



Pancreatectomies for pediatric pancreatic tumors: A single institute experience from 2007 to 2018

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ARTICLE INFO

Article history:

Received 20 June 2019

Received in revised form 18 August 2019

Accepted 31 August 2019

Key words:

Pediatric pancreatic tumors
Surgery
Perioperative management
Postoperative complication
Prognosis

ABSTRACT

Background: To investigate the safety, feasibility, and complications of pancreatectomies for pediatric pancreatic tumors.

Methods: The medical records of pancreatectomy patients from January 2007 to January 2018 were retrospectively analyzed for perioperative factors and complications. Patients were divided into pancreatic head (n = 43), body (n = 18) and tail (n = 43) groups.

Results: Seventy-two girls and 32 boys (median age 10 years at diagnosis, range: 0–15 years) were enrolled and had solid pseudopapillary tumors (n = 73), pancreatoblastoma (n = 19), neuroendocrine tumors (n = 9), and others. Primary surgical procedures included pylorus-preserving pancreaticoduodenectomy (n = 10) and distal pancreatectomy with splenectomy (n = 4), and organ-sparing resection procedures included duodenum-preserving pancreas head resection (n = 25), middle segmental pancreatic resection (n = 15), spleen-preserving distal pancreatectomy (n = 37) and local enucleation (n = 13), with a median blood loss of 20 cm³ (range: 10–300 cm³). Short-term complications included pancreatic fistula (35.6%), bile leakage (2.9%), intraabdominal infection (21.2%), delayed gastric emptying (23.1%), and postpancreatectomy hemorrhage (5.8%). After a median follow-up of 38 months (range: 3–143 months), 94 patients (90.4%) were alive without tumor recurrence, 2 were alive after tumor recurrence, 1 pancreatoblastoma patient died from tumor recurrence, and 7 were lost to follow-up. Only 14 patients (14/96, 14.6%) had long-term complications at the outpatient follow-up.

Conclusions: Surgical resection was the main treatment for pancreatic tumors. Organ-sparing resection procedures led to good long-term results for pediatric pancreatic tumors, even if these procedures could cause a relatively high incidence of short-term complications (especially pancreatic fistula and postpancreatectomy hemorrhage).

Level of evidence: Level IV.

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Pancreatic tumors are relatively frequent in adult patients; in contrast, this disease is very rare among the pediatric population. The pancreatic cancer represents 0.2% of all pediatric malignancies [1]. Among these tumors, solid pseudopapillary tumors (SPTs) can be observed in late childhood, while pancreatoblastoma (PB) is typical of early childhood [2]. Pancreatic adenocarcinomas are extremely infrequent in the pediatric population [3]. Other less common tumors have been reported, such as

inflammatory myofibroblastic tumors (IMTs), primitive neuroectodermal tumors (PNETs), neuroendocrine tumors, neuroblastoma (NB), and rhabdomyosarcoma (RMS) [4,5]. The main treatment for pancreatic tumors, regardless of tumor type (except lymphoma), is surgical resection [6]. While the overall morbidity and mortality rates associated with pancreatectomies in adults have been extensively studied, limited information is available about the outcomes in pediatric patients. This study reviews the authors' experiences with pancreatectomies in treating pediatric patients with pancreatic tumors over an 11-year period.

1. Methods

1.1. Patients

The medical records of pediatric patients with pancreatic tumors who underwent tumor resection from January 2007 to January

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2018 at Beijing Children's Hospital (BCH) were retrospectively analyzed. The demographic information, preoperative assessments, operative details, length of hospital stay, pathology results, and outcomes were extracted from the electronic medical records and analyzed. Specific outcomes of interest included the short-term postoperative complications that occurred during the initial hospital stay, as well as any evidence of long-term sequelae noted during the follow-up clinic visits. The patients were retrospectively divided into three groups according to the primary tumor site: pancreatic head group, pancreatic body group and pancreatic tail group. The perioperative factors and postoperative complications were compared among the three groups. This retrospective study was approved by the Medical Ethics Committee of the BCH (2018-k-29), and the patient informed consent requirements were waived.

1.2. Statistical analysis

Statistical analysis was performed with SAS 9.4. Continuous variables were presented as means with standard deviations, and variables with non-normal distributions were presented as the median and interquartile range. Student's t-tests or Mann–Whitney U tests were used to compare variables between different subgroups. Categorical variables were reported as counts and percentages and were studied using the chi-square test. $P < 0.05$ was considered statistically significant.

2. Results

2.1. Patient characteristics

Overall, 104 pediatric patients with pancreatic tumors were studied. Seventy-two of the patients were girls, and 32 were boys, with a median

age of 119 (89, 146) months (range: 0–15 years). The patient characteristics are listed in Table 1. The tumors were located in the pancreatic head (43, 41.4%), body (18, 17.3%), and tail (43, 41.4%). The most common presenting symptom in our cohort was abdominal pain (63, 60.6%). The second most common presenting symptom was a palpable abdominal mass (24, 23.1%), followed by vomiting (22, 21.2%). The other symptoms included pathoglycemia (9, 8.7%), jaundice (5, 4.8%), fever (4, 3.9%), upper gastrointestinal bleeding (1, 1.0%), and diarrhea (1, 1.0%); 11 patients had no obvious symptoms (11, 10.6%). The diagnoses included SPTs (73, 70.2%), PB (19, 18.3%), neuroendocrine tumors (9, 8.7%), pancreatic cyst (1, 1.0%), IMT (1, 1.0%), and PNET (1, 1.0%). The levels of alpha-fetoprotein (AFP), a common tumor marker, were clearly elevated in patients with PB, whereas the AFP levels were generally normal in patients with other tumors at diagnosis. The median maximum diameter of the primary tumor was 6.70 (4.40, 8.35) cm (range: 1.5–32 cm).

2.2. Surgical data and perioperative situations

As shown in Table 1, among the patients with pancreatic head tumors, pylorus-preserving pancreaticoduodenectomy (PPPD) was performed in 10 patients (10/43, 23.3%), duodenum-preserving pancreas head resection (DPPHR) was performed in 25 patients (25/43, 58.2%), and local enucleation was performed in 8 patients (8/43, 18.6%). Among the patients with pancreatic body tumors, middle segmental pancreatic resection was performed in 15 patients (15/18, 83.3%), and local enucleation was performed in 3 patients (3/18, 16.7%). Among the patients with pancreatic tail tumors, distal pancreatectomy with splenectomy (DPS) was performed in four patients (4/43, 9.3%), spleen-preserving distal pancreatectomy (SPDP) was performed in 37 patients (37/43, 86.1%), and local enucleation was performed in 2

Table 1
Patient characteristics.

Variables	Results
Sex (n, %)	Male Female
Age (median, month)	119 (89, 146)
Primary tumor site (n, %)	Pancreatic head Pancreatic body Pancreatic tail
Presenting symptom (n, %)	Abdominal pain Palpable abdominal mass Vomiting Pathoglycemia Jaundice Fever Upper gastrointestinal bleeding Diarrhea No obvious symptoms
Histopathology (n, %)	SPT PB Neuroendocrine tumor Pancreatic cyst IMT PNET
AFP (median, ng/ml)	PB Other tumors
Maximum diameter of primary tumor (median, cm)	6.70 (4.40, 8.35)
Surgical procedure (n, %)	Pancreatic head Pancreatic body Pancreatic tail
	PPPD DPPHR Local enucleation Middle segmental pancreatic resection Local enucleation DPS SPDP Local enucleation

AFP: alpha-fetoprotein, normal range: (0–9) ng/ml; SPT: solid pseudopapillary tumor; PB: pancreoblastoma; IMT: inflammatory myofibroblastic tumor; PNET: primitive neuroectodermal tumor; PPPD: pylorus-preserving pancreaticoduodenectomy; DPPHR: duodenum-preserving pancreas head resection; DPS: distal pancreatectomy with splenectomy; SPDP: spleen-preserving distal pancreatectomy.

patients (2/43, 4.7%). The data on the main surgical characteristics and complications were compared among the three groups with different primary tumor sites (Table 2). The operative time of the pancreatic head group was clearly longer than that of the pancreatic body and pancreatic tail groups ($P < 0.001$); however, no significant difference was found in the operation time between the pancreatic body and pancreatic tail groups ($P > 0.05$). The interval peritoneal drainage was used, time until liquids were started and length of hospital stay in the pancreatic head group were all clearly longer than those in the pancreatic tail group (all $P < 0.05$). Additionally, more patients were treated with parenteral nutrition in the pancreatic head group than in the pancreatic tail group ($P = 0.002$). Otherwise, no significant differences were found in the incidences of short- and long-term complications among the three groups (all $P > 0.05$).

2.3. Management of tumor thrombi

Tumor thrombus is a typical feature of malignant pancreatic tumors, and there were eight patients with tumor thrombi in this study (as shown in Supplementary Table 1). All eight tumors were located in the pancreatic tail, and the diagnoses were SPTs ($n = 1$), PB ($n = 6$), and neuroendocrine tumor ($n = 1$). All six PB patients and one SPT patient underwent surgery after neoadjuvant chemotherapy (3–7 cycles). Two patients underwent DPS, and six patients underwent the SPDP procedure. During surgery, splenic pedicle ligation was performed in five patients, resection of the tumor thrombi and segment vessels were performed in eight patients, removal of the tumor thrombi from the vein was performed in one patient, and anastomosis of the splenic vein was performed in one patient. After a median follow-up time of 64 (34, 72) months (range: 7–143 months), all 8 patients were alive and disease free.

2.4. Short-term complications

The short-term complications were assessed in concordance with the International Study Group of Pancreatic Surgery (ISGPS) criteria [7–11], and a total of 53 patients (53/104, 51.0%) had short-term complications (Table 2). As shown in Table 3, apart from delayed gastric emptying (DGE), there were no significant differences in the other short-term complications among the three groups. Postpancreatectomy hemorrhage (PPH) [11] occurred in six patients (one patient with Grade

A, 3 patients with Grade B and 2 patients with Grade C). One patient underwent middle segmental pancreatic resection, two patients underwent SPDP, and three patients underwent DPPHR. Three patients were stable after treatment with blood transfusion, somatostatin, total parenteral nutrition, hemostatics, and other supportive treatments. And other three patients underwent relaparotomy (as shown in Supplementary Table 2).

In addition to the above three patients who underwent short-term secondary surgery due to PPH (as shown in Supplementary Table 2), one patient had a grade B pancreatic fistula and bile leakage postoperatively and underwent endoscopic biliary stenting 2 months after the first DPPHR surgery.

2.5. Prognosis and long-term complications

In this study, after a median follow-up time of 38 (22, 66) months (range: 3–143 months), 94 patients (90.4%) were alive without tumor recurrence, 2 patients were alive after tumor recurrence (2.0%), 1 patient with PB died of tumor recurrence (1.0%), and 7 patients (6.7%) were lost to follow-up. The long-term outcomes were assessed with respect to chronic disability and chronic medication use. In total, 14 patients (14/96, 14.6%) had long-term complications at the outpatient follow-up, including fat malabsorption ($n = 9$), upper gastrointestinal bleeding ($n = 2$), chronic pancreatitis ($n = 1$), anastomotic stricture ($n = 1$), biliary obstruction ($n = 1$), endocrine insufficiency ($n = 1$), and abdominal pain ($n = 1$) (Table 4). Two patients complained of fat malabsorption postoperatively, and these patients were provided medication in the form of pancrelipase. Otherwise, none of the patients in this cohort received insulin therapy postoperatively.

In this study, five patients underwent long-term secondary surgery: one SPT patient underwent staged surgery for intravenous tumor thrombi 9 months after the first surgery; one SPT patient underwent recurrent tumor resection 5 years after the first surgery; one PB patient underwent secondary surgery for recurrent tumor and liver metastases 2 years after the first surgery; one patient who underwent DPPHR developed a biliary obstruction postoperatively and received endoscopic biliary stenting 7 months after the first surgery; and one patient who underwent PPPD developed stricture of the bilioenterostomy anastomosis and underwent open operation 4 years after the first surgery.

Table 2
Comparison of the surgical data and complication rates between different primary tumor sites.

Variables	Primary tumor site			Results	P
	Pancreatic head ^{a,b}	Pancreatic body ^c	Pancreatic tail		
Number of patients	43	18	43		
Operative time (median, min)	428.50 (337.50, 480.00) ^{a,b}	330.00 (266.50, 427.50)	265.00 (220.00, 345.00)	24.914	< 0.001
Blood loss (median, cm ³)	20 (10, 50)	10 (10, 33)	30 (10, 50)	2.794	0.230
Red blood cell transfusion (n, %)	Yes 7 (16.28)	1 (5.56)	7 (16.28)	1.387	0.500
	No 36 (83.72)	17 (94.44)	36 (83.72)		
Peritoneal drainage usage (median, day)	24 (15, 35) ^b	23.5 (15, 36)	15 (8, 24)	7.954	0.019
Feeding jejunostomy tube (n, %)	Yes 13 (30.23)	5 (27.78)	6 (13.95)	3.481	0.176
	No 30 (69.77)	13 (72.22)	37 (86.05)		
Somatostatin (n, %)	Yes 43 (100.00)	18 (100.00)	42 (97.67)	1.780	0.411
	No 0 (0)	0 (0)	1 (2.33)		
Somatostatin treatment (median, days)	14 (8, 19)	12 (8, 18)	10 (6, 14)	4.217	0.121
Parenteral nutrition (n, %)	Yes 35 (81.40) ^b	14 (77.78)	20 (46.51)	12.991	0.002
	No 8 (18.60)	4 (22.22)	23 (53.49)		
Parenteral nutrition treatment (median, days)	12 (8, 16)	12 (10, 23)	11 (7, 16)	1.596	0.450
Days until starting liquid diet (median, day)	6 (3, 9) ^b	6 (4, 7) ^c	4 (3, 6)	10.234	0.006
Hospital stay (median, day)	26 (16, 39) ^b	25 (16, 41)	18 (11, 28)	2.344	0.032
Short-term complications (n, %)	Yes 26 (60.47)	11 (61.11)	16 (37.21)	5.550	0.062
	No 17 (39.54)	7 (38.89)	27 (62.79)		
Long-term complications (n, %)	Yes 9 (9/40, 22.50)	2 (2/16, 12.50)	3 (3/40, 7.50)	3.890	0.143
	No 31 (31/40, 77.50)	14 (14/16, 87.50)	37 (37/40, 92.50)		

^a Result of the comparison between pancreatic head and pancreatic body tumors, which was considered statistically significant.

^b Result of the comparison between pancreatic head and pancreatic tail tumors, which was considered statistically significant.

^c Result of the comparison between pancreatic body and pancreatic tail tumors, which was considered statistically significant.

Table 3

Comparison of the short-term complications between the different primary tumor sites.

Short-term complications		Primary tumor site (n)			Results	P
		Pancreatic head ^a	Pancreatic body	Pancreatic tail		
Number of patients		43	18	43		
Pancreatic fistula	No	27	10	30	5.746	0.452
	Biochemical leak	4	4	6		
	Grade B	10	3	7		
Bile leakage	Grade C	2	1	0	5.426	0.066
	Yes	3	0	0		
Chyle leak	No	40	18	43	-	-
	Yes	0	0	0		
Intraabdominal infection	No	43	18	43	1.200	0.549
	Yes	10	5	7		
Delayed gastric emptying	No	33	13	36	15.208	0.004
	Grade A	27 ^a	13	40		
	Grade B	13	5	3		
	Grade C	3	0	0		
Postpancreatectomy hemorrhage	Grade C	0	0	0	-	-
	No	40	17	41		
	Grade A	0	0	1		
	Grade B	2	0	1		
	Grade C	1	1	0		

^a Result of the comparison between pancreatic head and pancreatic tail tumors, which was considered statistically significant.

3. Discussion

Primary pancreatic tumors are exceedingly rare in the pediatric population. One of the largest series of pediatric pancreatic tumors to date was jointly performed by two medical centers in the USA. The study retrospectively reviewed 31 pediatric patients between 1991 and 2011 [12]. In this study, we present the largest single institutional series of pancreatic tumors in children, with 104 cases treated over an 11-year period, and share some clinical treatment experiences.

The histopathology of primary pancreatic tumors in children is diverse across benign, low-grade malignant and malignant tumors (as shown in Supplementary Table 3). In our series, the most common histological subtype was SPTs, with a female-to-male ratio of 3.29:1, which accounted for 70.2% of all tumors; this incidence was similar to that published in most series [12,13]. In our series, the second most common type of pediatric pancreatic tumors was PB (18.3%), which was malignant and associated with poor prognosis.

Due to the rarity of primary pancreatic tumors, patient management is a challenge for pediatric surgeons who may lack experience with these tumors. The gold standard to treat pancreatic tumors, regardless of tumor type (except lymphoma), is surgical resection. The extent of resection required for complete debulking is dictated by the tumor location [14]. Whenever possible, less extensive resection is advocated [5]. An analysis of 58 pediatric pancreatic malignancies extracted from the Surveillance, Epidemiology, and End Results (SEER) registry in 2008

found that surgery was an independent predictor of survival [6]. The mortality of patients who did not undergo surgical debulking was 15-fold higher than that of patients who underwent surgery. Given that complete surgical resection provides the only potential cure for patients with malignant pancreatic tumors, various surgical techniques are constantly being improved, such as DPPHR, SPDP, and middle segmental pancreatic resection, with the goal to preserve as much normal tissue as possible while achieving complete tumor resection. Resection of metastases, especially solitary metastases and those confined to the liver, was also beneficial for SPTs and PB [15–17].

For pancreatic head tumors pathologically proven to be benign or low-grade malignant, DPPHR or local enucleation should be considered [18,19]. However, a minority of patients with PB or other malignant tumors will still need to undergo pancreaticoduodenectomy (PD) or PPPD to achieve a safe margin. In our cohort, all 4 patients with PB and one patient with PNET in the head of the pancreas underwent the PPPD procedure (5/43). However, most of the patients with low-grade malignant tumors and benign tumors of the pancreas head underwent DPPHR or local enucleation (32/43), and the prognoses were good.

For tumors in the tail of the pancreas, spleen preservation is a popular recommendation. In our cohort, there were a total of 41 patients with pancreatic tail tumors; of whom, 37 patients underwent SPDP, and 4 patients underwent DPS. In the 37 cases of SPDP, 25 (25/37) used the recommended Kimura's method [20], and 7 (7/37) used Warsaw's method [21]. Due to an insufficient blood supply, two of cases required hemisplenectomy. The remaining 5 patients (5/37) underwent splenic vein dissection, and the splenic artery was well preserved. One patient experienced a focal splenic infarction, and one patient developed a splenic abscess after SPDP; both patients recovered after conservative treatment.

Middle segmental pancreatic resection is a parenchyma-sparing technique that reduces the risk of postoperative endocrine and exocrine insufficiency and has been recommended for lesions on the neck or body of the pancreas [22]. There were 15 patients who underwent middle segmental pancreatic resection in our cohort. Since the normal digestive tract and pancreatic tissue were retained as much as possible, no patients developed diabetes in this group, and only one patient needed supplemental exogenous pancreatic enzymes.

Pancreatic tumor resection is usually a challenging operation for pediatric patients. The overall morbidity and mortality reported have decreased over the past years as the surgical techniques have improved. The surgical requirements for organ-preserving surgeries are higher and more difficult to achieve than those for radical surgery [5]. In our

Table 4

Comparison of the long-term complications between the different primary tumor sites.

Long-term complications	Primary tumor site (n)		
	Pancreatic head	Pancreatic body	Pancreatic tail
Long-term survivors	40	16	40
Fat malabsorption	6	1	2
Upper gastrointestinal bleeding	2	0	0
Chronic pancreatitis	1	0	0
Anastomotic stricture	1	0	0
Biliary obstruction	1	0	0
Endocrine insufficiency	0	0	1
Abdominal pain	0	1	0
Delayed gastric emptying	0	0	0
Chronic medications	Pancrelipase	1	0
	Insulin	0	0

cohort, the median operation time was 340 (262, 450) minutes (range: 120–636 min). The total operative time depends on the concrete disease states, but the reported operative time includes any necessary liver resection ($n = 1$), feeding jejunostomy tube insertion ($n = 24$), resection of the tumor thrombus and segment vessels ($n = 20$), removal of the tumor thrombus in the vein and anastomosis of the vascular features ($n = 1$). The median intraoperative blood loss was 20 (10, 50) cm^3 (range: 10–300 cm^3), and transfusions were required only for 15 of 104 (14.4%) patients.

Proper discussions of the risks and benefits of each surgical method are particularly difficult because of the scarcity of pediatric pancreatic tumors. We observed a relatively high rate of short-term complications, with an overall rate of 51% (53/104). We believe that this result may be related to the surgical theory of preserving as much normal pancreatic tissue as possible. In our cohort, PPH occurred in six patients, among whom, three patients underwent short-term secondary surgery. The other three patients recovered after conservative treatment. The occurrence of hemorrhage may be related to poor drainage of pancreatic fistula, and the resulting pancreatic juice is destructive for normal tissues and the vascular wall. Therefore, we have implemented improvements for postoperative management, such as double-tube drainage has been placed for continuous lavage in the early postoperative period and reducing the local pancreatic enzyme concentration. After using this technique for the past 4 years, no cases of PPH due to severe pancreatic fistula occurred again.

In the adult population, the reported rates for exocrine insufficiency are 56%–73%, and the rates for endocrine insufficiency following PD are 20%–25% [5]. We observed that 14 patients had long-term complications (14/96, 14.6%). Two patients complained of fat malabsorption postoperatively, and they were administered medication in the form of pancrelipase. In our series, none of the patients required treatment for endocrine failure, which further proves the benefits of retaining as much normal pancreas tissue as possible. To ensure the quality of life for many years in future, especially for children, it is worthwhile to perform organ-sparing surgical procedures.

Overall, this series shows that surgical treatment is associated with a high survival rate in children with pancreatic tumors, and we recommend that normal tissues and organs should be retained as much as possible. Although these procedures can cause a relatively high incidence of short-term complications, organ-sparing surgeries are of great significance to achieving normal long-term endocrine and exocrine functions for these pediatric patients, who have a life expectancy of at least 7 to 8 decades.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jpedsurg.2019.08.051>.

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