Research Article

Surgical outcomes and postoperative complications in patients undergoing Whipple's procedure: A tertiary academic center experience

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Abstract

Introduction: Whipple's procedure is the standard treatment for periampullary pathologies. Whipple's procedure is associated with high morbidity. Therefore, this study aims to report the surgical complications and identify the prognostic factors toward surgical complications and readmission in patients undergoing Whipple's procedure.

Methods: This is a retrospective cohort study of all patients who underwent Whipple's procedure from November 2015 to August 2022 at King Saud University Medical City (KSUMC).

Results: 72 patients underwent Whipple's procedure. 58 (80.6%) and 14 (19.4%) patients underwent Classic Whipple and pylorus-preserving Whipple, respectively. Postoperative complications were seen in 39 (54.2%) patients. Clavien-Dindo classification of postoperative complications grade ≥III was seen in 22 (30.6%) patients. Only ICU/HDU admission correlated significantly *(P<0.001)* toward postoperative complication and was insignificant in the regression test.

Prognostic variables toward readmission correlated significantly with the female gender *(P=0.017),* having asthma *(P<0.001),* taking Anticoagulant (Enoxaparin) *(P=0.002),* undergoing ERCP with stent placement *(P=0.044),* consultant experience <5 years *(P=0.003),* and postoperative complication *(P=0.007).* The multivariate analysis led only to statistical significance in the female gender *(P=0.048)* and postoperative complication *(P=0.035).*

Conclusion: This study's morbidity and mortality results are consistent with those reported internationally. The small volume of cases may have a major impact on the center experience and overall outcome. It is imperative that we establish a referral center that is equipped to provide prompt high-quality intervention in order to improve outcomes further.

Introduction

Allen Whipple reported the first description of Whipple's procedure (pancreaticoduodenectomy) in 1935 [1]. Since then, Whipple's procedure has been practiced by many surgeons and has undergone several technical improvements aiming to decrease its high operative morbidity and mortality [2]. Nonetheless, Whipple's procedure importance lies in its role as the standard treatment for periampullary pathologies [3,4].

Although mortality rates have been reduced to less than 5% [5], Whipple's procedure morbidity remained high, reaching 40-50% [4]. Postoperative complications embodied the core of its morbidity, with pancreatic anastomoses leakage as the main complication [6]. Several complications of Whipple's procedure have been described in the literature: postoperative pancreatic fistula, Delayed Gastric Emptying (DGE), biliary leak, wound infection, postoperative pancreatic hemorrhage, need for reoperations, and prolonged hospital stay [7]. Additionally, Whipple's procedure involves an extensive pancreatic parenchymal tissue resection of nearly 30-50%. Therefore, patients are at high risk of developing pancreatic exocrine insufficiency and new-onset Diabetes Mellitus (DM) [8].

There are two types of Whipple's procedure: either a classic Whipple in which part of the pancreas, the gallbladder, the duodenum, the pylorus (outlet of the stomach), and the distal (lower) part of the stomach are resected, and the so-called pylorus-preserving pancreaticoduodenectomy, or pylorus-preserving Whipple operation, in which the stomach and the pylorus are not removed [9]. A recent systematic review compared the effectiveness of classic Whipple's procedure and pylorus-preserving Whipple. It concluded that current evidence suggests no relevant differences in mortality, morbidity, and survival between the two operations. However, higher-quality RCTs are needed due to the study's evident clinical and methodological heterogeneity [9].

This study aims to report the surgical complications and identify the prognostic factors toward surgical complications and readmission in patients undergoing Whipple's procedure in a single tertiary academic center.

Materials and methods

Following the approval of the Institutional Review Board (IRB) at King Saud University, we retrospectively collected and reviewed the electronic medical records of all patients who underwent the Whipple procedure from November 2015 to August 2022 at King Saud University Medical City (KSUMC), an academic medical institution in Riyadh, Saudi Arabia. We included only patients who completed the procedure. Patients with aborted Whipple procedures were excluded from the study.

Whipple's procedure was performed and followed by specialized and well-qualified hepatobiliary surgeons in our center. Data collected included baseline demographics, perioperative and pathological variables, surgical intervention parameters and outcomes, and postoperative complications. Prognostic variables toward surgical complications and readmission were collected and analyzed.

Statistical analysis

Data were analyzed using Statistical Package for Social Studies (SPSS 22; IBM Corp., New York, NY, USA). Continuous variables were expressed as mean ± standard deviation. Categorical variables were expressed as percentages. The t-test was used for continuous variables with normal distribution, and the Mann-Whitney test was used for continuous variables without normal distribution. The chi-square test was used for categorical variables. Univariate and Multivariate regression analyses were used. A p-value <0.05 was considered statistically significant.

Results

Between November 2015 to August 2022, 72 patients underwent Whipple's procedure. Table 1 shows the baseline demographics of our patients. The mean age was 55.88 (SD 15.23) years. Forty-nine (68.1%) patients presented with abdominal pain, followed by 46 (63.9%) with jaundice. Thirty-three patients (45.8%) underwent preoperative ERCP with stent placement; only one had a failed ERCP. Adenocarcinoma was the most common etiology in 51 (70.8%) patients.

Surgical intervention parameters and outcomes are represented in Table 2. Fifty-eight (80.6%) and 14(19.4%) patients underwent Classic Whipple and pylorus-preserving Whipple, respectively. Of these, 63(87.5%) patients had pancreatojejunostomy, and 9(12.5%) had pancreaticogastrostomy. The mean total hospital stay and postoperative stay in days were 26.13 (SD23.84) and 20.21 (SD21.36), respectively. Additionally, 11 (15.3%) patients had readmission, and 10 (13.9%) patients had a reoperation. Thirty days and 90 days mortality were 4(5.6%) and 6(8.3%), respectively.

Postoperative complications were seen in 39(54.2%) patients. The most common complication was wound infection in 20(27.8%) patients, followed by abdominal collection in 16 (22.2%). Clavien-Dindo classification of postoperative complications grade ≥III was seen in 22(30.6%) patients. More details are in Table 3 and Figure 1.

Diabetes mellitus was reported in 34(47.6%) patients in our study. Figure 2 illustrates the diabetes status postoperatively, showing that 19(55.86%) patients had no change, and only one had new-onset diabetes.

Prognostic variables toward surgical complications are seen in Table 4. Only ICU/HDU admission correlated significantly (P<0.001) toward postoperative complication and was insignificant in the regression test.

Prognostic variables toward readmission correlated significantly with the female gender (P=0.017), having asthma (P<0.001), taking Anticoagulant (Enoxaparin) (P=0.002), undergoing ERCP with stent placement (P=0.044), consultant experience <5 years (P=0.003), and postoperative complication (P=0.007). More details are in Table 5.

Table 6 shows univariate and multivariate analysis of prognostic factors toward readmission, which led only to statistical significance in the multivariate analysis of female gender (P=0.048) and postoperative complication (P=0.035).

Table 1: Baseline demographics (N=72).

Variables		Number	%
Age*		55.88	15.23
Gender	Male	43	59.7
	Female	29	40.3
BMI*		27.18	6.38
Smoking		12	16.7
ASA Score	I	3	4.2
	II	44	61.1
	III	21	29.2
	IV	3	4.2
	V	1	1.4
Blood thinner	Aspirin	3	4.2
	Enoxaparin	4	5.6
Presenting Symptoms	Jaundice	46	63.9
	Abdominal pain	49	68.1
	Gastric outlet obstruction	1	1.4
	Weight loss	32	44.4
	Loss of appetite	27	37.5
Albumin (gm/L)*		28.60	5.99
Hemoglobin (g/L)*		118.89	15.43
Total Bilirubin (mcmol/L)*		61.70	88.70
Pre-op ERCP/ PTC	ERCP with Stent	33	45.8
	PTC	1	1.4
	Failed ERCP	1	1.4
	ERCP Diagnostic	2	2.8
Etiology	Adenocarcinoma	51	70.8
	Pancreatic cyst	6	8.3
	Chronic pancreatitis	3	4.14
	Pseudopapillary tumor	3	4.14
	Neuroendocrine	5	6.9
	Autoimmune pancreatitis	1	1.4
	Crohn's disease	1	1.4
	GIST	1	1.4
	Tuberculosis infection	1	1.4

*Mean, SD

Table 2: Surgical intervention parameters and outcome (N=72).

Variables		Number	%
Type of surgery	Classic Whipple	58	80.6
	Pylorus preserving	14	19.4
Pancreatic anastomosis	Pancreatojejunostomy	63	87.5
	Pancreaticogastrostomy	9	12.5
PV reconstruction		5	6.9
Open abdomen		2	2.8
Operative time (Minutes)*		463.03	127.33
pRBC transfusion		20	27.8
FFP transfusion		7	9.8
Platelet transfusion		3	4.2
Consultant experience ≥ 5 years		57	79.2
Total Hospital stay (days)*		26.13	23.84
Post operative stay (days)*		20.21	21.36
ICU/ HDU admission (days)*		3.39	6.03
ICU/HDU admission		68	94.4
Readmission		11	15.3
Re-operation		10	13.9
30 days mortality		4	5.6
90 days mortality		6	8.3

*Mean, SD

Table 3: Postoperative complication (N=72).

	Number	%
Abdominal Collection	16	22.2
Wound infection	20	27.8
Respiratory disease	6	8.3
VTE	2	2.8
Bleeding	8	11.1
Pancreatic anastomotic leak	9	12.5
Bile leak	2	2.8
Bowel leak	1	1.4
Pancreatic fistula	2	2.8
Clavien-Dindo grade ≥ III	22	30.6

Table 4: Prognostic variables toward surgical complication.

Variables		Number	%	P value
Gender	Male	24	61.54	0.733
	Female	15	38.46	
Age*		57.01	13.98	0.459
ASA Score	I	1	2.56	0.727
	II	25	64.10	
	III	11	28.21	
	IV	2	5.13	
DM		17	43.59	0.678
HTN		22	56.41	0.151

Table 5: Prognostic variables toward readmission.

Variables		Number	%	P value
Gender	Male	3	27.27	**0.017****
	Female	8	72.73	
Age*		56.91	13.44	0.908
ASA Score	I	1	9.09	0.773
	II	6	54.55	
	III	3	27.27	
	IV	1	9.09	
	V	0	0.00	
DM		4	36.36	0.473
HTN		5	45.45	0.483

Heart disease	IHD	2	5.13	0.300
	DLP	8	20.51	
	Cardiomyopathy	1	2.56	
Asthma		4	10.26	0.080
Renal disease		1	2.56	0.542
Blood thinner	Aspirin	2	5.13	0.613
	Enoxaparin	3	7.69	
CEA*		4.08	4.94	0.841
CA 19-9*		2066.86	5620.81	0.194
Albumin (gm/L)*		29.84	5.38	0.055
Hemoglobin (g/L)*		120.37	14.94	0.382
Total Bilirubin (mcmol/L)*		51.50	73.62	0.208
PV reconstruction		2	5.13	0.510
Pre-op ERCP/PTC	ERCP with Stent	18	46.15	0.430
	PTC	1	2.56	
	Failed ERCP	1	2.56	
	ERCP Diagnostic	2	5.13	
Surgery	Classic Whipple	29	74.36	0.126
	Pylorus preserving	10	25.64	
Abdomen left open		2	5.13	0.290
Pancreatic anastomosis	Pancreatojejunostomy	34	87.18	0.608
	Pancreaticogastrostomy	5	12.82	
Consultant experience ≥5 years		29	74.36	0.275
ICU/HDU admission		35	89.74	<0.001**
*Mean, SD **Significant p-value				

Heart disease	IHD	0	72.73	0.172
	DLP	2	0.00	
	Cardiomyopathy	0	18.18	
Asthma		4	36.36	<0.001**
Renal disease		1	9.09	0.153
Blood thinner	Aspirin	0	0.00	0.002**
	Enoxaparin	3	27.27	
CEA*		2.23	2.72	0.644
CA 19-9*		4175.46	6187.20	0.204
Albumin (gm/L)*		29.53	6.57	0.576
Hemoglobin (g/L)*		120.45	14.21	0.718
Total Bilirubin (mcmol/L)*		88.64	102.57	0.429
ICU/HDU admission (Days)*		3.64	2.25	0.067
PV reconstruction	Yes	2	18.18	0.165
Pre op ERCP PTC	ERCP with Stent	2	18.18	0.044**
	Failed ERCP	0	0.00	
	ERCP Diagnostic	0	0.00	
	PTC	1	9.09	
Surgery	Classic Whipple	8	72.73	0.362
	Pylorus preserving	3	27.27	
Abdomen left open		1	9.09	0.284
Pancreatic anastomosis	Pancreatojejunostomy	11	100.00	0.204
	Pancreaticogastrostomy	0	0.00	
Histology	Malignant	11	100.00	0.093
	Benign	0	0.00	
Consultant experience	≥5 years	5	45.45	0.003**
	<5 years	6	54.55	
Postoperative complication		10	90.91	0.007**
ICU/HDU admission		11	100.00	0.507
*Mean, SD **Significant p-value				

Table 6: Logistic regression analysis of prognostic factors toward readmission.

| Variable	Univariate logistic regression analysis			Multivariate logistic regression analysis		
	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value
Female gender	5.08	(1.22-21.19)	0.026	10.40	(1.02-106.17)	0.048*
Blood thinner (Enoxaparin)	21.38	(1.98-231.20)	0.012	13.71	(0.47-399.38)	0.128
ERCP with Stent	0.22	(0.04-1.11)	0.067	0.96	(0.10-9.38)	0.970
Consultant experience ≥5 years	0.14	(0.04-0.57)	0.006	0.16	(0.02-1.37)	0.095
Postoperative complication	11.03	(1.33-91.58)	0.026	29.36	(1.27-680.00)	0.035*
*Significant p-value						
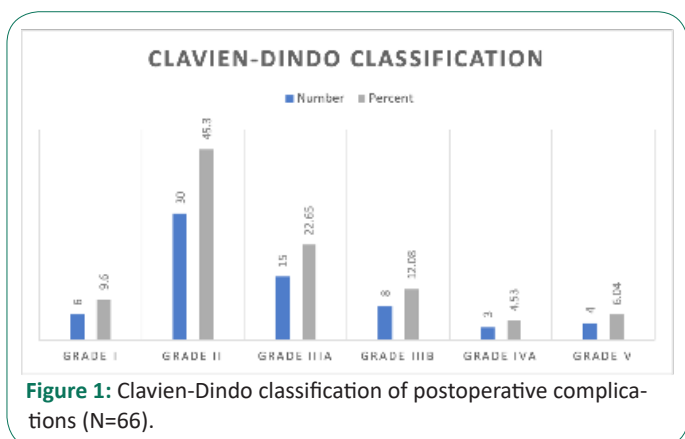
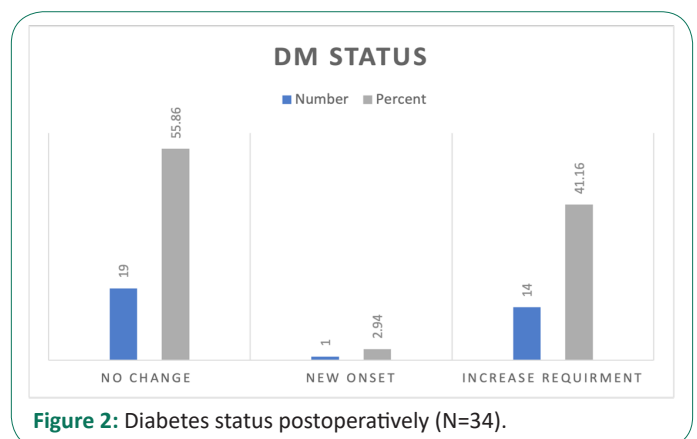**Figure 1:** Clavien-Dindo classification of postoperative complications (N=66).

Figure 2: Diabetes status postoperatively (N=34).

Discussion

While Whipple's procedure is currently associated with low mortality rates in experienced centers, morbidity rates remain high [5,10-12]. No local reports regarding surgical outcomes following Whipple's procedure in Saudi Arabia exist. This study aimed to report the surgical outcomes and prognostic factors in patients who underwent the Whipple procedure.

Postoperative complications were seen in 54.2% of patients, matching previous studies ranging from 38-58% [5,10-12]. Consistently, periampullary adenocarcinoma was the most common indication for Whipple's procedure. The distribution of age, gender, and presenting symptoms was similar to other studies elsewhere [4,7]. In contrast, the operative time, postoperative stay, and total hospital stay were more prolonged than reported in the literature [12,13]. This can be justified by the relatively small volume of procedures per consultant and the advanced stages of the disease with obstructive jaundice and large tumor sizes. Furthermore, 30% of our patients had postoperative complications graded III and above according to the Clavein-Dindo classification which mandates interventional management; further prolonging the postoperative stay and total hospital stay.

Wound infection was the most common postoperative complication (25%) reported by Arjunan et al. Similarly, the most common complication in our study was wound infection, seen in 20(27.8%) of our patients, followed by abdominal collection in 16 patients (22.2%) and pancreatic anastomotic leak in 9 patients (12.5%). On the other hand, Saraee et al. and Lakhey et al. reported delayed gastric emptying and pancreatic fistula as the most common complications [11,14].

New-onset DM post pancreaticoduodenectomy has ranged from 12-24% in the literature [8,15,16]. In our study, 19 (55.86%) patients had no change, whereas 14(41.16%) patients had increased requirements, and only one had new-onset DM (2.94%). On the other hand, several studies reported improvement in glucose control post pancreaticoduodenectomy [8,16,17].

Wu et al. has explored the resolution of DM post pancreaticoduodenectomy in patients with and without Pancreatic Ductal Cell Adenocarcinoma (PDCA) and reported similar rates of resolution between the two groups, however, differences were observed between patients with new-onset DM (41% in PDCA vs 63% in non-PDCA) and long-standing DM (9.1% in PDCA vs 9.8% in non-PDCA) [17]. Similarly, Saluja et al. found that diabetes did improve in 1 of 3 patients who had recent onset diabetes [8].

Prognostic variables toward surgical complications correlated significantly with ICU/HDU admission *(P<0.001)*. However, there was no statistical significance between a classic Whipple's procedure and pylorus-preserving Whipple's. This finding is supported by a systematic review by Hüttner et al., which compared the classic Whipple's procedure and the pylorus-preserving Whipple in terms of survival, postoperative mortality, complications, and quality of life and eventually concluded that no relevant difference is evident between the two surgical procedures for the treatment of pancreatic or periampullary cancer. Along similar lines, a recent meta-analysis has investigated the impact of gastric resection and enteric anastomotic configuration on delayed gastric emptying after pancreaticoduodenectomy and concluded that in studies that directly compared classic Whipple, pylorus-resecting, and pylorus-preserving approaches with gastric resection in pancreaticoduodenectomy, no statistically significant differences in the rates of overall DGE were found. However, pylorus-resecting pancreaticoduodenectomy ranked as the best approach for reducing DGE in 71% of comparisons [18].

Pancreatic anastomosis reconstruction, pancreaticogastrostomy versus pancreatojejunostomy, is another area of discussion. Contradictory results are found in the literature; Wellner et al. concluded that pancreaticogastrostomy is superior to pancreatojejunostomy regarding relevant postoperative pancreatic fistula (11.4% versus 22.6%, *P=0.03*) [11,14]. Similarly, Heeger et al. study showed that modified pancreaticogastrostomy seems to be superior to pancreatojejunostomy regarding pancreatic fistula *(P=0.029)*, especially in patients with a soft, non-fibrotic pancreas and/or a small duct *(P=0.023)* [19]. Meanwhile, a 2011 meta-analysis showed that the pancreatic fistula, postoperative complications, biliary fistula, mortality, reoperation, and length of hospital stay were not statistically different between the pancreaticogastrostomy and pancreatojejunostomy groups [20]. Anastomosis configuration was not associated with higher surgical complications in our study. Hence, the debate on the superiority of one over the other will continue. Surgeon experience plays an essential role in the outcome of Whipple's procedure [21].

This study has a few limitations that should be considered. First, it is a retrospective cohort study, where inherent bias may be present. Second, it's a single-center study with a small sample size, which could contribute to the statistical insignificance of different variables. Therefore, multi-center studies with larger sample sizes are warranted to confirm the results.

Conclusion

This study's morbidity and mortality results are consistent with those reported internationally. Increasing the number of cases is needed to refine the surgeons' experience and improve the patient's overall outcome. Hence, it is imperative that we establish a national referral center to concentrate the volume of cases and provide prompt high-quality interventions.

Conflicting interest: The authors have no conflict of interest to disclose.

References

1. Peters JH, Carey LC. Historical review of pancreaticoduodenectomy. Am J Surg. 1991; 161(2): 219-25. doi: 10.1016/0002-9610(91)91134-5

2. Mosca F, Giulianotti PC, Balestracci T, et al. Long-term survival in pancreatic cancer: Pylorus-preserving versus Whipple pancreatoduodenectomy. Surgery. 1997; 122(3): 553-66. doi: 10.1016/s0039-6060(97)90128-8

3. Surgical Treatment: Evidence-Based and Problem-Oriented. In: Holzheimer RG, Mannick JA, eds. Surgical Treatment: Evidence-Based and Problem-Oriented. Zuckschwerdt Copyright © 2001, W. Zuckschwerdt Verlag GmbH. 2001.

4. Reyna-Sepulveda F, Munoz-Maldonado G, Perez-Rodriguez E, Hernandez-Trejo F, Guevara-Charles A, et al. Prognostic factors for survival and surgical complications in Whipple's pancreatoduodenectomy during a 10-year experience. Cir Cir. 2019; 87(2): 205-210. Factores de pronostico de sobrevida y complicaciones quirurgicas en la pancreaticoduodenectomia de Whipple durante 10 anos de experiencia. doi: 10.24875/CIRU.18000526

5. DeOliveira ML, Winter JM, Schafer M, et al. Assessment of complications after pancreatic surgery: A novel grading system applied to 633 patients undergoing pancreaticoduodenectomy. Ann Surg. 2006; 244(6): 937-9. doi: 10.1097/01.sla.0000246856.03918.9a

6. Balzano G, Zerbi A, Capretti G, Rocchetti S, Capitanio V, et al. Effect of hospital volume on outcome of pancreaticoduodenectomy in Italy. Br J Surg. 2008; 95(3): 357-62. doi: 10.1002/bjs.5982

7. Arjunan R, Karthik SDS, Chowdappa R, Althaf S, Srinivas C. Contemporary Surgical, Oncological, and Survival Outcomes of Pancreaticoduodenectomy for Periampullary Tumours: A 5-Year Experience from Tertiary Cancer Center. Indian Journal of Surgical Oncology. 2021; 12(3): 603-610. doi: 10.1007/s13193-021-01385-7

8. Saluja SS, Kiran S, Mishra PK, et al. Long-Term Functional Outcome After Pancreatoduodenectomy for Periampullary Carcinoma With Morphological Correlation. Pancreas. 2019; 48(9): 1182-1187. doi: 10.1097/MPA.0000000000001392

9. Huttner FJ, Fitzmaurice C, Schwarzer G, et al. Pylorus-preserving pancreaticoduodenectomy (pp Whipple) versus pancreaticoduodenectomy (classic Whipple) for surgical treatment of periampullary and pancreatic carcinoma. Cochrane Database Syst Rev. 2016; 2: CD006053. doi: 10.1002/14651858.CD006053.pub6

10. Neupane HC, Tamang TY, Timalsina S, Tamrakar KK, Bhattarai A. Complications among Patients Undergoing Pancreaticoduodenectomy in Tertiary Care Centers of Nepal: A Descriptive Cross-sectional Study. JNMA J Nepal Med Assoc. 2022; 60(245): 77-82. doi: 10.31729/jnma.7050

11. Lakhey PJ, Bhandari RS, Ghimire B, Khakurel M. Perioperative outcomes of pancreaticoduodenectomy: Nepalese experience. World J Surg. 2010; 34(8): 1916-21. doi: 10.1007/s00268-010-0589-y

12. Schmidt CM, Powell ES, Yiannoutsos CT, et al. Pancreaticoduodenectomy: A 20-year experience in 516 patients. Arch Surg. Jul 2004; 139(7): 725-7. doi: 10.1001/archsurg.139.7.718

13. Cameron JL, Riall TS, Coleman J, Belcher KA. One thousand consecutive pancreaticoduodenectomies. Ann Surg. 2006; 244(1): 10-5. doi: 10.1097/01.sla.0000217673.04165.ea

14. Saraee A, Vahedian-Ardakani J, Saraee E, Pakzad R, Wadji MB. Whipple procedure: A review of a 7-year clinical experience in a referral center for hepatobiliary and pancreas diseases. World J Surg Oncol. 2015; 13: 98. doi: 10.1186/s12957-015-0523-8

15. Fang WL, Su CH, Shyr YM, et al. Functional and morphological changes in pancreatic remnant after pancreaticoduodenectomy. Pancreas. 2007; 35(4): 361-5. doi: 10.1097/MPA.0b013e3180d0a8d5

16. Hirata K, Nakata B, Amano R, Yamazoe S, Kimura K, et al. Predictive factors for change of diabetes mellitus status after pancreatectomy in preoperative diabetic and nondiabetic patients. J Gastrointest Surg. 2014; 18(9): 1597-603. doi: 10.1007/s11605-014-2521-5

17. Wu JM, Kuo TC, Yang CY, et al. Resolution of diabetes after pancreaticoduodenectomy in patients with and without pancreatic ductal cell adenocarcinoma. Ann Surg Oncol. 2013; 20(1): 242-9. doi: 10.1245/s10434-012-2577-y

18. Varghese C, Bhat S, Wang TH, O'Grady G, Pandanaboyana S. Impact of gastric resection and enteric anastomotic configuration on delayed gastric emptying after pancreaticoduodenectomy: A network meta-analysis of randomized trials. BJS Open. 2021; 5(3). doi: 10.1093/bjsopen/zrab035

19. Wellner U, Makowiec F, Fischer E, Hopt UT, Keck T. Reduced postoperative pancreatic fistula rate after pancreatogastrostomy versus pancreaticojejunostomy. J Gastrointest Surg. 2009; 13(4): 745-51. doi: 10.1007/s11605-008-0763-9

20. Yang SH, Dou KF, Sharma N, Song WJ. The methods of reconstruction of pancreatic digestive continuity after pancreaticoduodenectomy: a meta-analysis of randomized controlled trials. World J Surg. 2011; 35(10): 2290-7. doi: 10.1007/s00268-011-1159-7

21. Kennedy GT, McMillan MT, Maggino L, Sprys MH, Vollmer CM. Surgical experience and the practice of pancreatoduodenectomy. Surgery. 2017; 162(4): 812-822. doi: 10.1016/j.surg.2017.06.021