Original Article

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Evaluation of Factors Related to Pancreatic Fistula Development in Patients Undergoing Pancreaticoduodenectomy for Periampullary Tumours

Periampullar Tümör Nedeniyle Pankreatikoduodenektomi Uygulanan Hastalarda Pankreatik Fistülle İlişkili Faktörlerin Değerlendirilmesi

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ABSTRACT

Objective: This study aimed to investigate the factors associated with pancreatic fistula (PF) development after pancreaticoduodenectomy (PD) at our clinic.

Methods: Patients who underwent PD for periampullary tumours between 2010 and 2019 were included in the study and categorised into Group I (with PF) and Group II (without PF). The demographic and clinical characteristics, laboratory parameters, tumour characteristics and post-operative results were compared between the groups. Risk factors for PF were analysed by univariate analysis and multivariate logistic regression analysis.

Results: In total, 155 patients participated in the study (Group I: n=31; Group II: n=124). The rate of PF was 20%. The two groups were comparable with regard to sex (p=0.348) and age (64.8 vs 66.9 years, p=0.916). Compared with Group II, Group I had a higher number of metastatic lymph nodes (1.61 vs 0.87, p=0.041), a higher number of post-operative complications (58.1% vs 21.8%, p=0.000) and a longer duration of post-operative hospital stay (25.25 vs 16.43 days, p=0.000). Haemoglobin (p=0.493) and albumin (p=0.698) levels were similar between the groups. Total survival duration was shorter in Group I (23.9 vs 38.18 months, p=0.024). In multivariate analyses, being ≥65 years (p=0.040), tumour localisation (p=0.021), lymph node stage (p=0.008) and

ÖZ

Amaç: Bu çalışmada kliniğimizde pankreatikoduodenektomi (PD) sonrası gelişen pankreatik fistül (PF) ile ilişkili faktörleri araştırmayı amaçladık.

Yöntemler: 2010-2019 yılları arasında periampullar bölge tümörü nedeniyle PD, uygulanan hastalar çalışmaya dahil edili. Grup 1 (PF var) ve Grup 2 (PF yok) olmak üzere iki grup oluşturuldu. Gruplarda hastaların demografik ve klinik özellikleri, labrotuvar parametreleri, tümöre ait özellikler, postoperatif sonuçlar ortalama sağkalımları karşılaştırıldı. Pankreas fistülü (PF) için risk faktörleri tek değişkenli analiz ve çok değişkenli lojistik regresyon analizi ile analiz edildi.

Bulgular: Çalışmamıza 155 hasta katıldı. PF oranımız %20 olarak bulduk. Buna göre Grup 1: 31 Grup 2: 124 hastadan oluşuyordu. Gruplarda cinsiyet benzer özellikteydi (p=0,348). Gruplarda yaşlar benzer (64,8; 66,9, p=0,916). Metastastik lenf nodu sayısı Grup 1'de 2'ye oranla daha yüksek (1,61; 0,87, p=0,041) Post-operatif komplikayon Grup 1'de yüksek (%58,1; %21,8 p=0,000). Postoperatif yatış süresi Grup 1'de daha uzundu (25,25 vs 16,43 gün p=0,000). Gruplarda hemoglobin p=0,492, albumin p=0,698 benzer. Toplam sağkalım süresi Grup 1'de daha kısa (23,9 ay; 38,18 ay p=0,024). Çok değişkenli analizlerde >65 yaş p=0,040, Tümör

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tumour diameter ≥2 (p=0.021) were the independent risk factors for developing pancreatic fistula.

Conclusion: In our study, tumour diameter, patient age and lymph node status were associated with PF development. The development of PF reduced expected survival. We believe that identifying the pre-operative, intraoperative and post-operative factors related to PF formation may help decrease its development.

Keywords: Pancreatic fistula, pancreaticoduodenectomy, prognosis

lokalizasyon p=0,021 lenf nodu evresi p=0,008. Tümör çapının >2 p=0,021 pankreatik fistül için bağımsız risk faktörüydü.

Sonuç: Çalışmamızda tümör çapı hasta yaşı ve lenf nodu durumu PF gelişmesi ile ilişkiliydi. PF gelişimi beklenen sağ kalımı azaltmıştı. Preoperatif, intraoperatif ve postoperatif dönemdeki etkenlerin ortaya konulması ile PF oluşumunun azalabileceğini düşünmekteyiz.

Anahtar Sözcükler: Pankreatik fistül, pankreotikoduodenektomi, prognoz

Introduction

Pancreaticoduodenectomy (PD) is currently the standard method for the treatment of benign and malignant tumours of the periampullary region (pancreatic head, ampulla, duodenum and distal choledochus) (1-3). Although the results of PD have greatly improved with advances in surgical techniques and perioperative management, this procedure remains one of the most complex abdominal operations and results in high post-operative morbidity rates of 30%-40% (4).

Pancreatic fistula (PF) is the most common and severe complication following PD. Despite the advances and technical changes developed to prevent PF, the incidence of this terrible complication still ranges from 3% to 45% (5). PF can not only prolong hospital stay and increase the cost of treatment but also increase the risk of premature mortality after surgery and cause other complications (4,6,7). Till date, the risk factors of PF have been extensively studied to obtain recommendations for its prevention and treatment; in addition, many studies have investigated the correlation between PF and perioperative variables, but the results are not consistent (8,9).

Determining the factors related to PF development will help prevent and manage this feared complication. The literature has demonstrated that many pre-operative, perioperative and post-operative factors, such as sex, age, hyperbilirubinemia, duration of surgery, intraoperative blood loss, pancreatojejunal anastomotic technique, pancreatic duct size, use of somatostatin and surgeon experience, are related to PF development after PD (10,11).

In this study, we aimed to investigate the factors related to PF development after PD in our clinic during a 10-year period and to discuss our findings in the light of the literature.

Methods

We enrolled 172 patients who underwent PD for periampullary tumours (ampulla, distal choledochus, pancreas head and duodenum) between January 2010 and January 2019. Patients aged <18 years, whose records could not be obtained and whose pathological diagnosis was not adenocarcinoma (n=17) were excluded from the study. Finally, 155 patients were included in the study. Patient data were obtained retrospectively from electronic records, patient files, anaesthesia follow-up forms and nurse observation forms. Owing to the retrospective design of the study, an ethics committee approval was not received.

PF was defined as any measurable volume of drain fluid appearing on or after the 3rd post-operative day, with an amylase content three times higher than the upper normal serum value (12). Patients were divided into two groups: Group I included patients with PF and Group II included those without PF. Demographic and clinical data such as sex; age; presence of comorbidities; American Society of Anesthesiologists (ASA) score; tumour localisation; laboratory parameters such as complete blood count, albumin, bilirubin and tumour markers [carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9)]; pathological features (e.g. tumour differentiation, stage, diameter, number of dissected and metastatic lymph nodes and presence of positive lymph nodes) and post-operative follow-up data (e.g. the presence of non-PF complications, duration of post-operative hospital stay, 30-day post-operative survival, local recurrence status, current clinical status, cause of exitus and total survival time) were analysed. In addition, independent risk factors were evaluated using univariate and multivariate analyses.

Post-operative complications were defined as wound infection, evisceration, intraabdominal abscess, intraabdominal haemorrhage and anastomosis leakage. Tumour-node-metastasis 2010 and 2016 systems was used for tumour staging.

All patients were evaluated at the Hepatobiliary Tumour Council at our centre before the operation. In patients with severe hyperbilirubinemia, pre-operative biliary drainage was performed via percutaneous transhepatic cholangiography or endoscopic retrograde cholangiopancreatography.

Operation Details

Following laparotomy, the choledoch was incised just above the cystic duct choledoch junction (until the negative surgical margin was reached). Subsequently, the pancreas was rotated to reach the posterior and was cut from the superior mesenteric vein border. From the proximal end of the pylorus, the distal stomach was freed, rotated and cut. The Treitz ligament was then freed and incised at approximately 10 cm from the distal end of the jejunum. Ductojejunal anastomosis between the pancreatic duct and jejunum was completed using 5/0 PDS and 3/0 silk sutures in the end-to-side manner. To the proximal end of this anastomosis, biliary tract-jejunum anastomosis was performed-

first on the posterior wall using 4/0 or 5/0 PDS sutures and then on the anterior wall using 4/0 or 5/0 PDS single sutures. Lymph node dissection was advanced from the lymphatic tissue in the hepatoduodenal ligament to the level of the celiac trunk. Subsequently, a drain was placed in the subhepatic region.

Statistical Analysis

SPSS 23.0 (IBM Corp., Armonk, N.Y., USA) package programme was used for statistically analysing data. Categorical measurements were summarised as numbers and percentages, and continuous measurements were summarised as mean, deviation and minimum and maximum values. Pearson's chi-squared test was used to compare categorical variables. While comparing the continuous measurements between the groups, the distributions were assessed and binary variables identified were analysed using independent Student t-test. Cox regression was used for multivariate analyses. Kaplan-Meier analysis and log rank tests were used for survival analyses. Statistical significance was set at 0.05 in all tests.

Results

For the 155 patients who participated in our study, the PF rate was 20%. Group I (with PF) consisted of 31 and Group II (without PF) consisted of 124 patients. Male sex was dominant in both the groups (61.3% vs 66.9%, p=0.348). Both groups were comparable in terms of the mean age (64.6 vs 64.8 years, p=0.916). At least one comorbidity was noted in 41.9% patients in Group I and 52.4% patients in Group II. The most common ASA score was ASA I in both the groups (51.6% vs 42.7%, p=0.589). Choledochus localisation was more common in Group I than in Group II (32.3% vs 12.1%, p=0.001). The demographic and clinical features of the patients are shown in Table 1.

The following laboratory parameters were similar between the groups: white blood cell count (p=0.885), neutrophil count (p=0.671), lymphocyte count (p=0.494), platelet count (p=0.900), haemoglobin level (p=0.492), albumin level (p=0.698), total bilirubin (p=0.891), CEA level (p=0.499) and CA19-9 level (p=0.223). Laboratory parameters of patients in both groups are shown in Table 2.

Poorly differentiated tumours were dominant in both Group I and Group II (61.3% vs 49.2%, p=0.349). Stage T3 tumours were the most common in both the groups (41.9% vs 50.8%, p=0.079). Lymph node stage and positivity were higher in Group I (58.1% vs 38.7%, p=0.041). However, tumour diameter was similar between the groups (1.94 cm vs 2.36 cm, p=0.070). The characteristics of tumours in both groups are shown in Table 3.

The incidence of post-operative complications other than PF was higher in Group I (58.1% vs 21.8%, p=0.000); so was the length of hospital stay (25.25 vs 16.43 days, p=0.000). Post-operative 30-day mortality was similar between the groups (19.4% vs 9.7%, p=0.119). However, the rate of local recurrence was higher in Group I (45.2% vs 37.9, p=0.295). In terms of the cause, mortality caused by sepsis was higher in Group I (22.6% vs 10.5%, p=0.028). For both groups, post-operative follow-up results are shown in Table 4. The average survival duration was shorter in Group I (23.9 months vs 38.18 months, p=0.024), as shown in Table 5 and Graphic 1.

The univariate analysis demonstrated that tumour localisation (p=0.021) was the independent risk factor of PF. However, in multivariate analyses, the independent risk factors of PF were age ≥65 years [hazard ratio (HR) (95% confidence interval (CI)] =2.182 (1.034-4.602), p=0.040), lymph node stage [HR (95% CI) =2.739 (1.304-5.753), p=0.008], presence of post-operative complications [HR (95% CI) =0.275 (0.133-0.567), p=0.001] and tumour diameter >2 [HR (95% CI) =0.423 (0.204-0.879), p=0.021]. The results of the multivariate analysis are shown in Table 6.

Table 1. Characteristics of patients

		Group 1 (n=31) n (%)	Group 2 (n=124) n (%)	p
Sex	Male	19 (61.3)	83 (66.9)	0.348
	Female	12 (38.7)	41 (33.1)	
Age		64.61±11.55 (22-91)	64.87±14.12 (22-93)	0.916
Comorbidities	Yes	13 (41.9)	65 (52.4)	0.200
	No	18 (58.1)	59 (47.6)	
ASA score	1	16 (51.6)	53 (42.7)	0.589
	2	12 (38.7)	52 (41.9)	
	3	3 (9.7)	19 (15.3)	
Tumour localisation	Ampulla	12 (38.7)	52 (41.9)	0.001*
	Duodenum	2 (6.5)	0 (0.0)	
	Choledochus	10 (32.3)	15 (12.1)	
	Pancreas	7 (22.6)	57 (46.0)	

ASA: American Society of Anesthesiologists

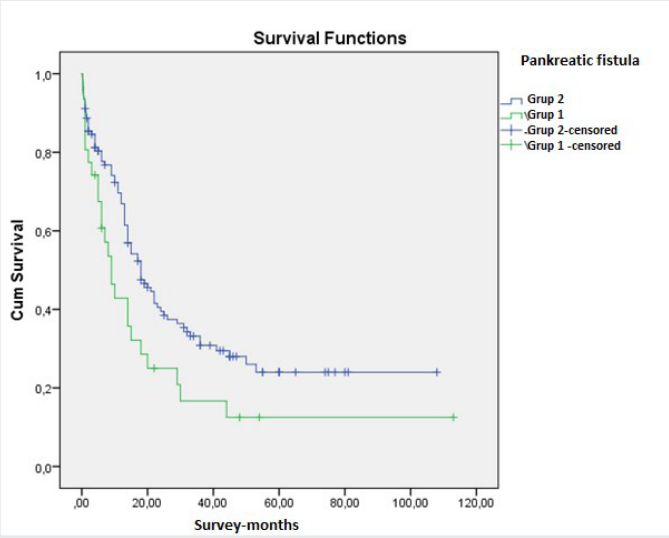
Table 2. Laboratory parameters

	Group 1 (n=31) Mean ± SD (Minimum-maximum)	Group 2 (n=124) Mean ± SD (Minimum-maximum)	
WBC (mm^3)	8285.48±2542.45 (3600-14410)	8202.01±2933.08 (1430-18390)	0.885
Neutrophil count (mm^3)	5785.16±2620.98 (1110-12310)	55868.48±2515.54 (840-15000)	0.671
Lymphocyte count (mm^3)	1627.74±785.51 (470-4490)	1728.22±714.73 (460-4630)	0.494
Platelet count (mm^3)	299.74±120.17 (104-684)	297.10±99.53 (92-690)	0.900
Haemoglobin (g/dL)	12.77±1.59 (9.8-15.6)	12.52±1.87 (7.4-17.7)	0.492
Albumin (g/dL)	3.48±0.80 (1.4-4.6)	3.53±0.68 (1.8-4.9)	0.698
Total bilirubin (mg/dL)	5.96±7.24 (0.2-29)	5.77±6.80 (0.1-34)	0.891
Pre-operative CEA (ng/mL)	5.81±15.57 (0.01-87.4)	4.30±9.71 (0-81.6)	0.499
Pre-operative CA19-9 (U/mL)	325.55±633.30 (2-2704)	671.96±1540.92 (1-9683)	0.223

WBC: White blood cell, SD: Standard deviation, CEA: Carcinoembryonic antigen, CA19-9: Carbohydrate antigen 19-9

Table 3. Characteristics of tumours

		Group 1 (n=31) n (%)	Group 2 (n=124) n (%)	p
Differentiation	Well	7 (22.6)	28 (22.6)	0.348
	Moderate	5 (16.1)	35 (28.2)	
	Poor	19 (61.3)	61 (49.2)	
T	T1	6 (19.4)	8 (6.5)	0.079
	T2	12 (38.7)	53 (42.7)	
	T3	13 (41.9)	63 (50.8)	
N	N0	13 (41.9)	76 (61.3)	**0.041***
	N1	18 (58.1)	48 (38.7)	
Number of total dissected lymph nodes (minimum-maximum)		10.48±8.08 (1-42)	10.45±5.71 (1-29)	0.982
Metastatic lymph node number (minimum-maximum)		1.61±2.38 (0-11)	0.87±1.58 (0-9)	**0.041***
Lymph node involvement	Negative	13 (41.9)	76 (61.3)	**0.040***
	Positive	18 (58.1)	48 (38.7)	
Tumour diameter		1.94±1.16 (0.7-5.0)	2.36±1.15 (0.4-6.5)	0.070



Graphic 1. Total survival duration of patients according to pancreatic fistula

Discussion

PD is one of the more complex abdominal surgical techniques and is associated with several post-operative complications. The most important complication that can develop following PD is a PF. The incidence of fistula formation after PD is much higher than that after other gastrointestinal operations and ranges from 3% to 45%. In addition, PF might lead to the development of other major complications (5,13).

The prognosis and aggressiveness of periampullary tumours vary according to tumour localisation. Overall, pancreatic head carcinoma is thought to have the worst prognosis among all periampullary tumour types (14). Reportedly, there are conflicting data regarding the effect of tumour localisation on PF development. Chen et al. (3) found that PF was associated with tumour localisation in periampullary tumours [odds ratio (OR) =3.00, p=0.029]. In contrast, Schmidt et al. (15) demonstrated that tumour localisation in the periampullary region was not associated with PF development. In addition, they reported that lymph node status was not a risk factor for

Table 4. Post-operative outcomes

		Group 1 (n=31) n (%)	Group 2 (n=124) n (%)	p
Post-operative complications other than pancreatic fistula	Yes	18 (58.1)	27 (21.8)	**0.000***
	No	13 (41.9)	97 (78.2)	
Length of hospital stay (minimum–maximum)		25.25±13.41 (6-56)	16.43±8.33 (5-43)	**0.000***
Post-operative 30-day mortality	Yes	6 (19.4)	12 (9.7)	0.119
	No	25 (80.6)	112 (90.3)	
90-day reoperation	Yes	3 (9.7)	6 (4.8)	0.258
	No	28 (90.3)	118 (95.2)	
Local recurrence	Yes	14 (45.2)	47 (37.9)	0.295
	No	17 (54.8)	77 (62.1)	
Current situation	Ex	25 (80.6)	80 (64.5)	0.063
	Alive	6 (19.4)	44 (35.5)	
Cause of death	None	7 (22.6)	54 (43.5)	**0.028***
	Cardiac causes	7 (22.6)	12 (9.7)	
	Sepsis	7 (22.6)	13 (10.5)	
	Tumour-related causes	10 (32.2)	45 (36.3)	

Table 5. Total survival duration according to pancreatic fistula groups

Group	Mean [Mean ± SD (minimum-maximum)]	Median [Mean ± SD (minimum-maximum)]	p
1	23.90±6.77 (10.62-37.18)	9.0±1.93 (5.20-12.79)	**0.024***
2	38.18±4.16 (30.01-46.35)	18.0±2.67 (12.76-23.23)	

SD: Standard deviation

Table 6. Univariate and multivariate analyses of factors associated pancreatic fistula in periampullary tumours

Measurements		Univariate	Multivariate	
		p	HR (95% Cl)	p
Age group (years)	<65	**0.036**	1.00	**0.040***
	≥65		2.182 (1.034-4.602)	
Sex	Male	0.893	1.00	0.862
	Female		1.053 (0.500-2.215)	
Localisation	Ampulla	**0.021***	1.00	**0.011***
	Duodenum		5.767 (1.276-26.074)	**0.023***
	Choledochus		2.011 (0.869-4.656)	0.103
	Pancreas		0.566 (0.212-1.513)	0.257
Differentiation	Well	0.765	1.00	0.192
	Moderate		1.135 (0.910-1.276)	0.213
	Poor		1.231 (0.876-1.652)	0.672
T	T1	0.444	1.00	0.391
	T2		0.535 (0.188-1.519)	0.240
	T3		0.494 (0.175-1.394)	0.183
N	N0	**0.007***	1.00	**0.008***
	N1		2.739 (1.304-5.753)	
Post-operative complication	Yes	**0.001***	1.00	**0.001***
	No		0.275 (0.133-0.567)	
Local recurrence	Yes	0.751	1.00	0.750
	No		0.887 (0.424-1.856)	
ASA score	1	0.928	1.00	0.932
	2		0.963 (0.449-2.065)	0.922
	3		0.787 (0.226-2.740)	0.707
Tumour diameter	Below 2	**0.020***	1.00	**0.021***
	2 and above		0.423 (0.204-0.879)	
Haemoglobin (g/dL)	Below 12	0.153	1.00	0.166
	12 and above		1.740 (0.794-3.813)	
Albumin (g/dL)	Below 3.5	0.963	1.00	0.963
	3.5 and above		0.983 (0.477-2.025)	
Bilirubin (mg/dL)	Below 5	0.525	1.00	0.522
	5 and above		1.277 (0.604-2.698)	

ASA: American society of Anesthiologists, HR: Hazard ratio, CI: Confidence interval

PF. In our study, tumour localisation was associated with PF and was an independent risk factor for PF development. In addition, PF was more common in patients with choledochal tumours. PF rate varied based on lymph node stage, tumour diameter, tumour differentiation and tumour localisation. We additionally noted that parallel to these factors, lymph node positivity and the number of metastatic lymph nodes were higher in the PF group. Lymph node positivity was an independent risk factor of PF development [HR (95% CI) =2.739 (1.304-5.753), p=0.008].

Several studies have indicated that a small diameter of the pancreatic duct (≤3 mm) is a risk factor for post-operative PF. When performing PD, surgeons should consider this risk factor and achieve a satisfactory pancreatic anastomosis to reduce PF formation (8,10,16,17). Notably, the debate on the relationship between tumour diameter and PF development is still ongoing. In their study, Polanco et al. (18) observed a smaller tumour diameter in the PF group (2.1 vs 2.9 cm, p=0.02; OR =0.594, 95% CI: 0.383-0.922, p=0.002). However, in another study, tumour diameters were similar in groups with and without PF (3.2 vs 3.1 cm, p>0.05) (15). We noted a similar result in our study. Although the tumour diameters were similar in the groups with and without PF (1.94 cm vs 2.36 cm, p=0.070), a tumour diameter of >2 cm was an independent risk factor for PF development.

The effect of intraoperative variables on PF development has been previously discussed in the literature. The type of

anastomosis performed during operation has also been cited as a predictor of PF (15,19,20). Schmidt et al. (15) reported that PJ invagination performed after PD resulted in a lower incidence of PF than Wirsung-jejunostomy (WJ). In addition, Bartoli et al. (20) reported that the incidence of PF development after WJ was the lowest compared to that after other anastomoses. Reportedly, soft pancreatic tissue is a strong risk factor for the development of PF (19). In the study by Sert et al. (19), PF was observed in 18 patients (75%) with soft pancreatic tissue, with the texture of pancreatic tissue being significantly associated with PF development (p<0.001). In the present study, we attempted to perform the same procedure in all patients. For this reason, we could not compare the details of operation because the surgical techniques were similar in both the groups.

Pancreatic duct stenting during anastomosis formation has been discussed in the literature (21,22). This was examined in a randomised trial by Winter et al. (22); they randomised 238 patients undergoing PD with or without internal pancreatic duct stent, with the endpoint being postoperative pancreatic fistula (POPF) development. The authors concluded that internal pancreatic duct stenting did not alter the incidence of POPF. Pancreatic duct drainage was also examined with external stents. In a study by Poon et al. (23), 120 patients undergoing PD with PJ duct-to-mucosa anastomosis were prospectively randomised to an external stent or no-stent group. Patients in the stent group had a significantly lower PF rate than those in the no-stent group (6.7% vs 20%, p=0.032) (23). In our routine practice, we use internal stents. In the present study, we used the same application in all patients; therefore, we could not evaluate the effect of stents.

In studies where the pancreatic duct is blocked with biological substances, the results have been reported to be very successful. For example, a group of authors have suggested that a possible anastomotic leak could be treated with fibrin glue around the anastomosis during surgery (24). However, we did not use these methods in our patients.

Despite the controversy regarding the preventive and therapeutic value of abdominal drains after pancreatic resection, several studies have highlighted the importance of drainage analysis for the prediction of POPF (25,26). In our study, we placed prophylactic abdominal drains in all patients. We believe that these abdominal drains contributed in the prediction of the incidence of PF development.

Reportedly, PF is associated with increased morbidity, mortality and longer hospital stay as well as additional cost. As pancreatic fluid is an enzymatically active and aggressive substance, it causes erosions in the surrounding tissue and may affect the intestinal, bile duct or vascular walls. PF has been associated with other non-fistula complications, particularly delayed gastric emptying, ileus, wound infection, intraabdominal abscess, pancreatitis, bleeding and sepsis. It has also been associated with significantly increased hospital costs and the rate of reoperation and admission to hospital (10,27).

In their series, Schmidt et al. (15) found that sepsis (21% vs 5%, p<0.001) and other infection-related complications were higher in the group with PF than in the group without PF. Similarly, Chen et al. (3) reported higher rates of post-operative haemorrhage in the group with PF development (33% vs 1.3, p=0.000). In both these studies, the length of hospital stay was longer in the PF group. Similarly, in our study, the incidence of post-operative complications other than PF was higher in the PF group than in the other group (58.1% vs 21.8%, p=0.000). Accordingly, the duration of hospitalisation in the PF group increased by 9 days compared to that in the other group. Prolonged hospitalisation might result in additional medical costs and a decrease in the quality of patient care. In our study, the post-operative complication rate was higher in the PF group, and the presence of post-operative complications other than PF was an independent risk factor for PF development. From this point of view, PF might increase post-operative complications, which may play a role in the development of PF.

PF development increases post-operative mortality through the complications it causes (28). In addition, post-operative complications in patients with cancer delay their oncological treatment and sometimes make treatment impossible. Accordingly, PF development is expected to increase post-operative mortality rates and decrease long-term survival. In our study, although the 30-day and 90-day mortality rates were higher in the PF group, the difference was not statistically significant. Regarding the causes of mortality in patients who developed PF, we noted that septic complications were more common (22.6% vs 10.5%, p=0.024). In our study, PF significantly reduced long-term survival (23 vs 38 months, p=0.024).

Study Limitations

Our study is limited by the small number of patients, the single-centre nature and the operative variables and features of the pancreatic tissue that were not adequately evaluated. However, we believe that our study will provide detailed data on PF to the literature.

Conclusion

In conclusion, we found that localisation, stage and diameter of the tumour were related to PF development. In addition, the development of PF contributed to post-operative complications, which consequently prolonged hospital stay. PF also significantly shortened long-term survival. Thus, PF formation after PD poses a great threat to patients' life and health. Therefore, an early estimation of PF development and the investigation of related risk factors are of great importance in preventing PF and its complications.

Ethics

Ethics Committee Approval: Owing to the retrospective design of the study, an ethics committee approval was not received.

Informed Consent: Due to the retrospective design of the study, patient consent was not obtained.

Peer-review: Externally peer reviewed.

Authorship Contributions

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