

# World Journal of *Gastroenterology*

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 Telephone: +1-925-2238242  
 Fax: +1-925-2238243  
 E-mail: [editorialoffice@wjgnet.com](mailto:editorialoffice@wjgnet.com)  
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## Retrospective Study

**Pancreaticoduodenectomy for duodenal papilla carcinoma: A single-centre 9-year retrospective study of 112 patients with long-term follow-up**

Pei-Long Lian, Yuan Chang, Xiu-Chun Xu, Zhen Zhao, Xian-Qiang Wang, Ke-Sen Xu

Pei-Long Lian, Zhen Zhao, Ke-Sen Xu, Department of Hepatobiliary Surgery, Qilu Hospital, Shandong University, Jinan 250012, Shandong Province, China

Yuan Chang, Department of Anesthesiology, Shandong Provincial Hospital Affiliated to Shandong University, Jinan 250021, Shandong Province, China

Xiu-Chun Xu, Department of Vascular Surgery, Binhai People's Hospital, Yancheng 224500, Jiangsu Province, China

Xian-Qiang Wang, Department of Hepatobiliary Surgery, the PLA General Hospital, Beijing 100853, China

**Author contributions:** Lian PL designed the research, analyzed the data, drafted and revised the paper; Wang XQ, Xu XC and Zhao Z performed the research; Chang Y searched the literature; Xu KS revised the paper, approved the final version.

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Correspondence to: Ke-Sen Xu, PhD, Professor, Department of Hepatobiliary Surgery, Qilu Hospital, Shandong University, 107 Wenhua Road, Jinan 250012, Shandong Province, China. [xukesen0519@sdu.edu.cn](mailto:xukesen0519@sdu.edu.cn)  
Telephone: +86-531-82169230  
Fax: +86-531-82169243

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**Abstract****AIM**

To retrospectively evaluate the factors that influence long-term outcomes of duodenal papilla carcinoma (DPC) after standard pancreaticoduodenectomy (SPD).

**METHODS**

This is a single-centre, retrospective study including 112 DPC patients who had a SPD between 2006 and 2015. Associations between serum levels of CA19-9 and CEA and various clinical characteristics of 112 patients with DPC were evaluated by the  $\chi^2$  test and Fisher's exact test. The patients were followed-up every 3 mo in the first two years and at least every 6 mo afterwards, with a median follow-up of 60 mo (ranging from 4 mo to 168 mo). Survival analysis was conducted using the Kaplan-Meier survival and Cox proportional hazards model analysis. The difference in survival curves was evaluated with a log-rank test.

## RESULTS

In 112 patients undergoing SPD, serum levels of CA19-9 was associated with serum levels of CEA and drainage mode (the *P* values were 0.000 and 0.033, respectively); While serum levels of CEA was associated with serum levels of CA19-9 and differentiation of the tumour (the *P* values were 0.000 and 0.033, respectively). The serum levels of CA19-9 and CEA were closely correlated ( $\chi^2 = 13.277$ ,  $r = 0.344$ ,  $P = 0.000$ ). The overall 5-year survival was 50.00% for 112 patients undergoing SPD. The Kaplan-Meier survival analysis showed that increased serum levels of CA19-9, CEA, and total bilirubin were correlated with a poor prognosis, as well as a senior grade of infiltration depth, lymph node metastases, and TNM stage (the *P* values were 0.033, 0.018, 0.015, 0.000, 0.000 and 0.000, respectively). Only the senior grade of infiltration depth and TNM stage retained their significance when adjustments were made for other known prognostic factors in Cox multivariate analysis ( $RR = 2.211$ ,  $P = 0.022$  and  $RR = 2.109$ ,  $P = 0.047$ ).

## CONCLUSION

For patients with DPC, the serum levels of CA19-9 and CEA were closely correlated, and play an important role in poor survival. Increased serum levels of total bilirubin and lymph node metastases were also correlated with a poor prognosis. The senior grade of infiltration depth and TNM stage can serve as independent prognosis indexes in the evaluation of patients with DPC after SPD.

**Key words:** Duodenal papilla carcinoma; CA19-9; CEA; Survival; Pancreaticoduodenectomy

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**Core tip:** For duodenal papilla carcinoma (DPC), standard pancreaticoduodenectomy (SPD) is still the most important treatment. However, the prognosis assessment for DPC after SPD is not yet clear. So we conducted a long-term follow-up and observation with a large sample. Our study demonstrated that the serum levels of CA19-9 and CEA were closely correlated and played an important role in poor survival. Increased serum levels of total bilirubin and lymph node metastases were also correlated with a poor prognosis. The senior grade of infiltration depth and TNM stage can serve as independent prognosis indexes for patients with DPC after SPD.

Lian PL, Chang Y, Xu XC, Zhao Z, Wang XQ, Xu KS. Pancreaticoduodenectomy for duodenal papilla carcinoma: A single-centre 9-year retrospective study of 112 patients with long-term follow-up. *World J Gastroenterol* 2017; 23(30): 5579-5588 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v23/i30/5579.htm> DOI: <http://dx.doi.org/10.3748/wjg.v23.i30.5579>

## INTRODUCTION

The incidence rate of primary duodenal papilla carcinoma (DPC) is low, only accounting for 0.01% of malignant tumours and accounting for 5% of gastrointestinal malignant tumours<sup>[1]</sup>. It has been reported in the literature that among malignant tumours primarily occurring in the duodenum, 60% are diagnosed as DPC<sup>[2]</sup>, and the incidence rate of DPC in periampullary carcinoma is the highest. A series of studies have demonstrated that there is a higher excision rate and better prognosis of DPC than other malignant tumours around the duodenal ampulla, and the survival rate within 5 years after the operation is in the range of 50%-60%<sup>[3]</sup>.

For DPC, Standard pancreaticoduodenectomy (SPD) is still the most important treatment mode<sup>[4-6]</sup>. Based on a large number of studies, there are still many disputes concerning the prognosis assessment for primary DPC after SPD, and there is lack of long-term follow-up and observation of a large sample.

Therefore, the main objective of this study was to review and report our own single-centre data of 112 patients with DPC at the PLA General Hospital between 2006 and 2015 to evaluate factors influencing outcome after radical SPD surgery.

## MATERIALS AND METHODS

### General data

A total of 112 patients with DPC who received SPD in the PLA General Hospital from August 2006 to November 2015 were enrolled. In this study, all patients were confirmed as DPC according to postoperative pathological examinations. There were 74 males and 38 females, with a median age of 57.95 years. The disease course was 0.13-15 years.

This study only enrolled patients who received SPD due to DPC. The following patients were not enrolled: patients who had received radiotherapy and chemotherapy before the operation; patients who received endoscopic local excision of benign tumours of the duodenum; patients who could not tolerate SPD because of body conditions; and patients with complicated malignant tumours at other sites.

All patients and/or a family member signed a written informed consent form, in which the nature of the diseases, possible therapeutic methods and postoperative potential complications were detailed. This study was approved by the ethics committee of the PLA General Hospital and was performed in accordance with the ethical standards specified in the 1964 Declaration of Helsinki and its later amendments.

### Clinical manifestations and concomitant diseases

The most common clinical manifestation was jaundice; other symptoms included body weight decreases and epigastric discomfort. In addition, there were

20 patients with cholangitis symptoms such as intermittent or acute fever. Common concomitant diseases included hypertension, heart diseases and diabetes mellitus. The medical history of other patients included 5 cases of endoscopic local excision and 4 cases of choledocholithotomy.

### **Preoperative evaluation**

Routine blood tests were carried out for all patients before the operation, including blood routine, hepatic and renal function, biochemical indicators, blood coagulation series and tumour markers.

There were 87 patients with increased bilirubin more than 17.1  $\mu\text{mol/L}$ , of whom there were 69 patients with increased bilirubin more than 34.2  $\mu\text{mol/L}$ . Preoperative tests of tumour markers mainly included CA19-9 and CEA. There were 39 patients with CA19-9 higher than 120 U/mL, while there were only 16 patients with CEA higher than 5 ng/mL.

Preoperative routine ultrasound and CT examinations were carried out. Intrahepatic and extrahepatic bile duct extension suggested that low-level biliary obstruction was the most common manifestation on CT. Preoperative endoscopic retrograde cholangiopancreatography (ERCP) examinations were carried out for 92 patients, during which the conditions of duodenal papilla were directly observed under an endoscope, and in 64 of them, biopsy and pathological examinations were performed before the operation, which confirmed the pathological diagnosis. In 34 patients, a biliary tract prosthesis or a drainage tube was inserted during ERCP to drain bile as an active preoperative preparation measure.

### **Operation procedures**

SPD was carried out for all patients. During the operation, it was found that in 2 cases, there was remote lymph node metastases, which made radical SPD impossible; therefore, they were excluded. For all pancreas stumps, anastomosis of the pancreatic duct and jejunum was carried out, and the anastomosis modes were categorized into anastomosis of the pancreatic duct and jejunal mucous membrane and invaginated pancreaticoenterostomy according to the diameter of the pancreatic duct and the size of pancreas amputation stump, with 90 cases and 22 cases, respectively. Intraoperative exploration found that in 34 cases, the diameter of the main pancreatic duct was greater than 4 mm; in 78 cases, it was smaller than 4 mm. For the intraoperative anastomosis of the pancreatic duct and jejunum, one end of a support tube was placed in the main pancreatic duct, and the other end was placed inside the jejunum or outside the abdominal wall to drain liquid. According to the position of the support tube, pancreatic duct drainage modes were divided into internal drainage and external drainage, with 85 cases and 27 cases, respectively. According to the different habits of operators, the jejunum input side to the output side

anastomosis (Braun anastomosis) was added, with the position 8 cm under the gastro-intestinal anastomotic stoma. In 54 cases, Braun anastomosis was added. All operations were performed by chief physicians with rich experience.

### **Postoperative complications**

For all patients, conventional postoperative treatment of the pancreas was carried out. Before being transferred back to the patients' rooms, they were observed for at least one day in the intensive care unit. After the operation, 100  $\mu\text{g}$  of octreotide was subcutaneously injected three times daily in all patients for 7 continuous days. On the second day after the operation, routine blood, liver and kidney function tests were carried out; on the third day after the operation, an abdominal Colour Doppler Ultrasound examination was carried out; and 7 d after the operation, an abdominal CT examination was carried out to observe the conditions of the abdomen. Before the end of the operation, a drainage tube was placed in the pancreaticoenteric anastomosis, cholecysto-colonic anastomosis and gastrojejunostomy anastomosis, and the amount, colour and description of the draining liquid were recorded every day.

After the operation, the pancreaticoenteric drainage tube was removed when the amylase level was less than 300 U/L (less than two times the serum amylase level) inside the drainage tube, the drainage amount was less than 50 mL each day, or the drainage duration exceeded 10 d after the operation.

According to the diagnosis criteria defined by the International Study Group on Pancreatic Fistula (ISGPF)<sup>[7]</sup>, a pancreatic fistula was defined as follows: 3 or more days after the operation, the draining liquid could be measured, and the activity of amylase was 3 times higher than that of the serum amylase activity. Pancreatic fistulas consisted of three grades (Grades A, B, and C) according to the clinical events of the patients' hospitalizations. Grade A pancreatic fistulas required no change from the normal clinical approach, did not delay discharge, and usually could be resolved through the removal of the retained operation drainage tube. Grade B pancreatic fistulas required a change of treatment strategy or adjustment of the clinical approach (for instance, fasting, total parenteral nutrition support, or the addition of antibiotics or somatostatin), delayed discharge, or needed readmission for treatment after discharge. If, according to the patients' pathogenetic conditions, invasive procedures were needed, the grade of the pancreatic fistula was upgraded to Grade C. Grade C pancreatic fistulas required a significant change of the treatment strategy or adjustment of the clinical approach; if clinical symptoms were aggravated and there were complications, such as sepsis and organ dysfunction, exploration through reoperation might be needed. Grade C pancreatic fistulas were often accompanied by complications, leading to an increased probability of

postoperative death.

A biliary fistula was diagnosed if there was persistent secretion of bilirubin-rich drainage fluid of more than 50 mL per day or if secretion continued after the 10<sup>th</sup> postoperative day<sup>[8]</sup>.

Postoperative bleeding was defined as the need for more than 2 units of red blood cells more than 2.4 h after surgery or relaparotomy for bleeding.

The nasogastric tube was removed when the drainage decreased to less than 200 mL per 24 h<sup>[8]</sup>.

Delayed gastric emptying was defined as gastric stasis requiring nasogastric intubation for 10 or more days or the inability to tolerate a regular diet on the 14<sup>th</sup> postoperative day<sup>[9]</sup>.

### Pathology

All excised specimens were examined in detail by two independent pathological experts; the contents observed included the nature of the tumours, size, infiltration depth, peripheral bile duct, nerves and pancreatic tissue infiltration, lymph node metastases, conditions of the tissue incisional margin (including common bile duct incisional margin, pancreas incisional margin, portal vein and mesenteric blood vessels incisional margin, stomach and jejunum incisional margin), tumour staging, etc. The TNM stage was done according to the UICC standard, version 7<sup>[10]</sup>.

According to the measurement of postoperative gross specimens, there were 36 cases with a diameter greater than 2 cm and 76 cases with a diameter smaller than 2 cm. In 24 patients, lymph node metastases were positive after the operation, and in 88 patients lymph node metastases were negative. The range of lymph node metastases included pancreas peripheral lymph nodes (10 cases), duodenum peripheral lymph nodes (8 cases), common bile duct peripheral lymph nodes (4 cases), and superior mesenteric lymph nodes (2 cases).

According to the infiltration depth of tumours into the duodenum wall, tumours involved the superficial muscular layer (14 cases), deep muscular layer or full-thickness (34 cases). While for tumours penetrating the intestinal wall and infiltrating the peripheral tissues, the peripheral tissues that were mainly involved included pancreas (35 cases), the bile duct (24 cases), nerves (5 cases), etc.

### Follow up

Telephone and outpatient follow-ups were performed. The patients were followed-up every 3 mo in the first two years and at least every 6 mo afterwards, with a median follow-up of 60 mo (ranging from 4 mo to 168 mo). When necessary, re-examinations by CT and MRI were carried out.

### Statistical analysis

Analysis was carried out with SPSS 16.0 statistical software. Associations between serum levels of CA19-9 and CEA and various clinical characteristics of

112 patients were evaluated by the  $\chi^2$  test and Fisher's exact test. Survival analysis was conducted using the Kaplan-Meier survival and Cox proportional hazards model analysis. The difference in survival curves was evaluated with a log-rank test. A value of  $P < 0.05$  was considered to be statistically significant.

## RESULTS

### Complications after the operation

In this study, no patients died during the operation. Forty-three patients developed one or more complications after the operation, with an incidence rate of 38.39% (43/112). The most common postoperative complications included pancreatic fistula, biliary fistula, intra-abdominal bleeding, gastric emptying disorders and peritoneal cavity infection.

Twenty-one patients developed postoperative pancreatic fistula, according to the diagnosis criteria of the ISGPF. There were 9 cases of Grade A pancreatic fistulas, 8 cases of Grade B pancreatic fistulas, and 4 cases of Grade C pancreatic fistulas. We also found that anastomosis of the pancreatic duct and jejunal mucous membrane and invaginated pancreaticoenterostomy had no influence on pancreatic fistulas. However, the incidence rate of pancreatic fistulas in patients with a pancreatic duct with a diameter greater than 4 mm was significantly lower than that in patients with a pancreatic duct with a diameter smaller than 4 mm. The incidence rate of postoperative biliary fistula was 1.78% (2/112). Seven patients developed a peritoneal cavity infection and 5 patients developed gastric emptying disorders.

After the operation, 2 patients needed reoperation, with an incidence rate of 1.78% (2/112). Of them, 4 patients received another laparotomy because of pancreatic fistulas and 2 patients underwent reoperation only because of intraabdominal bleeding. One patient experienced intraabdominal massive haemorrhage because of pancreatic fistulas, and although reoperation was performed, he still died.

### Associations between serum levels of CA19-9 and CEA and various clinical characteristics

We characterized the serum levels of CA19-9 and CEA from 112 DPC patients. For serum levels of CA19-9, 73 (65.17%) were lower than 120 U/mL, defined as negative, with 39 (34.82%) positive. For serum levels of CEA, 96 (85.71%) were lower than 5 ng/mL, defined as negative, with 16 (14.29%) positive.

As in our clinical correlation studies, serum levels of CA19-9 and CEA were compared with DPC characteristics and risk factors (Table 1). The following analysis showed that serum levels of CA19-9 was associated with serum levels of CEA and drainage mode (the  $P$  values were 0.000 and 0.033, respectively); While serum levels of CEA was associated with serum levels of CA19-9 and differentiation of the tumour (the  $P$  values

Table 1 The serum levels of CA19-9 and CEA and clinical characteristics for 112 patients with duodenal papilla carcinoma

Characteristic	No.	Serum CA19-9		P value	Serum CEA		P value
		Negative	Positive		Negative	Positive	
Gender				0.350			0.807
Male	74	46	28		63	11	
Female	38	27	11		33	5	
Age (yr)				0.621			0.699
< 60	61	41	20		53	8	
> 60	51	32	19		43	8	
Duration (yr)				0.938			0.699
< 1	54	35	19		47	7	
> 1	58	38	20		49	9	
Serum CA19-9 (U/mL)							0.000
< 120	73				69	4	
> 120	39				27	12	
Serum CEA (ng/mL)				0.000			
< 5	96	69	27				
> 5	16	4	12				
Serum total bilirubin ( $\mu$ mol/L)				0.105			0.526
< 34.2	43	32	11		38	5	
> 34.2	69	41	28		58	11	
Bile pre-drainage				0.945			0.933
No	78	51	27		67	11	
Yes	34	22	12		29	5	
Tumour diameter (cm)				0.820			0.934
< 2	76	49	27		65	11	
> 2	36	24	12		31	5	
Pancreatic duct diameter (mm)				0.351			0.015
< 4	78	53	25		71	7	
> 4	34	20	14		25	9	
Drainage mode				0.033			0.928
Inside	85	60	25		73	12	
Outside	27	13	14		23	4	
End-to-end invagination				0.184			0.145
No	90	56	34		75	15	
Yes	22	17	5		21	1	
Blood loss (mL)				0.786			0.059
< 400	67	43	24		54	13	
> 400	45	30	15		42	3	
Delayed emptying				0.227			0.350
No	107	71	36		91	16	
Yes	5	2	3		5	0	
Pancreatic fistula				0.874			0.166
No	91	59	32		76	15	
Yes	21	14	7		20	1	
Differentiation				0.253			0.033
Well	40	24	16		37	3	
Moderate	38	23	15		28	10	
Poor	34	26	8		31	3	
T stage				0.946			0.062
T1	14	10	4		14	0	
T2	34	22	12		31	3	
T3	35	23	12		30	5	
T4	29	18	11		21	8	
N stage				0.078			0.301
N0	88	61	27		77	11	
N1	24	12	12		19	5	
TNM stage				0.682			0.109
I A	14	10	4		14	0	
I B	27	18	9		25	2	
II A	28	20	8		24	4	
II B	14	7	7		12	2	
III							

were 0.000 and 0.033, respectively). The serum levels of CA19-9 and CEA were closely correlated ( $\chi^2 = 13.277$ ,  $r = 0.344$ ,  $P = 0.000$ ). No evidence of a significant

association was observed between alteration of serum levels of CA19-9 or CEA and other characteristics or risk factors.

### Associations between survival and various clinical characteristics

As of August 2015, we followed up all patients after the operation, with a median follow-up of 60 mo (ranging from 4 mo to 168 mo). There was a total of 52 patients with nodiseaseprogression, and of them, 48 patients lived longer than 5 years. A total of 60 patients died of this disease, with an median survival of 24.50 mo (ranging from 4 mo to 80 mo). The overall 5-year survival was 50.00% for 112 patients undergoing SPD (Figure 1A).

The Kaplan-Meier survival analysis showed that increased serum levels of CA19-9, CEA, and total bilirubin were correlated with a poor prognosis, as well as a senior grade of infiltration depth, lymph node metastases, and TNM stage (the *P* values were 0.033, 0.018, 0.015, 0.000, 0.000 and 0.000, respectively) (Tables 2 and 3, Figure 1B-F).

Only the senior grade of infiltration depth (T3/4) and TNM stage (II B/III) retained their significance when adjustments were made for other known prognostic factors in Cox multivariate analysis (*RR* = 2.211, *P* = 0.022 and *RR* = 2.109, *P* = 0.047).

## DISCUSSION

The incidence rate of DPC is low, only accounting for 5% of gastrointestinal malignant tumours<sup>[11-13]</sup>. However, because the special position of duodenal papilla, *i.e.*, it is located at the opening of pancreatic duct, early DPC may manifest as painless progressive jaundice. SPD has always been the most important treatment mode of DPC. According to the literature, it had different 5-year survival rates and factors influencing survival<sup>[14,15]</sup>. Therefore, in this study, we carried out long-term follow-up and prognosis analysis of patients with DPC who received SPD in our centre to provide a theoretical basis for prognosis improvement of the patients.

Jaundice is the most common early clinical symptom in patients with DPC, and whether treatment for jaundice should be performed before the operation is always a topic of dispute in surgery. Some scholars think that preoperative high bilirubin may inhibit hepatocyte function and induce endotoxin dysmetabolism, thereby increasing the incidence rate of postoperative complications and influences the prognosis of patients<sup>[16,17]</sup>. However, some scholars have opposing views<sup>[18,19]</sup>. In this experiment, a poor survival was found in patients with increased bilirubin more than 34.2  $\mu\text{mol/L}$ , with a 5-year survival rate of 40.6% (*P* = 0.015). Meanwhile, 34 patients who had placement of stents or drainage tubes before the operation, live longer than the other 78 patients who did not receive treatment for jaundice, with a 5-year survival rate of 55.9% vs 47.4%, although the difference was not significantly (*P* = 0.285). Based on these data, we proposed that increased bilirubin more than 34.2  $\mu\text{mol/L}$  plays a bad role in the survival of

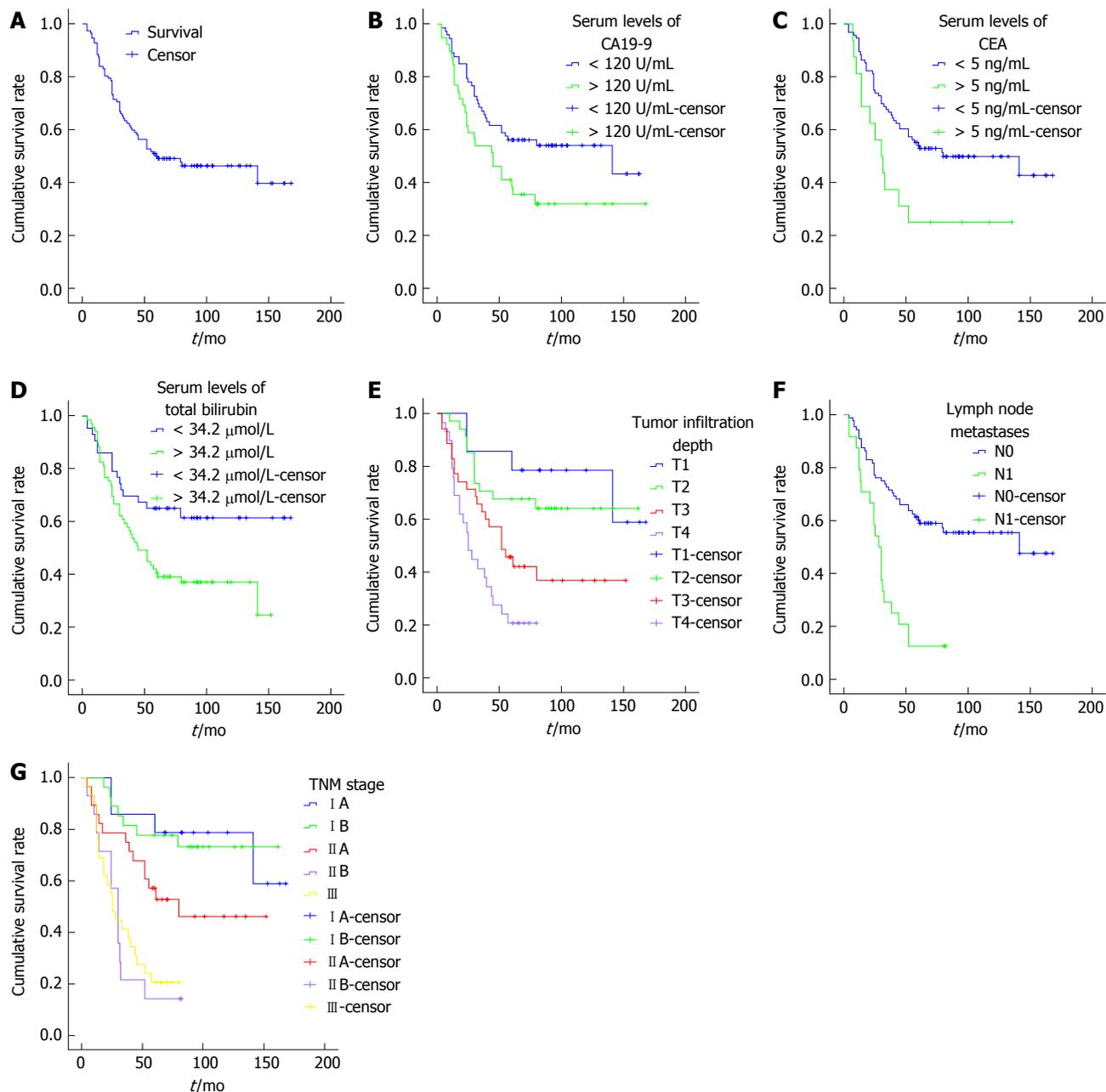
patients with DPC after SPD.

Tumour markers are mainly used for the detection of primary tumours and the differentiation of benign and malignant tumours, and they have good clinical guidance significance for the judgement of the efficacy of tumour treatment and their occurrence and prognosis of tumours. There is still a lack of specific tumour markers for DPC. In our study, serum levels of CA19-9 was associated with drainage mode (*P* = 0.033); While serum levels of CEA was associated with tumour differentiation (*P* = 0.033). Besides, the serum levels of CA19-9 and CEA were closely correlated (*r* = 0.344, *P* = 0.000). A study by Dorandeu *et al*<sup>[20]</sup> demonstrated that preoperative serum levels of CA199 and CEA were negatively related to the prognosis of patients with DPC; however, our study has opposing views. Among the 112 patients with DPC, there were 39 patients with increased serum CA19-9 and 16 patients with increased serum CEA levels. When the patients with increased levels of serum CA199 were compared with the others, the 5-year survival rates were significantly lower (38.3% vs 56.2%, *P* = 0.033). The same tendency was present in levels of serum CEA, with the 5-year survival rates of 25.0% vs 54.1% (*P* = 0.018). This indicated that the serum levels of CA19-9 and CEA are worth considering as the basis of diagnosis and prognosis for patients with DPC after SPD.

Pancreas-duodenum operations may cause great trauma, and there are many postoperative complications, of which pancreatic fistula is the most common complication<sup>[21,22]</sup>. In this study, the incidence rate of pancreatic fistula was 18.75% and was mainly Grade A and B pancreatic fistulas. However, we also found that whether there is a pancreatic fistula or not is not related with the long-term survival of patients (*P* = 0.500). In our study, we also investigated the influence of different factors on pancreatic fistulas, and our study found that anastomosis of the pancreatic duct and jejunal mucous membrane and invaginated pancreaticoenterostomy had no influence on pancreatic fistulas; different pancreatic duct drainage modes and whether Braun anastomosis was added also had no influence on the occurrence of pancreatic fistulas.

When it comes to the relationship between the size of tumour and the prognosis of patients, the study by Di Giorgio *et al*<sup>[23]</sup> demonstrated that among the 64 patients who underwent SPD, the prognosis of patients with tumours with a diameter greater than 2 cm was significantly inferior to those with tumours less than 2 cm. However, the results of our study were different; there was no significant difference in prognoses between the patients with tumours with a diameter greater than 2 cm and the others, and a diameter of 2 cm is not a boundary for the difference in prognosis.

We also found that the infiltration depth of tumours is an independent factor influencing the prognosis of patients after SPD. The study by Di Giorgio *et al*<sup>[4]</sup> demonstrated that for patients who underwent SPD



**Figure 1** Kaplan-Meier plots show the association of survival and significant factors. A: The overall 5-year survival was 50.00%, with a median follow-up of 60 mo (ranging from 4 mo to 168 mo); B: Increased serum levels of CA19-9 was associated with decreased survival ( $P = 0.033$ ); C: Increased serum levels of CEA was associated with decreased survival ( $P = 0.018$ ); D: Increased serum levels of total bilirubin was associated with decreased survival ( $P = 0.015$ ); E: The senior grade of infiltration depth was associated with decreased survival ( $P = 0.000$ ), with significant difference between T1 and T3, T4 ( $P = 0.022, 0.000$ ), as well as the difference between T2 and T3, T4 ( $P = 0.036, 0.000$ ) and the difference between T3 and T4 ( $P = 0.049$ ); F: The senior grade of lymph node metastases was associated with decreased survival ( $P = 0.000$ ); G: TNM stage was associated with decreased survival ( $P = 0.000$ ), with significant difference between I A and II B, III ( $P = 0.000, 0.000$ ), as well as the difference between I B and II B, III ( $P = 0.000, 0.000$ ) and the difference between II A and II B, III ( $P = 0.006, 0.000$ ).

because of duodenal ampulla tumours, the prognosis of patients with Stage T1/2 tumours was significantly better than that of patients with Stage T3/4 tumours. Our study also demonstrated that the infiltration depth of tumours has influence on the prognosis of patients; even when adjustments were made for other known prognostic factors in Cox multivariate analysis, the senior grade of infiltration depth (T3/4) and TNM stage (II B/III) retained their significance ( $RR = 2.211, P = 0.022$  and  $RR = 2.109, P = 0.047$ ).

Whether there are lymph node metastases is an important factor influencing the prognosis of malignant tumours. The study by Klein *et al.*<sup>[24]</sup> reported that lymph node metastasis was a key factor influencing tumour recurrence and the survival of patients with ampullary carcinoma. Other studies demonstrated that the number of lymph node metastases was related to the prognosis of patients with periampullary carcinoma<sup>[25,26]</sup>. Our experiment led to the same conclusion; *i.e.*, the 5-year survival rate of patients

**Table 2** Univariate analysis comparing overall survival to prognostic factors in 112 patients with duodenal papilla carcinoma

Factors	No.	5 years survival	$\chi^2$	P value
Gender			0.561	0.454
Male	74	48.6%		
Female	38	52.4%		
Age (yr)			0.022	0.883
< 60	61	46.3%		
> 60	51	48.9%		
Duration (yr)			0.409	0.523
< 1	54	41.7%		
> 1	58	53.4%		
Serum CA19-9 (U/mL)			4.566	0.033
< 120	73	56.2%		
> 120	39	38.3%		
Serum CEA (ng/mL)			5.554	0.018
< 5	96	54.1%		
> 5	16	25.0%		
Serum total bilirubin ( $\mu\text{mol/L}$ )			5.929	0.015
< 34.2	43	65.1%		
> 34.2	69	40.6%		
Bile pre-drainage			1.144	0.285
No	78	47.4%		
Yes	34	55.9%		
Tumour diameter (cm)			0.185	0.667
< 2	76	51.3%		
> 2	36	47.2%		
Pancreatic duct diameter (mm)			0.493	0.483
< 4	78	51.2%		
> 4	34	47.1%		
Drainage mode			0.006	0.939
Inside	85	48.2%		
Outside	27	55.3%		
End-to-end invagination			0.592	0.442
No	90	48.9%		
Yes	22	54.5%		
Blood loss (mL)			0.052	0.820
< 400	67	49.2%		
> 400	45	51.1%		
Delayed emptying			0.614	0.433
No	107	50.5%		
Yes	5	40.0%		
Pancreatic fistula			0.455	0.500
No	91	47.1%		
Yes	21	57.1%		
Differentiation			3.676	0.159
Well	40	62.4%		
Moderate	38	39.5%		
Poor	34	47.1%		
Infiltration depth			22.424	0.000
T1	14	78.6%		
T2	34	67.6%		
T3	35	45.7%		
T4	29	20.7%		
lymph metastases			21.187	0.000
N0	88	60.2%		
N1	24	12.5%		
TNM stage			35.041	0.000
I A	14	78.6%		
I B	27	77.8%		
II A	28	57.1%		
II B	14	14.3%		
III	29	20.7%		

with positive lymph node metastases was significantly lower than that of patients with negative lymph node metastases. However, lymph node metastases could not serve as an independent factor influencing the

prognosis of patients after SPD.

In conclusion, for patients with DPC, the serum levels of CA19-9 and CEA were closely correlated, and play an important role in poor survival. Increased

**Table 3** Multivariate analysis comparing overall survival to prognostic factors in 112 patients with duodenal papilla carcinoma

Factors	No.	5 years survival	Median survival (95%CI)(mo)	Relative risk (95%CI)	P value
CA19-9 (U/mL)					0.174
< 120	73	56.2%	141.0 (3.3-278.6)	1	
> 120	39	38.3%	45.0 (22.6-67.4)	1.550 (0.823-2.920)	
CEA (ng/mL)					0.528
< 5	96	54.1%	80.0 (10.4-149.5)	1	
> 5	16	25.0%	30.0 (18.2-41.8)	1.270 (0.605-2.663)	
Bilirubin ( $\mu$ mol/L)					0.264
< 34.2	43	65.1%		1	
> 34.2	69	40.6%	45.0 (29.9-60.1)	1.408 (0.772-2.566)	
Differentiation					0.137
Well	40	62.4%	141.0	1	
Moderate	38	39.5%	44.0 (3.09-57.1)	0.808 (0.399-1.635)	0.553
Poor	34	47.1%	52.0 (3.552-100.4)	1.636 (0.814-3.285)	0.167
Infiltration depth					0.022
T1 + T2	48	70.8%		1	
T3 + T4	64	34.4%	39.0 (26.3-51.7)	2.211 (1.119-4.367)	
lymph metastases					0.142
N0	88	60.2%	141.0	1	
N1	24	12.5%	28.0 (6.1-113.9)	1.744 (0.830-3.666)	
TNM stage					0.047
I A + I B + II A	69	69.5%		1	
II B + III	43	18.6%	28.0 (21.6-34.4)	2.109 (1.010-4.406)	

serum levels of total bilirubin and lymph node metastases were also correlated with a poor prognosis. The senior grade of infiltration depth and TNM stage can serve as independent prognosis indexes in the evaluation of patients with DPC after SPD.

## COMMENTS

### Background

For duodenal papilla carcinoma (DPC), standard pancreaticoduodenectomy (SPD) is still the most important treatment. However, the prognosis assessment for DPC after SPD is not yet clear.

### Research frontiers

Only a few researches have focused on the prognosis assessment for DPC after SPD. According to the literature, it had different 5-year survival rates and factors influencing survival.

### Innovations and breakthroughs

In this study, the authors carried out long-term follow-up and prognosis analysis of patients with DPC who received SPD in our centre to provide a theoretical basis for prognosis improvement of the patients.

### Applications

The senior grade of infiltration depth and TNM stage can serve as independent prognosis indexes in the evaluation of patients with DPC after SPD.

### Peer-review

This study is very interesting. Over all, the study was well designed, and the manuscript is well written.

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