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Distal Pankreatektomide Postoperatif Pankreatik Fistülü Öngören Faktörler

Predictive Factors for Postoperative Pancreatic Fistula in Distal Pancreatectomy

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ÖZ

Giriş: Pankreatektomi sonrası görülen postoperatif pankreatik fistül (POPF) major komplikasyonlara neden olabilmektedir. Bu çalışmanın amacı, distal pankreatektomi (DP) sonrası POPF'ü etkileyen risk faktörlerini değerlendirmek ve klinik önemini tartışmaktır.

Yöntem: Sakarya Üniversitesi Eğitim ve Araştırma Hastanesinde Ocak 2015 ve Ocak 2021 arasında distal pankreatektomi yapılan 37 hasta retrospektif incelendi. POPF'ye sebep olan risk faktörlerini belirlemek için hastaların demografik özellikleri, klinik parametreleri analizler kullanılarak değerlendirildi. P < 0.05 istatistiksel olarak anlamlı kabul edildi.

Bulgular: 37 hastanın 20'sinde (%54,05) POPF gelişirken, 17' sinde (%45,94) POPF gözlenmedi. Hastanın cinsiyetinin, yaşının, preoperatif serum-based inflammatory indicatorlerinin, cilt altı yağ dokusu, perinefrik yağ dokusu kalınlığının, psoas kası alanının POPF'e etkisi gözlenmedi. Pankreas kanal çapının 2mm'den büyük olması POPF'ü arttırdığı tespit edildi. (p=0,009).

Sonuç: Distal pankreatektomi sonrası POPF sık görülen komplikasyondur. Pankreas kanal çapının 2 mm'den büyük olması POPF' ü arttırabilir.

Anahtar Kelimeler: fistül, pankreatektomi, postoperatif, risk faktörleri

ABSTRACT

Objective: Postoperative pancreatic fistula (POPF) after pancreatectomy can cause major complications. The aim of this study is to evaluate the risk factors affecting POPF after distal pancreatectomy (DP) and to discuss its clinical significance.

Method: Data of TNBC patients treated with standard NACT protocol were analyzed retrospectively. ROC-curve analyzes were used for cutt-off determination. Binary logistic regression analysis was used for predictive markers.

Results: POPF was observed in 20 (54.05%) of 37 patients, while POPF was not observed in 17 (45.94%) patients. No effect of the patient's gender, age, preoperative serum-based inflammatory indicators, subcutaneous adipose tissue size, perinephric adipose tissue size, and psoas muscle area on POPF was observed. It was determined that pancreatic duct diameter greater than 2 mm increased POPF (p=0,009).

Conclusion: POPF is a common complication after distal pancreatectomy. Pancreatic duct diameter greater than 2 mm may increase the risk of POPF

Keywords: fistula, pancreatectomy, postoperative, risk factors

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INTRODUCTION

The incidence of POPF (Postoperative pancreatic fistula) after DP (distal pancreatectomy) is between 10% to 40% and remains the main cause of surgical morbidity (1).

As per the International Pancreatic Fistula Study Group, POPF is defined as a drain amylase level on the 3rd postoperative day that is more than 3 times the serum amylase level, irrespective of the drainage amount (2). POPF in pancreatic resections can result in bleeding, abscess formation, delayed gastric emptying, and sepsis. Several studies have recognized high body mass index (BMI), soft pancreatic parenchyma, transection technique, and excessive blood loss as factors that increase the risk of POPF (1,3,4,5,6).

In various types of surgery, there is a strong correlation between systemic inflammatory responses and the occurrence of surgical complications. (7,8). Indicators based on blood tests such as neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), systemic inflammatory index (SII) can be used as predictors of morbidity and mortality (9–11). Tumor-infiltrating lymphocytes serve as critical clinical biomarkers for patient stratification in diagnosed cancer patients, and can enhance conventional prognostic factors like stage and grade (12,13). Local increase in immune cell infiltration and increased systemic inflammatory responses in tumors may be important indicators of cancer progression and prognosis (14,15).

In our study, we aimed to investigate the predictive importance of preoperative serum-based inflammatory markers and preoperative computed tomography (CT) measurements for POPF.

MATERIALS AND METHODS

The data of 37 patients who underwent DP for different reasons between January 2015 and January 2021 in our center were retrospectively scanned. The preoperative serum-based laboratory results, demographic and computer tomography (CT) features of the patients were examined. Age, gender, location of pathology, surgery type, pancreatic duct diameter, pancreatic density, subcutaneous adipose tissue size, perinephric fat size, psoas volume, cancer antigen 19-9 (CA 19-9), hemoglobin (HGB), white blood cell (WBC), total bilirubin (Tbil), neutrophils, lymphocytes, platelets, mean platelet volume (MPV), amylase, lipase, albumin, PLR, NLR and SII values of the patients were evaluated. Density showing pancreatic consistency and pancreatic duct size measurements were made from the cut border of the pancreas in preoperative CT. Subcutaneous adipose tissue was measured at the umbilicus level, perinephric adipose tissue at the renal vein level, and psoas area at L3 level. After the postoperative 3rd day, the amylase values studied in the suspicious fluid sample taken from the abdominal drain were evaluated. If the amylase level in the fluid sample was more than 3 times the serum amylase, it was considered as POPF. The patients were divided into 2 groups as those with and without POPF. These two groups were compared with each other.

Statistical Analysis

The statistical analysis of the data was carried out using SPSS version 25.0, and the normality of the data was assessed using the Kolmogorov-Smirnov test. Descriptive statistics were used to express normally distributed quantitative data as mean±standard deviation, non-normally distributed quantitative data as median, minimum and maximum values, and categorical data as percentages. The independent samples T-test was applied for analyzing parametric quantitative data, Fischer's exact probability test was used for analyzing nonparametric quantitative data, and Chi-Square test was used for analyzing categorical data. A total type-1 error level of 5% was deemed statistically significant.

RESULTS

Of the 37 patients included in the study, 17 (45.9%) were male and 20 (54.1%) were female. The mean age of the patients was 57.8 (20-83). POPF was seen in 20 of 37 cases, but not in 17. When the patients with and without POPF were compared, no significant difference was observed in terms of gender and age (p=0.51 and p=0.68, respectively) (Table 1).

Table :1 Demographic Characteristics of All Patients, with and Without POPF

		POPF (-)	POPF (+)	All Patients	p Value
Age		56.82 ± 17.9	58.75 ± 9.85	57.86 ±13.9	0.68*
Gender	Male	8 (%47.1)	12 (%60)	17 (%45.9)	0.51 **
	Female	9 (%52.9)	8 (%40)	20 (%54.1)	

* Independent-Samples T Test
** Fisher's Exact Test

When the patients with and without POPF were compared in terms of the organ where the pathology originates, benign/malignant character, originating from the pancreas, no significant difference was found (p=0.33, p=0.416, p=1 respectively). When the types of surgery were compared between the groups in terms of conventional, laparoscopic and robotic surgery, no significant difference was found (p=0.406). When CT features were compared between the groups, no difference was found in terms of pancreatic density, subcutaneous adipose tissue thickness, perinephric adipose tissue, and psoas area (p=0.83, p=0.17, p=0.39 and p=0.10, respectively). It was observed that canal diameter greater than 2mm increased POPF significantly (p=0.009) (Table 2).

The effect of smoking habit on POPF was not observed (p=0,495) (Table 2). When serum-based laboratory results of patients with and without POPF were compared, no difference was found in terms of WBC, neutrophil, lymphocyte, MPV, CA 19-9, T.bil, HGB, platelet, amylase, lipase, albumin, NLR, PLR, SII (Table 2).

Table 2: Comparison of the Features of Patients with and Without POPF				
		POPF (-)	POPF (+)	p Value
Lesion Location	Pancreas	14 (%45.2)	17 (%54.8)	0.33*
	Colon	1 (%100)	0	
	Gastric	2 (%66.7)	1 (%33.3)	
	Spleen	0	2 (%100)	
Pathology Result	Benign	2 (%28.6)	5 (%71.4)	0.416*
	Malign	15 (%50)	15 (%50)	
Originating Organ	Pancreas	14 (%45.2)	17 (%54.8)	1*
	Non-Pancreatic	3 (%50)	3 (%50)	
Surgery Type	Open Surgery	15 (%48.4)	16 (%51.6)	0.406*
	Laparoscopic	2 (%50)	2 (%50)	
	Robotic	0	2 (%100)	
Cigarette	Yes	4 (%36.4)	7 (%63.6)	0.495*
	No	13 (%50)	13 (%50)	
Pancreatic Duct Diameter	<2 mm	17 (%56.7)	13 (%43.3)	0.009*
	>2 mm	0	7 (%100)	
WBC		7.60 ± 3.42	7.96 ± 2.45	0.71**
Neutrophil		5.09 ± 3.45	5.20 ±2.67	0.916**
Lymphocyte		1.75 ± 0.64	2.03 ± 0.79	0.255**
MPV		8.35 ± 1.81	8.39 ± 0.89	0.930**
Ca 19-9		8.14 (2–7274)	4.70 (2-23133)	0.479***
T.Bil		0.47 (0.10-1.26)	0.47 (0.11-2.71)	0.924***
HGB		11.9 (8.1-13.6)	12.6 (8.56-16.9)	0.20***
Platelet		224 (133-467)	211.5 (123-306)	0.24***
Amylase		48 (18-153)	61 (13-332)	0.27***
Lipase		28.5 (4-176)	26 (9-378)	0.466***
Albumin		3.51 ± 0.56	3.81 ± 0.61	0.145**
NLR		2.52 (0.89-54.1)	2.14 (0.8-38.02)	0.62***
PLR		129.5 (45.2-2349.65)	104.2 (46.4-721.5)	0.18***
SII		610.7 (146.06-18186.29)	513.2 (119.6-9163.7)	0.50***
Pancreatic Density (HU)		81.2 (30-117)	80 (39-109)	0.83***
Subcutaneous Adipose Tissue Size (mm)		22.6 (3.4-46)	25.5 (11-48)	0.17***
Perinephric Fat Size (mm)		9 (2-29)	11 (2-26)	0.39***
Psoas Area (cm^2)		5.9 (2-11)	7.75 (4.1-13)	0.10***

* Fisher's Exact Test
** Independent-Samples T Test
*** Mann-Whitney U Test

DISCUSSION

In this study, we examined the success of CT images together with preoperative serum-based inflammation indices in predicting POPF in patients who underwent DP.

POPF is identified as the primary major complication following pancreatic surgery, and is a severe, life-threatening complication that can extend the duration of hospitalization and increase medical expenses (16). The International Study Group on Pancreatic Fistula has established a universal and practical definition for postoperative pancreatic fistula (POPF) (16). The ISGPF defines POPF as the detection of a drain amylase greater than three times the serum amylase level on or after 3 days postoperatively, regardless of the amount of drainage (16).

It is known that POPF is primarily caused by the leakage of pancreatic fluid into the abdomen (17). POPF can lead to intraperitoneal abscesses and sometimes hemorrhages, which can cause life-threatening conditions with up to 40% fatality rates (17–19). A pancreatic duct diameter less than 3 mm, tumor localization in the ampullary and duodenal regions, presence of cystic or islet cell pathology, soft pancreatic parenchyma, and intraoperative blood loss exceeding 1,000 mL were identified as potential risk factors for an increased incidence of POPF. Moreover, these findings highlighted the cumulative effect of these risk factors and their adverse impact on clinical and cost-effective outcomes. Intraoperative risk assessment alone was found to be inadequate in predicting the occurrence of POPF, while preoperative risk stratification provided limited diagnostic value and was of little effect in altering the postoperative course (20).

The studies mentioned above, and general risk factors were determined mostly in patients who underwent pancreaticoduodenectomy (PD). Based on a meta-analysis conducted by Peng et al., it was concluded that soft pancreatic tissue, higher body mass index (BMI), blood transfusion, significant intraoperative blood loss, and prolonged operation time are potential risk factors that increase the likelihood of POPF in patients undergoing DP (21). In the meta-analysis of Chong et al., no effect of pancreatic consistency and BMI was observed, while smoking and diabetes increased POPF (22).

In our study, contrary to other studies, it was observed that larger canal diameter increased POPF. Most of the studies in the literature are studies on patients undergoing PD. Therefore, the risk of fistula increases after PD as the anastomosis safety will decrease with the small canal (23). However, since there is no anastomosis in distal pancreatectomy, this is not of major importance in terms of fistula development. In the study of Martin et al., it was determined that the consistency of the pancreatic tissue and the diameter of the duct were effective in the development of POPF, but not in the distal pancreatectomies. These data also support the results obtained in our study. In our study, we used radiological measurements to determine the intra-abdominal fat ratio instead of BMI. In the study of Morris et al., no effect of BMI on morbidity in abdominal surgery was observed, while the size of perinephric fat increased morbidity (24). Gonzalez et al. reported that total adipose tissue and perinephric fat thickness increased POPF in CT measurements (25). Balsam reported in her study that the psoas muscle area may affect functional recovery after major surgeries (26). However, no effect on POPF was observed in our study.

Inflammation has recently been thought to play an important role in cancer prognosis. In fact, prognostic factors based on inflammation such as NLR, PLR, LMR, SII have been defined (27). Preoperative and postoperative NLR associated with poor prognosis in gastric cancer (28). Like neutrophils, platelet is the blood cell responsible for the inflammatory response and is often elevated in solid tumors with chronic inflammation (29,30). It was found that high SII was associated with poor postoperative prognosis in patients with colorectal and endometrial cancer (10,31). Zhang et al. reported that high monocyte counts were associated with poor prognosis after curative surgery in 270 rectal cancer patients with pathological stage T3N0M0 (32).

Inflammatory biomarkers have been shown to play an independent prognostic role in predicting cancer-specific and postoperative survival in various malignancies, including periampullary malignancies (33,34).

Furthermore, the effectiveness of inflammatory markers in predicting postoperative morbidity has been investigated in various surgical procedures such as colorectal, esophageal, and otolaryngological surgery. Notably, a NLR of greater than 3 has been associated with an increased incidence of anastomotic failure in colorectal surgery (35). Low levels of albumin and lymphocytes have been linked to a higher occurrence of complications following esophageal surgery (36).

However, it is not clear enough in the literature whether preoperative serum-based inflammatory indicators have an effect on the risk of developing POPF after pancreatic surgery. In our study, it was observed that there was no effect of preoperative serum-based inflammatory indicators.

In conclusion, the findings of our study show that pancreatic consistency, psoas area, perinephric and subcutaneous adipose tissue blood count, NLR, PLR and SII are not clinically significant in predicting POPF in patients who underwent distal pancreatectomy. However, it was observed that pancreatic duct diameter greater than 2 mm increased the risk of POPF significantly. This result adds originality to our study. The limitations of our study are the retrospective nature of our study and the small number of cases. There is a need for prospectively planned multicenter studies with a large number of patients in this regard.

Ethics Committee Approval: Ethical approval was obtained. Clinical Research Ethics Committee (71522473/050.01.04/525).

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Data Collection:ATH, BU, NF, Analysis: EG, Literature search: ATH, NF, Writing:ATH, Review: ATH, FA, FÇ.

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Informed Consent: This study was conducted with a retrospective design.

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