

# The diversity between curatively resected pancreatic head and body-tail cancers based on the 8th edition of AJCC staging system: a multicenter cohort study

**Weiwei Sheng**

The first hospital of China medical university

**Ming Dong** (✉ [cmudongming@sohu.com](mailto:cmudongming@sohu.com))

First Affiliated Hospital of China medical University

**Guosen Wang**

The first hospital of China medical university

**Xiaoyang Shi**

China medical university

**Wei Gao**

The first hospital of China medical university

**Kewei Wang**

The first hospital of China medical university

**He Song**

The first hospital of China medical university

**Gang Shi**

Liaoning Cancer Institute and Hospital

**Xiaodong Tan**

Shengjing Hospital of China Medical University

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## Research article

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# Abstract

**Background** To our knowledge, there are no studies to systematically compare the detailed clinical significance between curatively resected pancreatic head (ph) and body-tail (pbt) ductal cancers based on the new 8th edition of AJCC staging system (8th AJCC stage) that was just applied in clinical practice in 2018. **Methods** 351 cases of curatively resected pancreatic adenocarcinoma (PC) patients from three center hospitals were entered into this multicenter cohort study. **Results** Increasing tumor size ( $P<0.001$ ), T stage (T1+T2 vs T3+T4,  $P=0.003$ ), frequent postoperative liver metastasis (PLM) ( $P=0.002$ ) and 8th AJCC stage (IA to VI,  $P<0.001$ ; I+II vs III+IV,  $P=0.002$ ) were closely associated with the progression of pbt cancers compared with that in ph cancer patients. Moreover, tumor size  $\geq 3$ cm ( $P=0.012$ ), 8th AJCC stage (III+IV) ( $P=0.025$ ) and PLM ( $P=0.010$ ) were identified as independent risk factors in pbt cancers in logistic analysis. Patients with pbt cancers had a significantly worse overall survival compared with ph cancer patients ( $P=0.007$ ). Moreover, pbt was an independent unfavorable factor in multivariate analysis ( $P=0.009$ ). In addition to 8th AJCC stage, vascular invasion and PLM, increasing tumor size and advanced T stage were also closely associated with the poor prognosis in 131 cases of pbt cancer patients compared with Ph cancers. **Conclusion** Pbt, as an independent unfavorable factor for the prognosis of PC patients, are much more aggressive than that in ph cancers according to 8th AJCC staging system. 8th AJCC staging system are more comprehensive and sensitive to reflect the malignant biology of pbt cancers.

## Background

From 2000 to 2011, pancreatic adenocarcinoma (PC) takes up the second upward trend of age-standardized mortality rates in the population of Chinese men [1]. Meanwhile, it is the fourth most common cause of cancer death in the United States and Japan [2, 3]. Despite advances in multimodality treatment, long-term survival hasn't shown improvement over the past several decades with five-year survival rate less than 5% [4]. The poor prognosis of PC is mainly due to the late diagnosis and advanced progression, most of patients with PC are diagnosed at stages III and IV [5]. Even following curative resection, the reported 5-year survival rate remains low (7-24%) [6]. Accurate evaluation of tumor stage is a prerequisite for further treatment and prognostic prediction. The AJCC TNM staging system has been widely applied worldwide as the most authorized tool for tumor staging assessment. AJCC released the 8th edition (8<sup>th</sup> AJCC stage), which incorporated significant changes in the T and N classification of PC [7].

Most investigation on PC has been focused on the head of the pancreas (ph), whereas rare data is regarding pancreatic tail and body (pbt) cancers. Previous studies investigate the incidence rate and survival time between ph and pbt ductal cancers [8]. However, the results remain controversial and the relationship between tumor location and clinical characters is rarely reported. Meanwhile, to the best of our knowledge, there is no studies to systematically compare the clinical significance between curatively resected ph and pbt cancers based on the new 8<sup>th</sup> AJCC stage [8]. Based on the new 8th AJCC stage, we

find new clinical difference between curatively resected ph and pbt cancers, which provides a new clinical sight in revealing the malignant biology and improving the treatment for PC, especially in pbt cancer.

## Methods

### *Patients*

This research protocol was approved by the ethical committee of the institutional review board of China Medical University and a consent form was signed by each participating patient. All patients enrolled from the First hospital of China Medical University, Shengjing hospital of China Medical University and Cancer hospital of China Medical University were histologically proven to be pancreatic ductal adenocarcinomas. Contrast computed tomography (CT)/positron emission tomography (PET), contrast nuclear magnetic resonance (MRI) and surgical exploration were used to ensure whether all PC patients meet our resection criteria as Sugiura et al previously reported [9], including: a) no distant metastasis, b) tumor extension to the superior mesenteric artery or celiac trunk was less than 90° and can be completely resected and constructed. The detailed enrollment procedure was shown in Fig 1. Based on above criteria, between 2008 and 2016, 351 cases of consecutive PC patients underwent radical pancreatectomy were finally entered into this study. Pancreatoduodenectomy (PD) and distal pancreatectomy (PDP) are two main surgical treatments. In order to achieve R0 resection, cancer resection margins were at least 1 mm as cut-off. Meanwhile, some cases underwent surrounding organ resection, such as spleen, left adrenal gland, gastrointestinal (partial stomach, duodenum, intestine or colon), artery (hepatic, superior mesenteric and celiac artery) and vein (portal or superior and inferior mesenteric vein). 6 PC patients were found a single liver metastasis (preoperative CT examination is not detected) in surgery, we additionally executed partial hepatectomy. A dedicated table for patients' characteristics was summarized in Table 1. Four classic samples from consecutive PC patients underwent radical PD and PDP resection showed in Fig 2.

### *Follow-up*

All patients were followed up by the operating surgeons. As described previously [6], postoperative patients were performed routinely laboratory examinations, including tumor markers, liver function, US, abdominal CT/PET or contrast MRI every 3-6 months. For postoperative live metastasis (PLM), if the liver metastasis showed no definite evidence of other metastasis or recurrence elsewhere, we characterized the newly developed hepatic lesion as PLM [10]. Patient follow-up examinations was performed each 3 months for the first 2 postoperative years, every 6 months for >2 years, and yearly thereafter. 125 cases of ph cancer patients and 73 cases of pbt cancer patients accepted postoperative gemcitabine-based chemotherapy, no difference was shown in two groups with or without chemotherapy treatment.

### *Statistical analysis*

Statistical analysis was performed using SPSS software 19.0. The differences between curatively resected ph and pbt cancers was analyzed using a Chi-Squared test. A logistic regression analysis was performed to determine the pathologic impact findings that were significant with regard to differences in

the univariate analysis. The Kaplan-Meier method was used to estimate survival in PC patients, and differences were analyzed by the log-rank test. The variables that were found to be significant by the univariate analysis were subjected to a multivariate Cox proportional hazards regression analysis in a stepwise manner. A value of  $P < 0.05$  was considered to be statistically significant.

## Results

### ***Comparison of the 7th and 8th editions of the TNM staging system for patients***

The detailed information of 7<sup>th</sup> and 8<sup>th</sup> AJCC stage in PC was summarized in supplemental Table 1 and Table 2. Briefly, in the 8th edition, stages T1-T3 are redefined according to tumor size. When the tumor invades the celiac axis, hepatic artery and/or superior mesenteric artery, it is defined as T4, and the classification as “unresectable” was removed. Because all the patients enrolled in this study accept the curative resection, 6 cases of T4 stage PC (III stage) patients based on 8<sup>th</sup> AJCC stage were excluded in 7<sup>th</sup> AJCC system (Table 1). In addition, the N classification was further subdivided according to the number of positive lymph nodes as N0, N1 and N2. T1-3N2M0 was defined as stage III in 8<sup>th</sup> AJCC stage, while it was defined as stage IIB in 7<sup>th</sup> AJCC stage. In current study, 14.9 % (16/107) of these patients had metastasis in more than 3 lymph nodes (pN2) (Table 1). The ratio of stage IA, IB, IIA, IIB, III and IV of 8<sup>th</sup> AJCC stage was 6.8%, 33.9%, 26.4, 24.3%, 6.5% and 1.7%, respectively, while the ratio of stage IA, IB, IIA, IIB and IV was 5.5%, 40.5%, 22%, 30.1% and 1.7% in 7<sup>th</sup> AJCC stage (III stage that was defined as “unresectable” PC were excluded).

### ***Different clinical significance between ph and pbt cancers in 351 cases PC patients with curative resection***

Chi-Squared test in Table 2 showed that tumor size, T stage, 8<sup>th</sup> AJCC stage and PLM were significantly different between ph and pbt cancers. Increasing tumor size ( $P < 0.001$ ), frequent PLM ( $P = 0.002$ ) and advanced T ( $P = 0.003$ ) and 8<sup>th</sup> AJCC stage (IA to VI,  $P < 0.001$ ; I+II vs III+IV,  $P = 0.002$ ) were closely associated with the progression of pbt cancers compared with that in ph cancers. However, age, gender, tumor differentiation, lymph nodes metastasis, CA199 level and perineural and vascular invasion showed no difference between two groups ( $P > 0.05$ ). A multivariate analysis (logistic regression analysis) identified tumor size  $\geq 3$ cm ( $P = 0.012$ ), 8<sup>th</sup> AJCC stage (III+IV) ( $P = 0.025$ ) and PLM ( $P = 0.010$ ) as independent risk factors in pbt cancers (Table 2). It is worthy noted that T and TNM stage based on 7<sup>th</sup> AJCC stage system showed no significant difference between ph and pbt cancers, which indicated that pbt cancers are closely associated with advanced clinical stage in 8<sup>th</sup> AJCC stage.

### ***Prognostic factors of PC patients who underwent curative pancreatectomy***

Univariate analysis showed that patients with pbt cancers had a significantly worse overall survival compared with ph cancer patients ( $P = 0.003$ ) (Table 3) (Fig 2a). Meanwhile, lymph nodes metastasis ( $P = 0.001$ ), 8<sup>th</sup> AJCC stage ( $P = 0.007$ ), vascular permeation ( $P = 0.004$ ) and PLM ( $P < 0.001$ ) were also

associated with PC patients' poor prognosis. In multivariate model, tumor location ( $P=0.011$ ), lymph nodes metastasis ( $P=0.004$ ), 8<sup>th</sup> AJCC stage ( $P=0.012$ ) and PLM ( $P=0.001$ ) were independent unfavorable prognostic indicators in PC (Table 3). 7<sup>th</sup> AJCC stage was also associated with the poor prognosis of PC patients ( $P=0.012$ ). Interestingly, previous studies show that pbt cancer patients have a better prognosis than ph cancer patients in early 7<sup>th</sup> AJCC I and II stage [11]. In current study, pbt cancer patients showed worse prognosis in both 8<sup>th</sup> AJCC I-III stage and I-II stage compared with ph cancer patients ( $P=0.032$ ) (Fig 2b, c). Only in 8<sup>th</sup> AJCC I stage, the median days of pbt cancer patients was longer than that in ph cancer patients, but there was no statistic difference (data not shown). In addition, lymph node metastasis (N0/N1) in 7<sup>th</sup> AJCC stage failed to stratify patients by survival, whereas lymph node metastasis (N0/N1/N2) based on 8<sup>th</sup> AJCC stage was an independent unfavorable prognostic indicator in our current study. It indicated that lymph node metastasis in 8<sup>th</sup> AJCC stage is more comprehensive to reflect the malignant progression and poor prognosis of PC patients.

### ***Different prognostic indicators in ph and pbt cancer patients with curative surgical resection.***

Lymph node metastasis, 8<sup>th</sup> AJCC stage and vascular invasion were associated with the poor prognosis in 220 cases of Ph cancer patients. In 131 cases of pbt cancer patients, in addition to 8<sup>th</sup> AJCC stage and vascular invasion, tumor size and T stage were also the poor prognostic indicators. Much more clinical factors based on 8<sup>th</sup> AJCC stage were associated with the prognosis in pbt cancer patients compared with the ph cancer.

## **Discussion**

In addition to positive reclassification outcomes, 8<sup>th</sup> AJCC stage demonstrates a more equal distribution among stages and increased prognostic accuracy compared with 7<sup>th</sup> AJCC stage. In an international multicenter cohort study including 1525 consecutive patients, the new T stage does not demonstrate significant correlation with survival on univariate or multivariate analysis, whereas the new N stage showed accurate discrimination of survival. These results were consistent with our current study [12]. However, the superiority of the 8th edition to the 7th edition at evaluating the relationship between tumor location and clinical characters has not been evaluated in PC patients, to our knowledge. Based on the new 8<sup>th</sup> AJCC stage, we found new diversity between ph and pbt cancers from a multicenter cohort study.

In anatomy, cell composition, blood supply, lymphatic and venous backflow,

and innervations are significantly different between ph and pbt cancers [13]. In clinic, tumors at different locations (ph vs pbt) display different clinical presentation,

treatment efficiency (surgery and chemoradiotherapy) and prognosis [14]. The incidence rate for ph cancer has remained at 5.6% per 100,000, whereas the rate for pancreatic body/tail cancers has increased by 46% between 1973 and 2002 in the SEER database [7]. Though both ph and pbt cancers had a higher proportion diagnosed in the distant stages (a neoplasm that has spread to parts of the body

remote from the primary tumor or to distant lymph nodes), patients with ph cancer were more likely to have localized and regional diseases (12.9% and 32.2%, respectively) as compared with patients with pbt cancer (6.6% and 13.9%, respectively) [7]. According to 7<sup>th</sup> AJCC stage, there was no significant difference in TNM stage between resected ph and pbt cancers [15]. However, in current study, we find new clinical difference between curatively resected ph and pbt cancers bases on 8<sup>th</sup> AJCC stage, which hasn't been reported previously to our knowledge.

The alteration of the definitions of T and N is main changes for 8th AJCC stage compared with the 7<sup>th</sup> AJCC stage [16]. Just shown in supplemental Table 1 and 2, extrapancreatic invasion can be difficult to predict accurately before surgery and may be inconsistently assessed by pathologists [17]. T3 tumors are now defined as those larger than 4 cm, while nodal involvement has been improved from a binary system to one based on extent of nodal involvement. In current study, increasing tumor size and advanced T stage and 8th AJCC stage were closely associated with the progression of pbt cancers compared with ph cancers. Only one study shows tumor size but not T and clinical stage in 7<sup>th</sup> AJCC stage exhibits difference in resected ph (56 cases) and pbt (24 cases) cancers [15], which is consistent with our study. Based on the alteration of T and N status in 8th AJCC stage, T1-3 stage was likely a stratified analysis of tumor size. Meanwhile, new 8<sup>th</sup> AJCC stage mainly increased III stage (16 vs 0) but decreased IIB stage (86 vs 104) in PC patients compared with 7<sup>th</sup> AJCC stage in our study, which is the critical reason for the discrimination in above results just as Omar Abdel-Rahman suggested [18]. Our study additionally found PLM was more frequent in pbt cancers, which is consistent with the study by Maria Chiara Ambrosetti et al [19]. However, Nakata B et al show that the recurrence of peritoneum, liver, lung and bone showed no difference in tumor location [15]. Among 707 unresectable PC patients with stage III, 30.1% developed PLM. However, no risk factors were identified among these patients [20]. The inconsistency might be due to the different sample size and diversity in national population included in the studies.

Currently, prognostic difference between ph and pbt cancer patients remain controversial. Data from SEER database (1988-2004) including 33752 PC patients presented a significant lower median survival (4 months vs 6 months) in

patients with pbt cancer compared with those with ph cancer [21]. However, data from the national PC registry of Japan showed a significant lower 5-year

survival rate (10.7% vs 13.8%) for patients with ph cancers (n=5788) than those with pbt cancers (n=1629) [22]. Both unresectable and resectable PC patients are enrolled in above studies. In our current study, we only enrolled curatively resected PC patients from three multiple centers. Our study showed that pbt cancer patients had a worse survival compared with ph cancers and was an independent unfavorable prognostic factor. Pbt cancer patients lack early symptoms but Ph cancer patients have (obstructive jaundice), which is a critical reason for the relationship between more advanced clinical stage and worse prognosis and pbt cancers patients as Melvin K et al suggested [7]. However, a Japanese study enrolling 80 consecutive

patients with resectable PC presented similar overall survival and recurrence

rates after a curative resection between ph (n=56) and pbt (n=24) cancers [15] Wentz SC et al. also showed no relationship of tumor location (151 cases of ph vs 18 cases of pbt) with resected PC patients [23]. Interestingly, using the surveillance, epidemiology, and end results (SEER) registry to identify 43,946 cases of PC, higher survival rates was shown in ph cancer compared with pbt cancer in several variables (age, sex, race, geography, and time). But the 3-year survival rate for local-stage (neoplasm confined to the organ of origin) pbt cancer is 20.0% compared with 9% for local-stage ph cancer [7]. In 32 cases of PC patients with 7<sup>th</sup> AJCC stage II, both overall and tumor-free survival were significantly higher in the patients with pbt cancer compared with those with ph cancers [11]. Our study showed that the survival time of pbt cancer patients was longer than that in ph cancer patients only in 8<sup>th</sup> AJCC I stage but no statistic difference. Indeed, some small metastases (liver metastasis) known as “micrometastases” from PC may be overlooked even with advanced imaging and surgical exploration [24], which affects the evaluation of TNM stage and the survival. In our study, 6 PC patients had a simultaneous single liver metastasis resection that was not detected in preoperative examination. 4 of 6 patients were evaluated in early stage (less than IIA) if we neglected the small single liver metastasis. Generally, pbt cancers were associated with much more advanced stage and worse prognosis in PC patients.

Finally, compared with ph cancers, we first showed tumor size and T stage were not only independent risk factors in the development of pbt cancers, but also poor prognostic indicators for pbt cancer patients based on 8<sup>th</sup> AJCC stage. Taking together, 8<sup>th</sup> AJCC stage are more comprehensive to reflect the poor prognosis of pbt cancer patients.

## Conclusions

Based on the 8<sup>th</sup> AJCC staging system, tumor size, T stage, AJCC stage and PLM are independent risk factors in the development of pbt cancer compared with ph cancers. Pbt, as an independent unfavorable factor for the prognosis of PC patients, are much more aggressive than that in ph cancers according to 8th AJCC staging system. 8th AJCC staging system are more comprehensive and sensitive to reflect the malignant biology of pbt cancers compared with ph cancers.

## Abbreviations

We thank for the clinical surgeons from the First hospital of China Medical University, Shengjing hospital of China Medical University and Cancer hospital of China Medical University for the clinical data collection.

## Declarations

### Authors' contributions

Weiwei Sheng and Ming Dong contributed the study design and concept. Data acquisition was performed by Weiwei Sheng, Guosen Wang, Gang Shi and Xiaodong Tan. Xiaoyang Shi and Wei Gao performed the statistical analysis. Ming Dong , Gang Shi and Xiaodong Tan contributed to the data analysis and interpretation. All of the authors read and approved the final manuscript

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## **Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request

## **Conflict of interest**

The authors declare no conflict of interest.

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## Tables

Table 1. The clinical data in 351 cases of PC patients with curatively surgical resection.

Parameters	No. of patients	Parameters	No. of patients
<b>Cases</b>	351	<b>Cases</b>	351
<b>Age(years)</b>		<b>Perineural invasion</b>	
≤65	240	Absent	278
>65	111	Present	73
<b>Gender</b>		<b>Vascular permeation</b>	
<b>Male</b>	210	Absent	266
<b>Female</b>	141	Present	85
<b>Tumor size(cm)</b>		<b>Pre-therapeutic CA19-9 level</b>	
<3	108	Mean±SD	355±283
≥3	243	<b>PLM</b>	
<b>Tumor location</b>		Absent	227
<b>Ph</b>	220	Present	124
<b>Pbt</b>	131	<b>7<sup>th</sup> AJCC stage<sup>a</sup></b>	
<b>Differentiation</b>		IA	19
<b>Well</b>	140	IB	140
<b>Moderate</b>	118	IIA	76
<b>Poor</b>	93	IIB	104
<b>8<sup>th</sup> T stage</b>		IV	6
<b>T1</b>	35	<b>Surgical procedures</b>	
<b>T2</b>	167	PD alone	196
<b>T3</b>	143	PD+gastrointestine	8
<b>T4</b>	6	PD+portal or superior	11
		mesenteric vein	
<b>7<sup>th</sup> T stage<sup>a</sup></b>		PD+ hepatic or superior	3
		mesenteric artery	
<b>T1</b>	27	PD +liver	2
<b>T2</b>	215	PDP alone	97
<b>T3</b>	103	PDP+gastrointestine	12
<b>Lymph nodes</b>		PDP +portal vein or inferior	6
<b>metastasis</b>		mesenteric vein	
<b>N0</b>	244	PDP + gastrointestine	5
		+left adrenal	
<b>N1</b>	91	PDP +liver+ left adrenal	1
<b>N2</b>	16	PDP +liver	3
<b>8<sup>th</sup> AJCC stage</b>		PDP + left adrenal	4
<b>IA</b>	24	PDP+ celiac artery	3
<b>IB</b>	119	<b>Postoperative chemotherapy</b>	
<b>IIA</b>	93	Ph cancers	125/220
<b>IIB</b>	86	Pbt cancers	73/131
<b>III</b>	23		
<b>IV</b>	6		

N1: Lymph nodes metastasis 1-3; N2: Lymph nodes metastasis>3; PLM: postoperative live metastasis; PD: Pancreatoduodenectomy; PDP: Distal pancreatectomy.

7<sup>th</sup> and 8<sup>th</sup> AJCC stage: 7th and 8th edition of AJCC staging system in PC; Ph: Pancreatic head; Pbt: Pancreatic body-tail. a 6 cases of T4 stage in 8<sup>th</sup> AJCC stage (III) were exclude in 7<sup>th</sup> AJCC stage.

Table 2. Clinical significance between ph and pbt cancers in 351 cases PC patients with curatively resection

Parameters	No. of patients	Chi square		<i>P</i>	Multivariate analysis	
		Head	Body-tail		Odds ratio (95% CI)	<i>P</i>
Cases	351					
Age(years)						
≤65	240	157	83	0.125		
>65	111	63	48			
Gender						
Male	210	131	79	0.911		
Female	141	89	52			
Tumor size(cm)						
<2	35	28	7	0.027		
≥2	316	192	124			
Tumor size(cm)						
<3	108	84	24	0.000	2.133(1.180-3.856)	0.012
≥3	243	136	107			
Differentiation						
Well	140	86	54	0.793		
Moderate	118	73	45			
poor	93	61	32			
Lymph nodes						
metastasis						
N0	244	155	89	0.101		
N1	91	59	32			
N2	16	6	10			
7 <sup>th</sup> T stage <sup>a</sup>						
T1+T2	151	159	83	0.114		
T3	103	58	45			
7 <sup>th</sup> AJCC stage <sup>b</sup>				0.360		
IA	19	13	6			
IB	140	86	54			
IIA	76	45	31			
IIB	104	71	33			
IV	6	2	4			
8 <sup>th</sup> T stage						
T1+T2	202	140	62	0.003	1.344(0.805-2.243)	0.258
T3+T4	149	80	69			
8 <sup>th</sup> AJCC stage				0.000		
IA	24	18	6			
IB	119	84	35			
IIA	93	42	51			
IIB	86	66	20			
III	23	8	15			
IV	6	2	4			
8 <sup>th</sup> AJCC stage						
I+II	321	209	112	0.002	2.520(1.121-5.665)	0.025
III+IV	30	11	19			
Perineural invasion						
Absent	278	180	98	0.118		
Present	73	40	33			
Vascular permeation						
Absent	266	172	94	0.174		
Present	85	48	37			

Pre-therapeutic  
CA19-9 level

Mean±SD	/	389.6±255.7	324.2±283.3	0.429		
PLM						
Absent	227	156	71	0.002	1.854(1.160-2.963)	0.010
Present	124	64	60			

N1: Lymph nodes metastasis 1-3; N2: Lymph nodes metastasis>3; PLM: postoperative live metastasis; 7<sup>th</sup> and 8<sup>th</sup> AJCC stage: 7th and 8th edition of AJCC staging system in PC; Ph: Pancreatic head; Pbt: Pancreatic body-tail. a, b 6 cases of T4 stage in 8<sup>th</sup> TNM stage (III) were exclude.

Table 3. Univariate and multivariate analysis for prognostic factors in 351 cases of PC patients with curatively surgical resection

Parameters	median survival (days)	Univariate analysis <i>P</i> (log rank)	Multivariate analysis hazard ratio (95% CI)	<i>P</i>
Age (<65/ ≥65 years)	432/421	0.127	–	
Gender (male/female)	421/472	0.366	–	
Tumor location (ph/pbt)	488/340	0.003	1.405(1.082-1.826)	0.011
Tumor size (<2/ ≥2 cm)	472/421	0.371	–	
Tumor size (<3/ ≥3 cm)	472/418	0.096	–	
Well/Moderate/poor	452/420/382	0.071	–	
Differentiation				
T stage (T1+T2/ T3+T4)	472/381	0.068	–	
Lymph nodes metastasis 8 <sup>th</sup> (N0/N1/N2)	480/330/284	0.001	1.451(1.123-1.874)	0.004
Lymph nodes metastasis 7 <sup>th</sup> (N0/N1+N2) <sup>a</sup> 8 <sup>th</sup> AJCC stage	472/399	0.090	–	
	468/284	0.007	1.442(1.085-1.915)	0.012
(I+II /III+VI)				
Perineural invasion (absent/present)	454/400	0.179	–	
Vascular permeation (absent/present)	480/330	0.004	1.401(0.905-2.168)	0.131
CA19-9 level (<37 U/ml/ ≥37 U/ml)	565/395	0.104	–	
PLM (absent/present)	499/330	0.000	1.594(1.224-2.076)	0.001
7 <sup>th</sup> AJCC stage	468/172	0.012	Not included	

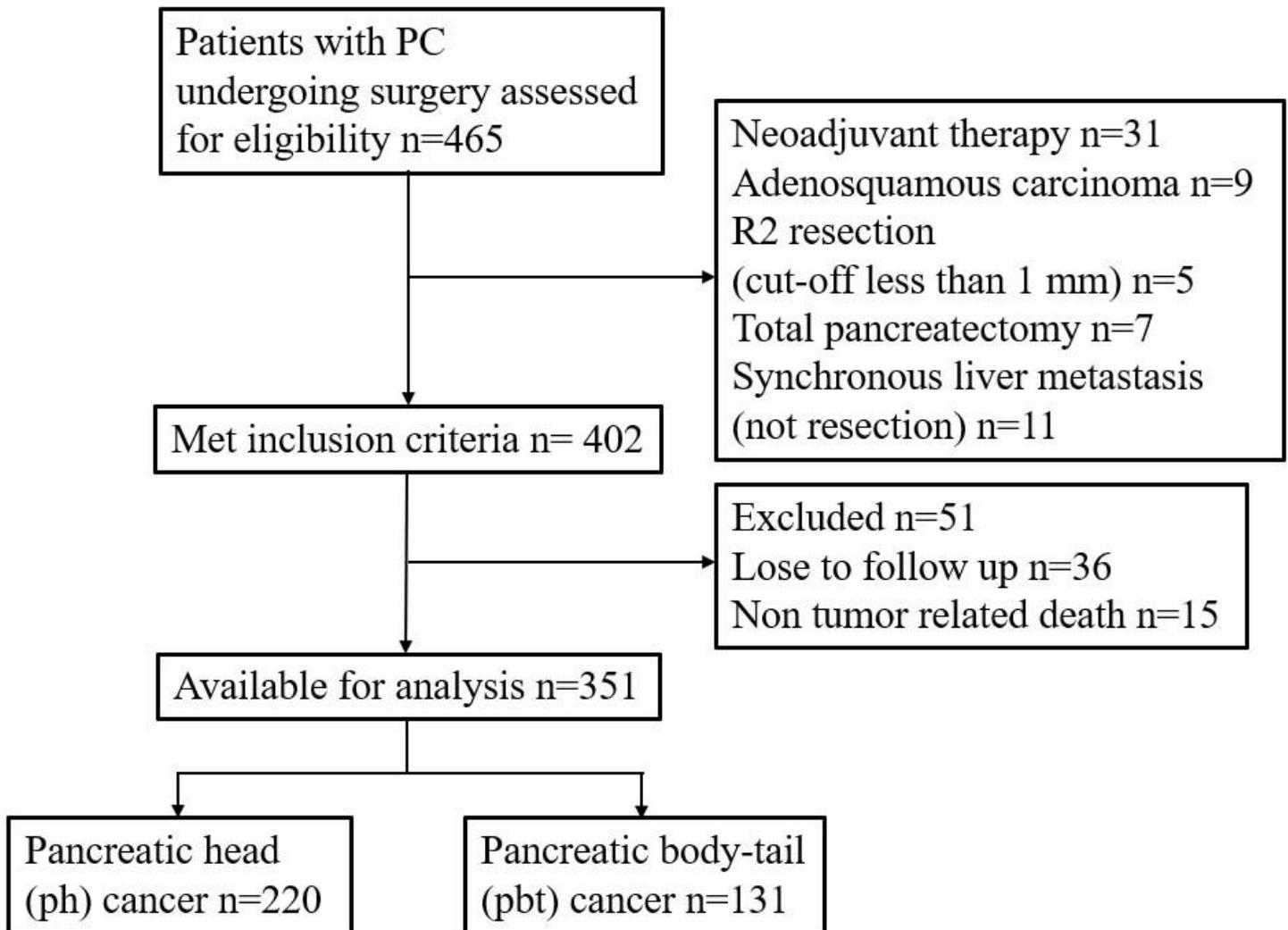
N1: Lymph nodes metastasis 1-3; N2: Lymph nodes metastasis>3; 7<sup>th</sup> and 8<sup>th</sup> AJCC stage: 7th and 8th edition of AJCC staging system in PC; Ph: Pancreatic head; Pbt: Pancreatic body-tail. a In 7<sup>th</sup> AJCC stage, N1 and N2 combined together.

Table 4. Difference of prognostic factors in Ph and Ptb cancer patients with curatively surgical resection.

Tumor location	Parameters	Median survival	Univariate analysis
		(days)	<i>P</i> (log rank)
220 Ph cancers	Age (<65/ ≥65 years)	499/480	0.131
	Gender (male/female)	454/615	0.335
	Tumor size (<3/ ≥3 cm)	555/488	0.358
	Well/Moderate/poor	615/555/411	0.155
	Differentiation		
	T stage	488/454	0.105
	(T1+T2/T3)		
	Lymph nodes metastasis (N0/N1/N2)	565/418/185	0.004
	8 <sup>th</sup> AJCC stage	360/273	0.017
	(I+II /III+IV)		
	Perineural invasion (absent/present)	880/545	0.298
	Vascular permeation	565/350	0.005
	(absent/present)		
	CA19-9 level	666/450	0.171
(<37 U/ml/ ≥37 U/ml)			
PLM			
absent/present	586/365	0.039	
131 Pbt cancers	Age (<65/ ≥65 years)	381/300	0.111
	Gender (male/female)	395/340	0.439
	Tumor size (<3/ ≥3 cm)	530/320	0.023
	Well/Moderate/poor	400/280/273	0.070
	Differentiation		
	T stage	418/320	0.016
	(T1+T2/ T3+T4)		
	Lymph nodes metastasis (N0/N1/N2)	360/259/234	0.007
	8 <sup>th</sup> AJCC stage	499/273	0.001
	(I+II /III+IV)		
	Perineural invasion (absent/present)	360/333	0.104
	Vascular permeation	400/265	0.009
	(absent/present)		
	CA19-9 level	468/331	0.099
(<37 U/ml/ ≥37 U/ml)			
PLM			
absent/present	432/275	0.001	

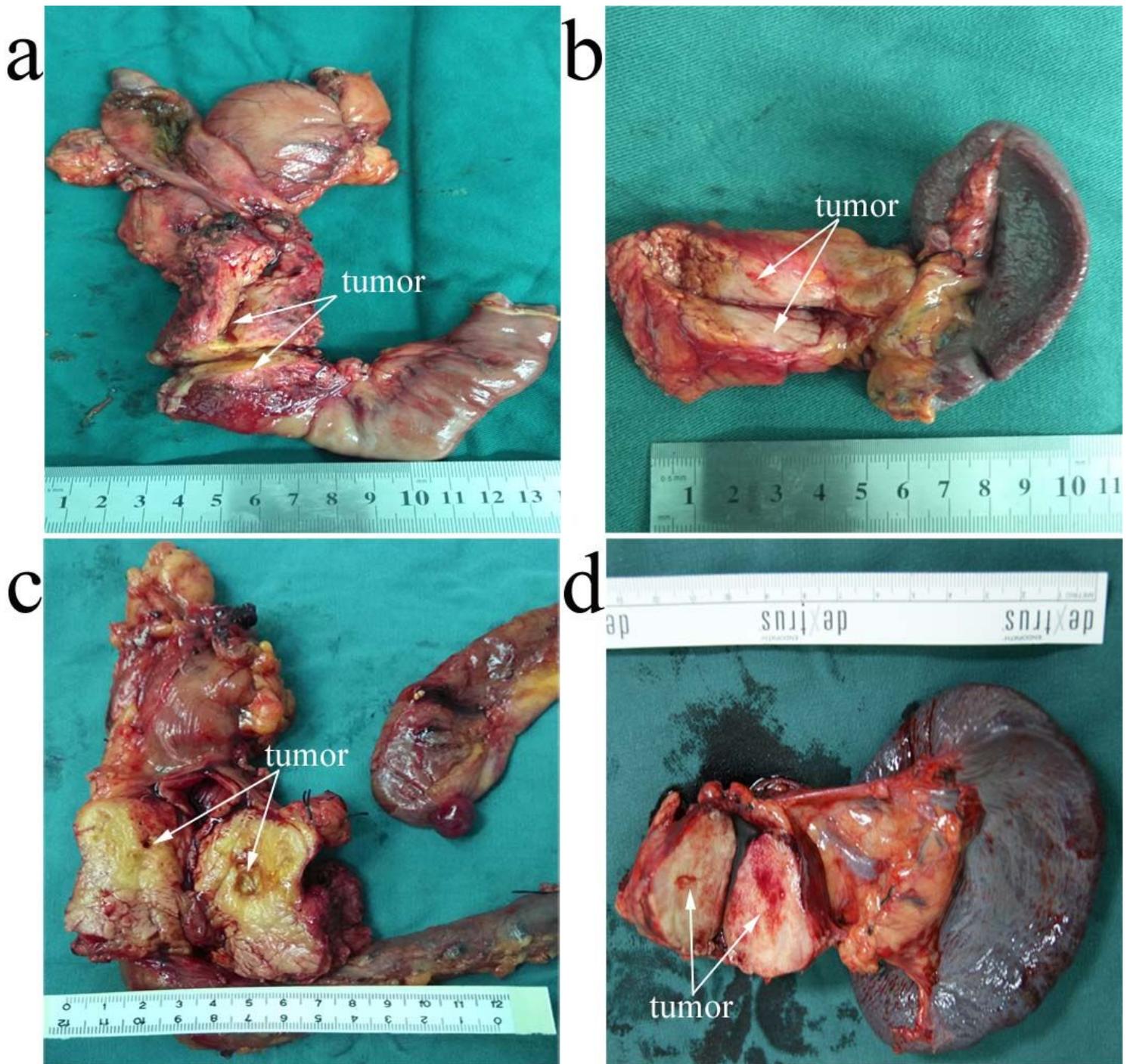
N1: Lymph nodes metastasis 1-3; N2: Lymph nodes metastasis>3; 8<sup>th</sup> AJCC stage: 8th edition of AJCC staging system in PC; Ph: Pancreatic head; Pbt: Pancreatic body-tail.

## Figures



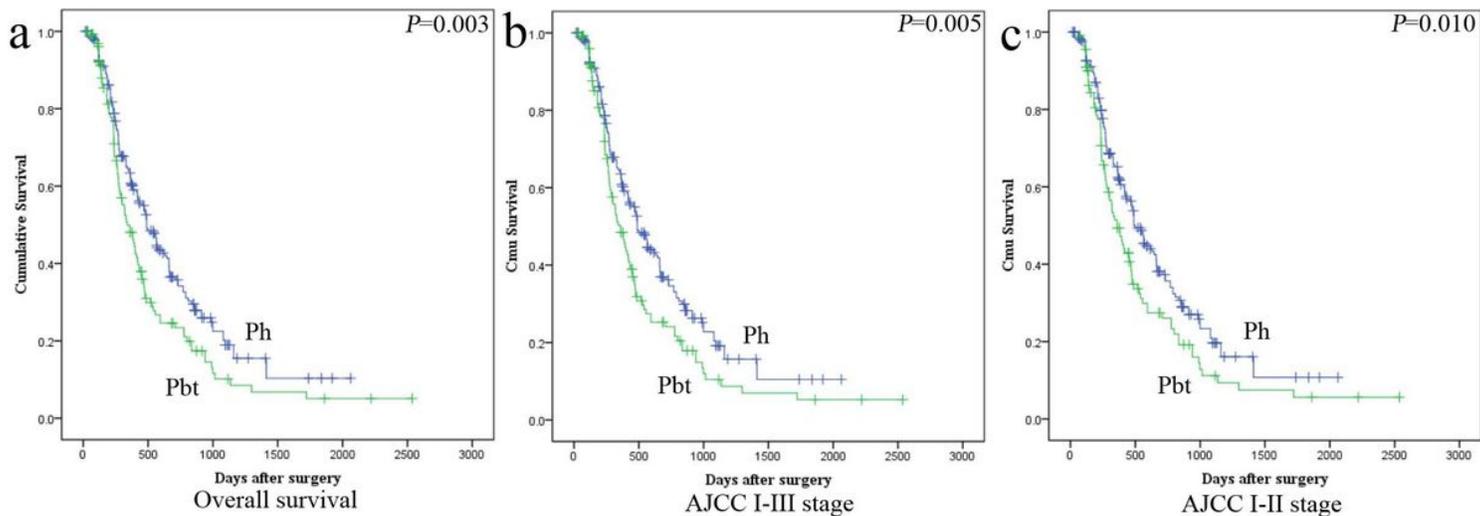
**Figure 1**

Study flow chart. Undergoing strict selection, 351 cases of PC patients were finally entered into this study from three multiple centers. PC: pancreatic adenocarcinoma; Ph: pancreatic head; Pbt: pancreatic body-tail.



**Figure 2**

Four classic samples from consecutive PC patients underwent PD or PDP. a, c Under PD treatment, two ph tumor samples was shown as arrows suggested. b, d Under PDP treatment, two pbt tumor samples was shown as arrows suggested. PD: Pancreatoduodenectomy; PDP: distal pancreatectomy. Ph: pancreatic head; Pbt: pancreatic body-tail.



**Figure 3**

The prognosis between ph and pbt cancers with different clinical stage of 8th AJCC. a. The prognosis between ph and pbt cancers in 8th AJCC stage I to III. b. The prognosis between ph and pbt cancers in 8th AJCC stage I to II.

## Supplementary Files

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