

Surgery of pancreas tumors in pediatric and adolescent patients: a single institution experience in South America

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Abstract

Purpose

Pancreas tumors are extremely rare in pediatric and adolescent patients. Surgical resection is the mainstay of treatment; however, the data is limited with respect to morbidity and mortality. We aimed to evaluate short- and long-term outcomes of pediatric and adolescent patients who underwent surgical resection of pancreatic tumors.

Methods

Patients \leq 18 years old who underwent resection of pancreas tumor at the National Institute of Neoplastic Diseases INEN during 2000–2020 were included.

Results

Thirty-four patients were diagnosed; 28 patients were female and 6 were male. The median age was 13.4 years old. Histological diagnosis was solid pseudopapillary neoplasm (SPN) ($n = 29$, 85.3%), pancreatoblastoma ($n = 3$), neuroendocrine carcinoma ($n = 1$), and insulinoma ($n = 1$). No patient experienced postoperative mortality and 15 (44.1%) patients developed postoperative complications including pancreatic fistula as the most frequent. Under a median follow-up period of 33.8 (0.5–138) months, 4 (11.8%) patients died. Of the 29 patients with SPN, the 3-and-5-year OS was 100% and 83.1%, respectively.

Conclusions

SPN was the most frequent cause of surgical treatment for pediatric and adolescent patients in the high-volume cancer center in Peru and was associated with favorable survival. Pancreaticoduodenectomy was safely performed in this patient group with acceptable morbidity and zero mortality.

Introduction

Pancreas tumors are extremely rare in pediatric and adolescent patients. Solid pseudopapillary neoplasm (SPN) and pancreatoblastoma are relatively common in this patient group [1, 2]. SPN was the most frequent pancreas tumor in patients with 10–20 years old, and pancreatoblastoma was generally found in patients < 10 years old [3, 4]. Other histological types including neuroendocrine tumors (NET), acinar carcinoma, ductal carcinoma, neuroblastoma, lymphoma were reported in pediatric and adolescent patients [2, 5–7]. Surgical resection is the mainstay of treatment and provides a better survival and lower recurrence rate [5]. Generally, radiotherapy and chemotherapy were used as adjuvant treatments.

Loading [MathJax]/jax/output/CommonHTML/jax.js he rates of morbidity and mortality in pediatric and

adolescent patients who underwent pancreatectomy [8]. The aim of this study is to evaluate clinical and pathological characteristics, short-term (morbidity and mortality) and long-term outcomes (overall and disease-free survival) in pediatric and adolescent patients who underwent pancreas resection for benign and malignant pancreas tumors.

Materials And Methods

Study population

Patients who underwent resection of pancreas benign and malignant primary tumors with curative intent at the National Institute of Neoplastic Diseases INEN from January 2000 through January 2020 were identified from a prospectively compiled database. Patients who underwent surgery at the age \leq 18 years old (i.e., pediatric and adolescent patients) were included in the study. Demographic characteristics and short- and long-term outcomes were evaluated. Pancreas tumors were diagnosed based on the current WHO classification[9]. The study was approved by the institutional review board at the National Institute of Neoplastic Diseases INEN.

Preoperative evaluation

All patients underwent computed tomography of the thorax, abdomen, and pelvis. A preoperative tumor biopsy was not routinely performed. Blood test including a complete blood count, hepatic, renal function, and a coagulation profile was performed. A cardiological, psychological, and nutritional evaluation was performed routinely before surgery. No patients received neoadjuvant chemotherapy and radiotherapy.

Surgical technique

The surgical procedure was performed based upon the tumor location and involvement of adjacent organs. For tumors located at the pancreas head, pancreaticoduodenectomy (PD) was performed using the conventional or pylorus preserving method. D2 lymph node dissection was generally performed. For patients with pancreatic tumors invaded to the portal vein and/or superior mesenteric vein, combined resection of the vessels and reconstruction were performed. The anastomosis of pancreas stump was performed depending on pancreas texture and main pancreatic duct diameter. In this series, we used duct to mucosa or modified telescopic anastomosis [10, 11]. For tumors located at the pancreas tail, distal pancreatectomy was performed, with or without splenectomy. For spleen-preserving distal pancreatectomy, Warshaw or Kimura technique was used depending on the surgeon's preferences [12, 13]. Central pancreatectomy was performed for tumors located at the neck and proximal body of the pancreas and the distal pancreatic stump was anastomosed using a Roux-en-Y jejunal loop or a pancreatic-gastric anastomosis [14]. For small tumors which are located away from the main pancreatic duct, enucleation was selected [15].

Postoperative management

An enteral feeding tube was routinely used in patients who underwent PD and central pancreatectomy. In patients who underwent distal pancreatectomy, an enteral feeding tube was only used in case of malnutrition and albumin < 35 g/dL. At the postoperative day (POD) 1 or 2 enteral nutrition was started through an enteral feeding tube, oral intake was started at POD 3 in patients who underwent an enteral anastomosis. Amylase levels in blood and fluid from abdominal drains were measured at POD 1, 3, 5, and 7. The discharge amount from abdominal drains was measured. When patients had pancreatic fistula, somatostatin analog was used [16]. Abdominal drains were removed when amylase level was < 5000 U/L; after POD 5 or on the day of patient discharge. Postoperative morbidity and mortality were defined as complications and mortality which occurred within 30 days after surgery. All complications were categorized according to the Clavien-Dindo classification [17].

Variable studied

Demographic characteristics (age, symptoms, tumor location, tumor size, and histology), surgical and pathological outcomes (surgical procedure, type of anastomosis, and nodal status), postoperative outcomes (hospital stay and postoperative complications), and long-term outcomes were evaluated. Tumors were classified according to the current WHO classification for pancreatic tumors [9].

Statistical analysis

Categorical variables are expressed as number (%) and continuous variables are expressed as median (ranges). Overall survival (OS) and recurrence-free survival (RFS) curves were constructed using the Kaplan-Meier method. Deaths without recurrence were censored for the RFS analysis. A p-value < 0.05 was considered statistically significant. Statistical analysis was conducted using SPSS 22.

Results

Study population

From 2000 to 2020, 34 patients underwent pancreas resection. The annual proportion of pancreatic malignancy in pediatric and adolescent patients at our institution is approximately 0.3% (1–2 pancreatic malignancy of 650 pediatric and adolescent patients with malignancy. Demographic and clinicopathologic characteristics were shown in Table 1. The median (range) age was 13.4 (3–18) years, and 28 (82.4%) patients were female and 6 (17.6%) were male. Symptoms were abdominal pain in 25 (73.5%) patients, palpation of intraabdominal mass in 3 (8.8%) patients, Cushing syndrome in 1 (2.9%) patient, and no symptoms in 5 (14.7%) patients.

Surgical and histopathologic outcomes

Table 2 shows surgical and histopathologic outcomes. Of the 34 patients, 19 (55.9%) underwent pancreaticoduodenectomy, 10 (29.4%) underwent distal pancreatectomy, 4 (11.8%) underwent central pancreatectomy, and 1 (2.9%) underwent enucleation. Pancreatic-jejunal anastomosis was performed in 22 (64.6%) patients, and pancreatic-gastric anastomosis was performed in 1 (2.9%) patient who

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underwent central pancreatectomy. Median (range) operative time was 343 (125–570) minutes and the median (range) estimated blood loss was 440 (20–3000) mL. Diagnoses of disease were SPN ($n = 29$, 85.3%), pancreatoblastoma ($n = 3$, 8.8%), neuroendocrine carcinoma ($n = 1$, 2.9%), and insulinoma ($n = 1$, 2.9%). Median (range) tumor diameter was 7.5 (2.0–13.5) cm. Lymph node metastasis was found in 2 (5.9%) patients who had a diagnosis of SPN. One patient underwent pylorus-preserving pancreaticoduodenectomy with vascular reconstruction because the superior mesenteric vein was involved by the tumor; the final pathology showed no vascular infiltration of the tumor.

Postoperative outcomes

Postoperative outcomes were shown in Table 3. No patient experienced postoperative mortality and 15 (44.1%) patients developed postoperative complications including pancreatic fistula ($n = 7$, 20.5%), pancreatitis ($n = 2$, 5.9%), intra-abdominal fluid collection ($n = 2$, 5.9%), postoperative hemorrhage ($n = 2$, 5.9%), delayed gastric emptying ($n = 1$, 2.9%) and intestinal obstruction ($n = 1$, 2.9%). Reoperation was performed in 2 (6.3%) patients undergoing pylorus-preserving pancreaticoduodenectomy because of intestinal obstruction in 1 (2.9%) patient and postoperative hemorrhage in 1 (2.9%) patient. The median (range) length of hospital stay was 12 (4–28) days. The postoperative complications by the type of procedures were summarized in Supplementary Table 1.

OS and RFS

Under a median follow-up period of 33.8 (0.5–138) months, 4 (11.8%) patients died. Of the 29 patients with SPN, 2 patients died; one patient because of liver cirrhosis and other patients because of liver metastasis. Of the 3 patients with pancreatoblastoma, 1 patient died because of liver metastasis. Of the 2 patients with NET/NEC, 1 patient died because of liver and lung metastases. Demographics and clinicopathologic factors only in patients with SPN were shown in Supplementary Table 2. Figure 1 shows OS and RFS curves in patients with SPN. The 3-and-5-year OS was 100% and 83.1%, respectively. The 3-and-5-year RFS was 100% and 93.3%, respectively.

Discussion

Primary pancreatic tumors are rare in pediatric and adolescent patients. Our study showed outcomes of the largest series in South America and the second largest single institution series worldwide. A total of 34 patients underwent resection without mortality.

In line with previous studies [1, 2, 5, 8, 18], the proportion of female sex was higher (82.4%) and the most common histology type was SPN in this population. Most of the patients were ≥ 10 years old (88.2%). The most frequent symptom was abdominal pain. These were also in line with previous studies, showing that the demographic characteristics of pediatric and adolescent pancreatic tumors may be common regardless of the regions worldwide [1, 2, 19, 20].

SPN is a low grade malignant pancreas tumors which contain solid and cystic components and mainly

SPN was 1: 9.5. The size of SPN is generally smaller in male patients than in female patients, and SPN diagnosed in male patients mainly contains solid components [19]. In pediatric and adolescent patients, SPN is generally found at the age from 10 to 20 years old [4]. Our study showed that the 3- and 5-year OS rates were 100% and 83.1% in pediatric and adolescent patients with SPN, respectively. This is in line with previous studies which showed that the OS in pediatric and adolescent patients with SPN was more than 95% and was better than OS in this patient group with other histology types of pancreas tumors [1, 5, 8, 20, 21].

Pancreatoblastoma is the second most common histology type in our study. Pancreatoblastoma was originally termed as infantile pancreatic carcinoma by Becker in 1957 [22] and is an extremely rare pancreas neoplasm which contains typical squamous corpuscles and tumor cells with acinar, glandular, or undifferentiated appearance [23]. It is predominant in male patients who are from 0 to 20 years old and has an association with Beckwith-Wiedemann syndrome [3, 24]. Serum alpha-fetoprotein level is elevated in most patients. Mylonas, et al reported 21 pediatric and adolescent patients with pancreatoblastoma. The median age of the patients 5.5 years old at the time of diagnosis [20]. In our study, of the three patients, two are alive with no evidence of recurrence after surgery and one died because of hepatic recurrence at 46 months after surgery. Bien, et al reported 20 pediatric and adolescent patients with pancreatoblastoma in a multicenter study [25]. The 5-year OS was 79.4% and the 5-year event-free survival was 58.8%. Complete surgical resection was a prognostic factor for a better event-free survival in univariate analysis.

The largest single institution retrospective study about this topic was reported in Asia [2]. The study included 104 pediatric and adolescent patients between 2007 and 2018. Other studies included approximately 30 patients mainly from North America. Our study is the largest series in the population of South America and found that female sex is dominant and SPN was the most common histology types in line with previous studies in other regions. Mylonas et al [20], reported a retrospective multicenter study using Surveillance, Epidemiology and, End Results (SEER) database, and included 114 pediatric and adolescent patients from 1973–2013. In this study, the most common histology type was NET with 40 (35%) patients followed by epithelial tumors with 29 (25%). A total of 73 (64%) patients had surgical treatment. Another study using the SEER database from 1973–2004, showing that the incidence of pancreas tumors in pediatric and adolescent patients was 0.018 per 100000 people [5].

Pancreaticoduodenectomy was the most frequent surgical procedure in our study which accounts for 19 patients (55.9%). Pancreaticoduodenectomy in pediatric and adolescent patients had been reported but the number of cases was low [26]. In children, pylorus-preserving pancreaticoduodenectomy may be considered to preserve gastric function [27, 28]. Mansfield et al reported that morbidity rate after pancreaticoduodenectomy was lower in patients \leq 30 years old than in adult patients [29]. In our study, no patient experienced postoperative mortality and 15 patients (44.1%) developed postoperative complications including 5 patients (14.7%) who had major complications. Pancreatic fistula was found in 6 (31.5%) patients undergoing pancreaticoduodenectomy versus 1 (10%) patient undergoing distal

Our study is a retrospective study with a small number of patients. Nonetheless, given the rarity of pancreas tumors in pediatric and adolescent patients, our study is the second largest series worldwide and showed outcomes of pancreas tumors for this patient group in South America. Another limitation is that the functional change after pancreatectomy was not followed because most patients lived in remote areas far from our institution.

In conclusion, SPN was the most frequent cause of surgical treatment for pediatric and adolescent patients in the high-volume cancer center in Peru and was associated with favorable survival. Pancreaticoduodenectomy was safely performed in this patient group with acceptable morbidity and zero mortality.

Declarations

Compliance with Ethical Standards

Conflicts of interest:

The authors declare that they have no conflicts of interest.

Ethics approval:

Ethical approval was waived by the local Ethics Committee of National Institute of Neoplastic Diseases in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

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Author contributions:

All authors contributed to the study conception and design. Conceptualization: Francisco Berrospi Espinoza; Methodology: Eduardo Payet Meza; Formal analysis and investigation: Eloy Ruiz Figueroa; Writing - original draft preparation: Oscar Paredes Torres; Writing - review and editing: Yoshikuni Kawaguchi; Supervision: Francisco Berrospi Espinoza. All authors read and approved the final manuscript.

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Tables

Due to technical limitations, the tables are only available as a download in the supplemental files section.

Figures

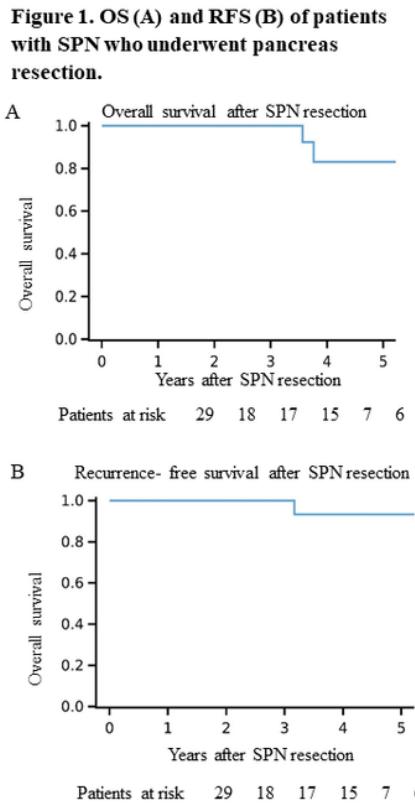


Figure 1

OS (A) and RFS (B) of patients with SPN who underwent pancreas resection.

Supplementary Files

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