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Long-term outcomes after pancreaticoduodenectomy using pair-watch suturing technique: Different roles of pancreatic duct dilatation and remnant pancreatic volume for the development of pancreatic endocrine and exocrine dysfunction

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ABSTRACT

Background: We evaluated long-term outcomes including endo- and exocrine functions after pancreaticoduodenectomy (PD) with standardized pancreaticojejunostomy, paying attention to postoperative pancreatic duct dilatation (PDD) and remnant pancreatic volume (RPV), and examined whether postoperative pancreatic fistula (POPF) influenced the configuration of remnant pancreas.
Methods: We analyzed the records of 187 patients with PD who could have RPV measured by CT volumetry at 1 month after operation and had been followed for more than 6 months. We assessed the risk factors of diabetes mellitus (DM) and PDD, and evaluated association between RPV and pancreatic endo- and exocrine functions assessed by several markers such as albumin, cholesterol, amylase and HbA1c.
Results: Regarding RPV, pancreatic exocrine functions were significantly impaired in the small-volume group (SVG: less than 10 ml) than in the large-volume group (LVG: 10 ml or more). The incidence of new-onset or exacerbation of DM did not differ between SVG and LVG. PDD and the primary disease (pancreatic ductal adenocarcinoma compared to bile duct cancer) were selected as the independent risk factors of new-onset or exacerbation of DM by multivariate analysis. Unexpectedly, there was no significant association between POPF and PDD.
Conclusions: Early occurrence of POPF after PD did not influence the development of PDD in late period, and long-term follow-up should be made by paying attention to PDD and RPV, because PDD was recognized as the most important risk factor of new-onset or exacerbation of DM and the patients with small RPV suffered from prolonged exocrine dysfunction rather than endocrine dysfunction.

Introduction

Pancreaticoduodenectomy (PD) has been more often carried out in recent years as a safe and proper operation in patients with malignant and benign diseases of the pancreas head and distal bile duct region. The probability of operative mortality after PD is now notably decreased in many high-volume centers. Despite the fact that a low mortality rate has been observed, the incidence of postoperative pancreatic fistula (POPF), which most negatively affects the patient's outcome, can reach 20–50% [1–3]. Furthermore, long-term survival after PD has been increased recently because of recent improvements in surgical techniques and postoperative care [4], which in turn raise the importance of long-term patient's administration, including preservation of endocrine and exocrine pancreatic functions.

Even in high-volume centers, the procedures of pancreaticodigestive anastomosis have not been standardized and each institution have employed each preferring procedures such as pancreaticogastrostomy (PG), pancreaticojejunostomy (PJ), external tube drainage, lost stent method and invagination et al.,

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and this diversity of procedures made it difficult to evaluate the frequency of POPF and several remnant pancreatic functions which are highly influenced by the type of pancreaticodigestive anastomosis. We previously reported the study regarding the validation of duct-to-mucosa pancreaticojejunostomy, named the "pair-watch suturing technique (PWST)", which allowed us to completely standardize the anastomotic procedures regardless of type of primary disease, grand texture of pancreas and caliber of main pancreatic duct (MPD) [5,6].

Regarding pancreatic exocrine deficiency, which is highly influenced by remnant pancreatic volume (RPV) after PD, we previously revealed that the patients whose pancreas cut line was made at the left side of superior mesenteric artery (SMA) highly developed postoperative non-alcoholic fatty liver disease (NAFLD) caused by the disruption of exocrine function and suggested a significant efficacy of exocrine enzyme replacement for those patients [7]. Furthermore, our institution recently published a study in which actual RPV significantly influences the occurrence of NAFLD and postoperative nutrition until a year after the surgery [8].

On the other hand, despite the fact that new-onset of diabetes mellitus (DM) was reported to develop in about 20% after PD [2,9–11], the precise incidence and its mechanism have not yet been covered. It is important to investigate its cause and what kind of patient could be categorized as a high risk group since this disease could ruin the patient's quality of life for a long term after PD once it occurs. Risk factors of new-onset of DM after PD were reported to be body mass index (BMI), hard pancreatic texture and postoperative pancreatic duct dilatation (PDD) [2,12]. In addition, previous clinical study revealed that pancreatic duct obliteration significantly exacerbated postoperative endocrine function with compare to duct to mucosa anastomosis group [13]. According to these article, the development of postoperative DM and PDD might be closely interacted each other, but there has been few report in which those risk factors were comprehensively assessed for more than 3 years postoperatively.

Regarding the association between POPF and postoperative long-term outcome, POPF after PD is considered to influence long-term outcomes such as new-onset and exacerbation of DM. In fact, it would be logical hypothesis that POPF could lead to the stenosis of pancreaticodigestive anastomosis resulting in PDD, which could cause the remnant pancreatic atrophy and ruin the pancreatic function. However, whether POPF influences long-term outcomes or not has been uncovered. To the best of our knowledge, only the Japanese multi-center study showed that POPF is a significant risk factor for new-onset or exacerbation of DM [14], but this retrospective study also had a strong limitation because of the diversity of pancreaticodigestive anastomosis.

Based on the results obtained from the long-term follow-up of patients who underwent PD using PWST, the present study was performed to evaluate how short-term outcomes such as POPF and RPV after PD influence long-term outcomes such as pancreatic functions, paying a special attention to PDD and the changes of RPV.

Patients and methods

Patients

All patients data including imaging studies were obtained from the electric medical records at Mie University Hospital Information Network Total System. The study design was approved by an ethics review board (*No.2857*). Among 284 patients who underwent PD from April 2007 to December 2015, PWST was performed in 263, of whom the subjects of the present study were 187 patients who could have RPV measured by CT volumetry at 1 month after operation and had been followed for more than 6 months (Fig. 1).

In these 187 patients, the median follow-up time was 26.6 months (6.1–114.2), the median age was 67.0 (39–86) years, and males/females were 112/75. The indication of PD was pancreatic ductal adenocarcinoma (PDAC) (n = 91), intraductal papillary mucinous neoplasm (IPMN) (n = 34), bile duct cancer (n = 34) and others (n = 28). Surgical procedure was conventional PD (n = 20), pylorus-preserving PD (PPPD) (n = 4) and subtotal stomach-preserving PD (SSPPD) (n = 163). Laparoscopic procedure was performed in 9 patients. Combined resection of the other organs was performed in 83 patients for the portal vein/superior mesenteric vein, in 11 for the hepatic artery, in 3 for the stomach, in 10 for the colon, in 5 for the liver and in 2 for the distal pancreas (middle pancreas was preserved). For the patients without PDAC, we did not perform the dissection of nerve plexus around SMA. Surgical reconstructions were performed according to our previous report: PJ using PWST, choledochojejunostomy, gastrojejunostomy (or duodenojejunostomy) and a Braun anastomosis were performed by turns [5].

At the time of 1 month after PD, we examined the status of pancreatic enzyme supplementation therapy: the dosage of pancreatic enzyme supplementation was no administration in 12 patient, low dose (pancreatin 1.5–3.0 g) in 15, and high dose (pancreatin 6 g or more or pancrealipase 900 mg or more) in 160.

After PD, all patients received enhanced multiditector-row computed tomography (MDCT) scan within one month to check the postoperative complications. The patients with the malignant disease such as PDAC or bile duct cancer had been followed by examining laboratory tests every 2 or 3 months and enhanced MDCT every 3 months within 2 years and every 6 months thereafter [15]. In the other patients, MDCT had been performed every 3–6 months with 2 years and thereafter every 6 or 12 months.

Methods

Assessment of pancreatic configuration

By using the images of preoperative MDCT, we evaluated the preoperative pancreatic configuration data such as MPD, pancreatic thickness, and MPD index which is the ratio of the MPD to pancreas body according to the previous literature [1]. Pancreatic duct size (3 mm or less, more than 3 mm) and the texture of the remnant pancreatic parenchyma were determined according to the medical records of intraoperative findings. RPV had been serially measured at 1, 3, 6, 12, 24 and 36 months after PD by CT volumetry according to our previous report [8].

Assessment of POPF after PWST

In all cases, amylase activities of abdominal drainage fluid and serum were measured on postoperative day 3–7. POPF was defined according to Bassi et al. [16]. Grading of POPF was calculated by using the web-based calculators which are available on Pancreas Club web site (http://pancreasclub.com/calculators/isgps-calculator/).

Association between RPV and NALFD or pancreatic functions

According to the RPV at 1 month, the 187 patients were classified into the two groups: small-volume group (SVG: RPV at 1 month of less than 10 ml) (n = 73) and large-volume group (LVG: RPV at 1 month of 10 ml or more) (n = 114) according to our previous study [8]. RPV ratio (RPV at 3 months or more/RPV at 1 month) was serially calculated to assess the shrinkage rate of the remnant pancreas.

Accurate methods for evaluation of pancreatic endocrine and