months, P=0.00046; median CSS: 26 *vs.* 23 months, P=0.00027, respectively, *Figure 3C,3D*). However, except for the CSS of patients with T3-stage tumors (median CSS:

 

**Table 2** Cox regression analyses for OS and CSS in all patients

| Variables | OS | | CSS | |
|---|---|---|---|---|
| | HR (95% CI) | P value | HR (95% CI) | P value |
| Race | | | | |
| White | Reference | | Reference | |
| Black | 1.076 (1.009–1.147) | 0.025 | 1.033 (0.959–1.112) | 0.393 |
| Other | 0.939 (0.873–1.009) | 0.085 | 0.932 (0.858–1.012) | 0.095 |
| Sex | | | | |
| Female | Reference | | Reference | |
| Male | 1.111 (1.069–1.154) | <0.001 | 1.080 (1.033–1.129) | 0.001 |
| Year of diagnosis | | | | |
| 2002–2007 | Reference | | Reference | |
| 2008–2011 | 0.911 (0.852–0.974) | 0.006 | 0.887 (0.819–0.960) | 0.003 |
| 2012–2015 | 0.830 (0.775–0.890) | <0.001 | 0.805 (0.742–0.874) | <0.001 |
| Location of PC | | | | |
| Head and neck | Reference | | Reference | |
| Body and tail | 0.838 (0.795–0.883) | <0.001 | 0.808 (0.758–0.862) | <0.001 |
| Overlapping | 0.925 (0.843–1.015) | 0.099 | 1.000 (0.897–1.115) | 0.994 |
| Not specified | 0.954 (0.859–1.060) | 0.382 | 0.992 (0.877–1.122) | 0.899 |
| Pathologic grade | | | | |
| I | Reference | | Reference | |
| II | 1.551 (1.451–1.658) | <0.001 | 1.646 (1.519–1.784) | <0.001 |
| III | 2.063 (1.926–2.209) | <0.001 | 2.171 (1.999–2.357) | <0.001 |
| IV | 1.673 (1.427–1.962) | <0.001 | 1.884 (1.565–2.268) | <0.001 |
| Pancreatectomy | | | | |
| Partial | Reference | | Reference | |
| Total | 1.061 (1.010–1.114) | 0.020 | 1.063 (1.004–1.126) | 0.036 |
| LN resection | | | | |
| 0 | Reference | | Reference | |
| 1–3 | 1.008 (0.866–1.172) | 0.923 | 1.029 (0.858–1.234) | 0.757 |
| >4 | 0.924 (0.808–1.057) | 0.251 | 0.997 (0.849–1.170) | 0.968 |
| Biopsy | 0.885 (0.662–1.183) | 0.410 | 1.006 (0.719–1.407) | 0.972 |
| Unknown | 0.962 (0.760–1.217) | 0.747 | 1.044 (0.798–1.366) | 0.752 |
| Tumor size (cm) | | | | |
| ≤2 | Reference | | Reference | |
| ≤4 | 1.406 (1.331–1.484) | <0.001 | 1.433 (1.344–1.529) | <0.001 |
| >4 | 1.687 (1.587–1.793) | <0.001 | 1.685 (1.568–1.811) | <0.001 |

**Table 2** (*continued*)

**Table 2** (*continued*)

| Variables | OS | | CSS | |
|---|---|---|---|---|
| | HR (95% CI) | P value | HR (95% CI) | P value |
| Other tumor history | | | | |
| No | Reference | | Reference | |
| Yes | 0.877 (0.838–0.917) | <0.001 | 0.108 (0.096–0.122) | <0.001 |
| Age (years) | | | | |
| ≤60 | Reference | | Reference | |
| >60 | 1.319 (1.263–1.377) | <0.001 | 1.239 (1.180–1.300) | <0.001 |
| Insurance | | | | |
| Uninsured | Reference | | Reference | |
| Insured | 1.049 (0.897–1.226) | 0.551 | 0.978 (0.828–1.156) | 0.796 |
| Medicaid | 1.309 (1.106–1.550) | 0.002 | 1.176 (0.980–1.411) | 0.082 |
| Unknown | 1.116 (0.943–1.320) | 0.203 | 1.050 (0.875–1.260) | 0.598 |
| Marital status | | | | |
| Unmarried | Reference | | Reference | |
| Married | 0.930 (0.874–0.990) | 0.023 | 0.950 (0.884–1.021) | 0.165 |
| Other[#] | 1.066 (0.995–1.140) | 0.068 | 1.065 (0.985–1.152) | 0.116 |

[#], divorced, separated, widowed and unknown. OS, overall survival; CSS, cancer-specific survival; PC, pancreatic cancer; LN, lymph node; HR, hazard ratio; CI, confidence interval.

22 *vs.* 20 months, P=0.047), no significant difference of OS and CSS of patients with T1- and OS of patients with T3-stage tumors were observed between groups (all P>0.05) (*Figure 3A*,*3B*,*3E*,*3F*).

### *Patients stratified by combination of tumor location and size*

To further investigate the survival effects of TP on pancreatic head and neck cancer, body and tail cancer, and overlapping cancer at different T stages, we stratified the patients based on tumor location combined with T-stage, resulting in 9 subgroups: head and neck-T1, head and neck-T2, head and neck-T3, body and tail-T1, body and tail-T2, body and tail-T3, overlapping-T1, overlapping-T2 and overlapping-T3. The baseline features of the patients in these 9 subgroups were comparable between the TP and PP groups (Tables S3-S5).

There was no significant difference in the OS and CSS between the two groups of patients with T1- and T3-stage tumors (both P>0.05) (*Figure 4A*,*4B*). Among the PC patients with T2-stage tumors located in the head and neck of pancreas, the OS and CSS of patients in the TP group were also significantly worse than those of patients in the PP group (median OS: 18 *vs.* 19 months, P=0.0016; median CSS: 22 *vs.* 24 months, P=0.00055, respectively) (*Figure 4C*,*4D*).The Cox proportional hazards model further demonstrated that TP was independently related to poorer OS and CSS of patients in the head and neck-T2 subgroup (OS: HR, 1.100; 95% CI, 1.027 to 1.179; P=0.007; CSS: HR, 1.112; 95% CI, 1.027 to 1.203; P=0.009) but not of patients in the other two subgroups (all P>0.05) (Table S6). Other independent predictors of OS and CSS, such as pathologic grade, other tumor history and age, are presented in Table S6. There was also no significant difference in the OS and CSS between the two groups of patients with T3-stage tumors (both P>0.05) (*Figure 4E*,*4F*).

In pancreatic body and tail cancer as well as overlapping cancer, the OS and CSS of patients with all T stages were not significantly different between the TP and PP groups (all P>0.05) (Figures S1,S2). The results of the Cox proportional hazards regression analyses of all these

 

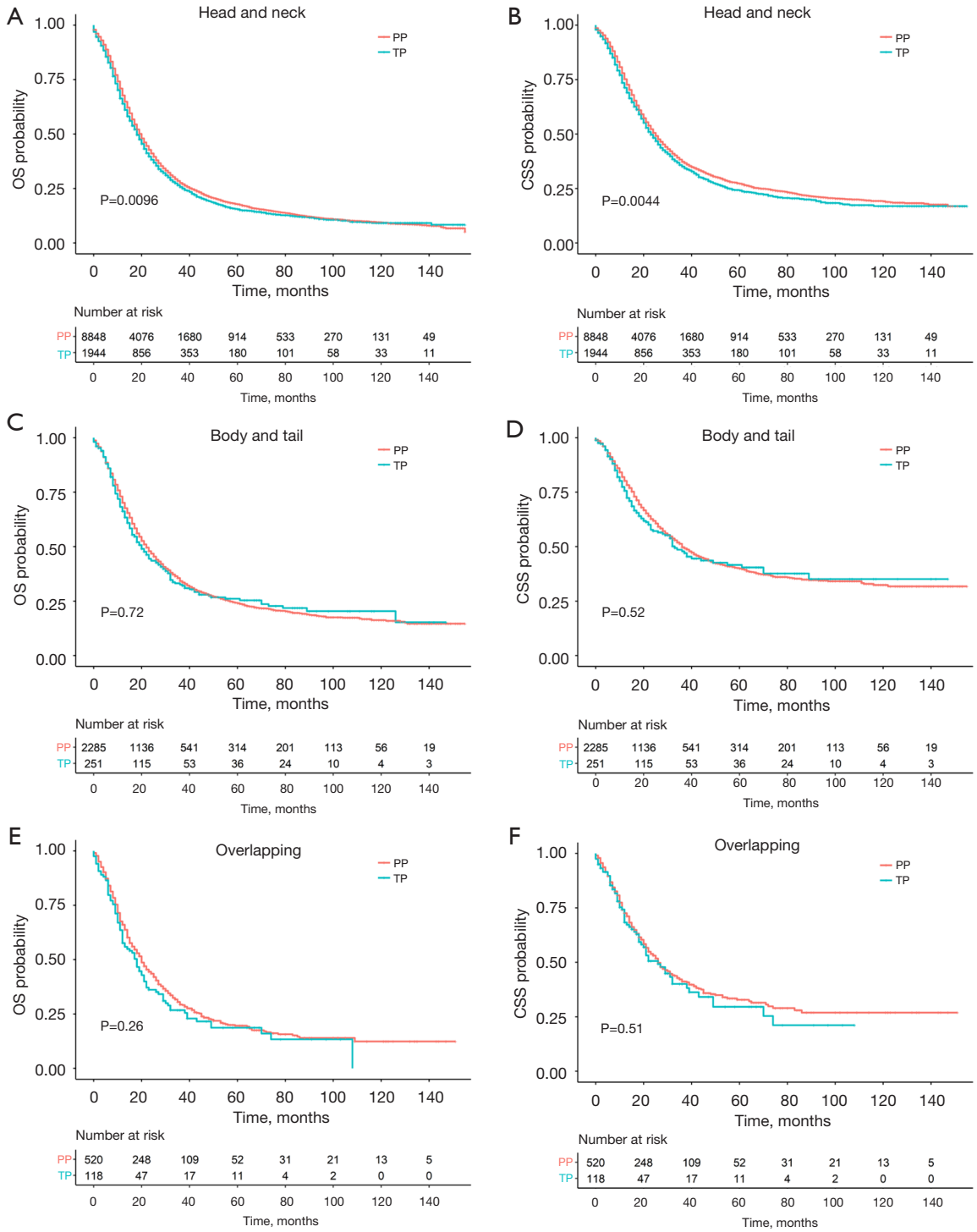


**Figure 2** Kaplan-Meier survival curves for patients undergoing TP or PP stratified by tumor location. OS and CSS for patients with tumors located in the pancreatic head and neck (A,B), body and tail (C,D), and overlapping location (E,F). OS, overall survival; PP, partial pancreatectomy; TP, total pancreatectomy; CSS, cancer-specific survival.

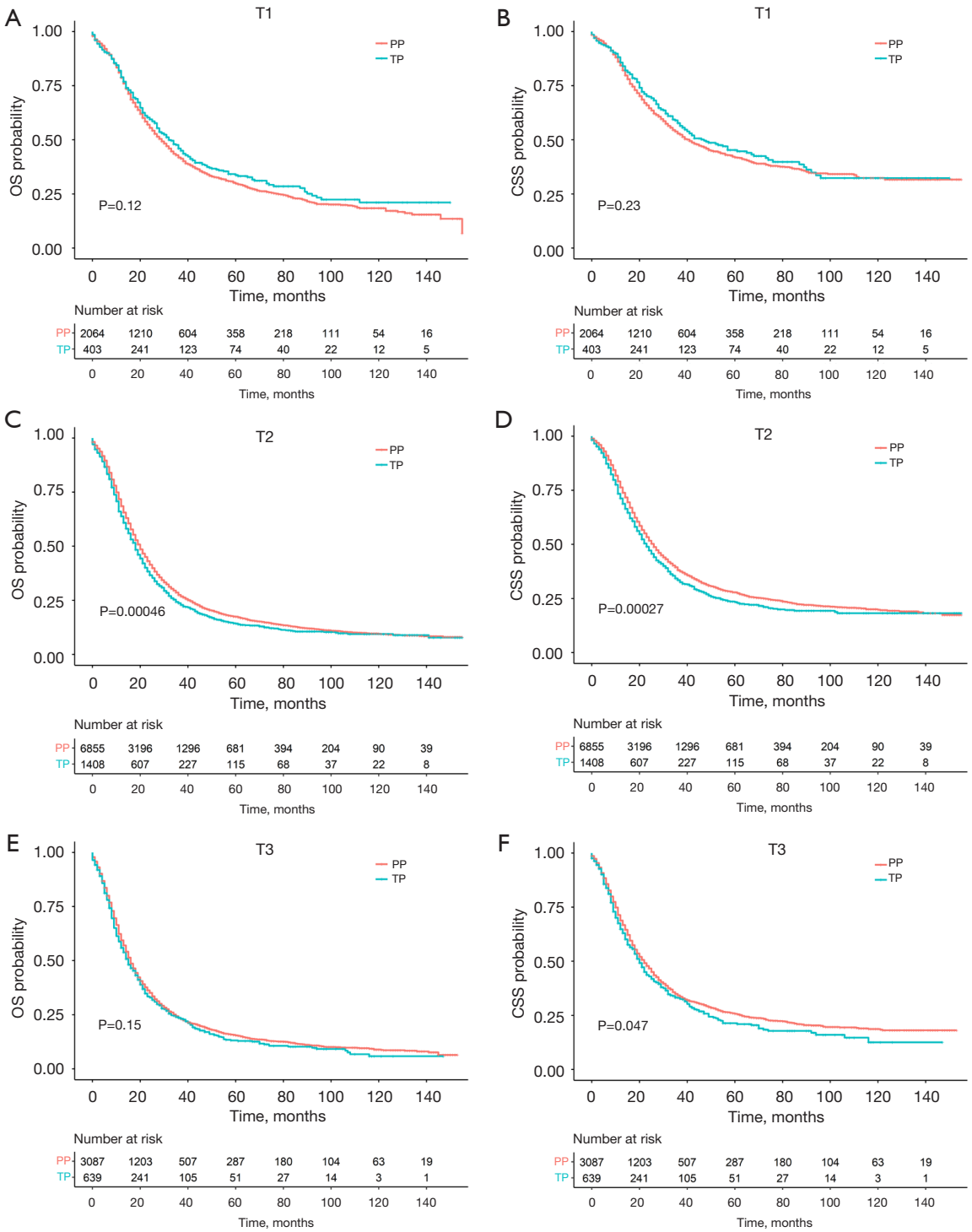


**Figure 3** Kaplan-Meier survival curves for patients undergoing TP or PP stratified by tumor size. OS and CSS for patients with T1-stage tumors (A,B), T2-stage tumors (C,D), and T3-stage tumors (E,F). OS, overall survival; PP, partial pancreatectomy; TP, total pancreatectomy; CSS, cancer-specific survival.

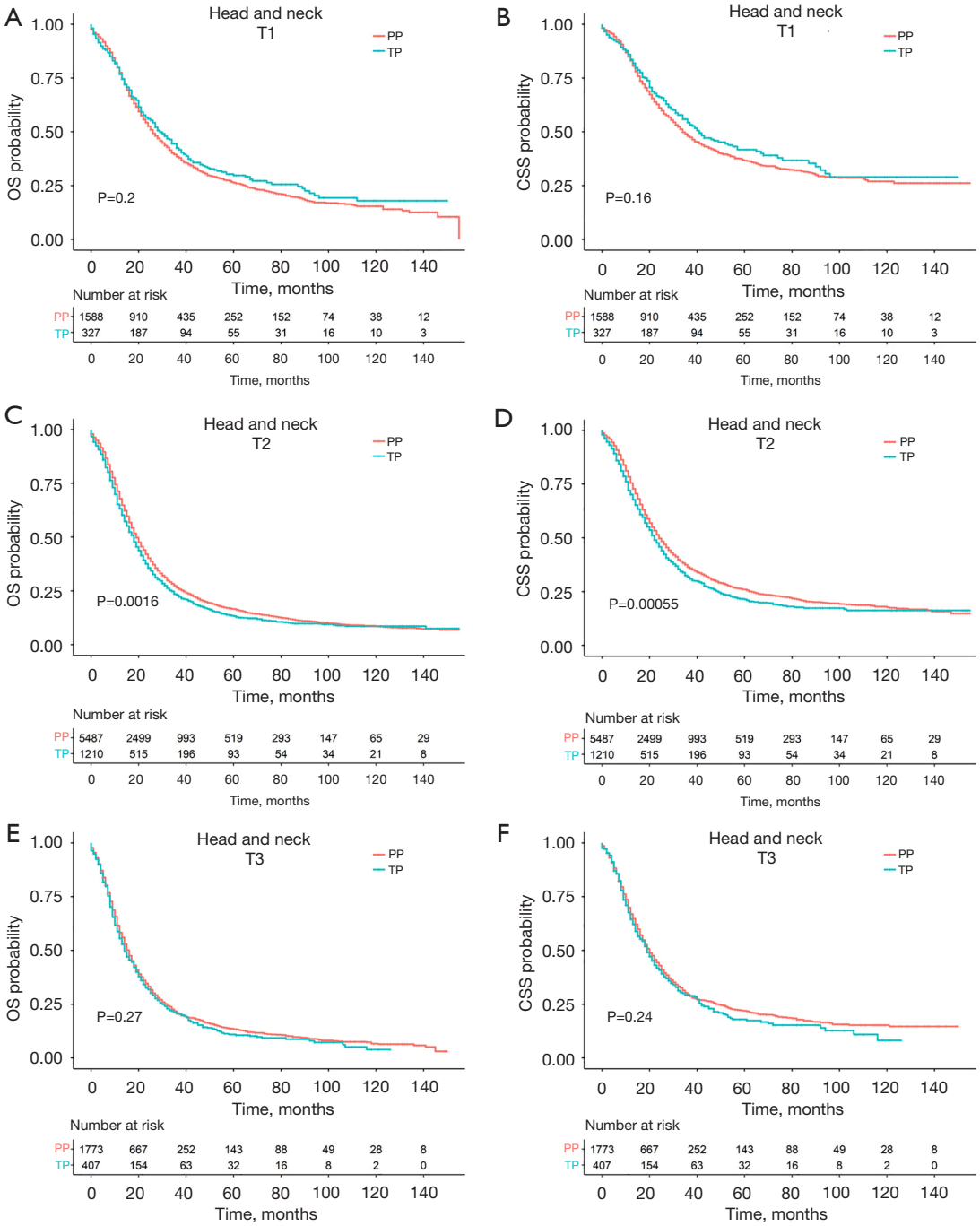


**Figure 4** Kaplan-Meier survival curves for patients undergoing TP or PP stratified by combination of tumor location and size. OS and CSS for pancreatic head and neck cancer patients with T1-stage tumors (A,B), T2-stage tumors (C,D), and T3-stage tumors (E,F). OS, overall survival; PP, partial pancreatectomy; TP, total pancreatectomy; CSS, cancer-specific survival.

subgroups are summarized in Tables S7,S8. TP was not associated with the OS and CSS of patients in any of these subgroups.

## Discussion

TP was initially introduced as a more thorough resection for PC, and was expected to produce better therapeutic effects (18). In the early years, because of the high perioperative morbidity and mortality after TP as well as lifelong diabetes mellitus and exocrine dysfunction, which affected the long-term outcomes and quality of life (QOL) of patients, surgeons preferred PP to TP (19-21). However, with the development of high-volume pancreatic centers, improved surgical techniques, and advances in perioperative care, the perioperative morbidity and mortality for TP have improved substantially (22-24). Furthermore, in recent years, the QOL of patients after TP has remarkably improved due to the wide clinical application of long-acting and medium-acting insulin and modern pancreatin drugs (25-27). Therefore, the appropriateness of TP has been reconsidered and it is being used in an increasing number of patients. Nevertheless, there is an ongoing debate as to whether TP leads to better long-term survival for PC compared with PP.

Using a large sample of data from the SEER database, we demonstrated a significant survival disadvantage for patients with PC after TP compared with PP. Because tumor location and size are significantly associated with PC prognosis (28-31), we further investigated the effect of TP on survival in PC patients with different tumor locations and tumor sizes. A negative effect on long-term prognosis was found for T2-stage pancreatic head and neck cancer after TP compared with PP. Several reasons might be accountable for our results. Firstly, patients in this study were enrolled from 2000 to 2016 and there was no appropriate endocrine therapy for TP patients in the early 2000's which might compromise the survival of patients who received TP. Secondly, the persistently high morbidity of complications associated with TP including total exocrine pancreatic insufficiency and postoperative brittle diabetes could also contribute to the poor survival (30). The diabetes post-TP led to prolonged hospital stay and increase 5–10% mortality rate (32). Finally, clinically relevant information like carbohydrate antigen 19-9 (CA 19-9), body mass index (BMI), comorbidities and chemotherapy, which are associated with survival, are lacking in the SEER database.

A study of 1,386 PC patients compared the effects of TP (n=100) and pancreaticoduodenectomy (n=1,286) on survival, and concluded that the long-term prognosis of both groups of patients was similar (5). A more recent study revealed that TP with a negative margin was associated with a more favorable survival outcome compared with marginal positive resection with PP; thus, TP was recommended when PP with negative margin was impractical (33). However, our present study showed that both the OS and CSS of the TP group were significantly worse than those of the PP group, and TP was an independent risk factor for OS and CSS. Most of the previous studies were retrospective single-center studies with relatively small sample sizes, whereas our study enrolled a large sample of patients from multiple centers and CSS was one of the primary study endpoints. Therefore, it is reasonable to believe that the results of this study are more reliable. Furthermore, previous studies generally focused on pancreatic head cancer including all T stages, whereas this study looked at potentially curable (AJCC T1–3) PC at all locations. This difference may also lead to differences in research results.

It is appropriate to speculate that the effect of TP is disparate for PC at different anatomical locations. Artinyan *et al.* reported that pancreatic body and tail cancer patients had a shorter median survival, a higher likelihood of distant metastasis, and a lower likelihood of surgical treatment than pancreatic head cancer patients (28). Two other studies verified the differences in both the genes and prognosis between pancreatic body and tail cancer and pancreatic head cancer (34,35). Our subgroup analyses results showed that in patients with tumors located in the head and neck of pancreas, TP was significantly associated with poorer OS and CSS, whereas in the body and tail subgroup and overlapping subgroup, the OS and CSS of the TP group resembled those of the PP group. In a previous study, Passeri *et al.* failed to find differences in survival between patients treated with TP and patients with tumors at different locations treated with PP. Although it stratified the patients undergoing PP according to tumor location, the patients who underwent TP were not stratified in the same way, which affects the credibility of the research results (9).

Tumor size is one of the three key aspects of the TNM staging system for solid tumors and a major predictor of tumor prognosis (36). Results of a study performed by Marchegiani *et al.* revealed different surgical outcomes between pancreatic ductal adenocarcinoma patients with tumor size ≤2 and >2 cm (37). Another study also found that the survival rate declined with increasing

 

tumor size in patients with localized pancreatic ductal adenocarcinoma (38). Johnston *et al.* reported that tumor size independently related to survival of PC patients undergoing TP (30). Therefore, stratification of PC according to tumor size is necessary to compare the influence of TP and PP on the survival of PC patients. The newest edition of the TNM staging of PC added tumor size of 4 cm as the cutoff of T2 and T3, which has been reported to be highly prognostic (16,39). Unfortunately, to our knowledge, no studies have been conducted to stratify patients according to this version of T-staging to compare the surgical outcomes of TP and PP. We found that TP led to decreased OS and CSS of patients with T2-stage tumors. In further analyses, we found that for PC patients with T2-stage tumors located in the head and neck of pancreas, the OS and CSS of patients in the TP group were significantly worse than for the PP group. In contrast, the same results were not found in other subgroup analyses.

Several limitations in our study need to be noted. Firstly, we stratified patients into three groups by the tumor size. According to the available information in the SEER database, the tumor size was obtained by measuring either pathologic specimen or pre-operative CT scans. However, the tumor size of measuring the pathologic specimens, the gold standard for determining tumor size, is usually slightly larger than that of measuring the pre-operative CT scans. Hence, it would be better to stratify patients according to tumor size measuring the pathologic specimen in the future study. Secondly, on account of the limited form of information available in the SEER database, information regarding clinical prognosis, such as BMI, CA 19-9 or other diseases, were not available. Therefore, the effect of this information on patient survival could not be studied. Thirdly, pancreatic neck cancer has different clinicopathologic characteristics compared to head or body-tail PC. A previous study reported that patients with pancreatic neck cancer had worse prognosis than patients with head or body-tail PC due to more frequently invading in peripheral major vessels (40). Therefore, it should be better to divide head and neck PC in two different subgroups. Finally, the current study analyses patients underwent TP and PP for all types of PC. Given different types of PC have different prognosis, it should be better to supplement additional analysis to investigate and compare the same data for each type of PC in the future.

## Conclusions

Survival was significantly poorer for patients with potentially curable PC who underwent TP than PP. In terms of different tumor locations and sizes, TP is significantly related to worse survival than PP for T2-stage pancreatic head and neck cancer patients. Further investigations are required to identify independent risk factors associated with the TP treatment.

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## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-2217/rc

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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 authors retrieved all patient information used in this study from the SEER database, so the institutional review board approval could be waived. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).



 

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