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Original Article

Survival outcomes of pancreaticoduodenectomy versus extended pancreaticoduodenectomy procedure for pancreatic head carcinoma: a propensity score matching study

Ning Pu[1#], Sucheng Mu[2#], Yuan Fang[1#], Hanlin Yin[1], Gao Liu[3], Guochao Zhao[1], Lei Zhang[1], Wenchuan Wu[1], Wenhui Lou[1]

[1]Department of General Surgery, [2]Department of Emergency Medicine, [3]Department of Liver Surgery and Transplantation, Zhongshan Hospital, Fudan University, Shanghai 200032, China

Contributions: (I) Conception and design: N Pu, S Mu, W Wu, W Lou; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: N Pu, Y Fang, G Liu, G Zhao, L Zhang; (V) Data analysis and interpretation: N Pu, S Mu; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Wenhui Lou, MD, PhD; Wenchuan Wu, MD, PhD. Department of General Surgery, Zhongshan Hospital, Fudan University, 180 Fenglin Road, Shanghai 200032, China. Email: lou.wenhui@zs-hospital.sh.cn; wu.wenchuan@zs-hospital.sh.cn.

Background: It is unclear if the modified extended pancreaticoduodenectomy (PD) has better outcome superior the conventional PD for patients with pancreatic head carcinoma (PHC). The objective of this study is to compare the survival outcomes of the classic PD procedure and the modified extended PD procedure for PHC.

Methods: A total of 7,084 resected PHC patients with PD and extended PD procedure from the SEER database from 2004 to 2014 were stratified. With the utilization of propensity score matching (PSM), patient baseline characteristics were balanced to decrease the bias. Overall survival (OS) and cancer-specific survival (CSS) were analyzed in both groups.

Results: Of the 7,084 patients, 6,541 (92.3%) and 543 (7.7%) patients received PD and extended PD surgical procedures, respectively. After 2:1 ratio of PSM, 543 patients with extended PD procedure and 1,084 patients with PD procedure were completely matched. The median CSS and OS for PD and extended PD group were 20.0 and 19.0 months, and 19.0 and 18.0 months, respectively. The 5-year CSS and OS rates for PD and extended PD group were 17.5% and 16.1%, and 13.9% and 13.1%, respectively.

Conclusions: There is no distinct difference in survival outcomes between PD and extended PD procedure in patients with PHC.

Keywords: Pancreatic head carcinoma (PHC); pancreaticoduodenectomy (PD); extended pancreaticoduodenectomy (extended PD); propensity score matching (PSM)

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Introduction

Pancreatic carcinoma has ranked as one of the most lethal diseases and its 5-year overall survival (OS) is less than 8%, which will become the second most common cause in the USA of cancer-related deaths by the year (1-3). Pancreaticoduodenectomy (PD) is the widely used operation in approximately 75% of patients with pancreatic head carcinoma (PHC). Current treatment strategies need to be highlighted and improved due to its highly aggressive nature with poor prognosis. Nowadays, surgical resection is considered as the potentially curative therapy. However, because of its difficulty in definite early diagnosis, merely

20% of patients have the opportunity for successful resection when diagnosed (4). Therefore, the established and promising surgical procedures will be focused to improve postoperative recovery and survival.

The classic PD procedure was considered as the operation of choice for PHC, which was refined and popularized by Whipple *et al.* in 1935 (5). In this procedure, an en bloc resection of the pancreatic head, the common bile duct, the gallbladder, the duodenum, the upper jejunum, the distal portion of the stomach and the adjacent lymph nodes was encompassed (6). In addition, the extended PD procedure included extended lymphadenectomy, extended organic resection, and extended vascular resection and reconstruction (7-10).

The benefits of extended lymphadenectomy had not been specified, and many multicenter randomized controlled trials reported that radical PD combined with extended lymphadenectomy was not beneficial to long-term survival in resectable PHC patients, and on the contrary, it may lead to levels of morbidity and mortality when compared to patients with standard lymphadenectomy (8,10,11). Besides, surgery for PHC commonly required vascular resection and reconstruction, such as the superior mesenteric vein (SMV) and portal vein (PV), however, the splenic vein (SV) sometimes also needed to be incised when it was involved by tumor (12).

The evidence of evaluating the safety and efficacy of vascular resection mainly came from single institutional retrospective studies, which showed mixed results in both perioperative complications and survival. Among these cases, some have reported decreased survival and elevated perioperative complication rates with extended resection (13,14), while others have demonstrated similar short- and long-term survival with or without extended resection (15,16), which is controversial.

In this study, the objective was to assess whether the results of extended PD procedure were equal to those of the classic PD procedure in PHC patients, especially concerning survival outcomes.

Methods

Patients and clinical data

The data of patients were obtained from the Surveillance, Epidemiology, and End Results (SEER) database in our study and the selection criterion were as previously described (17). Besides, patients diagnosed from 2004 to 2014 with PD or extended PD surgical procedures with following chemotherapy and having available data for sex, race/ethnicity, age, grade, tumor size, liver metastasis, lung metastasis, TNM stage, regional lymph node examined, regional lymph node positive, insurance, marriage, and survival information were analyzed. Other patients with partial pancreatectomy, total pancreatectomy, and pylorus-preserving PD were all excluded. The AJCC 8th staging system was still evaluated as previous publications (4,17). Following the criteria, the whole cohort was finally included.

Statistical analysis

In this study, R project version 3.3.4 (http://www.r-project.org/) and SPSS 21.0 statistical package (SPSS Inc., Chicago, IL, USA) were used in statistical analyses. Propensity score matching (PSM) was applied to cut down selection bias. The propensity scores, which were defined as the probability of being assigned to the PD or extended PD groups by considering all potential confounders, were computed by the MatchIt package in R project with an algorithm of 2:1 matching by age, race/ethnicity, and AJCC 8th staging system. The nearest neighbor matching with a caliper width of 0.05 was employed. Correlations and differences between categorical variables were analyzed by the χ^2 test and Fisher's exact test, while continuous variables by Student's *t*-test. The cancer-specific survival (CSS) and OS were depicted by Kaplan-Meier curves via Survminer package in the R project. CSS was calculated by the time from treatment to cancer-related death, while OS was defined as the time from treatment to the last follow-up or death. Univariate and multivariate analyses with Cox proportional hazards regression model were used to identify its independent prognostic factors. All P value <0.05 were considered the statistically significant difference.

Results

Demographic and clinicopathological characteristics

There were 7,084 histologically confirmed patients of PHC in this study, including 6,541 (92.3%) and 543 (7.7%) patients who received PD and extended PD surgical procedures, respectively. The mean ratio of extended PD procedure use was 7.7% (ranging from 5.9% in 2009 to 9.0% in 2005). There was no extensive application during these years; the detailed frequency of PD or extended

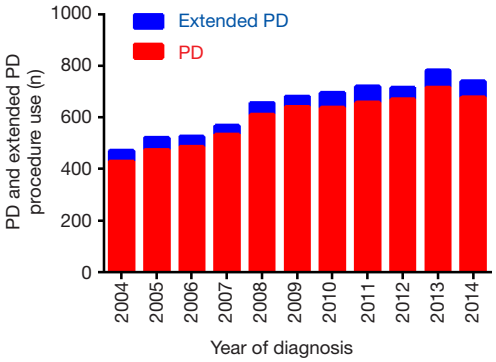

Figure 1 The frequency of PD and extended PD procedure used in 2004–2014. PD, pancreaticoduodenectomy.

PD procedure use is shown in *Figure 1*. In the whole cohort, there were 3,640 male and 3,444 female patients whose median age was 65.9 (ranging from 29 to 95) years old. Among these patients, liver metastasis was detected in 98 patients (1.4%) and lung metastasis in 24 patients (0.3%). The mean tumor size was 32.3±16.9 mm, and the average number of examined and positive lymph nodes was 15.9±10.3 and 2.6±3.3, respectively. For further analysis, the mean number of lymph nodes examined and positive with PD procedure was 15.9±10.3 and 2.6±3.3 respectively, while 16.1±10.1 and 2.6±3.1 respectively with extended PD procedure, which showed no significance between two groups. By the AJCC 8th TNM staging system, 659, 3,399, 2,499 and 527 patients were respectively classified into stage I, II, III and IV disease, respectively. The other detailed characteristics were displayed in *Table 1*.

PSM for PD and extended PD

Patients who were older, of white ethnicity, and with higher TNM stage were more likely to receive extended PD procedure. To reduce confounder and reflect the nature of two surgical procedures, a PSM model based on these three indicators was built. As a result, 543 patients with extended PD procedure and 1,084 patients with PD procedure were completely matched using PSM. The distribution and histograms of propensity scores before and after matching were shown in *Figure 2*. The detailed characteristics of the unmatched and matched cohorts were listed in *Table 1*.

The prognostic factors before or after matching

The older age, male, higher grade (P<0.001), larger

Table 1 Patient characteristics of unmatched and matched populations

Variables	Unmatched				Matched (2:1)			
	Patients (N)	Whipple, n (%)	Extended Whipple, n (%)	P value	Patients (N)	Whipple, n (%)	Extended Whipple, n (%)	P value
Age (years)				0.044				0.949
Mean ± STD	65.99	65.9±10.5	66.8±10.4		66.8±10.4	66.8±10.4	66.8±10.4	
Race/ethnicity				0.035				0.796
White	5,917	5,442 (92.0)	475 (8.0)		1,420	945 (66.5)	475 (33.5)	
Blank	654	615 (94.0)	39 (6.0)		112	73 (65.2)	39 (34.8)	
Others	513	484 (94.3)	29 (5.7)		95	66 (69.5)	29 (30.5)	
Sex				0.593				0.207
Male	3,640	3,355 (92.2)	285 (7.8)		818	533 (65.2)	285 (34.8)	
Female	3,444	3,186 (92.5)	258 (7.5)		809	551 (68.1)	258 (31.9)	

Table 1 (*Continued*)

Table 1 (*Continued*)

Variables	Unmatched				Matched (2:1)			
	Patients (N)	Whipple, n (%)	Extended Whipple, n (%)	P value	Patients (N)	Whipple, n (%)	Extended Whipple, n (%)	P value
Grade				0.265				0.206
I	659	609 (92.4)	50 (7.6)		151	101 (66.9)	50 (33.1)	
II	3,399	3,159 (92.9)	240 (7.1)		776	536 (69.1)	240 (30.9)	
III or IV	2,499	2,288 (91.6)	211 (8.4)		587	376 (64.1)	211 (35.9)	
Unknown	527	485 (92.0)	42 (8.0)		113	71 (62.8)	42 (37.2)	
AJCC 8th stage				0.042				0.160
I	1,590	1,493 (93.9)	97 (6.1)		330	233 (70.6)	97 (29.4)	
II	2,621	2,403 (91.7)	218 (8.3)		599	381 (63.6)	218 (36.4)	
III	2,524	2,328 (92.2)	196 (7.8)		594	398 (67.0)	196 (33.0)	
IV	349	317 (90.8)	32 (9.2)		104	72 (69.2)	32 (30.8)	
Tumor size (mm)				0.525				0.933
Mean ± STD	32.33±16.9	32.33±16.2	32.83±23.8		32.83±21.1	32.93±19.6	32.83±23.8	
Liver metastasis				0.086				0.908
Yes	98	86 (87.8)	12 (12.2)		35	23 (65.7)	12 (34.3)	
No	6,986	6,455 (92.4)	531 (7.6)		1,592	1,061 (66.6)	531 (33.4)	
Lung metastasis				0.303				0.375
Yes	24	24 (100)	0 (0)		4	4 (100.0)	0 (0)	
No	7,060	6,517 (92.3)	543 (7.7)		1,623	1,080 (66.5)	543 (33.5)	
Lesion number				0.615				0.973
1	6,053	5,593 (92.4)	460 (7.6)		1,379	919 (66.6)	460 (33.4)	
≥2	1,031	948 (91.9)	83 (8.1)		248	165 (66.5)	83 (33.5)	
Insurance				0.132				0.126
Yes	5,383	4,988 (92.7)	395 (7.3)		1,230	835 (67.9)	395 (32.1)	
No	123	110 (89.4)	13 (10.6)		30	17 (56.7)	13 (43.3)	
Unknown	1,578	1,443 (91.4)	135 (8.6)		367	232 (63.2)	135 (36.8)	
Marriage				0.742				0.670
Married	4,489	4,145 (92.3)	344 (7.7)		1,016	672 (66.1)	344 (33.9)	
Divorced	1,655	1,526 (92.2)	129 (7.8)		404	275 (68.1)	129 (31.9)	
Single	758	705 (93.0)	53 (7.0)		165	112 (67.9)	53 (32.1)	
Unknown	182	165 (90.7)	17 (9.3)		42	25 (59.5)	17 (40.5)	

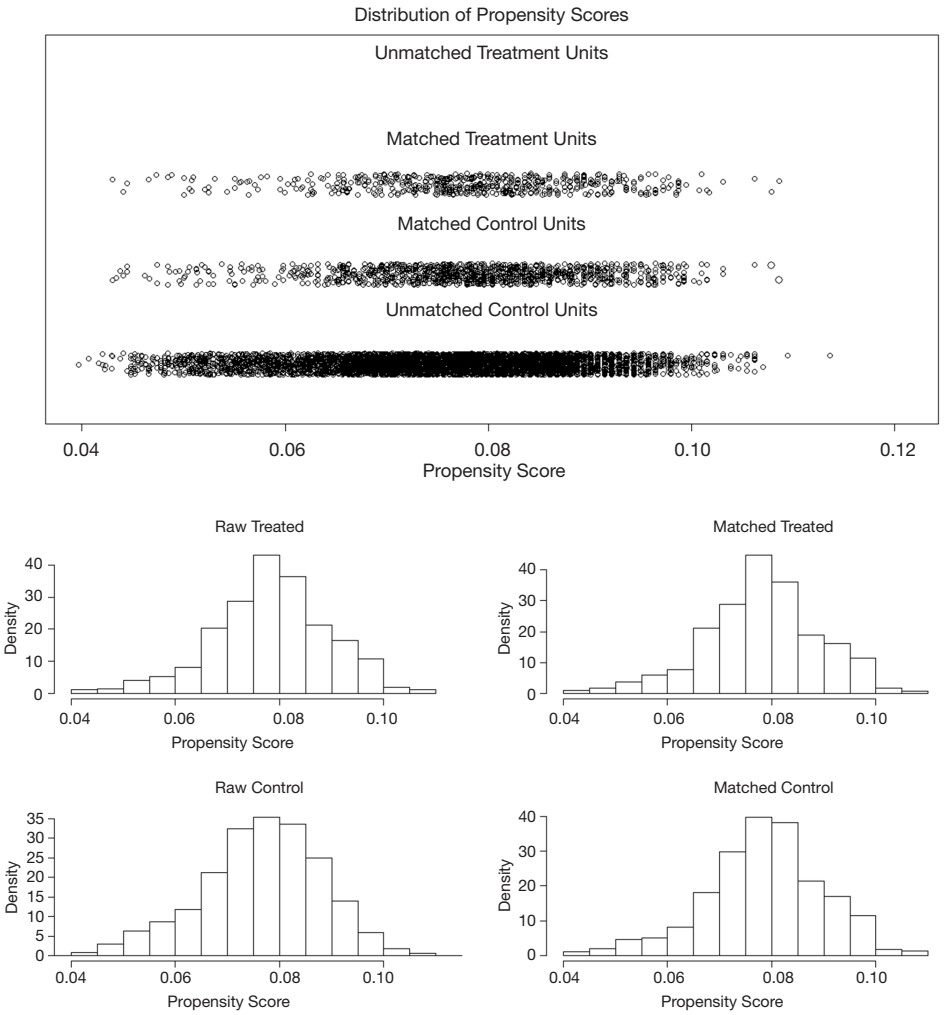

Figure 2 The distribution and histograms of propensity scores before and after matching.

tumor size, liver metastasis, lung metastasis and advanced TNM stage were significantly considered as risk factors for CSS before matching in univariate analysis. Besides these factors, divorce was also a risk factor for OS before matching. However, after matching, older age, higher grade, lung metastasis, and advanced TNM stage were still considered as risk factors for CSS, as well as divorce for OS (*Table 2*). In multivariate analysis, age, sex, grade, the AJCC 8th stage, and tumor size remained as independent prognostic indicators for CSS before matching, while only age, grade, and the AJCC 8th stage were independent prognostic factors after matching. For OS before matching, age, sex, grade, tumor size, marriage, and the AJCC 8th stage were all considered as independent risk factors, while after matching, there were only age, grade, marriage, and the AJCC 8th stage remaining (*Table 3*). In the matched populations, the surgical procedures had no effect on CSS [hazard ratio (HR): 1.030; 95% confidence interval (CI): 0.906–1.172, P=0.648] or OS (HR: 1.017; 95% CI: 0.900–1.148, P=0.790).

CSS and OS

The median CSS and OS of the whole population was 20.0 and 18.0 months, respectively. The 1-, 3- and 5-year CSS rates were 69.7%, 29.0% and 15.8%, respectively, while the OS rates at 1, 3 and 5 years were 66.3%, 25.2%, and 15.8%, respectively. Stratified by surgical procedures, the median CSS of patients received PD procedure were a little larger than that of patients with extended PD procedure

Table 2 Univariate prognostic analysis of unmatched and matched populations

Variables	Unmatched				Matched (2:1)			
	CCS		OS		CCS		OS	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Age (years)								
<65	1		1		1		1	
≥65	1.168 (1.101–1.239)	<0.001	1.208 (1.142–1.278)	<0.001	1.333 (1.177–1.509)	<0.001	1.400 (1.244–1.575)	<0.001
Race/ethnicity								
White	1		1		1		1	
Blank	0.956 (0.860–1.062)	0.835	1.039 (0.944–1.143)	0.436	0.869 (0.679–1.112)	0.264	0.914 (0.728–1.147)	0.437
Others	0.988 (0.878–1.110)	0.400	0.983 (0.879–1.143)	0.757	1.178 (0.905–1.533)	0.222	1.174 (0.915–1.507)	0.206
Sex								
Male	1		1		1		1	
Female	0.919 (0.867–0.975)	0.005	0.901 (0.852–0.952)	<0.001	0.899 (0.796–1.105)	0.085	0.881 (0.786–0.989)	0.031
Grade								
I	1		1		1		1	
II	1.396 (1.247–1.564)	<0.001	1.340 (1.207–1.487)	<0.001	1.364 (1.071–1.737)	0.012	1.229 (0.989–1.527)	0.062
III or IV	1.945 (1.733–2.182)	<0.001	1.799 (1.617–2.001)	<0.001	1.976 (1.547–2.525)	<0.001	1.712 (1.372–2.135)	<0.001
Unknown	1.227 (1.049–1.435)	0.011	1.193 (1.032–1.379)	0.017	1.354 (0.974–1.884)	0.072	1.199 (0.884–1.626)	0.244
AJCC 8th stage								
I	1		1		1		1	
II	1.678 (1.541–1.826)	<0.001	1.545 (1.429–1.670)	<0.001	1.435 (1.202–1.712)	<0.001	1.377 (1.168–1.623)	<0.001
III	2.079 (1.909–2.264)	<0.001	1.888 (1.745–2.042)	<0.001	1.815 (1.519–2.167)	<0.001	1.725 (1.462–2.036)	<0.001
IV	3.208 (2.794–3.683)	<0.001	2.788 (2.444–3.181)	<0.001	2.541 (1.953–3.306)	<0.001	2.331 (1.814–2.995)	<0.001
Tumor size (mm)	1.004 (1.003–1.005)	<0.001	1.003 (1.002–1.004)	<0.001	1.002 (1.000–1.003)	0.065	1.001 (1.000–1.003)	0.097
Liver metastasis								
No	1		1		1		1	
Yes	1.964 (1.537–2.510)	<0.001	1.818 (1.431–2.310)	<0.001	1.326 (0.877–2.005)	0.181	1.289 (0.867–1.916)	0.210
Lung metastasis								
No	1		1		1		1	
Yes	2.113 (1.330–3.358)	0.002	1.980 (1.262–3.107)	0.003	2.771 (1.037–7.404)	0.042	2.475 (0.927–6.609)	0.071
Lesion number								
1	1		1		1		1	
≥2	0.991 (0.910–1.079)	0.833	1.051 (0.972–1.137)	0.211	1.052 (0.886–1.250)	0.561	1.132 (0.966–1.326)	0.125

Table 2 (*Comtinued*)

Table 2 (*Continued*)

Variables	Unmatched				Matched (2:1)			
	CCS		OS		CCS		OS	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Insurance								
No	1		1		1		1	
Yes	0.836 (0.667–1.046)	0.117	0.820 (0.664–1.012)	0.064	0.933 (0.577–1.510)	0.778	0.804 (0.526–1.227)	0.311
Unknown	0.948 (0.754–1.192)	0.646	0.929 (0.750–1.151)	0.502	1.049 (0.643–1.712)	0.847	0.900 (0.584–1.386)	0.631
Marriage								
Married	1		1		1		1	
Divorced	1.059 (0.987–1.137)	0.111	1.098 (1.028–1.173)	0.006	1.129 (0.979–1.303)	0.095	1.174 (1.026–1.342)	0.019
Single	1.007 (0.912–1.112)	0.894	1.068 (0.974–1.170)	0.163	1.110 (0.903–1.365)	0.323	1.166 (0.962–1.414)	0.118
Unknown	0.962 (0.789–1.174)	0.706	0.943 (0.779–1.140)	0.543	0.587 (0.367–0.938)	0.026	0.584 (0.374–0.910)	0.018
Surgical procedure								
Whipple	1		1		1		1	
Extended Whipple	1.106 (0.992–1.233)	0.070	1.089 (0.982–1.208)	0.106	1.030 (0.906–1.172)	0.648	1.017 (0.900–1.148)	0.790

CSS, cancer specific survival; OS, overall survival.

(20.0 *vs.* 19.0 months), so did median OS (19.0 *vs.* 18.0 months). However, it was still lack of significant differences (*Figure 3A,B*). The cumulative CSS rates of patients with PD procedure at 1, 3 and 5 years were 70.0%, 29.2% and 19.7%, whereas in extended PD group, they were 65.8%, 26.3% and 16.1%, respectively. The cumulative OS rates of patients with PD procedure at 1, 3 and 5 years were 66.6%, 25.5%, and 16.0%, whereas in extended PD group, they were 62.6%, 22.5% and 13.1%, respectively.

After PSM, the median CSS and OS changed to 19.0 and 18.0 months, respectively. The CSS rates of 1, 3 and 5 years in the matching group were 67.3%, 27.2%, and 17.1%, whereas the OS rates were 63.6%, 23.6% and 13.7%, respectively. For further analysis of surgical effects, the median CSS of both PD and extended PD procedure groups was 19.0 months. In PD procedure group, the 1-, 3- and 5-year CSS rates were 68.1%, 27.7%, and 17.5%, respectively, while in extended PD procedure group, they were 65.8%, 26.3% and 16.1%, respectively. Regarding the OS, the median OS of both groups was 18.0 months. The cumulative OS rates in PD procedure group at 1, 3 and 5 years were 64.1%, 24.2%, and 13.9%, whereas in extended PD procedure group, they were 62.6%, 22.5%, and 13.1%, respectively. Therefore, the CSS and OS were still not comparable between two surgical groups after PSM (*Figure 3C,D*).

Discussion

In this study, we analyzed the outcomes of different surgical procedures on PHC patients. A total of 7,084 PHC patients with PD or extended PD procedure were enrolled in the unmatched group. After the PSM of age, race and TNM stage, 1,627 matched patients were finally analyzed. The results showed that the survival outcomes were similar between PD and extended PD procedure in both unmatched and matched groups.

Through the above analysis, we found that the average of lymph nodes examined and positive with PD procedure was 15.9±10.3 and 2.6±3.3 respectively, while 16.1±10.1 and 2.6±3.1 respectively with extended PD procedure, which showed no difference between two populations. After PSM, the average of lymph nodes examined and positive with PD procedure changed into 15.6±9.5 and 2.8±3.5 respectively, while 15.8±8.9 and 2.6±3.1 with extended PD procedure respectively. The results meant that the extended PD procedure in this study mainly included the PD with extended resection and reconstruction instead of the PD

Table 3 Multivariate prognostic analysis of unmatched and matched populations

Variables	Unmatched				Matched (2:1)			
	CCS		OS		CCS		OS	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Age (years)								
<65	1		1		1		1	
≥65	1.220 (1.149–1.295)	<0.001	1.256 (1.187–1.329)	<0.001	1.397 (1.232–1.584)	<0.001	1.466 (1.300–1.652)	<0.001
Sex					NA	NA	NA	NA
Male	1		1					
Female	0.926 (0.873–0.982)	0.011	0.878 (0.829–0.930)	<0.001				
Grade								
I	1		1		1		1	
II	1.387 (1.238–1.554)	<0.001	1.331 (1.199–1.478)	<0.001	1.353 (1.062–1.725)	0.014	1.224 (0.985–1.521)	0.069
III or IV	1.870 (1.666–2.099)	<0.001	1.740 (1.564–1.937)	<0.001	1.958 (1.532–2.502)	<0.001	1.695 (1.359–2.115)	<0.001
Unknown	1.144 (0.977–1.339)	0.094	1.122 (0.970–1.298)	0.122	1.258 (0.903–1.753)	0.174	1.125 (0.828–1.527)	0.452
AJCC 8th stage								
I	1		1		1			
II	1.608 (1.476–1.752)	<0.001	1.490 (1.376–1.612)	<0.001	1.457 (1.220–1.740)	<0.001	1.409 (1.194–1.662)	<0.001
III	2.005 (1.839–2.187)	<0.001	1.841 (1.700–1.995)	<0.001	1.919 (1.604–2.295)	<0.001	1.840 (1.557–2.175)	<0.001
IV	3.173 (2.710–3.716)	<0.001	2.799 (2.407–3.255)	<0.001	2.595 (1.984–3.395)	<0.001	2.459 (1.912–3.162)	<0.001
Tumor size (mm)	1.002 (1.001–1.004)	0.001	1.002 (1.001–1.003)	0.002	NA	NA	NA	NA
Liver metastasis					NA	NA	NA	NA
No	1		1					
Yes	1.037 (0.784–1.372)	0.800	1.013 (0.771–1.331)	0.925				
Lung metastasis							NA	NA
No	1		1		1			
Yes	0.973 (0.602–1.573)	0.912	0.982 (0.616–1.567)	0.940	1.843 (0.673–5.052)	0.234		
Marriage	NA	NA						
Married			1		1		1	
Divorced			1.156 (1.080–1.238)	<0.001	1.134 (0.982–1.309)	0.087	1.169 (1.022–1.339)	0.023
Single			1.123 (1.024–1.232)	0.014	1.224 (0.993–1.507)	0.058	1.284 (1.057–1.558)	0.012
Unknown			1.016 (0.840–1.229)	0.871	0.665 (0.416–1.064)	0.089	0.650 (0.416–1.016)	0.059

CSS, cancer specific survival; OS, overall survival; NA, not available.

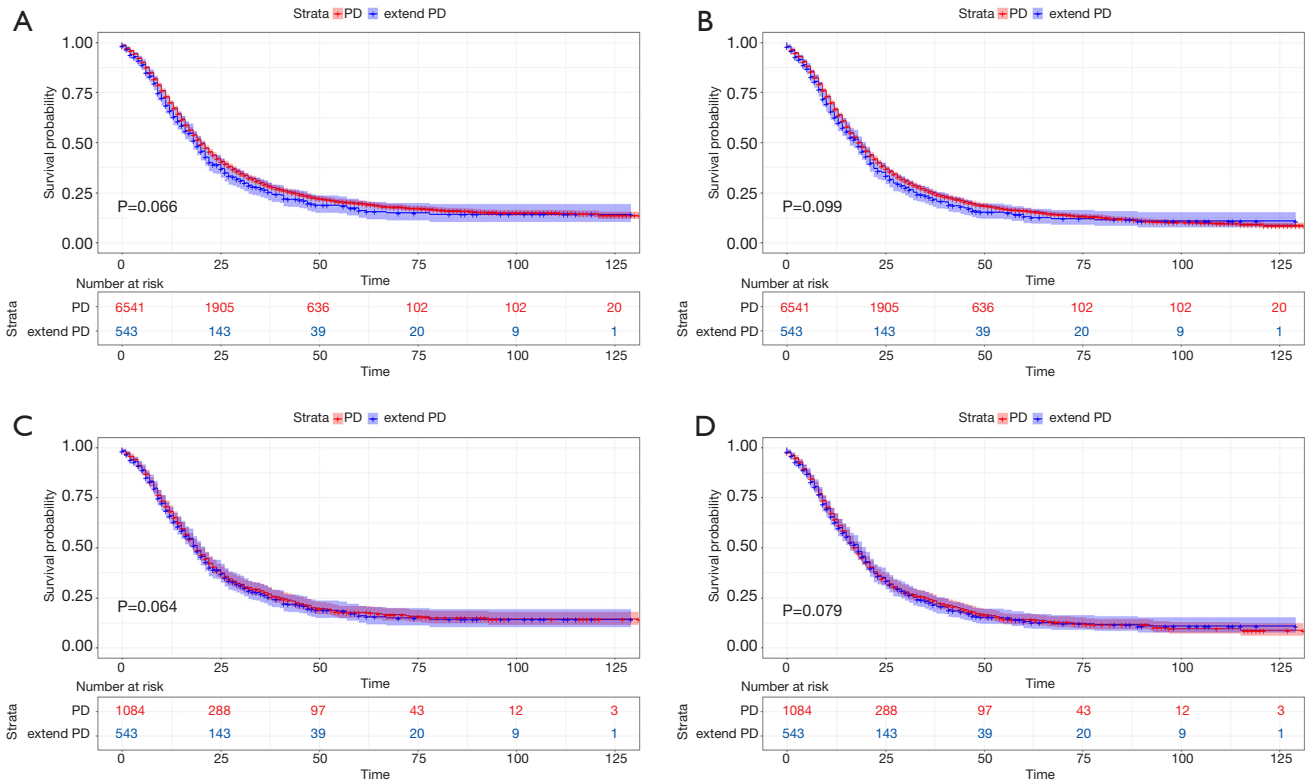

Figure 3 Kaplan-Meier survival curves for OS and CSS of patients with PD or extend PD procedures. CSS (A) and OS (B) between PD and extended PD in unmatched cohort. CSS (C) and OS (D) between PD and extended PD in matched cohort. OS, overall survival; CSS, cancer specific survival; PD, pancreaticoduodenectomy.

with extended lymphadenectomy. As the results showed, the CSS rate of 5 years in both matched populations was 17.5% and 16.1%, respectively. Regarding the 5-year OS, it was respectively 13.9% and 13.1%. Patients had no significant difference in CSS or OS, which was following many previous studies (16,18,19). However, Kantor *et al.* (20) demonstrated that PD with major vascular resection increased the rate of severe adverse effects, readmissions, a total length of hospital stay and costs. Despite the rates of R0 resection and overall relapse were similar between two cohorts, decreased OS occurred in combination with vascular resection. Podda *et al.* (16) obtained similar conclusions that the median OS for standard PD was 21 months and for PD with venous resection was 18 months (P=0.588). However, patients undergoing PD procedure with venous and arterial resection had a median OS of 7 months, which was less than standard PD procedure significantly (P=0.044). In addition, the PD with venous resection had no increased risk of procedure specific postoperative complications compared to standard PD. On the other hand, no survival benefit was obtained in PD procedure with venous resection and arterial resection. All of these studies indicated that the extended PD procedure had no survival benefit and may lead to a higher risk of morbidity and mortality (14,21).

It was not clear about the potential etiology for the growing complications with the extended PD procedure. The cross-clamping of the PV may consist of the higher complication profile, and then might result in growing propensity for ileus, malnutrition, and delayed gastric emptying induced by transient intestinal ischemia. All of the complications occurred among populations with extended PD procedure in increased frequency (22,23), which contributed to the prolonged hospitalization and admission. In addition, longer length of hospital stay, a principal adverse contributor to patient debilitation and quality of life, was a widely known risk indicator for delays to adjuvant chemotherapy (20).

From the results of multivariate analysis, we found age, differentiated grade, and TNM stage level were

independent prognostic factors for CSS. Intriguingly, marital status was an additional independent risk for OS. Asano *et al.* (24) reported that age contributed to the risk stratification in resected PC patients. In addition, differentiation grade, and TNM stage may reflect its biological activity highlighted in plenty of studies for its critical role in survival and some recent reports even combines these factors with other biomarkers to improve the predictive power (25-27). However, to our surprise, the single or divorced patients may have a poorer OS than those of being married. The reasons for that may include the lonely, anxious and depressed life, lack of enough care and high occurrence rate of accidents (28,29).

We recognize some possible limitations in this study. This study was limited as retrospective research, the data was lack of the morbidities and complications, and the extended PD was not classified specifically. Therefore, a multi-center and large-scale prospective study need be performed to eliminate the selective bias for further confirmation.

This population-based study shows that there is no distinctly different survival outcome between PHC patients with PD or extended PD procedure. The clinical indicators for the individual patient, such as age, differentiated grade, and TNM stage, may reveal a superior risk stratification to obtain an optimal treatment modality.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/tcr.2020.01.38). NP serves as an unpaid section editor of *Translational Cancer Research* from Jan 2020 to Dec 2021. The other authors have no conflicts of interest to declare.

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 Ethics Committees of Zhongshan Hospital, Fudan University, approved the design and analysis of this study (Ethical Committee No: B2017-006R). This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Individual informed consent was waived.

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