Original Article

Surgical treatment and survival analysis of primary duodenal malignant tumor: a retrospective cohort study

Zhicheng Zhao, Jiehong Zhang, Chuan Li, Tong Liu, Weidong Li

Tianjin General Surgery Institute, Department of General Surgery, Tianjin Medical University General Hospital, Tianjin, China

Contributions: (I) Conception and design: T Liu, Z Zhao; (II) Administrative support: T Liu, W Li; (III) Provision of study materials or patients: W Li; (IV) Collection and assembly of data: J Zhang; (V) Data analysis and interpretation: Z Zhao, C Li; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Weidong Li. Tianjin General Surgery Institute, Department of General Surgery, Tianjin Medical University General Hospital, Tianjin, China. Email: mzzlee@163.com.

Background: A primary duodenal malignant tumor (PDMT) is an extremely uncommon malignancy that originates from a gastrointestinal tract tumor. Currently, there is no unified, effective surgical treatment for PDMTs. In this retrospective study, we sought to analyze and evaluate the surgical procedure for PDMTs including pancreaticoduodenectomy (PD) and limited resection (LR), expect to inform the management of PDMT.

Methods: We retrospectively reviewed patients with PDMT who underwent PD and LR in General Surgery Department of Tianjin Medical University General Hospital from January 2014 to December 2019. The clinical characteristics of the malignant tumors among the different segment of the duodenum were analyzed. We analyzed and compared the efficacy and safety of these two surgical treatments. Through survival result of the patients, we analyzed the survival factors affecting the PDMT.

Results: Of the 94 patients, 60 (63.8%) were diagnosed with duodenal adenocarcinomas (DAs), 32 (34.1%) with duodenal gastrointestinal stromal tumors (d-GISTs), and 2 (2.1%) with duodenal lymphomas. Of the duodenal malignancies localized in the descending (D2) segment, 72.6% were DAs, and the initial symptom was jaundice (27.4%). Comparing with D2, d-GISTs were more common in the non-D2 segment (50.0%), and 46.9% of these patients presented with anemia as a primary symptom. PDs (87.1%) were more commonly performed for malignancies localized in the D2 segment, and LRs (59.4%) were more commonly performed for malignancies localized in the non-D2 segment ($P<0.05$).

Conclusions: In this study, we found that PDMT is more likely to occur in the D2 segment than the other segments, and the most common pathological type is DA. Treatment decisions for PD and LR might depend on the tumor type, location, and whether invasion of the pancreas. PD might be the first choice of treatment for PDMTs located in the D2 segment; otherwise, LR would be preferred. Further studies, preferably large randomized clinical trials, are needed to confirm these results.

Keywords: Primary duodenal malignancy; duodenal adenocarcinoma (DA); duodenal gastrointestinal stromal tumors (d-GISTs); pancreaticoduodenectomy (PD); limited resection (LR)

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Introduction

A primary duodenal malignant tumor (PDMT) is a rare malignant tumor of the digestive system that accounts for 0.3–1% of all gastrointestinal tract malignant tumors (1). PDMT is also highly prevalent in small intestinal malignancies that up to 45% of small bowel malignancies (2), even though the length of the duodenum is <10% of the small intestine. Additionally, the duodenum is the 1st part of the small

intestine, and tumor treatment is quite difficult due to its relationship with the hepatobiliary system and pancreas. There are several distinct subtypes of PDMT, including duodenal adenocarcinomas (DAs), which account for about 50–70% of PDMTs, duodenal gastrointestinal stromal tumors (d-GISTs), which account for nearly 30% of PDMTs, and neuroendocrine tumors, which account for 1–3% of PDMTs (3). There is no specific clinical presentation of PDMT at the early stage, which results in a low rate of diagnosis or misdiagnoses of other abdominal diseases.

PDMT treatment is mainly based on operation, which is the only hope for curing the tumor (4). The particularity of the anatomical location of the duodenum that the closeness of the tumor to the duodenal papilla, and the easy invasion of the pancreas have seriously troubled the appropriate choice of surgical approach for PDMT. Currently, the common surgical approaches include pancreaticoduodenectomy (PD) and limited resection (LR) (5). Due to the delicate vascular anatomy and complex anastomosis, PD is prone to high-risk complications such as pancreatic leakage and abdominal hemorrhage post operation. Therefore, PD has become one of the complex operations with high perioperative mortality. Compared with PD, LR can reduce the length of stay in hospital and the incidence of postoperative complications is lower. However, so far, due to the low incidence of PDMT and the lack of clinical studies, there is no consensus on whether it could be the alternative surgical approach for PDMT (6-8). In this retrospective study, we analyzed the clinical data and prognosis of patients with PDMT treated by surgery, and expect to give partial answer to this question. We present the following article in accordance with the STROBE reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-475/rc).

Methods

Ethics

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics committee of Tianjin Medical University General Hospital (No. IRB2021-036-01). Informed consent was taken from all the patients.

Materials and methods

This was a retrospective study of PDMTs. In this study, we collected the clinical data of 103 patients diagnosed with PDMT who had been admitted to the General Surgery Department of the Tianjin Medical University General Hospital from January 2014 to December 2019. All the patients' diagnoses were histopathologically confirmed. Among the patients, 9 who were diagnosed as low- or very low-risk d-GIST were excluded from the study, and 94 patients were deemed eligible for this retrospective analysis. Finally, there were 67 patients in PD group and 27 patients in LR group. This study compared the features of PDMT in different segments [i.e., the duodenal bulb segment (D1), the descending segment (D2), and the horizontal/ascending segment (D3/D4)].

Data on patients' basic clinical information including sex, age, smoking and drinking history, body mass index (BMI), previous medical history; laboratory tests such as white blood cell count (WBC), hemoglobin (Hb), alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin (ALB), total bilirubin (TBIL), direct bilirubin (DBIL); operation data (bleeding volume, operation time, transfusion volume); postoperative complications, and pathological examinations were reviewed from the medical records by trained investigators.

The tumor-node-metastasis (TNM) staging system for the Classification of Malignant Tumors (8th edition, Union for International Cancer Control and the American Joint Committee on Cancer) was used. The risk stratification for d-GIST was based on the 2008 revised National Institutes of Health classification system.

Follow up

Long-term complication, survival and disease progression after operation was assessed by calling to patients or family members as well as outpatient review. Overall survival (OS) was defined as the time from surgery to the end of follow-up or death from any cause. Progression-free survival (PFS) was defined as the time from surgery to the end of follow-up or disease progression from any cause.

Statistical analysis

SPSS 23.0 statistical software was used to test the normal distribution and homogeneity of variance of each measurement data. The consistent data with a normal distribution and homogeneity of variance are expressed as the ($\bar{x}$±s), and a *t*-test was used for the data statistics. The data that did not conform to a normal distribution

Table 1 PDMT patient characteristics and laboratory presentations

Characteristics	All patients (n=94)
Gender, n (%)	
Male	60 (63.8)
Female	34 (36.2)
Age (years), $\bar{x}$±s	62.5±10.2
Clinical presentation, n (%)	
Abdominal pain	25 (26.6)
Anemia	24 (25.5)
Digestive symptoms	20 (21.3)
Jaundice	17 (18.1)
No clinical symptoms	8 (8.5)
Laboratory test	
WBC[1] (×10^9/L), median ($X_{25\%}$–$X_{75\%}$)	5.77 (4.64–7.28)
Hb[2] (g/L), $\bar{x}$±s	107.5±24.9
ALT[1] (U/L), median ($X_{25\%}$–$X_{75\%}$)	25.0 (15.0–62.5)
AST[1] (U/L), median ($X_{25\%}$–$X_{75\%}$)	21.0 (16.0–48.0)
ALB[1] (g/L), median ($X_{25\%}$–$X_{75\%}$)	37.0 (33.3–40.0)
TBIL[1] (μmol/L), median ($X_{25\%}$–$X_{75\%}$)	11.8 (6.9–29.3)
DBIL[1] (μmol/L), median ($X_{25\%}$–$X_{75\%}$)	4.4 (2.8–18.8)

[1], the data are not normally distributed; [2], the data is normally distributed. PDMT, primary duodenal malignant tumor; WBC, white blood cell count; Hb, hemoglobin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, albumin; TBIL, total bilirubin; DBIL, direct bilirubin.

are expressed as the median ($X_{25\%}$–$X_{75\%}$), and the non-parametric rank-sum test (Mann-Whitney U test) was used. The counting data are expressed as the frequency and percentage. The chi-square test or Fisher's exact probability method was used to compare rates. The survival time is shown as the ($\bar{x}$±s). The cumulative OS rate and PFS rate were calculated by the Kaplan-Meier method. Survival curves were compared by the log-rank test. For the statistical results, a P value <0.05 was considered statistically significant.

Results

Basic clinical characteristic of patients

A total of 94 patients diagnosed with PDMT were included in this study, of whom 60 were male, and 34 were female (male-to-female ratio: 1.8:1). The patients had a mean age of 62.5±10.2 (range, 30–82) years. The most common clinical symptoms of PDMT patients were abdominal pain (26.6%), anemia (25.5%), and gastrointestinal symptoms (21.3%), which presented with nausea and vomiting as the primary clinical manifestations. There were 17 patients (18.1%) with jaundice, and 8 patients (8.5%) who displayed no clinical symptoms. Laboratory tests after patients' admission showed that the mean Hb was 107.5±24.9 g/L, the median WBC was 5.77 (4.64–7.28) ×10^9/L, the median ALT was 25.0 (15.0–62.5) U/L, the median AST was 21.0 (16.0–48.0) U/L, the median ALB was 37.0 (33.3–40.0) g/L, the median TBIL was 11.8 (6.9–29.3) μmol/L, and the median DBIL was 4.4 (2.8–18.8) μmol/L. For further details, see *Table 1*.

Among the 94 patients, 60 (63.8%) were diagnosed with adenocarcinomas, 32 (34.1%) with GISTs, and 2 (2.1%) with lymphomas. Stage II was the most common stage among the DA patients (n=24, 40.0%). Most of the patients were high-risk GIST patients (n=17, 53.1%). In this study, 7 patients (7.4%) with tumors located in the suprapapillary region (D1 segment), and 4 of the 7 patients underwent PD, and 3 underwent LR. A total of 62 patients (66.0%) with tumors located in the peripapillary region (D2), in which 54 patients was performed PD, and LR was performed in the remaining 8 patients.25 patients (26.6%) had tumors located in the subpapillary region (D3/D4), among which 9 patients in the D3 segment underwent PD and 10 patients underwent LR. All 6 patients with tumors in the D4 segment underwent LR surgery. Thus, PDMT more commonly presented in the D2 segment, and was more commonly diagnosed as DA. For further details, see *Table 2*.

PDMT comparison between the D2 segment and non-D2 segment

Among all the PDMT patients, whose tumor 62 located in the D2 segment, and others were in non-D2 segments. In clinical manifestations, the D2 patients most commonly presented with jaundice (27.4%), followed by abdominal pain (24.2%), and abdominal discomfort (21.0%). Anemia and having no apparent symptoms were relatively rare (14.5%, 12.9%). DA (72.6%) was the most common pathological type in D2 patients. d-GIST (50.0%) was the most common pathological type of the PDMT localized in the non-D2 segment. Anemia (46.9%) was the primary clinical symptom, followed by abdominal pain (31.2%), and abdominal discomfort (21.9%). The characteristic

Table 2 Surgery characteristics and clinical pathology

Characteristics	All patients (n=94)
Diagnosis, n (%)	
Adenocarcinoma	60 (63.8)
I	16 (17.0)
II	24 (25.5)
IIIA	14 (14.9)
IIIB	6 (6.4)
GIST	32 (34.1)
Intermediate risk	15 (46.9)
High risk	17 (53.1)
Malignant lymphoma	2 (2.1)
Surgery, n (%)	
PD	67 (71.3)
LR	27 (28.7)
Tumor location, n (%)	
D1	7 (7.4)
D2	62 (66.0)
D3	19 (20.2)
D4	6 (6.4)

GIST, gastrointestinal stromal tumor; PD, pancreaticoduodenectomy; LR, limited resection; D1, duodenal bulb segment; D2, descending segment; D3, horizontal segment; D4, ascending segment.

pathological type and clinical signs of PDMT in the D2 segment and non-D2 segment differed significantly (P<0.05). The average diameter of the D2 tumors was shorter than that of the non-D2 tumors (3.0 *vs.* 4.5, P<0.05); however, DA was more common in D2 PDMT and PD was performed as the surgical treatment, while LR was more common in patients with non-D2 PDMT (P<0.05). The results are set out in *Table 3*.

Resection comparison between the PD and LR groups

The 94 patients were divided into the PD group and LR group according to the surgical treatment. Of the 67 (71.3%) patients who underwent PD, 41 were male (61.2%), and 26 were female (38.8%) (male-to-female ratio: 1.5:1), and the patients had an average age of 64.1±9.0 years (see *Table 4*). Abdominal pain was the most common primary clinical symptom (n=19, 28.4%), followed by jaundice (n=17, 25.4%), and abdominal discomfort (n=14, 20.9%). There were 27 patients (28.7%) in the LR group, of whom 19 were male (70.4%) and 8 were female (29.6%) (male-to-female ratio: 2.7:1). The patients had an average age of 58.6± 12.1 years. Anemia was the most common clinical symptom (n=14, 51.9%), followed by abdominal pain (n=6, 22.2%), and abdominal discomfort (n=6, 22.2%); 1 patient (3.7%) showed no obvious clinical symptoms. Jaundice presented more in the PD group than the LR group (P=0.002), while anemia was more common in the LR group than the PD group (P<0.05). In terms of the preoperative examination, the levels of ALT, AST, TBIL, and DBIL were higher in the PD group than the LR group (P<0.05). For further details, see *Table 4*.

Comparison of the clinicopathological characteristics between the PD and LR groups

In this study, we analyzed the pathological data of the patients in the different groups. Of the 60 patients with DA, 32 patients with d-GIST were divided into the PD group and LR group according to the different surgical treatments for the D2 segments and the other duodenal segments, respectively. There were 45 patients with DA in the D2 segment, and 15 patients with DA in the non-D2 segment. PD was performed for all patients with DA in the D2 segment. Of the 15 non-D2 segment patients, PD was performed in 8 patients (53.3%) and LR was performed in 7 patients (46.7%), and the difference between the two groups was statistically significant (P<0.05).

A comparison of the clinicopathological data of the non-D2 adenocarcinoma patients showed that when the DA invaded the pancreas, PD was preferred for patients as a radical surgical treatment (P<0.05). In this study, no statistically significant difference was found between the tumor diameter and tumor stage and surgical option due to data limitations (P>0.05). Thus, PD should be the 1st choice for surgical treatment when DA is located in the D2 segment or invades the pancreas. For DA in the non-D2 segments, LR should be selected as the surgical option if the tumor does not invade the pancreas, and radical surgical treatment is guaranteed. The statistical results are set out in *Table 5*. Of the 16 patients with d-GIST in the D2 segment, 8 (50.0%) underwent PD, and 8 (50.0%) underwent LR. Of the 16 patients with d-GIST in the non-D2 segment, 5 (31.3%) underwent PD, and 11 (68.7%) underwent LR. The proportion of PD in patients with D2 d-GIST was higher than that of patients with non-D2 d-GIST, but the

Table 3 The clinical characteristic of the D2 segments and non-D2 segment

Characteristics	PD group (n=62)	LR group (n=32)	P value
Clinical symptom, n (%)			
Anemia	9 (14.5)	15 (46.9)	0.001
Jaundice	17 (27.4)	0	<0.05[1]
Abdominal pain	15 (24.2)	10 (31.2)	0.463
Digestive tract symptom	13 (21.0)	7 (21.9)	0.919
No symptom	8 (12.9)	0	0.048[1]
Clinical diagnosis, n (%)			
Adenocarcinoma	45 (72.6)	15 (46.9)	0.014
GIST	16 (25.8)	16 (50.0)	0.019
Malignant lymphoma	1 (1.6)	1 (1.6)	1.000
Surgical treatment, n (%)			<0.05
PD	54 (87.1)	13 (40.6)	
LR	8 (12.9)	19 (59.4)	
Tumor diameter[3] (cm), $\bar{x}\pm s$	3.0 (2.0–4.0)	4.5 (2.6–6.0)	0.002[2]
Pancreas invasion, n (%)			0.078
Yes	27 (43.5)	8 (25.0)	
No	35 (56.5)	24 (75.0)	

[1], P value was calculated by Fisher's exact test; [2], P value was calculated by the Mann-Whitney U-test; [3], the data are normally distributed. D2, descending; GIST, gastrointestinal stromal tumor; PD, pancreaticoduodenectomy; LR, limited resection.

difference was not statistically significant (P=0.473).

The comparison of the surgical and clinicopathological data of the D2 and non-D2 GIST patients revealed that the surgical choice of the non-D2 GIST patients was statistically correlated with the tumor diameter (P<0.05). Additionally, there were no significant differences in terms of the invasion of the pancreas, mitotic count, or risk stratification between the two groups (P>0.05). Thus, LR should be used as the surgical treatment for non-D2 GIST patients with small tumor diameters. Results are set out in *Table 6*.

Comparison of intraoperative and postoperative indexes between the PD and LR groups

In the PD group, the median operative time was 370.0 (313.7–416.3) minutes, the median intraoperative blood loss was 300 (200.0–400.0) mL, and the median intraoperative blood transfusion was 0 (0–400) mL. In the LR group, the median operative time was 255.0 (199.7–292.5) minutes, the median intraoperative blood loss was 125 (50.0–325.0) mL, and the median intraoperative blood transfusion was 0 (0–400) mL. The operative time of the PD group was longer than that of the LR group (P<0.05), the intraoperative blood loss of the PD group was higher than that of the LR group (P<0.05), and the postoperative hospital stay of the PD group was longer than that of LR group (P<0.05).

Postoperative complications occurred in a total of 40 (59.7%) patients in the PD group, of whom 21 (31.3%) had pancreatic leakage, 4 (6.0%) had bile leakage, 5 (7.5%) had gastrointestinal anastomotic leakage, 10 (14.9%) had gastric empties, 7 (10.4%) had intraperitoneal bleeding, 4 (6.0%) had gastrointestinal anastomotic bleeding, and 7 (10.4%) had postoperative incision problems. Postoperative complications occurred in a total of 14 patients in the LR group, of whom 1 had pancreatic leakage (3.7%), 1 had postoperative gastrointestinal anastomotic leakage (3.7%), and 12 (44.4%) had postoperative delayed gastric emptying (DGE).

The number of postoperative complications of the PD

Table 4 The characteristics of the PD group and the LR group

Characteristics	PD group (n=67)	LR group (n=27)	P value
Gender, n (%)			0.261
Male	41 (61.2)	19 (70.4)	
Female	26 (38.8)	8 (29.6)	
Age[1] (years), $\bar{x}$±s	64.1±9.0	58.6±12.1	0.020
Clinical symptom, n (%)			
Anemia	10 (14.9)	14 (51.9)	<0.05
Jaundice	17 (25.4)	0	0.002[3]
Abdominal pain	19 (28.4)	6 (22.2)	0.680
Digestive tract symptom	14 (20.9)	6 (22.2)	0.833
No symptom	7 (10.4)	1 (3.7)	0.433[3]
Laboratory tests			
WBC[2] ($\times10^9$/L), median ($X_{25\%}$–$X_{75\%}$)	6.08 (4.75–7.29)	5.18 (4.37–6.78)	0.125[4]
Hb[1] (g/L), $\bar{x}$±s	110.6±23.3	99.5±27.3	0.053
ALT[2] (U/L), median ($X_{25\%}$–$X_{75\%}$)	35.0 (16.8–106.8)	18.5 (11.0–29.3)	0.002[4]
AST[2] (U/L), median ($X_{25\%}$–$X_{75\%}$)	27.5 (16.8–76.3)	17.0 (14.0–21.0)	0.001[4]
ALB[2] (g/L), median ($X_{25\%}$–$X_{75\%}$)	37.0 (34.0–40.3)	37.0 (33.0–40.3)	0.768[4]
TBIL[2] (μmol/L), median ($X_{25\%}$–$X_{75\%}$)	15.6 (8.1–84.9)	8.2 (6.3–13.9)	0.006[4]
DBIL[2] (μmol/L), median ($X_{25\%}$–$X_{75\%}$)	5.3 (2.9–59.3)	3.4 (2.4–6.3)	0.011[4]

[1], the data are normally distributed; [2], the data are not normally distributed; [3], P value was calculated by Fisher's exact test; [4], P value was calculated by the Mann-Whitney U-test. PD, pancreaticoduodenectomy; LR, limited resection; WBC, white blood cell count; Hb, hemoglobin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, albumin; TBIL, total bilirubin; DBIL, direct bilirubin.

Table 5 Pathological information comparison of PD and LR in the non-D2 group

Pathological information	PD group (n=8)	LR group (n=7)	P value
Tumor diameter[1] (cm), $\bar{x}$±s	4.6±2.5	4.5±1.5	0.944
Pancreas invasion, n (%)			0.041[2]
Yes	6 (75.0)	1 (14.3)	
No	2 (25.0)	6 (85.7)	
Tumor stage, n (%)			0.822[3]
I	1 (12.5)	1 (14.3)	
II	4 (50.0)	3 (42.8)	
IIIA	2 (25.0)	1 (14.3)	
IIIB	1 (12.5)	2 (28.6)	

[1], the data are normally distributed; [2], P value was calculated by Fisher's exact test; [3], P value was calculated by the Mann-Whitney U-test. PD, pancreaticoduodenectomy; LR, limited resection; D2, descending segment.

group was about 2.9 times that of the LR group; however, the difference between the two groups was not statistically significant (P=0.553). The incidence of postoperative pancreatic leakage in the PD group was much higher than that in the LR group (P<0.05). Conversely, the rate of postoperative gastric emptying in the LR group was slightly higher than that in the PD group (12 *vs.* 10, P<0.05). A total of 2 patients died of postoperative complications, resulting in hemorrhagic shock due to anastomotic bleeding. All the patients who died were in the PD group, but there was no statistically significant difference in the number of deaths between the two groups (P=1.000; see *Table* 7).

Long-term effect evaluation

The follow-up duration ranged from 1 to 71 months. Among the 94 patients enrolled in this study, 54 patients survived till the end of follow-up period with the survival

Table 6 Clinical and pathological data of d-GIST comparing the D2 segment and non-D2 segment

Clinical and pathological data of d-GIST	D2 segment (n=16)			Non-D2 segment (n=16)		
	PD (n=8)	LR (n=8)	P value	PD (n=5)	LR (n=11)	P value
Tumor diameter[1] (cm), $\bar{x}$±s	6.2±3.4	4.3±2.8	0.262	6.0±1.6	4.1±1.5	0.039
Pancreas invasion, n (%)			0.077[2]			0.313[2]
Yes	4 (50.0)	0		1 (20.0)	0	
No	4 (50.0)	8 (100.0)		4 (80.0)	11 (100.0)	
Mitotic, n (%)			0.077[2]			0.299[2]
≤5	4 (50.0)	0		3 (60.0)	3 (27.3)	
>5	4 (50.0)	8 (100.0)		2 (40.0)	8 (72.7)	
Risk level, n (%)			1.000[2]			0.093[2]
Intermediate	4 (50.0)	5 (62.5)		5 (100.0)	5 (45.5)	
High	4 (50.0)	3 (37.5)		0	6 (54.5)	

[1], the data are normally distributed; [2], P value was calculated by Fisher's exact test. d-GIST, duodenal gastrointestinal stromal tumors; D2, descending; PD, pancreaticoduodenectomy; LR, limited resection.

Table 7 Comparison of intraoperative and postoperative indexes between the PD and LR groups

Intraoperative and postoperative indexes	PD group (n=67)	LR group (n=27)	P value
Operative time (min), median ($X_{25\%}$–$X_{75\%}$)	370.0 (313.7–416.3)	255.0 (199.7–292.5)	<0.05
Intraoperative blood loss (mL), median ($X_{25\%}$–$X_{75\%}$)	300.0 (200.0–400.0)	125.0 (50.0–325.0)	0.003
Intraoperative blood transfusion (mL), median ($X_{25\%}$–$X_{75\%}$)	0 (0–400)	0 (0–400)	0.180
Complication, n (%)	40 (59.7)	14 (51.9)	0.553
Pancreatic leakage	21 (31.3)	1 (3.7)	0.005
Bile leakage	4 (6.0)	0	0.574[2]
Gastrointestinal anastomotic leakage	5 (7.5)	1 (3.7)	0.514
DGE	10 (14.9)	12 (44.4)	0.002
Intraperitoneal hemorrhage	7 (10.4)	0	0.185[2]
Gastrointestinal anastomotic bleeding	4 (6.0)	0	0.574[2]
Postoperative incision problems	7 (10.4)	0	0.185[2]
Death after surgery, n (%)	2 (3.0)	0	1.000[2]
Hospitalization time after surgery[1] (days), median ($X_{25\%}$–$X_{75\%}$)	28.5 (23.7–35.3)	24.0 (16.0–31.0)	0.015

[1], the data are not normally distributed; [2], P value was calculated by Fisher exact test. PD, pancreaticoduodenectomy; LR, limited resection; DGE, delayed gastric emptying.

time ranged from 1 month to 69 months. Among the 60 patients with DA, OS at 1- and 3-year were 74.6% and 58.1%, and median OS was 26.3±2.2 months. Relapse-free survival (RFS) at 1- and 3-year were 78.5% and 62.4%, and median PFS was 26.7±2.2 months. Among the 32 patients with d-GIST, OS at 1- and 3-year were 93.6% and 72.5%, and median OS was 56.8±4.4 months. RFS at 1- and 3-year were 100% and 77.6%, and median OS was 59.2±3.9 months. There were significant statistical differences in OS and PFS between them (OS, P<0.05; PFS, P<0.05).

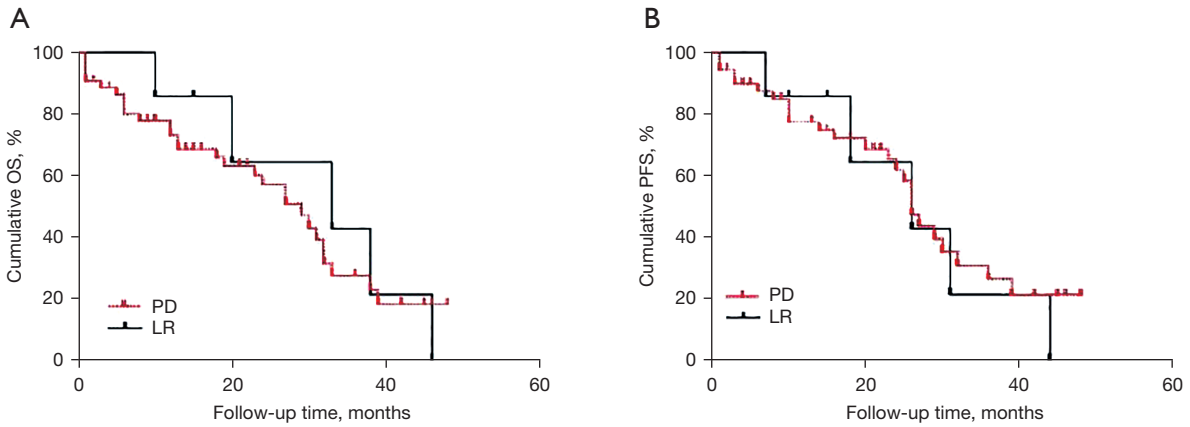

Figure 1 Kaplan-Meier curves of (A) OS and (B) PFS in the DA population with different surgery. PD, pancreaticoduodenectomy; LR, limited resection; OS, overall survival; PFS, progression-free survival; DA, duodenal adenocarcinoma.

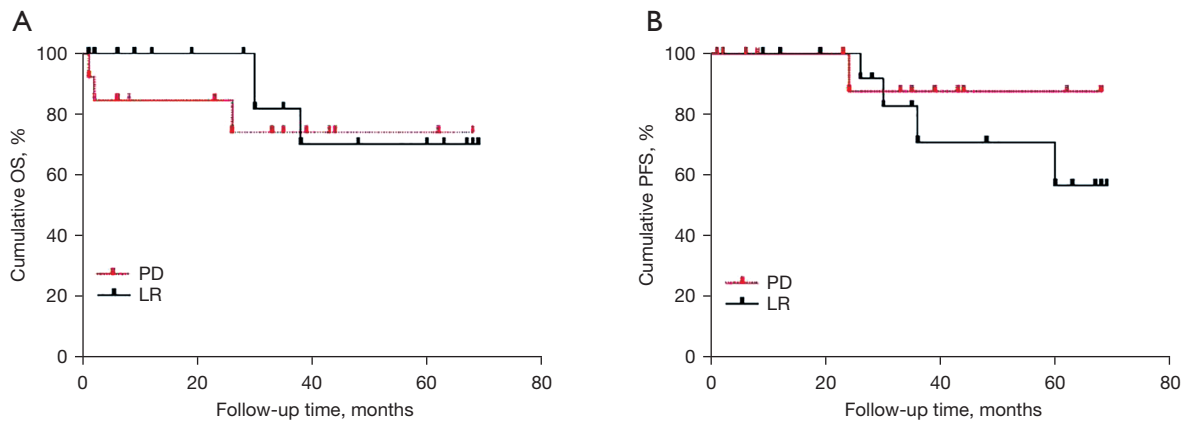

Figure 2 Kaplan-Meier curves of (A) OS and (B) PFS in the d-GIST population with different surgery. PD, pancreaticoduodenectomy; LR, limited resection; OS, overall survival; PFS, progression-free survival; d-GIST, duodenal gastrointestinal stromal tumors.

Fifty-three of 60 patients with DA underwent PD surgery with the rest 7 patients underwent LR surgery. OS at 1- and 3-year of DA patient underwent PD surgery were 73.2% and 57.2%, and median OS was 25.7±2.4 months. PFS at 1- and 3-year of patient underwent PD surgery were 77.5% and 26.5%, and median PFS was 26.8±2.5 months. The OS and PFS between the two groups did not have statistically significant difference (OS, P=0.732; PFS, P=0.777) (*Figure 1*). OS at 1- and 3-year of d-GIST patient underwent PD surgery were 84.6% and 74%, and median OS was 53.3±7.4 months. PFS at 1- and 3-year of patient underwent PD surgery were 100% and 87.5%, and median PFS was 62.5±2.5 months. The OS and PFS between the two groups did not have statistically significant difference (OS, P=0.614; PFS, P=0.413) (*Figure 2*).

In order to find out the factor correlated with prognosis, we performed Kaplan-Meier analysis and found that the pancreas invasion was highly correlated with the prognosis of DA patients. The median OS of DA patients with pancreas invasion was 20.6±2.7 months, while the median OS of DA patients without pancreas invasion was 31.9±3.2 months (P<0.05), in addition, the PFS of DA patients with pancreas invasion was longer significantly (P<0.05). The tumor location, complication, the infiltration depth, the distance between mesangial side of tumor and duodenal papilla were found no correlation with the prognosis of DA patients (OS, P=0.638, P=0.604, P=0.207, P=0.202; PFS, P=0.714, P=0.775, P=0.099, P=0.293).

However, for patients with d-GIST, neither of pancreas invasion, the tumor location, complication, the infiltration

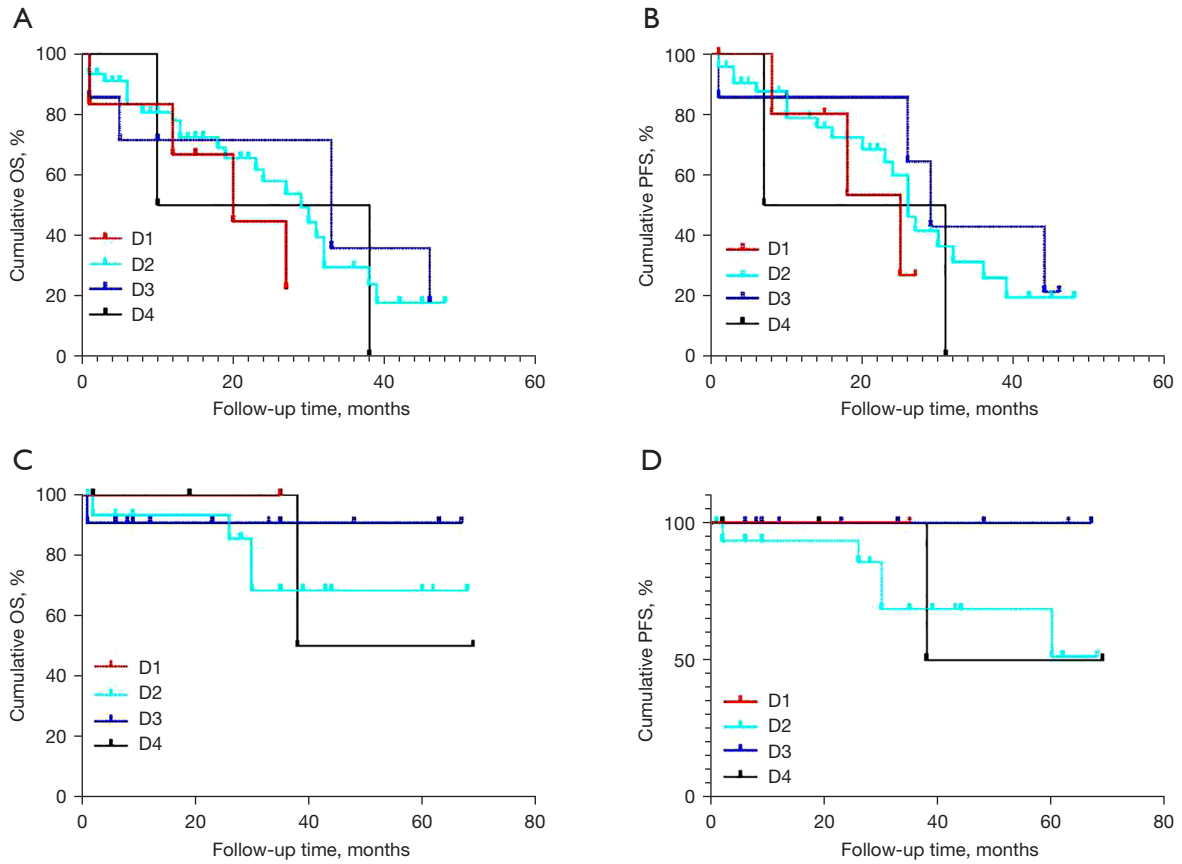

Figure 3 Kaplan-Meier curves of (A,C) OS and (B,D) PFS in the DA patients (A,B) and d-GIST patients (C,D) with different tumor location. D1, duodenal bulb segment; D2, descending segment; D3, horizontal segment; D4, ascending segment; OS, overall survival; PFS, progression-free survival; DA, duodenal adenocarcinoma; d-GIST, duodenal gastrointestinal stromal tumors.

depth, distance from the mesangial side of tumor to duodenal papilla showed significantly difference (OS, P=0.850, P=0.198, P=0.507, P=0.181, P=0.649; PFS, P=0.430, P=0.740, P=0.381, P=0.499, P=0.411) (*Figures 3*,*4*).

Discussion

A PDMT is a rare malignant tumor of the digestive system, which accounts for 0.3–1% of all gastrointestinal malignant tumors (1). Due to limited sample sizes and case studies, discussions of the medical evidence and the surgical treatment of PDMT are limited. PDMT is often associated with small intestinal malignant tumors, which comprise 2% of all gastrointestinal tumors (9). The D2 segment is the descending segment of the duodenum, and the non-D2 segments can be divided into the D1, D3, and D4. A total of 94 patients participated in this study, of whom 62 (66.0%) had tumors located in the D2 segment, which is consistent with previous studies (10).

The clinical symptoms of PDMT patients are diversified and lack clinical specificity, which results in no significant abdominal signs at the early stage and poses a significant challenge for a clinical diagnosis and the prevention of disease progression (11). In this study, DA was the most common pathological type and was defined by the histopathological classification of PDMT in the D2 segment. The tumor in this area was close to duodenal papilla, and DA often shows invasive growth in the intestinal cavity. Patients with tumors causing intestinal obstructions usually presented with jaundice and abdominal pain. However, d-GIST is the most common PDMT in the non-D2 segment, which is rich in blood supply. When the tumor penetrates the blood vessels, gastrointestinal bleeding can easily occur.

Surgical resection is the primary treatment for PDMT. The critical objective of the operation is to completely

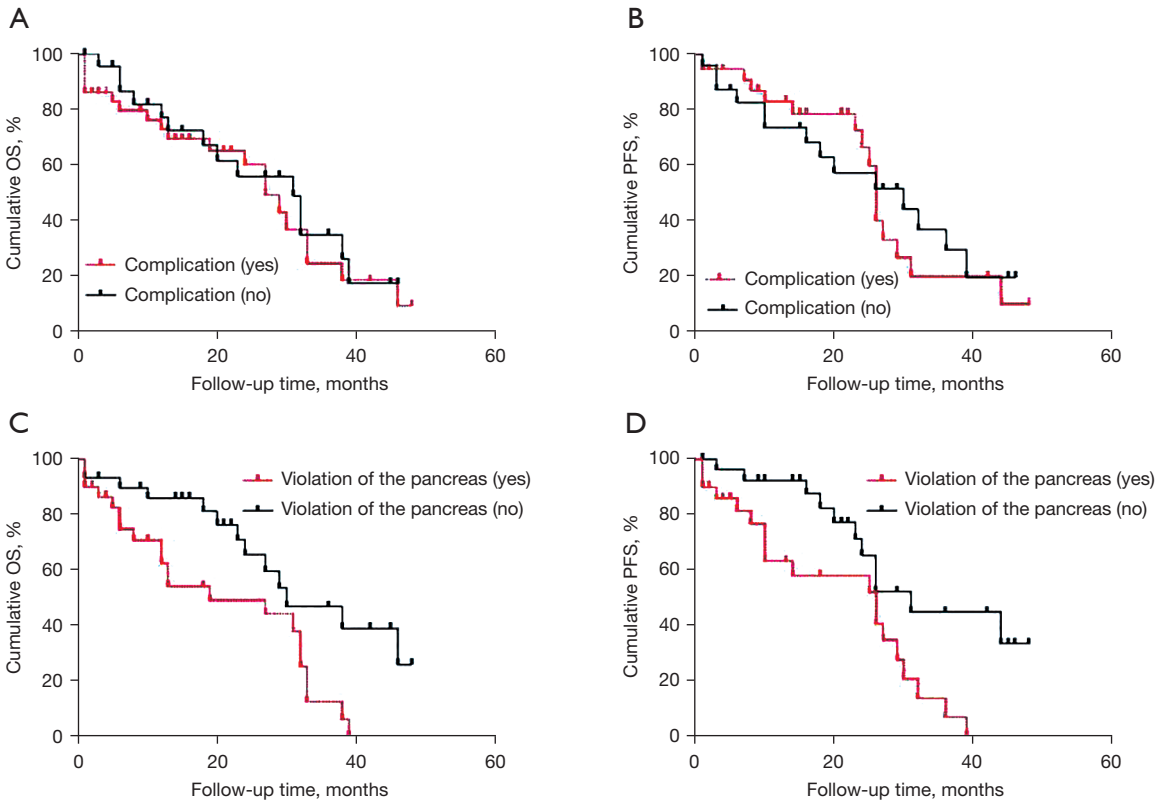

Figure 4 Kaplan-Meier curves of (A,C) OS and (B,D) PFS in the DA patients with complication (A,B) and pancreas invasion (C,D). OS, overall survival; PFS, progression-free survival; DA, duodenal adenocarcinoma.

remove the tumor and to achieve R0 resection and maintain the original anatomical and physiological functions of the duodenum as much as possible (12,13). Standard surgical methods include PD and LR. The choice of the appropriate method depends on many factors, and the standard for choosing the treatment is highly controversial due to the complexity of the duodenal anatomy.

PD is often used for surgical treatment when the tumor is located in the D2 segment or the D2/D3 junction of the duodenum and tumor involving the pancreas or duodenal papilla (14). In this study, the average diameter of the PDMT tumors in the D2 segment was smaller than that of tumors in the non-D2 segment, but the pathological type of PDMT tumors in the D2 segment was mostly DA. PD was also the most common surgical treatment and was used as a radical surgical treatment. However, due to the high incidence of complications and mortality after PD, new surgical methods need to be explored to reduce postoperative complications, shorten the length of hospital stay, and improve the quality of life of patients. Thus, the feasibility of LR, should be discussed and studied further by surgeons.

Meijer *et al.* found that when the margin resection was guaranteed to be negative, both LR and PD could completely remove the lymph nodes, and patients ultimately achieved a similar OS (15). In this study, LR was also used as an alternative surgical treatment for non-D2 adenocarcinoma. For patients with d-GISTs, both location and size of the tumor should be taken into consideration. When tumor volume is small and located in the superior area of duodenal papilla, wedge duodenectomy and primary sutures can contribute to close the incision.

The resection of larger volume tumors usually leads to more significant bowel wall defects, which require distal gastrectomy plus proximal duodenectomy and reconstruction of the digestive tract. When the tumor located in the subpapillary area, the recommended surgical treatment is a segmentectomy of the duodenum with primary anastomosis. Lee *et al.* (16) have confirmed its feasibility. This study attempted to confirmed the

correlation between tumor diameter and surgical choice. However, it failed to identify any other relevant factors that affect the surgical decision for treating d-GIST. This may be due to the small sample size.

Several studies have examined the efficacy and survival of LR and PD. For example, Zhou *et al.* found that PD had a longer hospitalization time than LR, and had higher postoperative morbidity, more intraoperative blood loss, and transfusion volume (12). Zhang *et al.* compared the 3-year PFS of the two types of surgery and found that the 3-year PFS of the PD group was significantly lower than that of the LR group (17). Conversely, Lee *et al.* found the two groups were similar in terms of their 5-year PFS rate and found no statistically significant differences between the two groups (18). The results of our study showed that the intraoperative blood loss and operative time of patients of the LR group were less than those of the PD group, and the postoperative discharge time of the LR group was shorter than that of the PD group. Thus, for non-D2 segment PDMT patients, LR is the first recommended surgical treatment when the tumor does not invade the pancreas.

In this study, the most common postoperative complication of LR was DGE, which resulted in a digestive symptom caused by impaired gastric motor function. The clinical presentation included vomiting, the high output of the nasogastric tube, and intolerance to oral consumption (19). The International Study Group of Pancreatic Surgery defines DGE as requiring the insertion or re-insertion of a nasogastric tube 3 days after surgery or the failure to resume an oral diet 7 days after surgery. However, the exact mechanism remains unclear.

In this study, we found there are a number of reasons why LR is likely to cause a high rate of DGE after surgery. First, the tumors in the LR group were mostly located in subpapillary region. Additionally, duodenum-jejunum anastomosis may result in postoperative gastrointestinal physiological pacemaker function disorder, which makes patients prone to functional gastrointestinal disorder, and results in postoperative DGE. Second, the LR operation destroys too many G cells, and decreases the secretion of gastrointestinal hormones and slows down the gastric movement. Third, LR damages or cuts off vagus nerves distributed in duodenum and jejunum, causing gastrointestinal motor dysfunction and delaying gastric emptying. Our findings are similar to the previous research (20,21). Thus, intraoperative jejunal nutrition tube placement may not only effectively prevent DGE but also provide adequate enteral nutrition for patients with DGE.

Due to the small sample size of patients with lymphoma in this study, long-term survival analysis could not be performed. In the remaining 92 patients, survival analysis of prognostic factors was performed for DA and d-GIST patients respectively, these factors included: choice of two surgical methods, tumor location, tumor invasion depth, distance from the mesangial side of tumor to duodenal papilla, postoperative complications and whether the tumor invaded the pancreas, etc. Among these factors, only tumor invasion into the pancreas was significantly associated with postoperative OS and PFS in DA patients in univariate analysis. In this study, d-GIST invaded the pancreas only in 5 patients (15.6%), so the same result was not obtained in this group. However, the choice of surgical method did not significantly affect the postoperative survival of patients with DA and d-GIST. Due to the small sample size, the independent risk factors affecting prognosis could not be found in this study.

In summary, PDMT mostly occurs in the D2 segment, and DA is the primary pathological type of PDMT. Surgical resection is advocated for the treatment of PDMT. The choice of the surgical methods depends on the pathological type of the tumor, the tumor location, the invasion of the pancreas, and other factors. Compared to PD, we found that LR has more clinical advantages, including a shorter hospitalization time, a shorter operative time, less intraoperative blood loss, and less anatomical and functional damage to the duodenum. Thus, PD should be the first surgical procedure choice when a PDMT is in the duodenal D2 segment or invades the pancreas. Conversely, when a tumor is in the non-D2 segment of the duodenum or does not invade the pancreas, LR should be the preferred.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-475/rc

Data Sharing Statement: Available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-475/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-475/coif). The 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 study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics committee of Tianjin Medical University General Hospital (No. IRB2021-036-01). Informed consent was taken from all the patients.

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