https://doi.org/10.55453/rjmm.2024.127.5.6
The article was received on November 27, 2023, and accepted for publishing on February 13, 2024.

ORIGINAL ARTICLE

Pyloric-preserving Pancreaticoduodenectomy with Duct to Mucosa Pancreatico-gastrostomy Reconstruction: Long-term Follow-up in a Tertiary Center

Shahriar Najafizadeh-Sari[1], Jamal A. Moghadam[2], Hamed Gholizadeh[2], Alireza Ranaei-Kenarsari[3], Mohammad Heiat[4], Mehdi Raei[5], Shahram Manoochehry[2]

[1] Baqiyatallah University of Medical Sciences, Tehran, Iran
[2] Department of General Surgery, Trauma Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran
[3] Department of Emergency Medicine, School of Medicine, Shahroud University of Medical Sciences, Shahroud, Iran
[4] Baqiyatallah Research Center for Gastroenterology and Liver Diseases, Baqiyatallah University of Medical Sciences, Tehran, Iran
[5] Health Research Center, Life Style Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran

Correspondence: Shahram Manoochehry, shahram.manoochehry@yahoo.com

Abstract: *Background: Duct to mucosa Pancreatico-gastrostomy (DMPG) is a method for reconstruction of pancreatic mass following pancreaticoduodenectomy (PD). There are still controversies about the benefits of this surgical technique compared to the old ones. Objectives: This study aimed to evaluate the long-term outcomes of DMPG reconstruction following PD operation. Method: Through a prospective observational setting, 164 patients, undergoing PD surgery, with diagnosed pancreatic head or peri-ampullary cancer, were enrolled. A pylorus-preserving PD and DMPG were done for all patients to reconstruct the pancreatic mass. Patients were followed up to a mean of 21.06±14.12 months. Demographic data, risk factors, tumoral staging, and postoperative follow-up data were collected for the analytic study. Results: The mean survival of the patients was 21.06±14.23 months after surgery. DGE (delayed gastric emptying) (34.75%), pancreatic fistula (21.34%), bile duct fistula (7.31%), and hemorrhage (5.5%) were recorded as the most important complication in patients. Some post-operative complications were significantly observed in patients with diabetes mellitus (pancreatic fistula, increased amylase, and DGE), Smokers (bile duct fistula, hemorrhage, and increased Amylase), and the elders (bile duct fistula) (p-value <0.05). Conclusions: Although our results indicate that DMPG reconstruction is a safe technique, our findings did not confirm the priority of this method over the older techniques.*

Keywords: *pancreatic neoplasms, gastrostomy, jejunostomy, pancreaticoduodenectomy*

INTRODUCTION

Pancreaticoduodenectomy (PD) is the main surgical treatment option for ampullary and peri-ampullary cancers, and some modifications have been described for this surgical operation. Therefore, these surgical modifications, complications, and outcomes need to be evaluated.

Despite the surgical techniques and management improvements, there are still many concerns about its high incidence of post-operative complications and morbidity rate (30-50%) [1,2]. Pancreatic fistula is considered the most common postoperative complication followed by bile duct fistula, thromboembolism, intra-abdominal hemorrhage, intra-abdominal abscess, wound infection, and gastro-intestinal bleeding as other important complications [2].

Reconstruction with pancreaticojejunostomy (PJ) is the preferred anastomosis technique following PD surgery. While this method has been commonly used for several decades, its high prevalence of complications (40-50%) prompts surgeons to come up with new approaches [3-5].

Duct to mucosa pancreaticogastrostomy (DMPG) is a method of reconstruction following PD surgery. There are still controversies about its benefits compared to previous ones. Few studies are available evaluating DMPG's outcomes, and complications [6-8]. This study aimed to evaluate the long-

term outcomes of DMPG reconstruction following PD operation.

MATERIALS AND METHODS

Patients

In this prospective observational study, patients with the diagnosis of pancreatic head or peri-ampullary tumors who underwent PD surgery at Baqiyatallah Hospital from January 2007 to February 2016 were enrolled. Informed consent was taken from patients. All operations were performed by the same surgeon. Patients were excluded from the study if failed to follow or their data were incomplete or inaccessible. Altogether 191 patients were included. During the study, 27 patients were excluded, (12, due to changes in their address, and 15, because of incomplete data and/or failure to follow). The study was approved by the ethics committee of Baqiyatallah University of Medical Sciences (national approval number: IR.BMSU.REC.1393.87).

Surgical Procedure

In all operations, a right subcostal incision was made and a pylorus-preserving PD and DMPG (using 4-0 polydioxanone sutures) were performed for the reconstruction. The Head of the pancreas was transected with at least a 2 cm macroscopic surgical margin from the mass, usually at the margin of the head and neck of the pancreas. The proximal duodenum was transected about 1.5-2 cm distal to the pylorus.

During the DMPG reconstruction, a small piece of the feeding tube was inserted into the DMPG anastomosis, like a stent, to secure the patency of the anastomosis within the first few days. The tube was not fixed with sutures. An end-to-side duodeno-jejunostomy hand-sewn anastomosis was made using 3-0 vicryl sutures. The coledoco-jejunostomy anastomosis was created about 50 cm distal to duodeno-jejunostomy using 3-0 Vicryl sutures. Tumor Lymphadenectomy was performed in all patients with palpable regional lymph nodes. A Penrose drain was inserted in the bed of the surgical site, and a closed-suction drain was placed in the Morison pouch.

Data Collection

Demographic information including age, sex, risk factors for the disease and surgery, history and laboratory, data essential to calculate the American Society of Anesthesiology scoring (ASA) class, and clinical staging of the tumor were collected and recorded into a checklist before surgery.

Duration of the operation, length of stay (LOS) in the hospital, post-operative complications, short- and long-term outcomes, pathologic result of the sample, morbidity, and mortality were recorded into the checklist during close follow-up. The patients were followed up to a maximum of 11 years or up to the date of death. The post-operative complications include pancreatic fistula, bile fistula, thromboembolic events, intra-abdominal fluid collection such as hemorrhage and abscess, wound infection, gastrointestinal bleeding, and gastroparesis. International Study Group on Pancreatic Fistulas (ISGPF) criteria was used to estimate pancreatic fistula [9]. Delayed gastric emptying (DGE) was graded according to the validated criteria of the ISGPF classification [10]. Pre-operative ASA classification was also assessed according to the ASA classification of physical status [11].

Statistical analysis

Data were analyzed using IBM SPSS Statistics for Windows (version 21, IBM Corp, NY). Averages were expressed as mean ± SD. Kolmogorov-Smirnov test was used to assess the normal distribution of data. Possible statistical relationships between the risk factors and complications after the surgery were calculated using student t-test, ANOVA, and Chi-Square tests. The p-values equal to or less than 0.05 were defined as statistical significance levels.

RESULTS

In this study, a total of 164 patients with a mean age of 62.21± 9.34 years (including 93 males and 71 females) were included. The demographic information, risk factors, and also the number of cases in each ASA class are demonstrated in Table 1. Most of the patients were in class II of ASA classification (45.73%). According to the exclusion criteria, the patients with class V of ASA classification were excluded from the study.

Table 1: Demographic information, risk factors, and ASA class of patients

Variable (N=164)		
Age, (Mean± SD)	62.21 ± 9.34	
Sex, n (%)	Male	93 (56.70)
	Female	71 (43.29)
Smoking, n (%)	58 (35.36)	
DM, n (%)	48 (29.24)	
IHD, n (%)	42 (25.60)	
ASA Class n, (%)	I	15 (9.14)
	II	75 (45.73)
	III	64 (39.02)
	IV	10 (6.09)
	V	0 (0.00)

DM: Diabetes Mellitus, IHD: Ischemic Heart Disease, ASA: American Society of Anesthesiology scoring

Adenocarcinoma was the most prevalent tumoral type in this study (41.46%). Less common pathologies were cholangio-

carcinoma, ampullary carcinoma, high-grade dysplasia, neuro-endocrine carcinoma, and intraductal papillary mucinous neoplasm (IPMN). The mean pancreatic duct size was 4±1 millimeters. According to the TNM tumoral staging, 55 (33.5%), 70 (42.7%), and 39 (23.8%) of tumors were classified as T1, T2, and T3, respectively.

Post-operative data such as complications, mortality rate, and their relationship with the risk factors are illustrated in Table 2. In brief, DGE (delayed gastric emptying) (34.75%), pancreatic fistula (21.34%), bile duct fistula (7.31%), and hemorrhage (5.5%) were recorded as the most important post-operative complications in patients. Some post-operative complications were significantly observed in patients with diabetes mellitus [pancreatic fistula (p-value 0.038), increased amylase (p-value 0.010) and DGE (p-value 0.024)], smokers [bile duct fistula (p-value 0.027), hemorrhage (p-value 0.026) and increased amylase (p-value 0.045)] and the elders [bile duct fistula (p-value 0.006)]. No patient reported a history of alcohol consumption as a risk factor for pancreatic cancers.

Table 2: Post-operative data; and their relationship with the risk factors

Complications		Descriptive, n(%)	Age (P)	Sex (P)	Smoking (P)	DM (P)	IHD (P)	HTN (P)
Pancreatic fistula	0	129 (78.65)	0.690	0.607	0.293	0.038*	0.777	0.919
	A	6 (3.65)						
	B	17 (10.36)						
	C	12 (7.31)						
Bile duct fistula		12 (7.31)	0.006*	0.626	0.027*	0.99	0.506	0.134
PGIB		9 (5.48)	0.075	1.00	0.722	0.722	1.00	0.733
IAAC		23 (14.02)	0.174	0.176	0.062	0.272	0.9701	0.120
TE		18 (10.97)	0.503	0.266	0.740	0.134	1.00	0.375
SSC		23 (14.02)	0.117	0.664	0.950	0.392	0.955	0.493
Amylase[a]		34 (20.7)	0.943	0.619	0.045*	0.010*	0.755	0.170
DGE		57 (34.75)	0.611	0.791	0.117	0.024*	0.418	0.949
Hemorrhage		9 (5.5)	0.409	0.459	0.026*	0.199	0.838	0.896
Reoperation		18 (10.97)	0.332	0.366	0.169	0.213	0.567	0.908
R-resection[b]		30 (18.29)	0.503	0.223	0.869	0.429	0.883	0.909
Survival (month)		21.06±14.23	0.282	0.915	0.665	0.924	0.616	0.291
LOS (day)		13.12±7.15	0.115	0.880	0.800	0.580	0.700	0.241

PGIB=Post-operative-Gastrointestinal Bleeding, IAAC= Intra-abdominal abscess collection, TE= Thromboembolism, SSC= Surgical Site Complication, DGE= Delayed gastric emptying, LOS= Long of stay, P= p-value

[a]: Significant increasing amylase = triple time level for more than 3 days

[b]: Surgical resection margins were not restricted to malignant tumors, and the surgeon had to conduct more resection to reach a free margin

*The character * in the above P values indicates that there is a significant statistical relationship between the two methods of surgery*

The mean follow-up time of the patients was about 21.06±14.12 months. The mean survival of the patients was 21.06±14.23 months after surgery. There were 5 early post-operative mortality; one case due to massive lung embolism, three because of post-operative intra-abdominal hemorrhage, and one patient due to myocardial infarction. The survival rate of patients who were diagnosed with adenocarcinoma was 19.93±15.02 months. Survival rates for other groups are shown in Table 3. Also, the mean survival years in each pathologic type of tumor are shown in Figure 1. The longest survival is seen in non-malignant masses and the shortest survival is seen in PMN tumors.

DISCUSSION

Pancreaticoduodenectomy is an accepted surgical treatment for pancreatic head and peri-ampullary cancers. However, its complications have made surgeons find a better surgical technique in recent years [12].

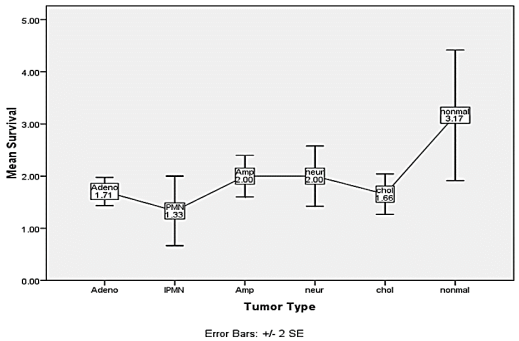

Figure 1: Mean survival year of the patients for each tumor type (*Adeno: Adenocarcinoma, IPMN: Intraductal papillary mucinous neoplasm, Amp: Ampullary Carcinomacarcinoma, Neur: Neuroendocrine tumor, Chol: Cholangiocarcinoma*)

PJ reconstruction is one of the accepted and common methods

of anastomosis after the excision of the pancreatic head and duodenum. However, the current method has many challenges such as a high rate of postoperative pancreatic fistula (POPF) and abdominal collections that are reported to be decreased in PG reconstruction in comparison to PJ reconstructions in different studies [13].

Table 3: The patients' survival rate (±SE); according to the pathologic type of tumor

Tumor / Survival	Ade (%)	IPMN (%)	Amp-Car (%)	Neur (%)	Chol (%)	Non-mal (%)	Total (%)
1-year	94±3	83±17	97±4	100	90±6	100	93.9±1.8
2-year	51±5	50±22	65±10	67±17	48±10	75±13	54.8±3.8
3-year	15±4	0	67±17	33±17	24±8	50±15	23.1±3.3
4-year	4±2	0	33±17	0	3±3	33±14	4.8±1.6
5-year	1±1	0	0	0	0	25±13	2.4±1.2
6-year	1±1	0	0	0	0	17±11	1.8±1.0
7-year	1±1	0	0	0	0	17±11	1.8±1.0
8-year	1±1	0	0	0	0	0	0.6±0.6
9-year	1±1	0	0	0	0	0	0.6±0.6
10-year	1±1	0	0	0	0	0	0.6±0.6

Ade: Adenocarcinoma, IPMN: Intra-ductal papillary mucinous neoplasm, Amp-Car: Ampullary Carcinomacarcinoma, Neur: Neuroendocrine tumor, Chol: Cholangiocarcinoma

Table 4: The Difference of Overall POPF Complication Rate in Recent Studies between PG and PJ Anastomosis after PD Surgery

Study	Year of Publication	PG		PJ		P value*
		N (%)	Total	N (%)	Total	
Wang et al. (DMPG) [7]	2014	2 (2.7)	75	-	-	-
Figueras et al. [4]	2013	10 (15.38)	65	20 (34.48)	58	0.006*
Topal et al. [14]	2013	13 (8.02)	162	33 (19.76)	167	0.002*
Wellner et al. (grade B/C) [20]	2012	6 (10.16)	59	7 (12.28)	57	0.775
Current study (DMPG)	2018	35 (21.32)	164	-	-	-

PG= Pancreatico-gastrostomy, PJ= Pancreatico-jejunostomy, DMPG= Duct to mucosa Pancreatico-gastrostomy
*The character of * in the above P values indicates that there is a significant statistical relationship between the two methods of surgery*

Table 5: Comparison of the various complication rates after PG Anastomosis in the previous studies

Complications/Study (Year, N)	Wang et al. (2014, 75) [7]	Figueras et al. (2013, 65) [19]	Topal et al. (2012, 162) [14]	Wellner et al. (2012, 59) [20]	Current Study (2018, 164)
Bile duct Fistula, n (%)	1 (1.3)	1 (2)	-	-	12 (7.31)
IAAC, n (%)	3 (4.0)	5 (8)	9 (6)	7 (12)	23 (14.02)
SSC, n (%)	3 (4.0)	-	65 (40)	_	23 (14.02)
DGE, N (%)	13 (17.3)	19 (29)	25 (15)	14 (27)	57 (34.75)
Hemorrhage, n (%)	2 (2.7)	13 (20)	21 (13)	6 (10)	9 (5.5)
Reoperation, n (%)	1 (1.3)	4 (6)	14 (9)	7 (12)	18 (10.97)
R-resection[a], n (%)	-	-	22 (10)	-	30 (18.29)
LOS (day, min-max)	19 (12-39)	12 (1-52)	19 (14-25)	15 (7-135)	14 (7-40)

PGIB=Post-GI Bleeding, IAAC= Intra-abdominal abscess collection, SSC= Surgical Site Complication, DGE= Delayed gastric emptying, LOS= Long of stay
a: Surgical resection margins were not restricted to malignant tumors, and the surgeon had to conduct more resection to reach a free margin

Duct to mucosa pancreatico-gastrostomy anastomosis is a method of anastomosis following PD surgery. There are few studies to show the distribution of complication rates after the DMPG surgical technique [7].

There are many accepted risk factors for POPF. Many risk factors are related to the pancreas itself and are different among patients; these include the size of the duct, histologic features, and the blood supply of the tail. However, many risk factors are related to the techniques of surgery such as anastomosis type after PD, stenting of the anastomosis, and blood loss during surgery [5,7,14].

In this study, there was also a significant relationship between the history of diabetes mellitus and the development of POPF (P=0.038). In a previous study, the risk of POPF was significantly higher in patients with diabetes mellitus (P=0.03). There was no significant relationship between age and POPF (P=0.69). Our finding in this regard is different from other studies [15]. Amylase levels and delayed gastric emptying (DGE) in diabetic patients were higher than in other patients.

In most studies, the male gender has a strong risk factor for pancreatic cancers. In our study, 56.7% of patients were male. However, gender was not an important risk factor for complications after surgery, the rate of bile duct fistula was higher in the elders significantly (P=0.006).

Smoking is another major risk factor for pancreatic cancer. The actual mechanism of this process is unknown. However, cigarettes contain thousands of carcinogenic compounds that can cause cancers [16]. Smoking is also an important risk factor for complications after surgery as seen in our study smokers developed higher rates of bile duct fistula and hemorrhage after the surgery. In these patients, the increase in amylase level was also higher than in other patients (Table 2).

In the current study, the prevalence of POPF was higher than the similar study on DMPG (21.32% vs. 2.7%), and also higher compared with PG (pancreatico-gastrostomy) reconstruction [17]. Although have no justification for that, it seems that DMPG doesn't have any priority in this regard. There are few reports on the comparison between POPF rates following DMPG and PJ anastomosis (21.32% vs. 12.28 and 34.48%) [18, 19]. In other studies, some complication rates such as hemorrhage, bile duct fistula, DGE, and also LOS are higher in PG in comparison to PJ anastomosis [17,19].

In this study, the prevalence of DGE was 34.75% which is higher compared to another study [5]. It might be because of the pylorus-preserving surgery done for the patient; however, this finding is not in favor of the priority of DMPG (Table 4). The prevalence of hemorrhage as a life-threatening post-operation complication was lower in this study (5.5%). On the other hand, the prevalence of bile duct fistula after PG was higher than in other studies. (7.31%, Table 5).

We calculated the DMPG survival rate for the first time according to a recommendation for future researchers by Topal et al [17]. The Survival rate after a mean follow-up of 21.06±12 months was 21.06±14.23 months in our study [17]. Survival rates for all pathologic types were similar and ranged from 1.33-2 years except for non-malignant tumors which resulted in a higher mean survival of 3.17 years (Figure 1).

Although our results indicate that DMPG reconstruction is a safe technique following PD, the claimed lower rate of post-operative complications and lower hospital stay is still in question and needs further investigation. Compared to other studies and the prevalence of this condition, the number of patients in this study is acceptable, however, it had some limitations. We did not perform subgroup analysis based on duct diameter. Also, pancreatic remnant consistency was not documented after our operations. Results might also be influenced by the surgical technique used for PG here. Also, we did not compare outcomes after DMPG with PJ anastomosis as a control group.

CONCLUSIONS

This study with a rather large number of patients and long-term follow-up after DMPG showed a lower rate of many post-operative life-threatening complications such as hemorrhage. On the other hand, the prevalence of bile duct fistula after PG was higher than in other studies. Though our results indicate that

Duct-to-mucosa pancreatico-gastrostomy reconstruction is a safe technique following PD however, does not confirm the priority of this method over older techniques. However, this contradiction calls for more studies including clinical trials and metaanalysis to clear all obscure dimensions.

Conflicts of interest and sources of funding

The authors declare no conflict of interest.

Acknowledgments

None

Authors' contribution

SNS, JAM, HG, ARK, MH, MR, SM were responsible for the study concept and design. SNS, JAM, HG, ARK, MH, MR, SM led data collection. SNS, JAM, HG, ARK, MH, MR, SM were responsible for the analysis and interpretation of data. SNS, JAM, HG, ARK, MH, MR, SM wrote the draft.

Ethics approval and consent to participate

This study was approved by the ethics committee of Baqiyatallah University of Medical Sciences. Throughout the study, researchers adhered to the Declaration of Helsinki. Written informed consent was obtained from the participants in this research.

Patient consent for publication

Informed consent was obtained from all subjects involved in the study.

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