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ORIGINAL ARTICLE

Retrospective evaluation of demographic data, clinical features and survival of patients with pancreatic cancer

Pankreas kanseri tanılı hastaların demografik verileri, klinik özellikleri ve sağkalım açısından retrospektif olarak değerlendirilmesi

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ABSTRACT • **Background and Aims:** This study aimed to evaluate the demographic characteristics, clinical features, and survival outcomes of patients diagnosed with pancreatic cancer. Additionally, patients diagnosed with pancreatic neuroendocrine tumors were included for comparative analysis. **Materials and Methods:** In this study, we retrospectively reviewed the records of 169 patients diagnosed with pancreatic cancer or pancreatic neuroendocrine tumors between January 1, 2011, and June 1, 2020, at Zonguldak Bülent Ecevit University Health Practice and Research Center. Demographic data, clinical characteristics, overall survival, and progression-free survival were analyzed. **Results:** Of the 169 patients, 152 (89.9%) had pancreatic cancer and 17 (10.1%) had pancreatic neuroendocrine tumors. The mean age at diagnosis was 60.7 years; 40.8% were female and 59.2% male. Median overall survival and progression-free survival for all patients were 11 and 6 months, respectively. In pancreatic cancer patients, overall survival was 10 months and progression-free survival 6 months, whereas in pancreatic neuroendocrine tumors patients, overall survival and progression-free survival were significantly longer (39 and 30 months, respectively). Eastern Cooperative Oncology Group performance status, body mass index, tumor-node-metastasis stage, surgery, and radiotherapy were significantly associated with overall survival and progression-free survival in both groups. In pancreatic cancer patients only, elevated carbohydrate antigen 19-9 levels and metastases (lymph node, liver, lung, peritoneum) negatively affected overall survival and progression-free survival. Factors such as alcohol/smoking habits, tumor size and location, chemotherapy, and biliary stenting showed no significant impact on survival in either group. **Conclusion:** Overall survival and progression-free survival were significantly worse in patients with pancreatic cancer compared with those with pancreatic neuroendocrine tumors. Consistent with the literature, advanced tumor-node-metastasis stage, poor ECOG performance status, and the presence of peritoneal metastasis at diagnosis had a statistically significant negative impact on both overall survival and progression-free survival in pancreatic cancer cases. In these patients, the presence of lymph node metastasis at diagnosis and elevated carbohydrate antigen 19-9 levels were found to negatively affect only overall survival. Although some studies have reported that biliary decompression provides an overall survival advantage in patients with pancreatic cancer, our study found no effect of biliary decompression on survival.

Key words: Pancreatic cancer, early stage, overall survival, progression-free survival

ÖZET • **Giriş ve Amaç:** Bu çalışmada, pankreas kanseri tanısı almış hastaların demografik verilerini, klinik özelliklerini ve sağkalım sürelerini analiz etmeyi amaçladık. Aynı zamanda, pankreatik nöroendokrin tümör tanısı almış hastalar da ayrı bir grup olarak çalışmaya dahil edilerek benzer analizler bu olgu grubu için de yapıldı. **Gereç ve Yöntem:** Bu çalışmada, 1 Ocak 2011 ile 1 Haziran 2020 tarihleri arasında Zonguldak Bülent Ecevit Üniversitesi Sağlık Uygulama ve Araştırma Merkezi'nde pankreas kanseri tanısıyla takip edilen 169 hastanın dosyaları retrospektif olarak incelendi. Hastaların demografik verileri, klinik özellikleri, genel sağkalım ve progresyonsuz sağkalım süreleri kaydedildi. **Bulgular:** Çalışmaya toplam 169 hasta dahil edildi; bunların 69'u (%40,8) kadın, 100'ü (%59,2) erkekti. Tanı anındaki ortalama yaş 60.78 yıl olarak bulundu. Ortanca sağkalım süresi 11 ay, progresyonsuz sağkalım süresi ise 6 ay olarak saptandı. Hastaların 152'sine (%89,9) pankreas kanseri, 17'sine (%10,1) ise pankreatik nöroendokrin tümör tanısı konulmuştu. Pankreas kanseri hastalarında genel sağkalım süresi 10 ay, progresyonsuz sağkalım süresi 6 ay iken; pankreatik nöroendokrin tümör hastalarında genel sağkalım 39 ay, progresyonsuz sağkalım 30 ay olarak bulundu. Hem pankreas kanseri hem de pankreatik nöroendokrin tümör hastalarında, ECOG performans durumu, vücut kitle indeksi, TNM evresi, cerrahi uygulanması ve radyoterapi alımı, sağkalım ve progresyonsuz sağkalım süreleriyle anlamlı şekilde ilişkili bulundu. Buna karşılık, sadece pankreas kanseri tanılı hastalarda karbonhidrat antijeni 19-9 düzeyleri ile lenf nodu, akciğer, karaciğer ve periton metastazlarının varlığı, sağkalım ve progresyonsuz sağkalım süreleri ile anlamlı şekilde ilişkiliydi. Alkol ve sigara kullanımı, tümör boyutu ve lokalizasyonu, kemoterapi alımı ve stent yerleştirilmesi, her iki grupta da sağkalım veya progresyonsuz sağkalım sürelerinde anlamlı bir fark göstermedi. **Sonuç:** Sağkalım ve progresyonsuz sağkalım süreleri, pankreatik nöroendokrin tümör hastalarına kıyasla pankreas kanseri hastalarında anlamlı derecede daha kötü saptandı. Literatürle uyumlu olarak, pankreas kanseri olgularında ileri tümör, nod, metaztaz evresi, kötü ECOG performans durumu ve tanı anında periton metastazı varlığı, hem sağkalım hem de progresyonsuz sağkalım üzerinde istatistiksel olarak anlamlı olumsuz etkiye sahipti. Bu hastalarda tanı anında lenf nodu metastazı varlığı ve yüksek karbonhidrat antijeni 19-9 düzeylerinin sadece sağkalım üzerinde olumsuz etkisi olduğu belirlendi. Bazı çalışmalarda biliyer dekompresyonun pankreas kanseri hastalarında genel sağkalım avantajı sağladığı bildirilmiş olsa da, bizim çalışmamızda biliyer dekompresyonun sağkalım üzerine herhangi bir etkisi saptanmadı.

Anahtar kelimeler: Pankreas kanseri, erken evre, genel sağ kalım, progresyonsuz sağ kalım

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INTRODUCTION

Worldwide, malignancies rank as the second most common cause of death after cardiovascular diseases (1). According to GLOBOCAN 2024 data, pancreatic cancer (PC) is the 12th most common cancer globally and the 7th leading cause of cancer-related mortality, with over 467,000 deaths annually. In Turkey, it ranks as the 8th most common cancer and is the 4th leading cause of cancer-related mortality after lung, colon, and gastric cancers (2). Based on Turkey's annual cancer statistics, the incidence of pancreatic cancer in 2016 was 5.7/100,000 in men, making it the tenth most common cancer, and 3.6/100,000 in women, ranking as the twelfth most common cancer (1). The prevalence of pancreatic cancer is approximately 1.5 times higher in men than in women (3). For both genders, the incidence of pancreatic cancer increases with age, peaking after 70 years. More than 90% of cases occur in individuals over the age of 55 (4). Pancreatic ductal adenocarcinoma (PDAC) and its variants account for 85-90% of all pancreatic neoplasms; therefore, the term "pancreatic cancer" generally refers to PDAC (5). Since pancreatic cancer is typically asymptomatic until diagnosis, most patients are in advanced stages at the time of detection. The 1-year survival rate for pancreatic cancer is below 25%, while the 5-year survival rate is approximately 5-6% (6). The median survival time is less than 12 months, with a mortality rate of nearly 99%. Less than 10% of patients are diagnosed at an early stage and are eligible for surgical resection. In these cases, survival is notably longer (7).

MATERIALS and METHODS

This retrospective study was conducted by analyzing the data of 169 patients diagnosed with pancreatic cancer, who were followed at the Gastroenterology and Medical Oncology outpatient clinics of Zonguldak Bülent Ecevit University Health Application and Research Center between January 1, 2011, and June 1, 2020. Patients without pathological diagnosis and those with incomplete data were not included in the study. The analyzed variables included socio-demographic characteristics, clinical features, laboratory and pathological findings, tumor localization, treatment modalities, metastasis status, survival outcomes, and patient status (live or dead). The staging was conducted based on the 7th edition of the American Joint Committee on Cancer (AJCC) staging system.

Statistical analyses were performed using SPSS 21.0 (IBM). Descriptive statistics for categorical variables were presented as frequencies and percentages, while numerical variables were summarized using mean, median, minimum, maximum, and standard deviation values. Some graphical representations of demographic variables were created using Microsoft Excel.

Non-parametric Mann-Whitney U tests were used for comparisons between two groups. General and progression-free survival analyses were conducted using the Kaplan-Meier method, and survival curves were generated. The Log-Rank test was used to assess differences in survival times between groups. Cox regression was used to examine the relationship between survival time and multiple variables. Statistical significance was set at $p < 0.05$ for all analyses.

This study was approved with Zonguldak Bülent Ecevit University Non-Interventional Clinical Research Ethics Committee dated 20.06.2020 and numbered 2020/13.

RESULTS

Of the patients included in the study 59.2% (n = 100) were male. The mean age at diagnosis was 59.7 ± 11.68 years for men and 62.33 ± 13.68 years for women, with no significant difference in the age at diagnosis between genders (p = 0.255) (Table 1).

Table 1 Patient characteristics

Parameters		Number (n)	Percentage (%)
Age (mean)	60.7 years		
Overall survival (median, months)	11 months		
Progression-free survival (median, months)	6 months		
Gender			
Male		100	59.2
Female		69	40.8
Pathological subtype			
PC		152	89.9
PNET		17	10.1
Current status			
Alive		34	20.1
Dead		135	79.9
Smoking			
Yes		107	63.3
No		62	36.7
Alcohol			
Yes		34	20.2
No		135	79.8
ECOG-PS			
ECOG 0 - 1		116	68.64
ECOG 2		35	20.71
ECOG 3		11	6.51
ECOG 4		7	4.14
Stage			
Stage 1		10	5.9
Stage 2		21	12.4
Stage 3		51	30.2
Stage 4		87	51.5
Tumor size			
< 2 cm		12	7.1
2 - 5 cm		107	63.3
> 5 cm		50	29.6
Tumor localization			
Head		106	62.7
Corpus		45	26.6
Tail		18	10.7
Chemotherapy regimen			
No		29	17.2
Gemsitabin- based regimens		93	55.0
5-Fluorouracil based regimen		38	22.5
Other regimen		9	5.3
Radiotherapy treatment			
Yes		44	26
No		125	74
Surgery			
Yes		99	58.6
No		70	41.4
Surgical type			
Whipple		67	39.6
Other procedures		32	18.9
Biliary stenting			
Yes		54	32
No		115	68

PC: Pancretaic cancer; PNET: Pancreatic neuroendocrine tumors; ECOG-PS: Eastern Cooperative Oncology Group Performance Status; ECOG: Eastern Cooperative Oncology Group.

The overall survival (OS) for all patients had a median of 11 months. The median OS was 12 months for men and 10 months for women, with no significant difference between genders in OS durations ($p = 0.781$). The progression-free survival (PFS) had a median of 6 months, and this duration was 6 months for both men and women, with no significant difference in PFS based on gender ($p = 0.700$). Of the 169 patients included in the study, 152 (89.9%) had a pathological diagnosis of PC, while 17 (10.1%) were diagnosed with PNET. In PNET patients, the median OS was 39 months, and the median PFS was 30 months. In PC patients, the median OS was 10 months, and the median PFS was 6 months. There was a significant difference in OS and PFS durations between PNET and PC patients ($p < 0.05$).

Of the patients included in the study, 34 (20.2%) had previously used alcohol, while 135 (79.8%) had not. A total of 107 patients (63.3%) had smoked or were still smoking at some point in their lives, while 62 patients (36.7%) had never smoked. There was no statistically significant difference in OS and PFS between both PC and PNET patients based on alcohol and smoking use. In our study, a family history was present in a total of 4 patients, with 2 having a history in their mothers and 2 in their fathers.

In the analysis based on body mass index (BMI), in the PC group, the median OS was 7 months for patients with BMI < 18, 11 months for those with BMI 18 - 25, and 10 months for those with BMI ≥ 25. There was a significant difference in OS durations based on BMI in the PC group ($p = 0.016$). Similarly, for PFS, the median was 3 months for patients with BMI < 18, 6 months for those with BMI 18 - 25, and 6 months for those with BMI ≥ 25. A significant difference in PFS durations based on BMI was also observed in the PC group ($p = 0.016$ for both OS and PFS). In the PNET group, the median OS was 4 months for patients with BMI < 18 and 29 months for those with BMI ≥ 25. Similarly, for PFS, the median was 3 months for patients with BMI < 18 kg/m^2 and 13 months for those with BMI ≥ 25. There was a significant difference in both OS and PFS durations based on BMI in the PNET group ($p = 0.001$ for both OS and PFS).

In the evaluation based on ECOG performance status, in PC patients, the median OS was 13 months for those with ECOG 0-1, while it was 1 month for those with ECOG 4. In PNET patients, the median OS was 33 months for those with ECOG 0-1, and 1 month for those with ECOG 4. ECOG performance status created a significant difference in both OS and PFS ($p < 0.001$). For more details, see Table 2 for PC patients and Table 3 for PNET patients.

In the evaluation based on tumor size (< 2 cm, 2 - 5 cm, and > 5 cm), no significant difference in OS or PFS was found in either the PC or PNET group. Regarding the tumor's localization in the pancreas, 62.7% of patients (96 with PC, 10 with PNET, total 106) had tumors in the head of the pancreas, 26.6% (41 with PC, 4 with PNET, total 45) in the body, and 10.7% (15 with PC, 3 with PNET, total 18) in the tail. Similarly, no significant difference in OS or PFS was observed based on tumor localization in either the PC or PNET group.

According to the tumor, node, metastasis (TNM) stage, in PC patients, the median OS was 17 months for stage 1, while it decreased to 7 months for stage 4. In PNET patients, these durations were 40 months for stage 1 and 14 months for stage 4. Regarding PFS, in PC patients, the median PFS was 13 months for stage 1, while it dropped to 5 months for stage 4. In PNET patients, PFS decreased from 38 months to 8 months. There was a significant difference in both OS and PFS durations based on TNM stage in both patient groups ($p = 0.000$ and $p = 0.000$, respectively).

Table 2 Impact of clinical and demographic variables on overall survival and progression-free survival in PC patients

	Pancreatic Cancer (n: 152)			
Variable	**Overall Survival (OS) (month)**	**Progression-Free Survival (PFS) (month)**	**p for OS**	**p for PFS**
BMI (kg/m²)			**0.016**	**0.016**
< 18	7	3		
18 - 25	11	6		
≥ 25	10	6		
Alcohol			0.135	0.087
Yes	10	6		
No	10	6		
Smoking			0.610	0.601
Yes	9	5		
No	11	6		
ECOG			**0.001**	**0.001**
0 - 1	13	7		
2	10	5		
3	4	3		
4	1	1		
Tumor Size			0.259	0.363
< 2 cm	12	6		
2 - 5 cm	10	6		
> 5 cm	10	6		
Tumor localization			0.428	0.252
Head	11	7		
Corpus	9	5		
Tail	8	4		
TNM stage			**0.000**	**0.000**
Stage 1	17	13		
Stage 2	15	8		
Stage 3	13	7		
Stage 4	7	5		
LN metastasis			**0.009**	**0.000**
Yes	10	5		
No	20	12		
Liver metastasis			**0.000**	**0.000**
Yes	6	4		
No	14	8		
Lung metastasis			**0.001**	**0.001**
Yes	10	5		
No	11	6		
Peritonium metastasis			**0.000**	**0.000**
Yes	4	3		
No	11	6		
CA 19-9 level (U/mL)			**0.001**	**0.001**
< 100	15	8		
100 - 500	10	6		
≥ 500	7	4		
Operation			**0.000**	**0.002**
Whipple precedure	13	7		
Subtotal resection	14	6		
Inoperable	6	3		
Chemotherapy			0.460	0.390
Yes	10	6		
No	6	4		
Radiotherapy			**0.001**	**0.002**
Yes	18	8		
No	8	5		
Biliary stent			0.335	0.253
Yes	12	7		
No	10	5		

PC: Pancreatic cancer; OS: Overal survival; PFS: Progression-free survival; BMI: Body-mass index; TNM: Tumor-node-metastasis; ECOG: Eastern Cooperative Oncology Group Scale; LN: Lymph node; CA 19-9: Carbohydrate antigen 19-9.

Table 3 Impact of clinical and demographic variables on overall survival and progression-free survival in PNET patients

	Pancreatic Neuroendocrine Tumors (n: 17)			
Variable	**Overall Survival (OS) (month)**	**Progression-Free Survival (PFS) (month)**	**p for OS**	**p for PFS**
BMI (kg/m²)			**0.001**	**0.001**
< 18	4	3		
18 - 25	*	*		
≥ 25	29	13		
ECOG				
0 - 1	33	30	**0.001**	**0.001**
2	*	*		
3	2	2		
4	1	1		
Tumor Size			0.863	0.867
< 2 cm	*	*		
2 - 5 cm	39	30		
> 5 cm	33	24		
TNM Stage			**0.000**	**0.002**
Stage 1	40	38		
Stage 2	38	36		
Stage 3	21	17		
Stage 4	14	8		
Operation			**0.001**	**0.001**
Whipple precedure	36	30		
Subtotal resection	35	27		
Inoperable	16	12		

OS: Overal survival; PFS: Progression-free survival; BMI: Body-mass index; TNM: Tumor-node-metastasis; ECOG: Eastern Cooperative Oncology Group Scale.
* No patients with this characteristic

In our study, when the metastatic status at the time of first diagnosis was analyzed, metastasis was detected in 128 patients (75.7%) in the lymph nodes, 66 patients (39%) in the liver, 25 patients (14.8%) in the lungs, 10 patients (5.9%) in the peritoneum and 6 patients (%3.5) in the bones. In 31 patients (18.3%), no metastasis was present at the time of diagnosis. During the follow-up period, liver metastasis developed in 34 patients, lung metastasis in 42 patients, peritoneal metastasis in 46 patients, and new lymph node metastasis in 24 patients. Overall, 152 patients (89.9%) had lymph node metastasis, 100 patients (59.1%) had liver metastasis, 67 patients (39.6%) had lung metastasis, and 56 patients (33.1%) had peritoneal metastasis. In the analysis based on the location of metastasis, the presence of lymph node, liver, lung, and peritoneal metastasis in PC patients created a significant difference in both OS and PFS durations. Due to insufficient data, an evaluation could not be performed for PNET patients.

Among the laboratory markers, carbohydrate antigen (CA) 19-9 levels (< 100, 100 - 500, > 500) showed a significant difference in both OS and PFS in PC patients (p = 0.001 for both OS and PFS).

In our study, 70 out of 169 patients (41.5%) had not undergone surgery, while 67 patients (39.6%) had undergone a Whipple procedure, 58 of whom were diagnosed with PC and 9 with PNET. Thirty-two patients (18.9%) had undergone subtotal surgeries, 28 of whom had PC and 4 had PNET. There was a significant difference in both OS and PFS durations between patients who underwent surgery and those who did not (p = 0.001 and p = 0.002, respectively).

Out of the 169 patients included in the study, 44 (26%) received both chemotherapy (CT) and ra-

Table 4 Multivariate Cox regression analysis of factors affecting OS for PC

Variable	B	SE	Exp (B)	%95 CI		P value
ECOG*	0.425	0.268	1.795	1.061	3.038	0.001
CA19-9*	0.004	0.022	1.530	1.189	1.968	0.029
Age	0.000	0.000	1.000	1.000	1.010	0.087
CT	0.584	1.014	1.014	0.998	1.030	0.128
BMI	0.009	0.030	1.006	0.962	1.048	0.840

B: Beta coefficiency; SE: Standart error; OR: Odds Ratio; CI: Confidence interval; ECOG: Eastern Cooperative Oncology Group; CA 19-9: Carbohydrate antigen 19-9; CT: Chemotherapy; BMI: Body-mass index.

diotherapy (RT), while 125 (74%) did not receive RT. Among PNET patients, only 2 received CT and RT, and no further evaluation was performed regarding the combination of CT and RT for these patients. In PC patients, the median OS was 18 months for those who received RT, while it was 8 months for those who did not. The median PFS for these groups was 8 months and 5 months, respectively. Receiving RT in PC patients created a significant difference in both OS and PFS durations ($p = 0.001$ and $p = 0.002$, respectively). In our study, 54 patients (31.95%) who were all diagnosed with PC underwent biliary stent placement. In the stented group, the median OS was 12 months, while it was 10 months for those without a stent. The median PFS was 7 months and 5 months, respectively. No significant difference in OS or PFS durations was observed between the stented and non-stented patients ($p = 0.335$ and $p = 0.253$).

In the multivariate Cox regression analyses, ECOG performance status and CA 19-9 levels were found to have a negative impact on both overall survival OS for PC. See Table 4 for details.

DISCUSSION

According to GLOBOCAN 2024 data, pancreatic cancer (PC) is the 12th most common cancer globally and the 7th leading cause of cancer-related mortality, with over 467,000 deaths annually. In Turkey, it ranks as the 8th most common cancer and is the 4th leading cause of cancer-related mortality after lung, colon, and gastric cancers (2). In a large-scale study conducted by Sun et al. in 2014, which covered the past thirty years, the 5-year survival rate for PC patients was found to be only 6.9%, despite an increase in recent years, with a median survival of approximately 6 months (8). In a study by Çetin et al. the median overall survival of patients with pancreatic cancer was reported as 11 month (9). In a retrospective study by Chu et al. involving 50 PNET patients, the overall survival (OS) duration was determined to be 40 months (10).

In our study, 107 patients (63.3%) had smoked or were still smoking at some point in their lives, with smoking being more common among male patients. No significant difference was found in OS and PFS between smokers and non-smokers in all patients. However, patients with a history of smoking were diagnosed at a younger average age. Another significant modifiable risk factor in the development of pancreatic cancer is alcohol consumption. In our study, only 20.2% of the patients had a history of alcohol consumption. However, the average duration and amount of alcohol use in these patients are unknown. In our study, no significant difference was observed in OS and PFS between patients who consumed alcohol and those who did not.

Patients with periampullary and PC often present to the hospital with cachexia resulting from malnutrition. Weight loss and cachexia have been reported in approximately 80% of patients with PC (10). In our study, when patients were grouped according to their BMI, a significant difference was found in OS and PFS among PC patients based on BMI values. In a recent study by Latenstein et al., cachexia (BMI < 20 kg/m^2) was found to have a negative impact on survival (12). Similarly, in a study by Ekeblad et al. involving 324 PNET patients, a low BMI (< 20 kg/m^2) was associated with a worse prognosis (13). Our findings were consistent with the literature.

The anatomical localization of pancreatic tumors has been proposed as a potential determinant of survival. There is a potential survival difference between tumors in the head and tail regions, which is attributed to patients with lesions in the tail region presenting relatively later clinically. In a 2008 study by Artinyan et al., it was stated that tumor location is a prognostic factor for survival, and tumors in the body and tail regions were found to have shorter survival durations compared to those in the head region. The authors attributed this to the fact that tumors in the head region present earlier with symptoms, leading to earlier diagnosis, while lesions in the tail region are more likely to cause distant metastases and have fewer surgical options (14). In our study, when we examined patients according to tumor location, 106 (62.7%) patients had tumors in the head of the pancreas, 45 had tumors in the body, and 18 had tumors in the tail region. The median OS was 11 months for patients with tumors localized in the head, 9 months for those with tumors in the body, and 8 months for those with tumors in the tail. Although survival times were numerically longer in the head region, the difference was not statistically significant. In this context, our findings are somewhat consistent with the literature.

In a study by Park et al. on unresectable pancreatic cancer patients, the ECOG performance status was identified as a prognostic factor for survival in univariate analyses (15). In a cohort study conducted by Dai et al., multivariate analysis revealed that poor ECOG performance status was associated with lower overall survival (16). In PC patients, the OS was determined to be 13 months for the ECOG 0-1 group and 1 month for the ECOG 4 group. In the study by Taş et al., multivariate analyses revealed that poor baseline performance status was associated with worse survival in stages other than locally advanced disease (17). In our study, consistent with the literature, there was a statistically significant difference in OS between the ECOG performance status groups. Additionally, the multivariate Cox regression analysis revealed that a lower ECOG performance status had a negative impact on OS for PC patients.

Many studies have shown that disease stage is one of the most important prognostic factors for survival in pancreatic cancer. In our study, according to TNM staging, 10 of 169 patients (5.9%) were in stage I, 21 (12.4%) in stage II, 51 (30.1%) in stage III, and 87 (51.4%) in stage IV. Because most patients remain asymptomatic for a long time, they are often diagnosed at advanced stages, which leads to significantly shorter survival. In a study conducted by Yılmaz et al. in 2019, it was demonstrated that stages II, III, and IV were associated with a higher risk of mortality compared to stage I in patients with pancreatic cancer (18).

Due to its late symptom onset, patients with pancreatic cancer are often diagnosed only at the metastatic stage. Approximately 20% of patients present with localized and potentially resectable disease (stage I–II), while about 50% present with metastatic disease (stage IV). The remaining 30% are detected in a borderline resectable or locally advanced stage (stage III), involving major vascular structures. In a study by Peixoto et al. on un-

resectable locally advanced pancreatic cancer patients, multivariate analysis found that peritoneal metastasis was considered a prognostic factor for OS (19). In our study, the presence of lymph node, liver, lung, and peritoneal metastasis at the time of diagnosis in PC patients created a significant difference in both overall survival OS and PFS, consistent with the literature.

As with all gastrointestinal malignancies, many tumor markers have been investigated in pancreatic cancer to detect the disease at an early stage and for monitoring during treatment. Serum CA 19-9 levels have been found to be a useful tumor marker in distinguishing benign pancreatic lesions from malignant ones and in monitoring tumor response during treatment (20). In the ACCORD1/PRODIGE4 study, a significant decrease in CA 19-9 levels after treatment was reported as a prognostic factor for overall survival OS and PFS (21). In our study, pancreatic cancer (PC) patients were divided into three groups based on CA 19-9 levels: < 100, 100 - 500, and ≥ 500. In the group with CA 19-9 < 100, the median OS was 15 months, while in the group with CA 19-9 ≥ 500, it was 7 months. Similarly, in terms of PFS, the median PFS was 8 months in the first group and 4 months in the third group. A significant increase in mortality rate was observed in parallel with the rise in CA 19-9 levels. Additionally, in the multivariate Cox regression analysis, high CA 19-9 levels were found to have a negative impact on OS in PC patients.

Whether a patient undergoes surgery and, if so, whether a complete resection is performed, significantly affects the prognosis (22). Surgical resection is the only potentially curative treatment option for pancreatic cancer. Unfortunately, due to the late-stage detection of the disease, only 15-20% of patients are candidates for pancreatectomy (23). In our study, 70 out of 169 patients (41.5%) were not operated on, 67 patients (39.6%) underwent a Whipple procedure, and 32 patients (18.9%) received various palliative surgeries. In our study, among PC patients, those who underwent a Whipple procedure had a median OS of 13 months, while those who underwent subtotal surgery had 14 months, and those who did not undergo surgery had 6 months. In both PC and PNET patients, there was a statistically significant difference in OS and PFS between those who underwent surgery and those who did not. Although undergoing a major surgery like Whipple carries a higher risk of complications and offers slightly shorter survival compared to subtotal surgeries, it still provides significantly better survival compared to those who did not undergo surgery.

In our study, out of the 169 patients, 29 (17.2%) did not receive any chemotherapy (CT), 93 (55%) received a gemcitabine-based chemotherapy protocol, 38 (22.5%) received a 5-fluoro uracil-based (FOLFOX or FOLFIRINOX) chemotherapy protocol, and 9 (5.3%) received various other chemotherapy protocols. Since patients were included in our study starting from 2011, the majority of those who received chemotherapy were treated with gemcitabine-based regimens. However, in recent years, most patients have been receiving the FOLFIRINOX regimen. In PC patients, those who received chemotherapy had a median OS of 10 months, while those who did not receive chemotherapy had 6 months. Although there was a notable difference in survival durations between the chemotherapy and non-chemotherapy groups, no statistically significant difference was found in terms of OS. The results for PFS were similar. In the CONKO-001 study published by Sinn et al. in 2013, adjuvant chemotherapy after surgery was found to be an independent prognostic factor for long-term survival (24). Pancreatic cancer has a very poor prognosis, with a 5-year survival rate of less than 10%. In fact, long-term survival has not been significantly affected by the introduction of new chemotherapy treatments. It is predicted that by 2030, pancre-

atic cancer will become the second leading cause of cancer-related deaths (25). Most patients are diagnosed at advanced stages, and less than one-third of them are candidates for surgical resection. Therefore, systemic chemotherapy remains an important treatment option for patients, including those with locally advanced disease, who are treated in the metastatic stage. The results of the PRODIGE/ACCORD study conducted in 2011 on metastatic pancreatic cancer patients showed that FOLFIRINOX, despite having higher toxicity compared to gemcitabine monotherapy, significantly improved survival and quality of life. The median overall survival was 11.1 months in the FOLFIRINOX group, compared to 6.8 months in the gemcitabine group, while progression-free survival was 6.4 months in the FOLFIRINOX group and 3.3 months in the gemcitabine group. As a result of this study, it was shown that FOLFIRINOX is a good treatment option for patients with a good performance status (26). The most recent PRODIGE 24 study also demonstrated favorable results for FOLFIRINOX, similar to the previous study (27).

There is no consensus on the optimal treatment for pancreatic cancer. The primary goal is to perform surgical resection whenever possible. Adjuvant therapy is recommended for patients who undergo pancreatic resection. For patients with localized pancreatic cancer who are not candidates for resection, radiotherapy (RT) has been found to be beneficial. In our study, 44 out of 169 patients (26%) received chemotherapy with RT (CRT). In the PC patients who received CRT, the median OS was 18 months, while it was 8 months for those who did not receive radiotherapy. A statistically significant difference in OS was found between the two groups, and similarly, a significant difference in PFS was also observed.

The majority of pancreatic cancer patients are diagnosed only after biliary obstruction occurs. Jaundice is a symptom observed in 51-72% of patients with unresectable pancreatic cancer and develops in more than 80% of patients during the natural course of the disease. The mechanism of jaundice is due to the compression and/or invasion of the bile duct by a periampullary and/or head region mass, which is found in over 60% of patients (28). Unresolved cholestasis can lead to hepatic dysfunction and even liver failure. Surgical decompression of the obstruction or endoscopic stenting (ES) are available treatment options for these patients. In a study conducted by Macias et al. on pancreatic cancer patients following pancreatoduodenectomy, preoperative biliary drainage was found to be a prognostic factor for survival (29). In our study, 54 of the 169 patients (31.95%) underwent biliary stenting via endoscopic retrograde cholangiopancreatography (ERCP). In patients with biliary stenting, the median overall survival (OS) was 12 months, whereas in the 115 patients (68.05%) without stenting, it was 10 months. There was no statistically significant difference in median OS between the two groups, and our findings were somewhat consistent with the literature.

In conclusion, pancreatic cancer, despite not having a very high incidence, is a type of cancer with extremely high mortality. The main reasons for this are its asymptomatic nature until late stages and its generally nonspecific symptoms, which lead to delayed hospital visits by patients. Since the majority of patients are diagnosed at advanced stages, the chance for curative surgery is significantly low. Combined with these factors, the 5-year survival rate remains very low (around 9-10%) despite a slight increase in the last decade. Pancreatic cancers are a heterogeneous group due to the pancreas being both an endocrine and exocrine organ. Pancreatic cancer, which constitutes the majority of all pancreatic cancers, has a much higher mortality rate compared to PNET, which are less common.

Advancements in imaging techniques will help de-

tect the disease at earlier stages before metastasis occurs, thereby increasing the chances for surgery. Earlier diagnosis also means patients are in better performance status, are better nourished, are not cachectic, and have improved survival outcomes. In the adjuvant setting, chemotherapy or chemoradiotherapy alone still does not provide the desired efficacy. Effective treatments are urgently needed to reduce mortality and improve survival in pancreatic cancer patients.

Ethics Committee: *Ethics committee approval for this study was obtained at the meeting of the Zonguldak Bülent Ecevit University Non-Interventional Clinical Research Ethics Committee dated 20.06.2020 and numbered 2020/13. The study was complied with The World Medical Association Declaration of Helsinki.*

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