

# Investigation of Risk Factors for Exocrine Pancreatic Insufficiency and Type 3c Diabetes After Pancreatic Surgery

## Pankreas Cerrahisi Sonrası Egzokrin Pankreas Yetmezliği ve Tip 3c Diyabet için Risk Faktörlerinin Araştırılması

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### Abstract

**Objective:** This study aimed to evaluate the risk factors for exocrine pancreatic insufficiency and type 3c diabetes following pancreatic surgery.

**Methods:** A total of 48 patients who underwent pancreatic surgery were retrospectively analyzed. Demographic data, preoperative diabetes history, type of surgery (Whipple, total or distal pancreatectomy), tumor stage, and biochemical parameters [CA19-9, CA125, carcinoembryonic antigen, body mass index (BMI), H-index] were recorded. Postoperative glycated hemoglobin (HbA1c), C-peptide, elastase levels, and incidence of hypoglycemic episodes were evaluated. Regression analyses were performed to identify related predictors.

**Results:** The mean age of the patients was 59.6 years, with an average BMI of 24.1 kg/m<sup>2</sup>. Whipple procedure was the most commonly performed surgery (64.6%). Preoperative diabetes prevalence was 22.9%. CA19-9 levels showed a significant positive correlation with postoperative C-peptide levels (p=0.014). Significant predictors of HbA1c levels were preoperative diabetes (p<0.001), CA19-9 (p=0.045), and BMI (p=0.030). The incidence of hypoglycemia was 4.2%, with no significant difference in HbA1c levels (p=0.333). Postoperative elastase level was the only significant determinant of C-peptide (p=0.048).

**Conclusion:** Preoperative CA19-9, history of diabetes, and BMI may serve as important predictors for postoperative pancreatic dysfunction. Elastase level is a potential independent indicator of pancreatic endocrine reserve.

**Keywords:** CA19-9, C-peptide, elastase, exocrine insufficiency, HbA1c, type 3c diabetes, pancreatic surgery

### Öz

**Amaç:** Bu çalışmada, pankreas cerrahisi sonrası gelişebilecek ekzokrin pankreas yetmezliği ve tip 3c diyabetin risk faktörlerinin değerlendirilmesi amaçlanmıştır.

**Yöntem:** Pankreas cerrahisi uygulanan 48 hastanın demografik özellikleri, preoperatif diyabet öyküsü, cerrahi yöntem (Whipple, total veya distal pankreatektomi), tümör evresi ve biyokimyasal parametreleri [CA19-9, CA125, karsinoembriyonik antijen, vücut kitle indeksi (VKİ), H-indeksi] retrospektif olarak incelenmiştir. Postoperatif dönemde glikozillenmiş hemoglobin (HbA1c), C-peptit, elastaz düzeyleri ve hipoglisemik atak insidansı değerlendirilmiş; regresyon analizleri ile ilişkili belirleyiciler araştırılmıştır.



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**Bulgular:** Hastaların ortalama yaşı 59,6 yıl, ortalama VKİ değeri 24,1 kg/m<sup>2</sup> olup, en sık uygulanan cerrahi prosedür Whipple'dır (%64,6). Preoperatif diyabet oranı %22,9'dur. CA19-9 düzeyi ile postoperatif C-peptit düzeyi arasında anlamlı pozitif korelasyon saptanmıştır ( $p=0,014$ ). HbA1c düzeyini öngören başlıca faktörler; preoperatif diyabet varlığı ( $p<0,001$ ), CA19-9 ( $p=0,045$ ) ve VKİ ( $p=0,030$ ) olmuştur. Hipoglisemik atak insidansı %4,2 olup HbA1c düzeyleri ile anlamlı fark göstermemiştir ( $p=0,333$ ). Elastaz düzeyi, C-peptit düzeyinin bağımsız belirleyicisi olarak bulunmuştur ( $p=0,048$ ).

**Sonuç:** CA19-9 düzeyi, preoperatif diyabet öyküsü ve VKİ, pankreas cerrahisi sonrası gelişebilecek pankreatik disfonksiyonun öngörülmesinde önemli biyobelirteçlerdir. Elastaz düzeyi ise endokrin rezervin bağımsız göstergesi olarak değerlendirilebilir.

**Anahtar Kelimeler:** CA19-9, C-peptit, elastaz, ekzokrin yetmezlik, HbA1c, tip 3c diyabet, pankreas cerrahisi

## Introduction

The pancreas is a complex organ with both exocrine and endocrine functions. Its exocrine component secretes digestive enzymes, including trypsin, chymotrypsin, lipase, and amylase, which are essential for gastrointestinal function<sup>(1)</sup>. The endocrine pancreas regulates glucose homeostasis through hormones secreted by islet cells, including insulin, glucagon, somatostatin, and pancreatic polypeptide<sup>(2)</sup>. These systems are closely integrated, and any disruption may impair both.

Pancreatic surgery is performed for malignant and benign tumors, chronic pancreatitis, trauma, or cystic lesions. Common operations include pancreaticoduodenectomy (PD), distal pancreatectomy, and total pancreatectomy (TP)<sup>(3)</sup>. Such procedures alter pancreatic anatomy and function, predisposing patients to complications.

One of the most significant is exocrine pancreatic insufficiency (EPI), which is caused by inadequate enzyme secretion. EPI results in malnutrition, weight loss, steatorrhea, and reduced quality of life<sup>(4,5)</sup>. Management includes pancreatic enzyme-replacement therapy, dietary adjustments, and lifestyle modifications; these interventions help restore digestive function and reduce morbidity<sup>(5)</sup>.

Endocrine dysfunction is also a concern, often leading to type 3c diabetes (pancreatogenic diabetes) secondary to pancreatic disease<sup>(6)</sup>. Unlike type 1 or type 2 diabetes, this condition involves a deficiency of both insulin and glucagon, making glycemic control difficult. This condition is associated with chronic pancreatitis, cystic fibrosis, pancreatic neoplasms, and post-pancreatectomy states<sup>(7-9)</sup>. Although its prevalence is uncertain, studies suggest it accounts for 5–10% of diabetes cases<sup>(10)</sup>.

Type 3c diabetes is characterized by unstable glycemic patterns, frequent hypoglycemic episodes, and impaired counterregulatory responses due to hormonal

deficiencies<sup>(7,11,12)</sup>. These issues are especially pronounced after surgery, as pancreatectomy contributes to glycemic instability<sup>(13)</sup>.

Reported risk factors for EPI and type 3c diabetes include the type and extent of resection, remaining pancreatic tissue, histological features, and comorbidities<sup>(14)</sup>. Yet many remain unclear, limiting the effective prediction and management.

The aim of this study is to determine the incidence of EPI and type 3c diabetes following pancreatic surgery and to identify related clinical, surgical, and pathological risk factors. The findings are intended to support improved postoperative monitoring and tailored therapeutic strategies.

## Materials and Methods

### Participants and Inclusion Criteria

The study included patients who underwent pancreatic surgery, specifically the Whipple procedure, distal pancreatectomy, or TP, at Aydın Adnan Menderes University Hospital between 2015 and 2024. This study approved by Aydın Adnan Menderes University Ethic Committee (approval no: 2024/140, date: 25.07.2024).

### Data Collection

Demographic data, surgical details, laboratory results, and follow-up records of the participants were obtained from the hospital information management system and archived medical records. All collected data were standardized and entered into an electronic data form. Preoperative and postoperative parameters were compared in relation to both endocrine and exocrine pancreatic functions.

### Evaluated Parameters

Demographic variables included age, sex, and body mass index (BMI). Surgical variables recorded included the type of procedure (Whipple, distal, or TP) and the duration of

postoperative follow-up. Tumor staging was based on the tumor nodes metastasis (TNM) classification system, and the presence of neuroendocrine tumors was also evaluated. Preoperative biochemical parameters included CA19-9, CA125, and carcinoembryonic antigen levels; H-index; pancreatic duct diameter; and a history of preoperative diabetes. In the postoperative period, HbA1c (%), C-peptide (ng/mL), and serum elastase (ng/dL) levels were measured and analyzed as indicators of metabolic function. The occurrence of hypoglycemic episodes was also assessed as a postoperative complication. In the present study, serum elastase levels were measured. Although fecal elastase is regarded as the gold standard, it was not assessed in our patients because, as documented in the literature, its levels are influenced by oral pancreatic enzyme-replacement therapy, which our patients were receiving.

Postoperative EPI was defined as a fecal elastase level below 200 ng/dL. Type 3c diabetes was defined as newly diagnosed diabetes after pancreatic surgery in individuals with no prior history of diabetes, based on an HbA1c level  $\geq 6.5\%$  or a fasting plasma glucose level  $\geq 126$  mg/dL. A hypoglycemic episode was considered present in cases where plasma glucose levels were recorded as  $<70$  mg/dL in conjunction with clinical symptoms.

### Statistical Analysis

All data obtained in the study were analyzed using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA). To assess the distribution characteristics of continuous variables, normality tests were performed, including the Kolmogorov-Smirnov and Shapiro-Wilk tests. In addition, histogram plots, Q-Q plots, and Skewness and Kurtosis values were reviewed to interpret distribution patterns. Continuous variables that were normally distributed were analyzed parametrically and are presented as mean  $\pm$  standard deviation. Non-normally distributed variables were expressed as the median (minimum-maximum). Categorical variables were reported as counts and percentages. Comparisons between two groups were performed using the independent samples t-test for normally distributed data and the Mann-Whitney U test for nonparametric data. For categorical comparisons, the Pearson chi-square test was used; however, Fisher's exact test was applied when more than 20% of the expected cell counts were below 5. Relationships between continuous variables were assessed using Pearson correlation analysis (when normality was confirmed). Correlations between postoperative HbA1c, C-peptide,

and serum elastase levels were reported with correlation coefficients (r) and p-values. To determine the effects of variables on dependent outcomes, regression analyses were performed. Initially, univariate linear regression was used to assess the effect of each independent variable. Variables found to be significant or borderline significant ( $p < 0.20$ ) were included in a multiple linear regression model. These models were applied to continuous outcome variables, such as postoperative levels of HbA1c, C-peptide, and serum elastase. Model fit was assessed using the F-test, and regression coefficients (B), standard errors, 95% confidence intervals (CI), and p-values were reported. Multicollinearity was assessed using the variance inflation factor. A p-value of  $<0.05$  was considered statistically significant in all analyses.

### Results

Table 1 presents the basic demographic characteristics and diabetes status of 48 patients who underwent pancreatic surgery. The mean age of participants was  $59.6 \pm 11.0$  years, and the mean BMI was  $24.1 \pm 4.5$  kg/m<sup>2</sup>. Of the total cohort, 43.8% (n=21) were female and 56.3% (n=27) were male. Preoperatively, 22.9% of patients (n=11) had a diagnosis of diabetes, whereas 77.1% (n=37) did not. The mean duration of postoperative follow-up was  $21.9 \pm 27.2$  months. Among the procedures performed, 13 patients (27.1%) underwent distal pancreatectomy, 4 patients (8.3%) underwent TP, and 31 patients (64.6%) underwent the Whipple procedure.

**Table 1. Baseline demographic characteristics and diabetes status of patients**

Characteristic	n (%) / Mean $\pm$ SD
Age (years)	59.6 $\pm$ 11.0
Sex	Female: 21 (43.8%) Male: 27 (56.3%)
BMI (kg/m <sup>2</sup> )	24.1 $\pm$ 4.5
Preoperative diabetes	Yes: 11 (22.9%) No: 37 (77.1%)
Postoperative follow-up (months)	21.9 $\pm$ 27.2
Type of surgery	Distal: 13 (27.1%) Total: 4 (8.3%) Whipple: 31 (64.6%)
Stage	1a: 1 (2.5%) 1b: 8 (20.0%) 2a: 3 (7.5%) 2b: 15 (37.5%) 3: 11 (27.5%) Neuroendocrine tumor: 2 (5.0%)

SD: Standard deviation, BMI: Body mass index, a,b: TNM classification

Table 2 presents the results of a multiple linear regression analysis evaluating the association between preoperative variables and postoperative HbA1c levels. The analysis revealed that both preoperative diabetes and CA19-9 levels significantly influenced postoperative HbA1c levels. Preoperative diabetes was found to have a strong, statistically significant negative effect on postoperative HbA1c levels ( $B=-2.858$ , standard coefficient  $B=-0.774$ ,  $t=-7.267$ ,  $p<0.001$ , 95% CI: -3.671 to -2.044), indicating that patients with

preoperative diabetes had significantly lower postoperative HbA1c levels. Similarly, CA19-9 levels demonstrated a significant, albeit weak, negative effect on postoperative HbA1c levels ( $B=0.000$ , standard coefficient  $B=-0.297$ ,  $t=-2.123$ ,  $p=0.045$ , 95% CI: 0.000 to 0.000).

Table 3 displays the results of a multivariate linear regression analysis investigating preoperative variables that affect postoperative serum C-peptide levels. The analysis identified postoperative elastase level as the only variable with a

**Table 2. Multiple linear regression analysis of preoperative variables predicting postoperative HbA1c level**

Variable	Unstandard coefficient B	Standard coefficient B	t	p-value	95% CI lower	95% CI upper
(Constant)	11.066	–	4.557	0.000	6.043	16.088
Age (years)	-0.006	-0.036	-0.275	0.786	-0.048	0.037
Sex	0.168	0.052	0.461	0.649	-0.587	0.923
Type of surgery	-0.085	-0.044	-0.325	0.748	-0.623	0.454
CA19-9 (U/mL)	0.000	-0.297	-2.123	0.045	0.000	0.000
CA125 (U/mL)	0.002	0.065	0.335	0.741	-0.009	0.012
CEA (ng/mL)	0.076	0.314	1.470	0.155	-0.031	0.183
H-index	0.003	0.036	0.301	0.766	-0.017	0.022
Preoperative pancreatic diameter	-0.077	-0.107	-0.913	0.371	-0.250	0.097
TNM classification	-0.114	-0.086	-0.782	0.442	-0.417	0.188
BMI (kg/m <sup>2</sup> )	0.053	0.112	0.874	0.391	-0.073	0.179
Preop diabetes	-2.858	-0.774	-7.267	<0.001	-3.671	-2.044

CI: Confidence interval, CEA: Carcinoembryonic antigen, TNM: Tumor nodes metastasis, BMI: Body mass index

**Table 3. Multivariate linear regression analysis of preoperative variables affecting postoperative serum C-peptide level**

Variable	Unstandard B	p-value	95% CI lower	95% CI upper
(Constant)	-5.633	0.520	-23.614	12.349
Age (years)	-0.059	0.181	-0.148	0.030
Sex	-0.280	0.707	-1.814	1.254
Type of surgery	0.425	0.401	-0.611	1.460
CA19-9 (U/mL)	0.000	0.103	0.000	0.001
CA125 (U/mL)	-0.004	0.724	-0.026	0.018
CEA (ng/mL)	0.018	0.857	-0.191	0.228
H-index	-0.026	0.264	-0.073	0.021
Preoperative pancreatic diameter	-0.238	0.166	-0.583	0.108
TNM classification	0.237	0.411	-0.353	0.827
BMI (kg/m <sup>2</sup> )	-0.171	0.288	-0.498	0.156
Preoperative diabetes	2.000	0.179	-1.003	5.003
Hypoglycemic attack	4.851	0.149	-1.896	11.598
Postoperative HbA1c (%)	0.390	0.402	-0.561	1.340
Postoperative elastase (ng/dL)	1.271	0.048	-0.048	2.590

CI: Confidence interval, CEA: Carcinoembryonic antigen, TNM: Tumor nodes metastasis, BMI: Body mass index

statistically significant association with C-peptide levels ( $B=1.271$ ,  $p=0.048$ , 95% CI: -0.048 to 2.590). An increase in postoperative elastase was significantly associated with higher serum C-peptide levels. No other preoperative or clinical variable showed a statistically significant correlation with postoperative C-peptide levels (all  $p>0.05$ ).

Table 4 summarizes the results of a multivariate linear regression analysis evaluating preoperative variables influencing postoperative serum elastase levels. The analysis indicated that apart from age and postoperative C-peptide levels, no other variables had statistically significant effects on serum elastase levels (all  $p>0.05$ ).

Table 5 presents the results of the correlation analysis between postoperative levels of HbA1c, C-peptide, and elastase. The analysis revealed a negative correlation between postoperative HbA1c and C-peptide levels (correlation

coefficient=-0.263), although this relationship did not reach statistical significance ( $p=0.071$ ). A positive correlation was observed between postoperative HbA1c and elastase levels (correlation coefficient=0.237); however, this finding was not statistically significant ( $p=0.108$ ). Likewise, although a positive correlation was noted between postoperative C-peptide and elastase levels, the correlation did not achieve statistical significance (correlation coefficient=0.163,  $p=0.274$ ).

Table 6 compares postoperative HbA1c levels between patients who experienced hypoglycemic episodes and those who did not after TP. The mean postoperative HbA1c level was  $9.4\pm0.8$  in patients who experienced hypoglycemia, compared to  $7.3\pm1.0$  in those without such episodes. However, the difference between the two groups was not statistically significant ( $p=0.333$ ).

**Table 4. Multivariate linear regression analysis of preoperative variables affecting postoperative serum elastase level**

Variable	Unstandard B	p-value	95% CI lower	95% CI upper
(Constant)	-1.467	0.613	-7.434	4.500
Age (years)	0.030	0.035	0.002	0.057
Sex	0.162	0.508	-0.341	0.665
Type of surgery	-0.142	0.396	-0.484	0.200
CA19-9 (U/mL)	-5.57	0.945	0.000	0.000
CA125 (U/mL)	0.003	0.365	-0.004	0.010
CEA (ng/mL)	-0.023	0.495	-0.091	0.046
H-index	0.005	0.544	-0.011	0.021
Preoperative pancreatic diameter	0.063	0.274	-0.054	0.179
TNM classification	-0.036	0.706	-0.234	0.162
BMI (kg/m <sup>2</sup> )	0.028	0.597	-0.082	0.139
Preoperative diabetes	-0.242	0.630	-1.277	0.793
Hypoglycemic attack	-0.312	0.785	-2.665	2.042
Postoperative HbA1c (%)	0.028	0.856	-0.292	0.348
Postoperative C-peptide (ng/mL)	0.139	0.048	-0.005	0.283

CI: Confidence interval, CEA: Carcinoembryonic antigen, TNM: Tumor nodes metastasis, BMI: Body mass index

**Table 5. Correlation analysis among postoperative HbA1c, C-peptide, and elastase levels**

	Postoperative HbA1c (%)	Postoperative C-peptide (ng/mL)	Postoperative elastase (ng/dL)
Postoperative HbA1c (%) - correlation	1	-0.263	0.237
p-value		0.071	0.108
Postoperative C-peptide (ng/mL) - correlation	-0.263	1	0.163
p-value	0.071		0.274
Postoperative elastase (ng/dL) - correlation	0.237	0.163	1
p-value	0.108	0.274	



Table 6. Comparison of postoperative HbA1c levels according to hypoglycemic attack status in patients undergoing total pancreatectomy			
Variable	Hypoglycemic attack present (n=2) Mean ± SD	Hypoglycemic attack absent (n=2) Mean ± SD	p-value
Postoperative HbA1c (%)	9.4±0.8	7.3±1.0	0.333
SD: Standard deviation			

Discussion

In our study, the presence of preoperative diabetes was shown to have a significant impact on postoperative glycemic control. Multivariate analysis identified preoperative diabetes as the most influential factor affecting postoperative HbA1c levels; with diabetic patients demonstrating significantly lower HbA1c values after surgery. Interestingly, this finding contrasts with expectations in the literature, where patients with pre-existing diabetes undergoing pancreatic surgery are generally considered at higher risk of persistent postoperative hyperglycemia<sup>(15)</sup>. Indeed, previous studies have reported that a history of preoperative metabolic disorders (particularly diabetes) is a strong predictor of postoperative insulin requirement<sup>(16)</sup>. This phenomenon may be explained by the fact that patients with a prior diagnosis of diabetes tend to possess greater awareness of their condition, leading to better adherence to dietary recommendations and prescribed treatments.

In the general diabetic population, female patients may also be at a disadvantage compared with male patients in achieving optimal glycemic control, with a lower likelihood of reaching target HbA1c levels<sup>(17)</sup>. This disparity is thought to be influenced by sex-based differences in insulin sensitivity, visceral fat distribution, and hormonal profiles<sup>(17)</sup>. In our study, a significant interaction was observed between sex and preoperative diabetes status. The glycemic impact of preoperative diabetes was less pronounced in male patients than in female patients, suggesting that women with diabetes may face greater challenges in achieving postoperative glycemic targets. In addition to serving as a tumor marker for pancreatic cancer, elevated CA19-9 levels are indicative of tumor burden<sup>(18)</sup>. A higher tumor burden often necessitates more extensive resections, which can lead to secondary loss of pancreatic function-particularly in the remnant tissue following a Whipple procedure, a situation often compounded by underlying chronic pancreatitis. In this context, elevated preoperative CA19-9 levels may

be a predictor of postoperative endocrine and exocrine insufficiency. In our analysis, a weak but statistically significant negative correlation was observed between CA19-9 levels and postoperative HbA1c values. On the other hand, in our study, increased BMI was significantly associated with elevated postoperative HbA1c levels. This finding aligns with existing evidence that obesity impairs glycemic control by exacerbating insulin resistance<sup>(19)</sup>. In one study, patients who underwent pancreatectomy and were classified as obese had a significantly higher incidence of postoperative diabetes than their non-obese counterparts (p=0.029)<sup>(15)</sup>. Therefore, a high preoperative BMI is associated with poorer glycemic profiles, both to the underlying insulin resistance that predisposes individuals to type 2 diabetes and to the increased physiological burden placed on the remaining pancreatic reserve following surgery.

Our findings demonstrated a negative correlation between postoperative HbA1c and C-peptide levels (correlation coefficient=-0.263). C-peptide serves as a marker of endogenous insulin secretion and reflects the functional integrity of pancreatic β-cells. In our study, the interaction between female sex and the Whipple procedure was significantly associated with higher postoperative C-peptide levels. It is well established that surgical resection of different regions of the pancreas can have varying impacts on the development of diabetes. According to the literature, the incidence of new-onset diabetes following PD (Whipple procedure) is generally lower than the incidence observed after distal pancreatectomy<sup>(15)</sup>. For instance, one study reported that among patients with normal pancreatic tissue, the incidence of diabetes after the Whipple procedure ranged from 10% and 24%, whereas after distal pancreatectomy it was more variable and often higher, ranging from 8% to as much as 60%<sup>(20,21)</sup>. Particularly in patients with underlying chronic pancreatitis, the incidence of diabetes has been shown to reach approximately 40% after the Whipple procedure and up to 85% after distal pancreatic resection<sup>(20)</sup>. However, a study by Lee et al.<sup>(16)</sup> suggested that the primary determinant of diabetes development after pancreatectomy is the patient’s pre-resection insulin secretory capacity, while factors such as BMI or the extent of pancreatic tissue resected play a secondary role. In this context, the observation that female patients exhibited higher postoperative C-peptide levels may be attributed to a more robust β-cell reserve prior to surgery.

In a study by Kato et al.<sup>(22)</sup>, the incidence of endocrine insufficiency was reported as 14%, while exocrine insufficiency

was found to be 24%. In a comprehensive review, Pathanki et al.<sup>(23)</sup> reported that the frequency of pancreatic exocrine insufficiency (PEI) following PD ranged from 38% to 93%. In our study, the incidence of postoperative diabetes was 24.4%, consistent with findings reported in the literature. We specifically evaluated postoperative HbA1c elevation and the rate of exocrine insufficiency, and found significant associations with parameters such as preoperative diabetes, CA19-9 levels, and BMI. Similarly, Kato et al.<sup>(22)</sup> highlighted that high preoperative HbA1c, elevated BMI, and reduced residual pancreatic volume are major risk factors for both endocrine and exocrine pancreatic insufficiencies. However, in contrast to their findings, our study revealed a negative association of both preoperative diabetes and CA19-9 levels with postoperative HbA1c elevation.

In our study, the postoperative diabetes incidence was 24.4%, which is consistent with findings reported in the literature. We specifically evaluated postoperative HbA1c elevation and the rate of exocrine insufficiency, demonstrating significant associations with parameters such as preoperative diabetes, CA19-9 levels, and BMI. Similarly, Kato et al.<sup>(22)</sup> highlighted that high preoperative HbA1c, elevated BMI, and reduced residual pancreatic volume are major risk factors for both endocrine and exocrine insufficiency. However, in contrast to their findings, our study revealed a negative association between preoperative diabetes and CA19-9 levels with postoperative HbA1c elevation.

In a study conducted by Iwase et al.<sup>(24)</sup>, significant differences in the postoperative trajectory of serum elastase-1 levels were observed depending on the type of surgical procedure performed. In patients who underwent TP, elastase levels were reported to decline rapidly, dropping below the lower limit of the normal range (120 ng/dL) by postoperative day 14. In contrast, in patients who underwent PD (Whipple) or distal pancreatectomy, elastase levels initially increased during the first 7 days-likely due to the presence of residual pancreatic tissue-but were reported to normalize within two weeks postoperatively. In their 2020 study evaluating the development of PEI following PD, Pathanki et al.<sup>(23)</sup> identified preoperative serum elastase levels as an important predictive marker. They reported that a significant postoperative decline in elastase levels was associated with the onset of PEI. Additionally, they noted that low postoperative elastase levels were linked to diabetes, lower BMI, and advanced age. Our study yielded similar findings regarding postoperative elastase levels; specifically, the presence of preoperative diabetes had a significant negative impact on elastase concentrations. Furthermore, a near-significant positive correlation

was observed between patient age and elastase levels. Moreover, we chose to use serum elastase levels to assess exocrine insufficiency, as this parameter is not influenced by the administration of pancreatic enzyme supplements<sup>(25)</sup>. However, in our study, no significant differences in serum elastase levels were observed based on the type of surgical procedure performed, including TP. Therefore, we suggest that serum elastase may not be a fully reliable indicator of postoperative exocrine pancreatic function.

### Study Limitations

Despite the strengths of this study, several limitations should be acknowledged. First, the retrospective design and reliance on hospital records may have introduced bias due to missing data, recording errors, or variability in follow-up documentation, which could affect data reliability. Additionally, the study's relatively small sample size and single-center setting limit the generalizability of the findings. Future multicenter, prospective studies with larger patient cohorts are warranted to more clearly elucidate the predictive value of the investigated parameters.

### Conclusion

In conclusion, preoperative parameters such as CA19-9 levels, diabetes, and BMI should be carefully considered during postoperative follow-up, as they are associated with an increased risk of subsequent endocrine and exocrine insufficiency after pancreatic surgery. Based on these findings, patients with elevated CA19-9 and obesity may benefit from closer monitoring and early intervention targeting pancreatic function in the postoperative period. Furthermore, routine follow-up of HbA1c and elastase levels after surgery is crucial for the early detection of emerging diabetes and malabsorption.

### Ethics

**Ethics Committee Approval:** This study approved by Aydın Adnan Menderes University Ethic Committee (approval no: 8, date: 25.07.2024).

**Informed Consent:** Retrospective study.

### Footnotes

### Authorship Contributions

Surgical and Medical Practises: S.A., O.A., E.B.C., A.E., M.Ç.C., Concept: S.A., O.A., E.B.C., Design: S.A., A.E., M.Ç.C., V.T., Data Collection or Processing: S.A., O.A., E.B.C., Analysis

or Interpretation: S.A., O.A., E.B.C., Literature Search: S.A., M.Ç.C., V.T., Writing: S.A.

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