ARAŞTIRMA MAKALESİ / RESEARCH ARTICLE

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Birinci Basamak Sistemik Tedavi Alan İnoperabl Pankreas Kanserli Hastalarda Malnütrisyon, Kırılganlık ve Kaşeksinin Sağkalım Üzerindeki Etkisi: Tek Merkezli Prospektif Kohort çalışması

The Survival Effect of Malnutrition, Frailty, and Cachexia in Unresectable Pancreatic Cancer Patients Received First-Line Systemic Treatment: A Single-Center Prospective Cohort Study

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ÖZ

Giriş: Pankreas kanseri düşük insidanslı ancak ölümcül bir malignitedir. Bu çalışma, inoperabl (lokal olarak ilerlemiş veya metastatik) pankreas kanseri olan hastalarda sıklıkla karşılaşılan malnütrisyon, kırılganlık ve kaşeksi prevalansını ve bu durumların genel sağkalım (OS) üzerindeki etkilerini araştırmak için yürütülmüştür.

Yöntem: Bu prospektif, gözlemsel, müdahalesiz, tek merkezli çalışmaya yeni teşhis konulmuş inoperabl pankreas kanseri olan 65 yetişkin hasta dahil edildi. Malnütrisyon, kırılganlık ve kaşeksi skorları tanı anında hesaplandı ve kaydedildi. Mini Beslenme Değerlendirmesi-Kısa Form (MNA-SF) malnütrisyonu değerlendirmek için kullanıldı; Yorgunluk, Direnç, Ambulasyon, Hastalıklar ve Kilo Kaybı (FRAIL) ölçeği kırılganlığı değerlendirmek için kullanıldı; son 6 ayda içindeki kilo kaybı kaşeksiyi değerlendirmek için kullanıldı.

Bulgular: Örneklemin medyan yaşı 65 (aralığı 35-84) yıldı. Tanı anında hastalarda malnütrisyon, kırılganlık ve kaşeksi prevalansı sırasıyla %47,7, %63.1 ve %58,5 idi. Genel sağkalımı etkileyen risk faktörlerini belirlemek için yapılan çok değişkenli analizde tanı anında malnütrisyon ($p<0,001$) varlığı, kırılganlık ($p=0,02$) varlığı ve albumin ($p<0,001$) düşüklüğü daha kısa genel sağkalım süresi ile ilişkili bulundu; ancak kaşeksinin sağkalım üzerinde etkili olmadığı görüldü.

Sonuç: Bulgularımız, inoperabl pankreas kanserli hastalarda tanı anında malnütrisyon, kırılganlık ve düşük albümin varlığının daha kısa genel sağkalım süresi ile ilişkili olduğunu göstermektedir. Bu risk faktörleri, özellikle birlikte mevcut olduklarında, pankreas kanserli hastaların genel sağkalım süreleri daha da kötüleşebilir.

Anahtar Kelimeler: malnütrisyon, kırılganlık, kaşeksi, hipoalbuminemi, genel sağkalım, pankreas kanseri

ABSTRACT

Objective: Pancreatic cancer is a low-incidence yet fatal malignancy. This study was carried out to investigate the prevalence of malnutrition, frailty, and cachexia, which are frequently encountered in unresectable (locally advanced or metastatic) pancreatic cancer patients, and their effects on overall survival (OS).

Method: The sample of this prospective, observational, non-interventional and single-center study consisted of 65 adult patients with newly diagnosed unresectable pancreatic cancer. The patients' malnutrition, frailty, and cachexia scores were calculated and recorded at the time of diagnosis. Mini Nutritional Assessment-Short Form (MNA-SF) was used to assess malnutrition; Fatigue, Resistance, Ambulation, Illnesses, and Loss of weight (FRAIL) scale was used to assess frailty; weight loss rates in the last 6 months were used to assess cachexia.

Results: The median age of the sample was 65 (range, 35-84) years. The prevalence of malnutrition, frailty, and cachexia in patients at the time of diagnosis was 47.7 %, 63.1% and 58.5%, respectively. The multivariate analysis conducted to identify the risk factors for OS revealed that the presence of malnutrition ($p<0.001$), frailty ($p=0.02$), and hypoalbuminemia ($p<0.001$), at the time of diagnosis were associated with shorter OS, whereas cachexia was not.

Conclusion: Our findings indicated that the presence of malnutrition, frailty, and hypoalbuminemia at the time of diagnosis were associated with shorter OS in patients with unresectable pancreatic cancer. These risk factors, especially when present together, may worsen the overall health of pancreatic cancer patients.

Keywords: malnutrition, frailty, cachexia, hypoalbuminemia, overall survival, pancreatic cancer

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INTRODUCTION

Pancreatic cancer is one of the deadliest known cancers, with a low incidence (4.9/100000) but high mortality rates (5-year survival: 10%) worldwide (1,2). Malnutrition, frailty, and cachexia are frequently encountered in pancreatic cancer patients, as pancreatic cancer occurs at older ages (median age of diagnosis: 70) (3), requires the use of heavy chemotherapy regimens and causes deterioration of digestive functions (4-6).

Malnutrition can be caused by a primary condition, such as lack of food, or a secondary condition, such as cancer (7,8). Malnutrition increases length of hospital stay, hospital-acquired infections and mortality rates. In a meta-analysis including 15 studies evaluating various heterogeneous cancer types, Dadi Peng et al. found that malnutrition was associated with lower OS (9).

Frailty is defined as a medical condition of reduced function and health in individuals (10). Many reasons may contribute to the development of frailty, such as increasing age, lower weight, female sex, living alone, low levels of exercise, polypharmacy, higher education level, smoking, drinking, malnutrition, and lower vitamin D levels (11). In a prospective study evaluating patients with advanced pancreatic cancer, Ngo-Huang et al., found that anorexia was associated with poorer quality of life (12).

Cachexia is a complex metabolic syndrome characterized by pathological weight loss, involving the loss of both muscle and fat tissues (13). Its clinical impact is significant; in a retrospective study of pancreatic and gastric cancer patients, Bozzetti et al. reported that cachexia correlated with poorer quality of life and increased chemotherapy toxicity (14).

The fact that the limitation in energy intake in gastrointestinal cancers is higher than in other types of cancer causes conditions such as malnutrition, frailty, and cachexia to occur more frequently. Although it has been shown in many studies that these conditions negatively affect the quality of life and survival in cancer patients, most of these studies were conducted retrospectively and consisted of heterogeneous patient groups. In this context, we aimed to determine the prevalence of malnutrition, frailty, and cachexia in pancreatic cancer patients who were in unresectable (locally advanced or metastatic) stages at the time of diagnosis and investigate the effects of these conditions on their prognoses in a prospectively designed study.

MATERIALS AND METHODS

Study Design

This study was designed as a prospective, observational, non-interventional and single-center study.

Population and Sample

The study population consisted of the patients diagnosed with unresectable pancreatic cancer who applied to the Medical Oncology outpatient clinic, between March 2022 and July 2024. The patients' demographic characteristics, clinical characteristics related to cancer diagnosis (localization and size of the tumor, vascular invasion, presence of diabetes mellitus (DM), ascites, metastasis, and the chemotherapy regimens administered), laboratory test results, malnutrition, frailty, and cachexia scores were calculated and recorded at the time of diagnosis.

Study's inclusion criteria were determined as follows:

- ✓ having locally advanced or metastatic disease,
- ✓ being over 18,
- ✓ agreeing to receive first line chemotherapy,
- ✓ having given voluntary consent to participate in the study,
- ✓ not having had surgery or chemotherapy before.

On the other hand, the exclusion criteria of the study were determined as follows:

- ✓ having a history of pancreatic cancer-related surgery,
- ✓ having been diagnosed with a second primary cancer,
- ✓ having an Eastern Cooperative Oncology Group (ECOG) performance status of 4,
- ✓ having a rheumatic disease,
- ✓ having a musculoskeletal disease of inflammatory or mechanical character,
- ✓ having a neuromuscular and neurological muscle disease.

In the end, a total of 65 pancreatic cancer patients, 52 males and 13 females, were included in the sample.

The Assessment of Malnutrition

Mini Nutritional Assessment-Short Form (MNA-SF) was used to assess patients' malnutrition status. MNA-SF consists of six screening criteria: food intake, unintentional weight loss, mobility, psychological stress or acute illness, neuropsychological problems, and body mass index (BMI) or calf circumference. MNA-SF scores of 12 to 14, 8 to 11, and 0 to 7 points indicate normal nutritional status, risk of malnutrition, and malnutrition, respectively (Supplementary Table 1) (15).

The Assessment of Frailty

Fatigue, Resistance, Ambulation, Illnesses, and Loss of weight (FRAIL) scale was used to assess patients' frailty status. The FRAIL scale is a 5-point (0 = not frail, 1-2 = pre-frail, 3-5 = frail) scale consisting of 5 items (Supplementary Table 2) (16,17).

The Assessment of Cachexia

Patients' weight loss rates in the last 6 months were used to assess their cachexia status. Accordingly, a weight loss of more than 5% in the last 6 months or a BMI of less than 20 kg/m2 and a weight loss of more than 2% in the last 6 months were considered to indicate cachexia (18).

Statistical Analysis

Statistical analyses were performed using SPSS Statistics 27(ver. 20.2.1.15749). Categorical variables were presented as numbers and percentages and continuous measures as the mean and standard deviation. Malnutrition was classified as present or absent based on MNA-SF scores. Frailty was categorized as frail or not frail using the FRAIL scale.

Supplementary Table 1. Mini Nutritional Assessment-Short (MNA-S) Form	
Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties? 0= Severe decrease in food intake 1= Moderate decrease in food intake 2= No decrease in food intake	
Weight loss during the last 3 months 0= Weight loss greater than 3 kg (6.6 ıbs) 1= Does not know 2= Weight loss between 1 and 3 kg (2.2 and 6.6 ıbs) 3= No wight loss	
Mobility 0= Bed or chair bound 1= Able to get out of bed/chair but does not go out 2= Goes out	
Has suffered psycgological stres sor acute disease in the past 3 months? 0= Yes 2= No	
Neuropsychological problems 0= Severe demantia or depression 1= Mild demantia 2= No psychological problems	
Body mass index (BMI) (weight in kg)/ (height in m^2) 0= BMI less than 19 1= BMI 19 to less than 21 2= BMI 21 to less than 23 3= BMI 23 or greater	
Screening score (Total max. 14 points)	12-14 points: Normal nutritional status 8-11 points: At risk of malnutrition 0-7 points: Malnutrition

Supplementary Table 2. Fatigue, Resistance, Ambulation, Illnesses, and Loss of weight (FRAIL) Scale	
Criterion	Description Score
Fatigue	How much of the time during the past 4 weeks did you feel tired? All of the time = 1, Most of the time = 2, Some of the time = 3, A little of the time = 4, None of the time = 5. 0 = Responses of “3” or “4” or “5” 1 = Responses of “1” or “2”
Resistance	By yourself and not using aids, do you have any difficulty walking up 10 steps without resting? 0 = No 1 = Yes
Ambulation	By yourself and not using aids, do you have any difficulty walking a couple of blocks (e.g. several hundred yards)? 0 = No 1 = Yes
Illness	Did a doctor ever tell you that you have [illness]? How many (see list below): The illnesses include hypertension, diabetes, cancer (other than a minor skin cancer), chronic lung disease, heart attack, congestive heart failure, angina, asthma, arthritis, stroke, and kidney disease. 0 = The total illnesses (0-4) 0 = The total illnesses (5-11)
Loss of Weight	How much do you weigh? Percent weight change is computed as: [[weight 1 year ago - current weight]/weight 1 year ago]] * 100. 0 = Percent change < 5% 1 = Percent change > 5%
Screening score (Total max. 5 points)	0 points: Robust health status 1-2 points: Pre-frail 3-5 points: Frail

Cachexia was defined as present or absent based on weight loss criteri. The optimum cutoff values were determined based on the median values and used to separate the 'low' and 'high' groups. Survival was analyzed using the Kaplan–Meier method and the log-rank test was used for group comparison. Univariate and multivariate Cox proportional hazards models were used to analyze factors affecting survival. For multivariate analysis, the "Enter" method was used. The hazard ratio (HR) was reported with the corresponding 95% confidence intervals (95% CI). The endpoint for progression free survival (PFS) was defined as clinical or radiological disease progression after starting first-line chemotherapy, and the endpoint for OS was defined as death after starting first-line chemotherapy or the date of last follow-up. Statistical significance was accepted as $p < 0.05$.

RESULTS

Demographic Findings & Oncologic Features

The median age of the 65 patients in the sample was 65 years (range: 23-84 years), with 80% male and 20% female. At the time of diagnosis, metastases were detected in 67.7% of the patients and DM in 32.3%. The tumor originated from the head and neck region in 44 (67.7%) patients, the trunk in 16 (24.6%) patients, and the tail region of the pancreas in 5 (7.7%) patients. Modified FOLFIRINOX (Folinic acid, Irinotecan, 5-Fluorouracil, Oxaliplatin) regimen was preferred as the treatment method in most (52.3%) of the patients. The demographic and clinical characteristics of the patients are shown in Table 1.

Table 1. Clinicopathological, measured and laboratory parameters of the patients.

Features		N	(%)
Gender	Male	52	(80.0)
	Female	13	(20.0)
Age at diagnosis	≥65	31	47.7
ECOG PS	≤1	17	(26.2)
Diabetes mellitus	Available	21	(32.3)
Primary tumor location	Head and neck	44	(67.7)
	Corpus	16	(24.6)
	Tail	5	(7.7)
Vascular involvement	Available	38	(58.5)
Ascites	Available	10	(15.4)
Metastasis	Available	44	(67.7)
Biliary Stent	Available	36	(55.4)
Chemotherapy protocols	Gemcitabine	6	(9.2)
	Gemcitabine - Cisplatin	8	(12.3)
	Gemcitabine - Nab-Paclitaxel	1	(1.5)
	CAPOX	5	(7.7)
	Modified FOLFIRINOX	34	(52.3)
	Gemcitabine-Capecitabine	9	(13.8)
	Gemcitabine - Oxaliplatin	2	(3.1)
Malnutrition (MNA-SF)	Available	31	(47.7)
Fragility (FRAIL scale)	Available	41	(63.1)
Cachexia (Weight loss%)	Available	38	(58.5)
Weight*	(Unit-kg)	68±22	38-164
Height*	(Unit-cm)	170±11	110-182
BMI*	(Unit-kg/m^2)	25±6	15-41
Leukocyte*	(Unit-10^9 /L)	7±6	2-32
Platelet*	(Unit-10^9 /L)	252±83	86-393
Hemoglobin*	(Unit-g/dL)	12±2	8-15
CRP *	(Unit-mg/dL)	13±35	0-136
Total protein*	(Unit-g/dL)	69±25	48-84
Albumin*	(Unit-g/dL)	40±25	31-53
Ca 19-9	(Unit-IU/mL)	421±1465	4-7658

*Median ± standard deviation was given instead of "N", minimum-maximum were given instead of "%"; BMI, Body Mass Index; Ca 19-9, carbohydrate antigen 19-9; CAPOX, Capecitabine and Oxaliplatin; CRP, c-reactive protein; ECOG-PS, Eastern Cooperative Oncology Group-Performance Status; FOLFIRINOX, Folinic acid, Irinotecan, 5- Fluorouracil, Oxaliplatin; FOLFOX: Folinic acid, 5- Fluorouracil, Oxaliplatin; FRAIL, Fatigue, Resistance, Ambulation, Illnesses, and Loss of weight; MNA-SF, Mini Nutritional Assessment-Short Form.

Table 2. Univariate and Multivariate Analysis of Characteristic Parameters Related to Progression Free Survival.

PFS		Univariate Analysis		Multivariate Analysis	
Characteristics	**Category**	**HR(95% CI)**	**P**	**HR(95% CI)**	**p-value**
Age	<65 vs ≥65	0.46(0.22-0.95)	**0.036**	0.56(0.26-1.23)	0.148
Sex	Female vs male	0.69(0.24-2.02)	0.501		
BMI	<25 vs ≥25	1.08(0.51-2.22)	0.856		
ECOG PS	≤1 vs >1	0.87(0.38-1.99)	0.747		
Diabetes mellitus	Yes vs no	1.37(0.67-2.82)	0.390		
Malnutrition (MNA≤7)	Yes vs no	1.50(0.69-3.27)	0.305		
Fragility (FRAIL scale ≥3)	Yes vs no	1.69(0.80-3.57)	0.170		
Cachexia (Weight loss ≥5%)	Yes vs no	2.22(1.08-4.54)	**0.031**	1.78(0.82-3.86)	0.146
Ascites	Yes vs no	1.62(0.69-3.83)	0.270		
Metastasis	Yes vs no	1.88(0.84-4.23)	0.127		
Biliary Stent	Yes vs no	1.38(0.66-2.88)	0.397		
CRP	<13 vs ≥13	0.61(0.29-1.30)	0.204		
Albumin	<40 vs ≥40	1.54(0.75-3.13)	0.237		
Ca 19-9	<421 vs ≥421	1.01(0.43-2.34)	0.986		

BMI, Body mass index; Ca 19-9, carbohydrate antigen 19-9; CI, Confidence interval; CRP**,** c-reactive protein; ECOG-PS, Eastern Cooperative Oncology Group-Performance Status; FRAIL, Fatigue, Resistance, Ambulation, Illnesses, and Loss of weight; MNA-SF, Mini Nutritional Assessment-Short Form.

Table 3. Univariate and Multivariate Analysis of Characteristic Parameters Related To Overall Survival.

OS		Univariate Analysis		Multivariate Analysis	
Characteristics	**Category**	**HR(95% CI)**	**P**	**HR(95% CI)**	**p-value**
Age	<65 vs ≥65	0.73(0.29-1.85)	0.512		
Sex	Female vs male	0.60(0.22-1.64)	0.313		
BMI	<25 vs ≥25	2.04(0.88-4.74)	0.097		
ECOG PS	≤1 vs >1	0.40(0.15-0.81)	**0.049**	0.72(0.16-3.33)	0.681
Diabetes mellitus	Yes vs no	1.37(0.54-3.45)	0.508		
Malnutrition (MNA≤7)	Yes vs no	1.70(1.49-3.09)	**0.005**	1.45(2.22-3.33)	**<0.001**
Fragility (FRAIL scale ≥3)	Yes vs no	1.33(1.22-2.15)	**0.019**	1.82(1.24-3.84)	**0.020**
Cachexia (Weight loss ≥5%)	Yes vs no	1.51(0.59-3.88)	0.395		
Ascites	Yes vs no	1.09(0.25-4.72)	0.908		
Metastasis	Yes vs no	1.06 (0.56-1.86)	0.231		
Biliary Stent	Yes vs no	1.17(0.47-2.89)	0.738		
CRP	<13 vs ≥13	0.80(0.34-1.91)	0.614		
Albumin	<40 vs ≥40	1.33(2.33-4.67)	**<0.001**	1.53(1.86-3.50)	**<0.001**
Ca 19-9	<421 vs ≥421	0.59(0.22-1.56)	0.291		

BMI, Body mass index; Ca 19-9, carbohydrate antigen 19-9; CI, Confidence interval; CRP**,** c-reactive protein; ECOG-PS, Eastern Cooperative Oncology Group-Performance Status; FRAIL, Fatigue, Resistance, Ambulation, Illnesses, and Loss of weight; MNA-SF, Mini Nutritional Assessment-Short Form.

Laboratory Test Results & Anorexia, Malnutrition and Cachexia Findings

The laboratory parameters were including leukocyte, platelet, hemoglobin, C-reactive protein, total protein, albumin, carbohydrate antigen 19-9 (CA 19-9). The prevalence of malnutrition, frailty, and cachexia in patients at the time of diagnosis was 47.7%, 63.1% and 58.5%, respectively. Patients' laboratory test results, malnutrition, frailty, and cachexia findings are shown in Table 1.

Risk Factors For Progression Free Survival

The median PFS of our patients was 4.5 months. In the univariate analysis, age 65 or older (p = 0.036), and the presence of cachexia (p=0.031) were identified as negative risk factors for PFS. Further analysis of these two parameters with multivariate analysis did not corroborate the univariate analysis finding that they were significant risk factors for survival. Table 2 shows the factors affecting PFS.

Risk Factors for Overall Survival

The median OS of our patients was 8.8 months. In the univariate risk assessment, the presence of poor ECOG PS (p=0.049), malnutrition (p=0.005), frailty (p=0.019) and hypoalbuminemia (p<0.001) were identified as negative risk factors for OS. In the multivariate analysis, the presence of malnutrition (p < 0.001), the presence of frailty (p = 0.020), and the presence of hypoalbuminemia (p < 0.001) were identified as negative risk factors for OS. Table 3 shows the factors affecting OS.

Kaplan-Meier Survival Analysis

Patients who were not malnutrition at the time of diagnosis had longer OS than patients who were malnutrition (8.8 months vs. 6.4 months; p = 0.002). Patients who were not frailty at the time of diagnosis also had longer OS than patients who were frailty (Non-Reach (NR) vs. 6.9 months; p = 0.011). Patients who were not hypoalbuminemia at the time of diagnosis also had longer OS than patients who were hypoalbuminemia (NR vs. 6.4 months; p < 0.001). Kaplan-Meier analyses for the presence of malnutrition, frailty, and hypoalbuminemia as risk factors affecting survival outcomes are shown in Figure 1, Figure 2, and Figure 3 respectively.

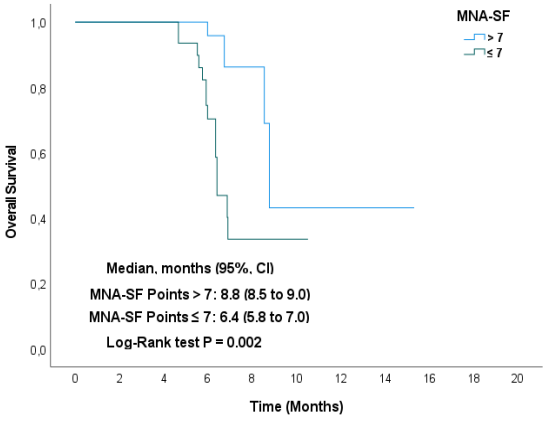

Figure 1. Kaplan Meier survival curves for Overall Survival according to Malnutrition.

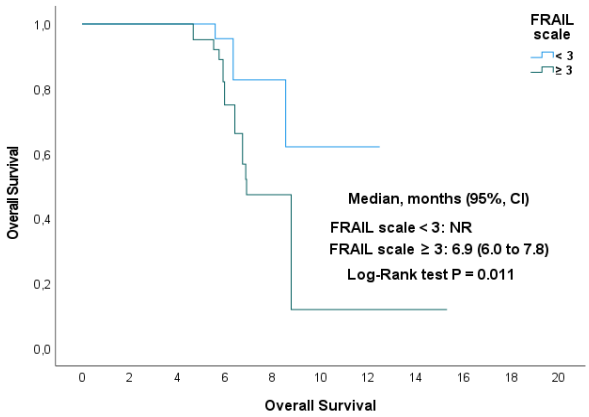

Figure 2. Kaplan Meier survival curves for Overall Survival according to Frailty.

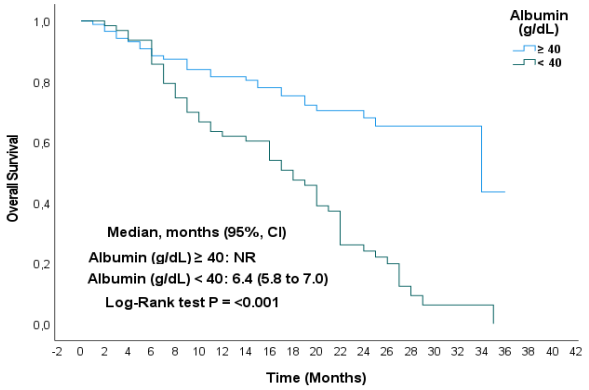

Figure 3. Kaplan Meier survival curves for Overall Survival according to Albumin.

DISCUSSION

The pancreas is a vital organ that produces the enzymes necessary for digestion. Pancreatic cancer, in addition to deteriorating the normal function of the pancreas, can also cause malnutrition, thus leading to a further increase in energy demand (19). Malnutrition-related fat and muscle loss, which is exacerbated by increased energy demand, causes frailty, and cachexia, also known as pathological weight loss. In this context, we prospectively evaluated the malnutrition frailty, and cachexia symptoms of patients with unresectable pancreatic cancer.

In a prospective study conducted with 97 pancreatic cancer patients, most of whom were not operated on, evaluating the relationship between the prevalence of malnutrition and factors limiting nutritional status and the risk of mortality, Kalliopi-Anna Poulia et al. found that the prevalence of malnutrition was 44.3%, and the presence of risk factors that limit food intake, such as nausea, vomiting and constipation, was associated with a significantly higher risk of mortality (20). In an observational study conducted with 41 pancreatic cancer patients, Santos I et al. found that the

prevalence of malnutrition was 73.2% (21).The higher prevalence of malnutrition in the study by Santos I et al. compared to the study by Kalliopi-Anna Poulia et al. may be attributed to the fact that all patients in Santos I et al.'s study had stage 4 disease and most of them were selected from inpatients (20,21). In parallel with the study by Kalliopi-Anna Poulia et al., we found that the prevalence of malnutrition in our cohort was 47.9%, and malnutrition was associated with a significantly shorter OS duration.

In a systematic review and meta-analysis study evaluating patients with resectable or unresectable pancreatic cancer, the prevalence of frailty was found to be 42% and 45%, respectively. In both studies, the presence of frailty was associated with increased relative risk for mortality (22,23). We found that the prevalence of frailty was 63.1%. The high prevalence of frailty in our patient population is due to the fact that all of our patients have unresectable disease. Similarly, we found that the presence of frailty was associated with shorter OS.

In a retrospective study investigating survival duration of 35 unresectable pancreatic cancer patients, Ohta R et al. found that the presence of hypoalbuminemia was associated with shorter OS (24). Similarly, in a prospective study involving 194 patients with advanced pancreatic cancer, Partelli S et al. identified the presence of hypoalbuminemia (≤40 g/L; hazard ratio 1.64, P=0.010) as an independent predictor of shorter survival time (25). Along these lines, we found that the patients with hypoalbuminemia had shorter OS than those without hypoalbuminemia.

One of the key parameters of our hypothesis, the prevalence of cachexia, was found to be 50% in a retrospective study of 150 patients (26), and 54.7% in another study involving 334 stage-IV pancreatic cancer patients (27), In our patient group, the prevalence of cachexia was 58.5%, which is consistent with these findings. Regarding survival analysis, the presence of cachexia was found to affect PFS in the univariate analysis; however, this effect was not statistically significant in the multivariate analysis. Additionally, no significant results were found for OS in either the univariate or multivariate analyses. Although the literature includes studies both supporting and not supporting the effect of cachexia on survival (28,29), a study by Hendifar AE et al. found that the presence of cachexia did not impact the mortality risk in patients receiving chemotherapy (27). As all patients in our study received chemotherapy,we can conclude that our results are consistent with those of Hendifar AE al.'s study. These findings suggest that further comprehensive and detailed studies are needed.

Limitations of the Study

Despite its strengths, such as its prospective design, the fact that more than one factor was investigated simultaneously in the patient population, and that it is the first study in which the prognostic significance of malnutrition, frailty and cachexia conditions were investigated simultaneously, the study also had some limitations. These limitations were mainly the single-center study design, small sample size, and short follow-up period.

CONCLUSIONS

The findings of this study indicated that the presence of malnutrition, frailty, and hypoalbuminemia at the time of diagnosis were associated with shorter overall survival (OS) in patients with unresectable pancreatic cancer. These risk factors, especially when present together, may exacerbate the overall health of pancreatic cancer patients and shorten their OS. Therefore, the management and treatment of these conditions is crucial at diagnosis and throughout the course of pancreatic cancer treatment. To this end, adopting a multidisciplinary approach and providing holistic care to patients may improve the chances of successful treatment outcomes.

Ethics CommitteeApproval: This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee (Date: March-2022, KAEK/2022.03.09).Written informed consent was obtained from all patients before the conduct of the study.

Authors'contributions: All authors contributed to the study conception and design. Material preparation, data collection by TK, FF, NB and GUE. Data analysis was performed by TK and FF. The first draft of the manuscript was written by TK and FF. All authors read and approved the final manuscript.

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Informed Consent: Written informed consent was obtained from all patients before the conduct of the study.

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