

DOES THE PRESENCE OF CHRONIC NONSPECIFIC PANCREATITIS IN THE PATHOLOGY SPECIMEN AFFECT THE PREVALENCE OF PANCREATIC FISTULA DEVELOPMENT FOLLOWING PANCREATICODUODENECTOMY?

¹Doğan Erdoğan and ²Mehmet Ali Uzun

¹Department of General Surgery, Haydarpaşa Numune Training and Research Hospital, Istanbul, Turkey.

²Department of General Surgery, University of Health Sciences Turkey, Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Turkey,

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Corresponding Author: Doğan Erdoğan

Department of General Surgery, Haydarpaşa Numune Training and Research Hospital, Istanbul, Turkey.

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ABSTRACT

Introduction: Postoperative pancreatic fistula (POPF) is the most important complication occurring after pancreaticoduodenectomy (PD). It is essential to identify the causes of POPF development and to take preventive measures. **Method:** The data of 113 patients who underwent PD in our hospital with a diagnosis of periampullary tumor were reviewed retrospectively and were divided into two groups as those without chronic nonspecific pancreatitis (Group 1) and those with chronic nonspecific pancreatitis (Group 2) accompanying the tumor in the pathology specimens. The demographic data and frequency of POPF development in the two groups were compared. **Results:** Groups 1 and 2 comprised 42 and 71 patients, respectively. There were no significant differences between the groups in terms of age, sex distribution, American Society of Anesthesiologists (ASA) scores, preoperative laboratory data, operation time, pancreaticojejunostomy (PJ) procedure or mortality ($p > 0.05$). Biochemical leakage was observed in 17 patients (33.3%) in Group 1 and in seven patients (9.9%) in Group 2. There was no clinically relevant leakage (Grade B and C) observed in Group 2, whereas four patients in Group 1 (9.5%) had clinically relevant leakage. The rates of biochemical leakage and clinically relevant leakage were significantly higher in Group 2 than in Group 1 ($p < 0.05$). **Conclusion:** The present study found the incidence of POPF to be significantly lower in the pathology specimens of patients with accompanying chronic nonspecific pancreatitis. The authors believe that the preoperative or intraoperative detection of nonspecific pancreatitis could be an important predictor of POPF development.

KEYWORDS: Pancreaticoduodenectomy, postoperative pancreatic fistula, chronic pancreatitis.

INTRODUCTION

Pancreaticoduodenectomy (PD) is the standard approach to the treatment of periampullary tumors. Postoperative pancreatic fistula (POPF) development is the most common and serious complication occurring after PD, affecting the postoperative course of patients. The incidence of POPF ranges from 3–45% depending on the experience of the center

and the surgeon.^[1,2] Pancreaticojejunostomy (PJ) is an important procedure used in cases of PD, and there have been many studies to date evaluating its safety and the risk of POPF development, identifying such risk factors as age, male sex, body mass index, pancreatic duct size, pancreatic tissue, intraoperative blood loss, operation time, anastomosis technique and surgical experience.^[3,4] Previous studies, however, have identified the status of pancreatic tissue as the primary risk factor, associating a soft pancreas with a higher risk of POPF development than a hard pancreas.^[5,6]

The present study investigates the effect of the presence of chronic nonspecific pancreatitis in pathology specimens on the incidence of POPF development after PD.

MATERIALS AND METHOD

After gaining ethics committee approval (No:HNEAH-KAEK 2022/KK/228), 113 patients who underwent PD procedures with a diagnosis of periampullary tumor in the General Surgery Clinic of Haydarpaşa Numune Training and Research Hospital between January 2014 and December 2019 were included in the study. Patient data were retrieved retrospectively from the hospital records, and those who underwent PD due to trauma, those who received chemotherapy or radiotherapy, and those with missing data were excluded from the study. The PJ procedures included end-to-end (dunking), end-to-side, duct-to-mucosa anastomosis and simple invagination techniques.

Clinical, laboratory, radiological, pathological and surgical data (operation time, hemorrhage) and postoperative data (length of hospital stay and mortality) were collected from the hospital database. All postoperative complications were evaluated according to the modified Clavien-Dindo classification system.^[7,8]

The 2016 update of the International Study Group for Pancreatic Surgery (ISGPS) was used for the definition and grading of POPF, according to which amylase concentrations in the abdominal drain greater than three times the upper limit of the serum amylase concentration on postoperative day 3 or after were identified as POPF. The condition is defined as biochemical leakage (Grade A) if the drain does not persist longer than three weeks (21 days) and does not lead to additional problems or require additional interventions, while grade B and C biochemical leakages are defined as clinically relevant pancreatic fistula. Drainage persisting for more than 3 weeks, changes in clinical condition, the need for percutaneous or endoscopic drainage, the need for an angiographic procedure, and signs of infection without evidence of organ failure raise the category of POPF to Grade B. In addition to the characteristics of Grade B leakage, Grade C includes also a reoperation need, organ failure and mortality.^[8]

The patients were divided into two groups depending on the presence or absence of chronic nonspecific pancreatitis accompanying the tumor identified in the pathology specimen. The demographic data and the incidence of POPF development in patients without chronic nonspecific pancreatitis (Group 1) and those with chronic nonspecific pancreatitis (Group 2) were compared.

Statistical Analysis

Descriptive statistics included mean, standard deviation, median, minimum, maximum, frequency and ratio. A Kolmogorov-Smirnov test was used to test for the normality of the distribution of variables, and a Mann-Whitney U test was used for the analysis of quantitative independent variables. A Chi-square test was used to analyze qualitative variables and Fisher's exact test was used if the assumptions of the Chi-square test were not met. IBM SPSS Statistics (Version 28.0. Armonk, NY: IBM Corp.) was used for the statistical analysis. A *p*-value of less than 0.05 was considered statistically significant.

RESULTS

There was no significant difference between Groups 1 and 2 in terms of the patients' age, sex distribution, ASA scores and laboratory parameters (albumin, GGT, total bilirubin, direct bilirubin) ($p > 0.05$) (Table 1).

The pancreaticojejunostomy technique, operation time, intraoperative blood loss, postoperative bile leakage, wound site infection, delayed gastric emptying, length of hospital stay and mortality rates did not differ significantly between the two groups ($p > 0.05$). The incidences of biochemical leakage (POPF) and clinically relevant biochemical POPF (CR-POPF) were significantly lower in Group 2 than in Group 1 ($p < 0.05$) (Table 2).

Table I: Demographic and clinicopathological characteristics of the groups.

	Group 1 (n:42) n (%) or mean (\pm SD)	Group 2 (n: 71) n (%) or mean (\pm SD)	p-value
Age	63.2 \pm 11.7	64.2 \pm 12.4	0.511 ^m
Sex			0.122 ^{X²}
Male	21 (50.0%)	46 (64.8%)	
Female	21 (50.0%)	25 (41.2%)	
Albumin (g/dl)	3.9 \pm 3.4	3.5 \pm 0.6	0.778 ^m
ALP (IU/L)	328.1 \pm 273	379.5 \pm 299.7	0.293 ^m
GGT (IU/L)	417.9 \pm 470.4	496.9 \pm 501.3	0.213 ^m
Total Bilirubin (mg/dl)	9.6 \pm 5.8	9.2 \pm 7.8	0.054 ^m
Direct Bilirubin (mg/dl)	4.4 \pm 4.5	6.5 \pm 5.8	0.065 ^m
ASA Score			0.243 ^{X²}
I	0 (0.0%)	2 (2.8%)	
II	12 (28.6%)	26 (36.6%)	
III	29 (69.0%)	39 (54.9%)	
IV	1 (2.4%)	4 (5.6%)	

ALP: Alkaline Phosphatase; GGT: gamma-glutamyl transferase; ASA: American Society of Anesthesiologists; SD: Standard Deviation; ^t: t test; ^{X²}: Chi-square test (Fischer's exact test); ^m: Mann-Whitney U test

Table II: Operative and postoperative characteristics of groups.

	Group 1 (n:42) n (%) or mean (\pm SD)	Group 2 (n: 71) n (%) or mean (\pm SD)	p-value
Pancreaticojejunostomy Technique			
Duct-to-Mucosa	11 (26.2%)	28 (39.4%)	0.152 ^{X²}
End-to-End Dunking	23 (54.7%)	38 (49.3%)	0.617 ^{X²}
End-to-Side Dunking	4 (9.5%)	3 (4.2%)	0.259 ^{X²}
Simple Invagination	4 (9.5%)	5 (6.9%)	0.222 ^{X²}
Operation Time (min)	362.1 \pm 86.8	353 \pm 59.9	0.962 ^m
Intraoperative Blood Loss (ml)			0.404 ^{X²}
<400	14 (33.3%)	22 (31%)	
401-700	19 (45.2%)	24 (33.8%)	
701-1000	8 (19%)	20 (28.2%)	
>1000	1 (2.4%)	2 (7%)	
Postoperative Pancreatic Fistula(POPF)			
Biochemical Leakage	14 (33.3%)	7 (9.9%)	0.000 ^{X²}
Clinically Relevant POPF			0.017 ^{X²}
POPF B	3 (7.1%)	0 (0.0%)	
POPF C	1 (2.4%)	0 (0.0%)	
Postoperative Biliary Leakage	3 (7.1%)	1 (1.4%)	0.144 ^{X²}
Other Postoperative Complications			0.460 ^{X²}
Wound Site Infection	0 (0.0%)	5 (7%)	
Delayed Gastric Emptying	2 (4.8%)	1 (1.4%)	
Length of Hospital Stay (day)	18.5 \pm 3.6	16.3 \pm 3.7	0.300 ^m
Mortality	2 (4.8%)	1 (1.4%)	0.554 ^{X²}

POPF: Postoperative Pancreatic Fistula; SD: Standard Deviation ^t: t test; ^{X²}: Chi-square test (Fischer's exact test); ^m: Mann-Whitney U test

DISCUSSION

POPF remains one of the main complications associated with pancreatic surgery, with high incidence rates despite surgical advances.^[2] POPF itself or the associated comorbidities increase the duration of hospital stays, hospitalization costs, and more importantly, mortality rates.

It is essential to carry out a risk assessment for the development of POPF as part of effective postoperative management procedures following PD, given the various preoperative, intraoperative and postoperative risk factors reported for the development of POPF. A fistula risk score (o-FRS) based on pancreatic tissue, pancreatic duct diameter, pathological diagnosis, body mass index (BMI) and intraoperative blood loss was proposed by Calley et al.^[10] In an update to the original FRS (o-FRS) in 2017, an alternative FRS (a-FRS) was developed that incorporates pancreatic tissue, pancreatic duct diameter and BMI.^[11] There have been many studies to date reporting soft pancreatic tissue to be a risk factor for the development of POPF, although most of these studies had a retrospective design^[5], and the identification of soft and hard pancreatic tissue is based on the subjective intraoperative assessment of the surgeon.^[12,13] An objective preoperative assessment of pancreatic tissue is possible through the use of such radiological methods as magnetic resonance imaging (MRI) and elastography, although there is a need for further studies in this regard.^[14,15]

To evaluate the predictive value of pancreatic tissue for the development of POPF, the present study evaluates the relationship between the finding of chronic nonspecific pancreatitis in pathology specimens in the absence of a preoperative diagnosis of chronic pancreatitis developing in relation to ductal obstructions caused by the tumor, and the incidence of POPF. In a univariate analysis of the study findings, the identification of chronic nonspecific pancreatitis in pathology specimens appeared to be a protective factor against the development of POPF. Although the present study focused on retrospective analysis of postoperative outcomes, the findings may have intraoperative implications that have the potential to predict the risk of POPF. The results of the present study support an objective histopathological assessment approach over the subjective intraoperative assessment of soft or hard pancreatic tissue by surgeons, proposing a different point of view to the widely acknowledged effect of pancreatic tissue on the development of POPF.^[11,16]

In conclusion, the authors believe that an intraoperative histopathological examination of the anastomosis site can contribute to other risk-scoring models in predicting the risk of POPF development, and may aid in improving overall patient care.

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