Shark mouth pancreaticojejunostomy: a new enteric reconstruction procedure of pancreatic stump

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Abstract

Background: The enteric reconstruction procedure of pancreatic stump after pancreaticoduodenectomy remains to be the critical factor influencing the mortality and morbidity. No widely accepted surgical procedure for the pancreaticojejunostomy has been erected yet. We have developed a new technique of pancreaticojejunostomy named "shark mouth pancreaticojejunostomy." The aim of this study is to assess the efficacy of "shark mouth pancreaticojejunostomy."

Methods: This is a prospective single-arm observational study to evaluate the clinical efficacy of "shark mouth pancreaticojejunostomy." Patients with diseases, in whom a pancreaticoduodenectomy is indicated, would be recruited from Peking University Third Hospital. The hypothesis to be tested is that a "shark mouth pancreaticojejunostomy" will reduce fistula rate from around 20% to less than 10%. A sample size of 120 patients will be needed. The primary endpoint is the incidence rate of postoperative pancreatic fistula (POPF). The secondary endpoints of the study are anastomosis time, postoperative hospital stay, and morbidities besides the POPF such as the hemorrhage. Enrolled patients will undergo pancreaticoduodenectomy and be followed up for 3 months. The relevant data will be monitored and recorded.

Conclusions: The current trial will explore the therapeutic value of the newly raised pancreaticojejunostomy procedure as the "shark mouth pancreaticojejunostomy." Its theoretical base and pragmatic feature will promise high external validity.

Trial registration: Clinical Trials.gov: NCT03366038; https://www.clinicaltrials.gov.

Keywords: Shark mouth pancreaticojejunostomy; Efficacy; Safety; Pancreaticoduodenectomy

Introduction

Pancreaticoduodenectomy is one of the most complicated surgical procedures and one of the standard therapies for benign and malignant lesions of pancreatic head and periampullary region.[1,2] Developments in surgical techniques and the perioperative management have reduced the mortality of pancreaticoduodenectomy to less than 3% in high-volume surgery centers.[3] However, the incidence of postoperative complication remained high, which ranged from 30% to 50% and the pancreatic fistula rate ranged from 5% to 40%.[4]

Since the International Study Group of Pancreatic Surgery (ISGPF) classification of postoperative pancreatic fistula (POPF) published in 2005, it has been widely accepted.[5,6] The rate of clinically relevant (CR)-POPF continued to persist at 20%. CR-POPF is one of the most important life-threatening complications that could lead to an intra-abdominal abscess, hemorrhage, and sepsis. The mortality rate of POPF will be amplified if pancreatic fistula related hemorrhage occurs.[7-9] The exocrine output from the pancreatic remnant was widely implicated as the initial promoter of fistula. The underlying process was the continuous leakage of caustic proteases and lipolytic enzymes, with significant local consequences (abscess, pancreatic fistula, pseudoaneurysm, hemorrhage) and systemic sequelae (sepsis, shock). The higher body mass index, thinner main pancreatic duct, soft gland, and the surgical procedure were widely accepted as the risk factors of CR-POPF.[10,11] Among them, only the surgical procedure could be improved by the surgeons. Therefore, an easy, feasible and efficient way to avoid the CR-POPF is to improve the enteric reconstruction technique of pancreatic stump.

There were different techniques of enteric reconstruction procedures such as invagination pancreaticojejunostomy, binding pancreaticojejunostomy, duct-to-mucosa pancreaticojejunostomy, Roux-en-Y pancreaticojejunostomy, and

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pancreaticogastrostomy. Each technique has its advantages and disadvantages.[12] Several anastomotic techniques have been introduced to reduce the incidence of pancreatic fistula in recent decades, including Peng binding method, and Bulgmart method.[12,13] However, large prospective studies and meta-analyses showed no significant differences in postoperative complications and mortality among these reconstruction methods.[12,14] Invagination pancreaticojejunostomy and duct-to-mucosa pancreaticojejunostomy still were the most popular reconstruction procedures. Invagination pancreaticojejunostomy is difficult to perform in the case of larger pancreatic remnant and soft gland. Duct-to-mucosa pancreaticojejunostomy is difficult to perform in the case of thinner pancreatic duct. The uncompleted drainage of the pancreatic remnant is also considered to be an important reason of CR-POPF. So we established a new procedure, named "shark mouth pancreaticojejunostomy," with theoretical advantages to facilitate the pancreaticojejunostomy. And we registered a clinical trial to reveal the superiority of the new procedure. This study will aim to evaluate the efficacy of "shark mouth pancreaticojejunostomy," which is theoretically considered to be with lower rate of complications, especially the POPF.

Methods

Ethical approval

This study was approved by the Medical Science Research Ethic Committee of Peking University Third Hospital (No. LM2017253). The trial protocol has also been registered at ClinicalTrials.gov (identifier: NCT03366038). The protocol, informed consent form, recruitment materials, and all participant materials will be submitted to the Medical Science Research Ethic Committee of Peking University Third Hospital for review and approval. The data monitoring committee of Medical Science Research Ethic Committee of Peking University Third Hospital and the sponsor will conduct the trial separately. The monitor from the Ethics Committee of Peking University Third Hospital will conduct the monitoring every 2 weeks throughout the study. Random review of the study data will be performed. Independent audits will be conducted by the Ethics Committee of Peking University Third Hospital to ensure monitoring practices are performed consistently across all participating sites. All patients involved will be scheduled only after comprehensive information concerning the nature, scope, and possible consequences of the clinical trial have been provided to them in an understandable way by the investigator. Written informed consent for the trial will be collected from each patient before the research. The clinical trial procedure, risks, benefits, and data management will be clarified in detail during the recruitment conversation. This is a clinical research sponsored by the primary investigator, and there is no conflict to disclose.

Type of trial

This study is a prospective single-arm observational clinical trial and will be performed in the Department of General Surgery, Peking University Third Hospital.

Sample size determination

Sample size calculation is based on the primary endpoint: POPF rate. An assumed absolute risk of 10% difference in POPF occurrence is the appropriate basis for the calculation assuming 10% POPF in the "shark mouth pancreaticojejunostomy" group and 20% in the previously published data.[15] This calculation yields a total of 108 patients in the "shark mouth pancreaticojejunostomy" technique group, which assures a power of 80% at a two-sided level of significance of 5% using NCSS&PASS 11 (NCSS Statistical Software, Kaysville, UT, USA). Assuming an expected withdrawal rate of 10% during the trial, 12 additional patients will be included; therefore, the total sample size required is 120 patients.

Inclusion criteria

Patients who meet the following criteria will be included in the study: (1) patients diagnosed with pancreatic cancer or other diseases which has the indication of pancreaticoduodenectomy; (2) operation-tolerated; and (3) informed consent.

Exclusion criteria

Patients who meet any of the following criteria will be excluded from the study: (1) history of abdominal operation; (2) pancreaticoduodenectomy is given up during operation; (3) patients require to exit from the study anytime; or (4) pregnancy.

Strategies for recruitment and retention

Posters will be displayed in the outpatient and inpatient departments of Peking University Third Hospital in order to enroll the potential participants. The brief introduction of the clinical trial and the contact information will be printed on the posters.

Withdrawal

Patients can withdraw from the trial on their own willing or at the request of their legal representative at any time. Patients may be removed if in the investigator's opinion, continuation of the trial could be detrimental to the patient's health or if a pancreaticoduodenectomy is not performed due to technical unresectability, metastasis, or any other reasons. Every withdrawal case will be recorded in the clinical report forms and in the patient's medical records.

Performance of shark mouth pancreaticojejunostomy

The "shark mouth pancreaticojejunostomy" will be performed according to the standard procedure by the same surgeon to improve adherence to intervention protocols [Figure 1]. The remnant of jejunum is closed by continuous suture. The transverse incision is made on the posterior wall of the jejunum (5.0 cm distal to remnant), which starts at 0.2 cm to the mesenteric border and should never exceed the anti-mesenteric border. In case of large pancreas remnant, a longitudinal incision will

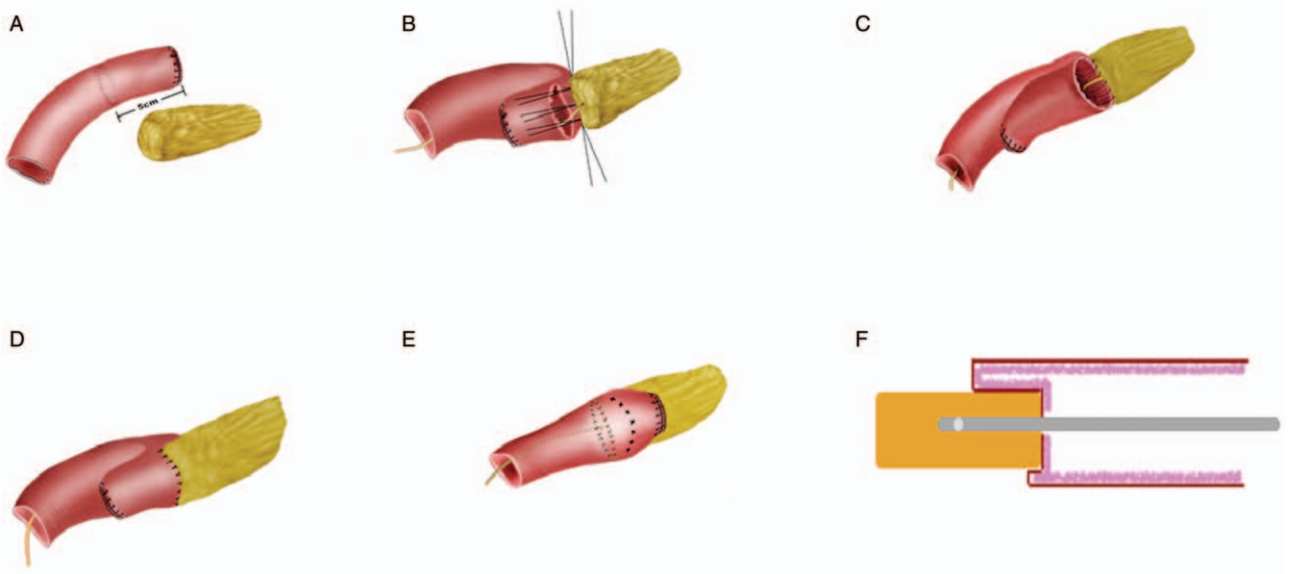

Figure 1: The procedure of "shark mouth pancreaticojejunostomy." (A) The jujunum remnant and the pancreatic stump. (B) The posterior seromuscular layer suture. (C) The posterior full thickness layer suture and internal silicone tube is inserted as the stent tube. (D) The anterior full thickness layer suture. (E) The seromuscular layer of the proximal jejunum is sutured with the anterior pancreatic capsule to cover the anterior part of anastomosis. (F) The schematic map of the "shark mouth pancreaticojejunostomy".

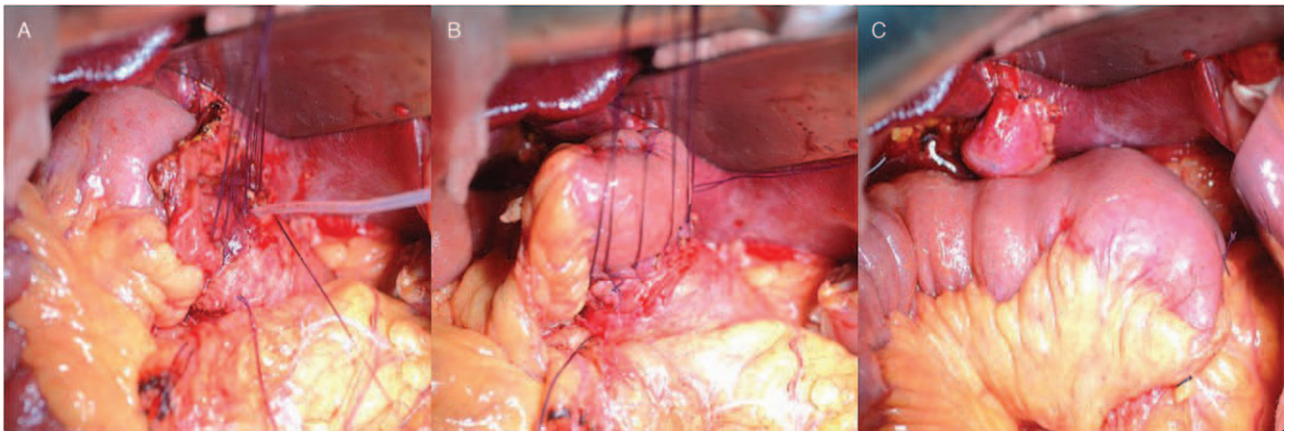

Figure 2: The operative photograph of "shark mouth pancreaticojejunostomy." (A) The posterior seromuscular layer and full thickness layer suture. (B) The anterior full thickness layer suture. (C) The closure of "shark mouth pancreaticojejunostomy."

be done at anterior part of anastomosis. The posterior part of anastomosis is two layers of intermittent suture, including seromuscular suture layer and full thickness suture layer. The anterior part of anastomosis is a single layer full thickness suture. At last, the seromuscular layer of the proximal jejunum is sutured with the anterior pancreatic capsule to cover the anterior part of anastomosis [Figure 2].

Concomitant therapy

In this protocol, a prescription medication is defined as a medication that can be prescribed only by a properly authorized/licensed clinician. Medications to be reported in the Case Report Form are concomitant prescription medications, over-the-counter medications, and supplements. The use of somatostatin, somatostatin analogs, antibiotics, and acid inhibitors should be recorded.

Primary and secondary endpoints

The primary endpoint of the study is the occurrence of POPF. The secondary endpoints of the study are the anastomosis time, morbidities besides the POPF, and postoperative hospital stay.

All outcome variables will be evaluated according to internationally accepted standards and scoring systems if available, that is, the consensus definitions for pancreatic fistula of the ISGPS.[6,16] The efficacy of the "shark mouth pancreaticojejunostomy" will be comprehensively assessed

by the symptoms (eg, febrile, abdominal pain, exsufflation), signs (eg, tenderness, rebound tenderness, increased amount of drainage fluids), laboratory examinations of the blood (eg, blood routine test), drainage fluids (eg, amylase, bacteria culture), and imaging examinations (eg, abdominal computed tomography scanning). Anastomosis time is defined as time from beginning to end of shark mouth pancreaticojejunostomy. Morbidities besides the POPF such as hemorrhage are classified according to the Clavien-Dindo definition as grade I to grade V.[17] Post-operative hospital stay is defined as the length of hospital stay after the operation.

Statistical analysis

Clinical data (including adverse events, concomitant medications, and expected adverse reactions data) and clinical laboratory data will be entered into the record system provided by the Ethics Committee of Peking University Third Hospital. Categorical data will be presented in numbers with percentages. Continuous data will be presented in means with standard deviations or medians with ranges. The subgroup analyses will be analyzed based on age, gender, the texture of the pancreas, diameter of the main pancreatic duct, and the primary diseases. A two-tailed $P < 0.05$ was considered statistically significant. For these analyses, SPSS for Windows version 19.0 (SPSS Inc., Chicago, IL, USA) software was used.

Discussion

Having been performed for around 100 years, pancreaticoduodenectomy is still one of the standard surgeries for lesions locating at pancreatic head and peri-ampullary region. The pancreaticoenteric reconstruction remains to be the "Achilles heel" of the pancreaticoduodenectomy procedure, and the CR-POPF represents one of the most fatal complications. Moreover, CR-POPF was closely related with the occurrence and severity of some other morbidities such as hemorrhage and sepsis. However, current clinical evidences fail to erect any "golden standard" procedure for pancreaticoenteric reconstruction.

The risk factors of POPF can be classified into three categories: the patient-related factors (body mass index), operative factors (surgeon's experience, operation time, blood loss, type of anastomosis, pancreatic duct stent, drain management, adjuvant medications, and others), and pancreatic factors (gland texture, diameter of the pancreatic duct, blood supply, and others). In these three categories of risk factors, the operative factors were the only kind of factors that could be controlled by the surgeons. Hence, the improvement and modification of pancreaticoenteric reconstruction was the key point to make the pancreaticoduodenectomy a safer operation.

Compared with the previously reported pancreaticojejunostomy procedures, our new technique, the shark mouth pancreaticojejunostomy, has several advantages. First, being composed of several layers of sutures, it reduces the tension of the anastomotic stoma of pancreaticojejunostomy; second, the shark mouth pancreaticojejunostomy creates wide contact surface between the pancreatic remnant and jejunum; third, the serosa of the pancreatic capsule is directly anastomosed to the serosa of the small intestine wall. The serosa-to-serosa fashion corresponds with the demand of alimentary tissue healing process; fourth, a duct-to-mucosa anastomosis can be technically difficult when dealing with a soft, friable, and fatty pancreas with a thinner duct. The "shark mouth pancreaticojejunostomy" is applicable for pancreas featured by these characteristics.

In summary, the current trial is designed to evaluate the superiority of "shark mouth pancreaticojejunostomy". Before it becomes widely accepted, further studies to strengthen its therapeutic value are also warranted.

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Conflicts of interest

None.

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