**A single centre analysis of clinical characteristics and treatment of pancreatic head and periampullary lesions with new modified pancreatoduodenectomy**

**Yingchen Xu 1, Dongxin Zhang 1, Guangming Li 2, Jiajun Ji 1, Lijun Zhang 1**

1. Department of Surgery of Hepato-biliary and pancreas, Beijing Tong Ren Hospital, Capital Medical University, Beijing,100730, china

2. Department of Surgery of Hepato-biliary and pancreas, Beijing YouAn Hospital, Capital Medical University, Beijing,100069, china

**Correspondence to:** Prof. Lijun Zhang**,** Department of Surgery of Hepato-biliary and pancreas, Beijing Tong Ren Hospital, Capital Medical University, 1# Dongjiaominxiang Street, Beijing, 100730, China.

E-mail: zhlj1968@126.com

**Abstract**

**Background:** Pancreatoduodenectomy (PD) remains the only chance of improving long-term survival for carcinoma originated from pancreatic head and periampullary region. However, severe postoperative complications are still the main risk factors for mortality.

**Methods:** This report reviewed the record of our institutional experience with PD which we designed as a combination of standard Whipple with modified CHILD procedure to rebuild the alimentary tract continuity. Patients with tumor original from head of pancreas and periampullary lesions were operated with the designed procedure at our department from Jan. 2013 to Dec. 2021. Medical data including demographics, clinical manifestations, laboratory results, surgery notes, postoperative hospital stay, complications, and pathological reports were reviewed.

**Results:** Altogether 70 patients were operated. The mean operation time was 4.5 hours, 100% survived at least 30 days after surgery, and the complications were 22.9 % after resection. The surgical complications and survival for patients greater than 70 year of age did not differ from that of younger patients. Hospital stay time and perioperative complication rate are much lower than other published data.

**Conclusions:** Our data indicated that our designed standard Whipple with modified CHILD method could be advantageous in restoration of continuity, low perioperative morbidity and mortality. Our new method should be the surgical procedure of choice for pancreatic head and periampullary tumors.

**Keywords:** Pancreatoduodenectomy, Whipple procedure, pancreatic cancer

**INTRODUCTION**

Although the diagnosis of pancreatic and periampullary tumors has been greatly improved duo to the development of advanced imaging technique, less than 40% of malignancies received effective treatment [1-3]. Advanced stage at diagnosis and postoperative complications are the reasons for poor prognosis. No more than 5% of all patients with pancreatic cancer survived for 5 years, the lowest long-term survival rate of any cancer [4]. A potentially curative resection for localized disease can be the only chance of long-term survival.

Pancreatoduodenectomy (PD, also as Whipple procedure) has been described in literature dating back to as early as the 1890s[5-7]. It became a more frequently performed procedure since 1980s with the advances in surgical technique and postoperative care, which allowed the procedure to be done with acceptable low morbidity and mortality. Currently, PD and pylorus-persevering pancreatoduodenectomy (PPPD) were the most common procedures for neoplasm originated from pancreatic head and periampullary/lower end of common bile duct. However, because of the complexity of surgical procedure, more excessive postoperative complications exists those results in higher morbidity and mortality.

Here we report a modified PD procedure employed in our hospital for pancreatic and periampullary tumor treatment that demonstrated convincing advantages over traditional PD in mortality and morbidity. In the new procedure, a distal jejunum loop was used to anastomose remnant pancreas and common hepatic bile duct, and gastrojejunostomy was finished with proximate jejunum arm, which was significant different from traditional CHILD methods. Our retrospective data analysis proved that our new modified PD can significantly decrease the perioperative morbidity and mortality compared with previously reported data.

**METHODS**

***Patients***

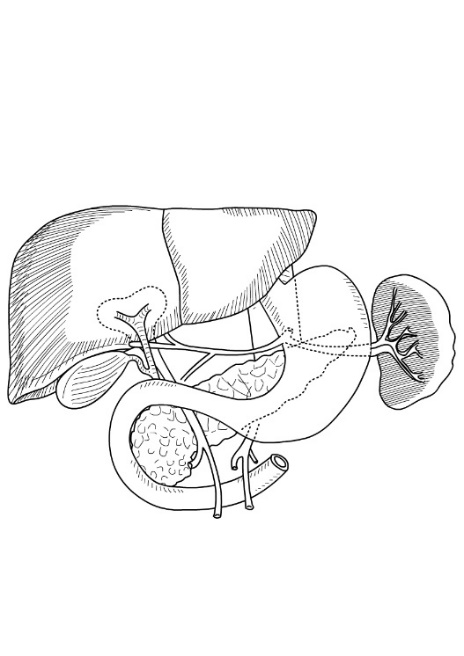
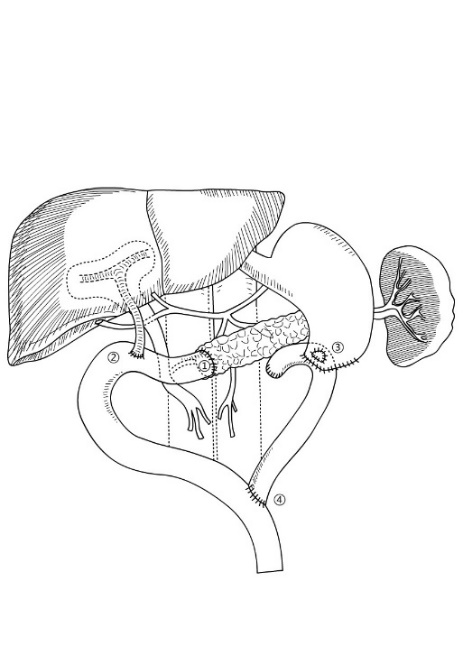
This retrospective study was approved by the Institutional Review Board of Beijing Tongren Hospital. Medical records of 70 patients under went modified PD in our hospital from Jan. 2013 to Dec. 2021 was reviewed. All preoperative diagnoses were neoplasms originated from either pancreas or periampulla region. Preoperative CT scans were used to characterize lesions for size and location, as well as to assess the possibility of resection (TNM staging before surgery). Patients are deemed un-resectable if there is involvement of the celiac axis or superior mesenteric artery (stage IIIB) or if metastatic disease is present (stage IV).

***Data Collection***

Data collected included: demographics, clinical manifestations, laboratory results, surgery notes, postoperative hospital stay, complications, and pathological reports.

***Surgery Procedure***

The surgery procedure consists of standard PD with a modified CHILD procedure for reconstitution. The first phase of surgery included excision and lymph nodes removal, and normal related structures sites as illustrated in **Figure 1a**. The procedure consisted of complete resection of the pancreatic head, i.e. transection of the pancreas above the portal vein/superior mesenteric vein, as well as duodenum, distal part of the stomach, common bile duct, and gallbladder. The ligament of Treitz was divided and the first part of the jejunum was also resected. Dissection and removal of the lymph-node stations included the anterior and posterior pancreatoduodenal lymph nodes, pyloric and biliary duct lymph nodes, superior and inferior pancreatic head and right pancreatic body lymph nodes. In addition, extended lymphadenectomy included the removal of lymph nodes along the aorta from the hepatic hilum to the inferior mesenteric artery and lateral to right renal hilum, with circumferential clearance to the origin of the celiac trunk.

（a）  （b）

**Figure 1.** Schematic image of Modified Whipple for pancreatic and periampullary neoplasm (n = 70). (a) The normal situs before surgery. (b) The standard Whipple and lymph nodes be cleared with the following anastomoses: ① pancreatojejunostomy, ② choledochojejunostomy, ③ gastrojejunostomy, ④ jejunojejunostomy.

The second phase of surgery was reconstitution process with modified the CHILD procedure (as illustrated in **Figure 1b**). First, the jejunum was transected at the line near the proximate residual end of jejunum, with a distance of 40-50 cm. Second, the distal end of jejunum was pulled through the transverse mesocolon, and pancreatic anastomosis (pancreatojejunostomy) was performed as following: the pancreatic stump was anastomosed with the jejunum end-end as a two-layer single-stitch pancreaticojejunostomy (5/0 PDS outer suture rows: seromuscular on to the pancreatic capsule/parenchyma; inner suture rows: mucosa to duct mucosa of the pancreatic duct) with a fitful drainage tube be fixed in pancreatic duct. Thirdly, choledochojejunostomy was performed by anastomosing the orifice of the common hepatic duct with the arm of jejunum in which pancreatojejunostomy was done with end-side method, with the distance between those anastomoses being 10-15 cm. Proximate jejunum loop (kept in its original position) was then anastomosed to gastric posterior wall in a side-side method to finish the gastrojejunostomy. Lastly, jejunojejunostomy was performed, in which the distal part of jejunum where pancreatojejunostomy and choledochojejunostomy had been completed was anastomosed to proximate part of jejunum where gastrojejunostomy was performed in an end-side method. The distance between choledochojejunostomy and jejunojejunostomy was 40-50 cm.

***Statistical Analysis***

Results were presented as mean ±SD and range where applicable. Comparison between groups was made in percentages and numbers or using independent t-test or chi-square test depending on the variables and distribution of data. These tests were 2-sided and a P value less than 0.05 considered statistically significant.

**RESULTS**

Between January 2013 and December 2021, there were 70 patients underwent modified pancreatoduodenectomy in our hospital. The average age of the patients was 58.6 years (range: 42 - 83 years). There was no significant gender differences within this cohort of 37 (52.8%) males. Twenty-eight (40%) patients were diagnosed with pancreatic carcinoma, 37 (52.8%) had periampullary carcinoma and 3 (4.3%) had pancreatic endocrine neoplasm (PEN). The remaining 2 (2.9%) patients were pathologically diagnosed as chronic massive pancreatitis in the pancreatic heads.

Patients’ characteristics were shown in **Table 1**. Thirty one (44.3%) tumors were located in the pancreatic head and uncinate process, and 37 patients (52.9%) were in the ampulla of duodenum and the lower end of common bile duct. Twenty-six patient of 65 malignant tumors had positive lymph nodes (40%). One pancreatic cancer and 1 PEN showed multi-nodes involvement in different pancreas section which were treated with total pancreatectomy. Two cases were diagnosed post-surgically as chronic pancreatitis (CP) through pathological analysis (inflamed mass in pancreatic head and unicinate process).

Table 1. Neoplastic location of 70 patients.

|  |  |
| --- | --- |
| Tumor location | Total  (n) |
| Head | 23 |
| Head+uncinate | 8 |
| Uncinate+neck+tail | 2 |
| Lower end of common bile duct | 31 |
| Ampulla of Vater or duodenum | 6 |
| TOTAL (n) | 70 |

PEN: Pancreatic Endocrine Neoplasm CP: Chronic Pancreatitis

R1 resection: positive resection margin LN (+): positive lymph node

Eight (11.4%) cases were Stage I neoplasm, 42 (60%) were stage II (IIA of pancreatic cancer), and 15 (21.4 %) were stage III (IIB of pancreatic cancer) per WHO (2010) classification [8]. All three PEN were nonfunctioning. When the alternative Ki-67 index cut-off value of 5% and 20% was applied [9,10], the number of grade G1 and G2 tumors was 1 and 2 of three PEN patients, respectively. The mean tumor size was 3.5 cm (range: 0.5–8.0 cm).

Abdominal pain/dullness was the most common symptom with incidence of 66 in 70 patients (94.3%), and jaundice was found in 58 (82.9%) cases. There were 6 patients manifested an abdominal mass by physical examination, and 5 showed interrupt vomiting suggesting of obstructive upper alimentary tract. Four (5.7%) cases were diagnosed incidentally from routine physical examination with no symptoms attributable to ultrasound and abdominal CT scan. The patient characteristics and pathological reports are listed in [**Table 2**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4475697/table/tab4/).

[Table 2](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4475697/table/tab4/). Presenting complaints, pathological report and the types of surgeries performed of 70 cases.

|  |  |  |  |
| --- | --- | --- | --- |
| **Post-operative manifestation** | **Pathology** | **Modified Whipple** | **%** |
| Abdominal pain/dullness | Duct adenocarcinoma (16)  Carcinoma (48)  CP (2)  PEN (1) | 67 | 95.7 |
| Obstructive jaundice | Duct adenocarcinoma (42)  Carcinoma (9)  Duodenal cancer (7) | 58 | 82.9 |
| Abdominal mass | Carcinoma(3)  CP (2)  PEN (1) | 6 | 8.6 |
| Gastric out obstruction | Carcinoma (1)  CP (2)  PEN (2) | 5 | 7.1 |
| No symptom | Duct adenocarcinoma (3)  Solid pseudopapillary tumor (1) | 4 | 5.7 |

Modified Whipple: Standard Whipple with modified CHILD procedure;

TP: Total pancreatectomy, CP: Chronic pancreatitis, PEN: Pancreatic endocrine neoplasm.

To investigate the safety of the modified PD procedure, patients were divided into two groups based on their tumor locations, and their clinical characteristics and postoperative data were compared in [**Table 3**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4475697/table/tab4/). The results showed no significant difference in all items that were compared.

[Tabel](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4475697/table/tab5/) 3. Comparisons of demographics, tumor size, operative time, loss of blood, postoperative complications, and in- hospital stay of our 70 patient.

|  |  |  |  |
| --- | --- | --- | --- |
| Characteristics | Pancreatic head cancer | Periampullary cancer | P value |
| Age (mean, years) | 56.4 | 61.5 | >0.05 |
| Sex (n) | | | |
| Males | 16 | 21 | >0.05 |
| Females | 12 | 21 | >0.05 |
| Tumor staging (n) | | | |
| Ⅰ | 3 | 5 | >0.05 |
| II(IIA of PC) | 19 | 22 | >0.05 |
| III(IIB of PC) | 6 | 10 | >0.05 |
| Operative time (mean, hours) | 4.6 | 3.5 | >0.05 |
| Loss of blood in operation (mean, ml) | 286.5 | 249.8 | >0.05 |
| Mean hospital stay (Day) | 26.2 | 25.5 | >0.05 |
| Postoperative complications (n, %) | | | |
| Pancreatic fistula | 2, 7.1% | 2, 4.8% | >0.05 |
| Bile leakage | 1, 3.6% | 2, 4.8% | >0.05 |
| Postoperative fever | 3, 10.7% | 4, 9.5% | >0.05 |
| Abdominal cavity abscesses | 1, 3.6% | 2, 4.8% | >0.05 |
| Wound infection | 1, 3.6% | 0 | <0.05 |
| Diabetes | 1, 3.6% | 1, 2.4% | >0.05 |
| Alimentary tract bleeding | 1, 3.6% | 1, 2.4% | >0.05 |
| Delayed gastric empting | 0 | 1, 2.4% | <0.05 |
| Total (n, %) | 6, 21.4% | 10, 23.8% | >0.05 |

*﹡*PC: pancreatic adenocarcinoma

The mean duration of in-hospital stay was 25.8 days (range: 18～50 days). Postoperative complications occurred in 16 patients (22.8%). Seven (10 %) patients developed postoperative fever, 4 (5.7%) had pancreatic fistula, and 3 (4.3%) cases had bile leakage, all of whom responded to conservative treatment. One (1.5%) patient had delayed gastric emptying (associated with pancreatic fistula and bile leakage), 1 (1.5%) had wound infection, 2 patients who underwent a total pancreatectomy developed type 2 diabetes, and 3 (4.3%) patients had abdominal abscess which was drained percutaneously. One died of fungal sepsis on the day of 31 after surgery.

We compared the clinical outcome between different age groups of <70 years old (n=49, 70%) and ≥70 years old (n=21, 30%). The postoperative complications were listed in **Table 4**. The results showed that there was no significant difference in two groups in all the items of postsurgical complications.

[Tab](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4475697/table/tab5/)le 4. Comparisons of characteristics in two different age groups of patients.

|  |  |  |  |
| --- | --- | --- | --- |
| Characteristics | >70 years old | ≤70 years old | P value |
| Mean age (years, n) | 73.4, 21 | 57.5, 49 | <0.05 |
| Sex (n) | | | |
| Males | 12 | 25 | >0.05 |
| Females | 9 | 24 | >0.05 |
| Tumors staging (n) | | | |
| Ⅰ | 2 | 6 | >0.05 |
| II(IIA for PC) | 13 | 29 | >0.05 |
| III(IIB for PC) | 4 | 11 | >0.05 |
| Mean Operative time (hours) | 4.4 | 3.8 | >0.05 |
| Loss of blood in operation (mean, ml) | 276.5 | 238.1 | >0.05 |
| Period of in hospital stay (mean, days) | 29.2 | 24.5 | >0.05 |
| Postoperative complications (n, %) | | | |
| Pancreatic fistula | 3, 14.3% | 1, 2.0% | >0.05 |
| Bile leakage | 1, 4.8% | 2, 4.1% | >0.05 |
| Postoperative fever | 2, 9.5% | 5, 10.2% | >0.05 |
| Abdominal cavity  abscesses | 1, 4.8% | 2, 4.1% | >0.05 |
| Wound infection | 1, 4.8% | 0 | <0.05 |
| Diabetes | 1, 4.8% | 1, 2.0% | >0.05 |
| Alimentary tract bleeding | 1, 4.8% | 1, 2.0% | >0.05 |
| Delayed gastric empting | 1, 4.8% | 0 | <0.05 |
| Total (n, %) | 9, 42.9% | 7, 14.3% | <0.05 |

**DISCUSSION**

The major objective of surgery for pancreatic and periampullary carcinoma has been focused on achieving acceptable low perioperative morbidity and mortality. Whipple procedure was adapted by oncologist worldwide, yet this primary goal was not met. We created a combination of PD with modified CHILD procedure that retained the advantages of Whipple procedure and complement its weaknesses, and applied this procedure on 70 patients between 2013 and 2021. We found this method was as effective and safe in patients with pancreatic carcinoma as in periampullary neoplasm (malignant and benign lesions) group. Also similar safety and efficacy of this method was found despite of age difference.

Prior to 1970, surgical complications of Whipper procedure including intra-abdominal abscess, pancreatic fistula, bile leak, delayed gastric emptying, and severe diarrhea were the major reason for higher than 25% postoperative mortality [6,11]. Other modified procedures have been published, such as pylorus-preserving Whipple and standard Whipple with Roux-en-Y reconstruction for the continuity of alimentary tract, yet these efforts has generated limited clinical progresses [12].

Factors being associated with postoperative prognosis include surgical times, intraoperative blood loss, surgeon experience and skill, and operative volume in centers with a particular interest in the care of patients with pancreatic cancer[13]. In this retrospective study, we found that the 30-day postoperative mortality was 0%, and 6-months postoperative mortality was 1.4% (1 of 70 cases), a dramatic improvement from the rates observed prior to the 1980s.

We performed an online search for all publications for post-operational prognosis since 2000, and found our clinical outcome superior over the published data with regard to operation time and postoperative morbidity and mortality rates [14-18]. Classical Whipple procedure required a prolonged operation time, and was associated with a significant higher surgical complications such as pancreatic fistula and bile leakage, resulted in a reduced quality of life [19]. Delayed gastric emptying had been reported more frequently in patients underwent pylorus-preserving Whipple procedure. No significant differences were found between our study and the others with respect to intra-operative blood loss, transfusion requirements, location of the tumor, mean tumor size, positive lymph-node status, or positive margin status on final permanent sections. However, the mean operative time in our study was 4.2 hours, which was much less than those in earlier publications. We had an overall post-operational complication rate of 22.9%, much lower than the published data of 29%, which subsequently resulted in shorter mean hospital stay period [16]. This may be due to preservation of the proximate jejunum in its original place instead of pancreatojejunostomy and choledochojejunostomy with flexible distal jejunum.

Study found that the risk of perioperative mortality in hospitals with fewer than 5 pancreatic resections performed annually was nearly 20 times that in hospitals where more than 20 pancreatectomies done. Settings like pancreatic centers with high caseload, experienced surgeon, and standardized perioperative management could also be important factors for improved outcome and formation of a proper pancreaticointestinal anastomosis. Our result demonstrated a safe outcome with superior perioperative prognosis over previously published results.

**CONCLUSIONS**

In reviewing of our 3-year experience of resection of pancreatic and periampullary neoplasm with modified Whipple procedure, we were convinced that our procedure offered a chance for patients with less postoperative complications and possibly better quality life of long-term survival [20]. Further randomized controlled studies with larger patient groups would be necessary to demonstrate the definite advantages and possible side effects.

**Strengths of the Study**

1. Published data on modified pancreatoduodenectomy is rare, and this study provides a most recent achievement in this regard.
2. This study provides a comprehensive analysis from a single institution of a designed surgical procedure for one of the most difficult neoplasms.
3. This study provides a paradigm for future analysis over larger data and multicenter research.

**Weaknesses of the Study**

1. The study is a retrospective cohort analysis of a modified procedure which may not very well designed for a faultless comparison among groups. The size of clinical sample is relatively small.
2. Although about 35% of patients with pancreatic carcinoma which accepted our surgical treatment died in 2 years, the period of follow-up was short, so the long time following up data should be assessed in coming future.

**DECLARATIONS**

**Authors’ contributions**

Made substantial contributions to the conception and design of the study and performed data analysis and interpretation: Yingchen Xu, Dongxin Zhang

Performed data acquisition, as well as provided administrative, technical, and material support: Guangming Li, Jiajun Ji, Lijun Zhang

**Availability of data and materials**

Not applicable.

**Financial support and sponsorship**

This work was supported by the Open Research Fund from Beijing Advanced Innovation Center for Big Data-Based Precision Medicine, Beijing Tongren Hospital, Beihang University & Capital Medical University, Grant No.BHTR-KFJJ-202011

**Conflict of Interests**

The authors declare that there is no conflict of interest regarding the publication of this paper.

**Ethical approval and consent to participate**

Not applicable.

**Consent for publication**

Not applicable.

**References**

1. Parul J Shukla, George Barreto, Shailesh V Shrikhande, et al.The evolution of pancreatoduodenectomy. Hepatogastroenterology. Jul-Aug 2011;58(109):1409-12.

2. Jonyvan Hilst,Thijsde Rooij, KoopBosscha, et al.Laparoscopic versus open pancreatoduodenectomy for pancreatic or periampullary tumours (LEOPARD-2): a multicentre, patient-blinded, randomised controlled phase 2/3 trial. Lancet Gastroenterol Hepatol. 2019 Mar;4(3):199-207.

3. Jemal A, Siegal R, Ward E, et al. Cancer statistics, 2008. CA Cancer J Clin. 2008: 58(2):71-96.

4. Niraj Jani, A. James Moser, Asif Khalid, et al. Pancreatic Endocrine tumors. Gastroenterology Clinics of North America.2007;36(2):431–439.

5. Howard J. History of pancreatic head resection–the evaluation of surgical technique. Am J Surg 2007; 194:S6–S10.

6. Bilimoria KY, Bentrem DJ, Ko CY, et al. National failure to operate on early stage pancreatic cancer. Ann Surg. 2007; 246(2): 173-180.

7. Crist DW, Cameron JL. Current status of pancreaticoduodenectomy for periampullary carcinoma. Hepatogastroenterology. 1989; 36(6):478-485.

8. Mahul B Amin, Frederick L Greene, Stephen B Edge, et al. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin.2017 Mar;67(2):93-99.

9. G. Rindi, M. Falconi, C. Klersy, et al. TNM staging of neoplasms of the endocrine pancreas: results from a large international cohort study. Journal of the National Cancer Institute. 2012; 104(10):764–777.

10. Rindi, Guido & R, Arnold, et al. Nomenclature and classification of neuroendocrine neoplasms of the digestive system. Nomenclature,2010. 13–14p.

11. Crist DW, Sitzmann JV, Cameron JL, et al. Improved hospital morbidity, mortality and survival after the Whipple procedure. Ann Surg. 1987;206(3):358-365.

12. Knut Jørgen Labori, Tore Tholfsen, Sheraz Yaqub, et al. Gastro- or Duodenojejunostomy Leaks After Pancreatoduodenectomy: Single Center Experience and Narrative Literature Review. J Gastrointest Surg. 2021 Dec;25(12):3130-3136.

13. Monish Karunakaran, Savio G Barreto, et al. ERAS® following pancreatoduodenectomy - more than just reducing hospital stay. HPB (Oxford). 2021 Feb;23(2):321.

14. Winter JM, Cameron JL, Campbell KA, et al. 1423 Pancreaticoduodenectomies for pancreatic cancer: a single-institution experience. J Gastrointest Surg. 2006;10(9):1199-1210; discussion 1210-1211.

15.  Castillo CF, Morales-Oyarvide V, McGrath D, et al. Evolution of the Whipple procedure at the Massachusetts General Hospital. Surgery 2012; 152:S56–S63.

16. Kimura W, Miyata H, Gotoh M, et al. A pancreaticoduodenectomy risk model derived from 8575 cases from a national single-race population (Japanese) using a web-based data entry system: the 30-day and in-hospital mortality rates for pancreaticoduodenectomy. Ann Surg 2014; 259:773–780.

17. Kawai M, Kondo S, Yamaue H, et al. Predictive risk factors for clinically relevant pancreatic fistula analyzed in 1,239 patients with pancreaticoduodenectomy: multicenter data collection as a project study of pancreatic surgery by the Japanese Society of Hepato-Biliary-Pancreatic Surgery. J Hepatobiliary Pancreat Sci 2011; 18:601–608.

18. Leichtle SW, Kaoutzanis C, Mouawad NJ, et al. Classic Whipple versus pylorus-preserving pancreaticoduodenectomy in the ACS NSQIP. J Surg Res 2013; 183:170–176.

19. D S Gorin, A G Kriger, G V Galkin, et al. Predicting of pancreatic fistula after pancreatoduodenectomy. Khirurgiia (Mosk). 2020;(7):61-67.

20. Afaneh C, Gerszberg D, Slattery E, et al. Pancreatic cancer surgery and nutrition management: a review of the current literature. HepatoBiliary Surg Nutr 2015;4(1):59-71.