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Rezektabl Pankreas Kanserinin Klinikopatolojik Özellikleri

A Clinicopathological Aspects of Resectable Pancreatic Neoplasm

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ÖZET

Amaç: Pankreas kanseri, en ölümcül malign neoplazmlardan biridir. Birçok malign neoplazmda olduğu gibi, hayatta kalma oranları kanserin histopatolojik tipine, evresine, tümör boyutuna ve tedaviye bağlıdır. Bu çalışmada pankreas kanserinin klinikopatolojik özelliklere ve histolojik alt tiplere göre sınıflandırmayı amaçladık.

Materyal ve Metot: Kliniğimizde pankreas neoplazmı nedeniyle teşhis ve tedavi edilen tüm yetişkin hastaların verileri hastanenin bilgisayarlı veri tabanından ve tıbbi dosyalarından geriye dönük olarak toplanmıştır. Hastalar klinikopatolojik özelliklerine göre kategorize edildi. Gruplar arası karşılaştırmalar için, ki-kare testi ve Fisher'in kesin testi kullanıldı ve nicel veriler için bağımsız örnekler için t-testi kullanıldı. Veriler, sürekli değişkenler ve sayılar için ortalama ± SD ve kategorik değişkenler için yüzdeler olarak ifade edildi. $p<0.05$ değeri anlamlı kabul edildi.

Sonuçlar: Hastaların ortalama yaşı 60,5 yıl, %70,8'i erkekti. Histopatolojik olarak tanımlanan beş tip tümör vardı ve bunlar arasında en sık tanı adenokarsinom (%76,9) idi. Tümörün en yaygın lokalizasyonu baş-boyun (%44,4) yerleşimliydi. Whipple cerrahisi ağırlıklı olarak hastaların %69,2'sine, distal pankreatektomi ise %29,0'ına uygulandı. Postoperatif komplikasyonlar hastaların üçte birinden fazlasında (%34) gözlendi. Ana komplikasyonlar pankreas kisti (%16,3) idi. Kaplan-Meier testi ile yapılan sağkalım analizinde 30,5 aylık medyan sağkalım, 1, 2 ve 5 yıllık genel sağkalım (OS) oranları sırasıyla %67,8, %40,5 ve %16.6 idi.

Tartışma: Sonuçlarımız literatürle uyumludur. Ancak sağkalım analizi sonuçları hastaların hepsinin rezektabl tümörlere sahip olması nedeniyle popülasyon tabanlı çalışmalara göre iyimserdi.

Anahtar Kelimeler: Pancreatik Neoplazmlar, Histolojik Tiplerine Göre Neoplazmlar, Pankreatektomi

ABSTRACT

Aim: Pancreatic cancer is one of the deadliest malignant neoplasms. As with many malignant neoplasms, survival rates depend on the histopathological type of cancer, its stage, tumor size, and treatment. In this study, we aimed to classify pancreatic cancer according to clinicopathological features and histological subtypes.

Material and Method: The data of all adult patients diagnosed and treated for pancreatic neoplasm in our clinic were collected retrospectively from the hospital's computerized database and medical files. Patients were categorized according to their clinicopathological features. Chi-square test and Fisher's exact test were used for between-group comparisons, and t-test was used for independent samples for quantitative data. Data were expressed as mean ± SD for continuous variables and numbers and percentages for categorical variables. A value of $p<0.05$ was considered significant.

Results: The mean age of the patients was 60.5 years, 70.8% were male. There were five types of tumors defined histopathological, and the most common diagnosis was adenocarcinoma (76.9%). The most common localization of the tumor was head and neck (44.4%). Whipple surgery was performed predominantly in 69.2% of patients, and distal pancreatectomy in 29.0%. Postoperative complications were observed in more than one third (34%) of the patients. The main complications were

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pancreatic cyst (16.3%). In the survival analysis performed with the Kaplan-Meier test, median survival of 30.5 months, and overall survival (OS) at 1.2 and 5 years were 67.8%, 40.5%, and 16.6%, respectively.

Discussion: However, survival analysis results were optimistic compared to population-based studies as all patients had resectable tumors**.**

Keywords: Pancreatic Neoplasms, Neoplasms by Histologic Type, Pancreatectomy

Introduction

Pancreatic cancer remains to be one of the most fatal malignant neoplasms and is the seventh leading cause of cancer deaths worldwide [1,2]. More than 450000 new cases are diagnosed annually and only 5.8% of cases survive [3]. The incidence of the pancreatic cancer increases in the aging population, in developed countries and in men which also correlates with mortality [1]. Smoking habits, obesity, genetics, family history, alcohol, physical inactivity, diabetes mellitus, chronic pancreatitis, and obesity are considered to be the certain risk factors [4].

As in many malignant neoplasms, the survival rates depend on the histopathological type of the cancer, stage, tumor size, and the treatment. Therefore, primary prevention is the most important measure because there is not a valid screening method available and most of patients are diagnosed at an advanced stage [5].

Most of the pancreatic cancers are ductal adenocarcinomas (DA) which represent 85% of all cases and arise in exocrine glands. Neuroendocrine tumors are less common (<5%) and related to the endocrine tissue of the pancreas [4].

Ductal neoplasia is the most important category among pancreatic tumors. It is important to understand different ductal tumor types because the vary in clinicopathological features and prognosis. Understanding molecular mechanism of the ductal carcinogenesis will aid effective prevention and develop treatment modalities [5].

Although a low proportion of patients (10-20%) are diagnosed at a resectable stage, surgery remains the only curative treatment option for pancreatic carcinoma [6]. A resectable stage was defined as the absence of distal organ and lymph node metastasis, absence of invasion of superior mesenteric vein and portal vein, tumor thrombus, and existence of clear fat planes around the celiac axis, hepatic artery, and superior mesenteric artery [7].

The treatment should be directed in a multimodal fashion including surgery and adjuvant chemotherapy because surgical treatment alone could not result in promising results due to local and distant relapses [8].

Studies have revealed that the prognosis depends on the clinicopathological features of the pancreatic carcinoma and histological confirmation is widely accepted as a cornerstone in the determination of treatment options as well as the outcomes.

The aim of this study is to retrospectively evaluate the data of 338 consecutive patients with resectable tumor diagnosed as pancreatic neoplasm between January 2010 and May 2021 in the surgical oncology clinic of an academic tertiary hospital. The primary outcome measure was to classify the diagnosis according to clinicopathological features and to histological subtypes.

Methods

This observational and retrospective study was conducted in a tertiary hospital from October 2010 to June 2021. After obtaining hospitals ethic committee approval, data were retrospectively collected from the hospital's computerized database and medical files of all adult patients who was diagnosed and treated due to pancreatic neoplasm. The study followed the strengthening the reporting of observational studies in epidemiology (STROBE) guidelines [9,10,11].

Obtaining informed consent was waived with respect to the retrospective design of the study. Inclusion criteria were resectable primary pancreatic neoplasms with histopathological diagnosis. Patients with insufficient data and lost during follow-up and non-resectable patients were excluded from the study.

Statistical Analysis

The data were analyzed using the Statistical Packages for Social Sciences for Windows version 11.5 pocket program (IBM Corp., Chicago, IL, USA). For intergroup comparisons, the Chi-square test and Fisher's exact test were used to analyze nominal data and the t-test for independent samples was used for quantitative data. Data were expressed as means ± SD for continuous variables and numbers, and percentages for categorical variables. The value of $p<0.05$ was considered significant.

Results

Medical records of 377 patients were reviewed. A total of 39 patients were excluded from the study due to the insufficient data (n=21) and lost in the follow-up period (n=18) (Figure 1). Mean age of patients was 60.5 +- 7.2 years (median, 62.3 years; range, 44-79 years); 70.8 % were men (Table 1). There were five types of the tumor was histopathological identified and among them, adenocarcinoma was the most common diagnosis (76.9%) followed by neuroendocrine tumor, solid pseudopapillary neoplasia, Intraductal papillary mucinous neoplasm and cystic neoplasia (Table 1). The tumor was localized predominantly at head - neck (44.4%) than the body - tail (27.2%) and ampulla (26.3%) of the pancreas.

Whipple surgery was performed predominantly in 69.2% of patients whereas distal pancreatectomy in 29.0%. Postoperative complications were observed in more than one third of patients (34%). The main complications were pancreatic cyst (16.3%), biliary fistula (4.1%), surgical site infection (3.6), multiorgan failure 3.0%).

The median survival time of 30.5 months, 1,2, and 5-year overall survival (OS) rates in the survival analysis performed with the Kaplan-Meier test were 67.8%, 40.5%, and 16.6%, respectively. The survival curve is shown in Figure 2. Survival analysis was also performed according to the histopathological features of the tumor (Table 2).

Discussion

Pancreatic cancer is defined as a group of malignancies with several histological subtypes that are originated from the pancreatic tissue. Adenocarcinoma is the most common subtype and the other types are uncommon with an incidence up to 15%. But these uncommon subtypes represent 27.3% of all resectable pancreatic cancer which is attributable to the less aggressive behavior of the uncommon subtypes. Unfortunately, most of adenocarcinoma cases are still diagnosed at a late stage for the surgical cure. More than 80% of patients have positive lymph modes or distant metastasis at diagnosis. In those patients, surgical resection does not increase the curability.

The results of the study showed that the ranking and proportion regarding the incidence of pancreatic tumor subtypes were found different than the studies in the literature. Pancreatic adenocarcinoma has been found to be the most common type as in the literature but the incidence was reduced to the 76.9% in our study which has been generally reported more than 85% [12].

It was interesting that the rank of the IPMN was changed to four which was known as the second common subtype of pancreatic tumor. The incidence of IPMN was 3.6% in our study which is reported as 7.0% in the literature. Also, the incidence of the neuroendocrine tumors was found to be higher than the literature (rank 2; 11.2% vs rank 3; 5.2%). The other uncommon types were increased according to the study [13].

With improvements in the medical technology, there is a rise in diagnosis of uncommon pancreatic tumors compared to the intraductal adenocarcinoma. A study revealed that the diagnosis of IPMN was 14-fold increase in twenty years [15].

Survival analysis results were more optimistic when compared with the literature, as they included resectable tumors. The median survival time of 30.5 months, 1,2, and 5-year overall survival (OS) rates in the survival analysis performed with the Kaplan-Meier test were 67.8%, 40.5%, and 16.6%, respectively [16].

Especially, indolent subtypes including pNET, IPMN, MCN, SPT, and ACC have better prognosis compared to adenocarcinoma when they are diagnosed at a localized stage. Therefore, the higher incidence of the uncommon subtypes may be promising since they are less aggressive and the survival rates are higher than pancreatic adenocarcinoma. But it should be noted that this condition is valid for early stages. At the stage III or IV the prognosis is as poor as the ductal adenocarcinoma [17]. Therefore, early diagnosis plays the most important role in the survival of the patients.

Another different result from the current study was the incidence of the tumor localization. Although it was reported that pancreatic cancer occurs approximately in 65% of the cases in the head and in 15% cases in the body and tail (18), our results indicated that the tumor is located with an incidence of 44.4% in the head, 27.2% in the body and tail, and 26.3% in the ampulla. We think that this result is considerable because tumor survival of the body and tail is much worse than those located in the head due to the late clinical manifestations.

The overall incidence of postoperative complications was 34.0% in our study. The morbidity rate after pancreatic surgery has been reported to range from 30 to 65% (19). The relatively high incidence of postoperative complications is related to the complexity of the surgery with multiple anastomoses, poor nutritional status of the patients or accompanying comorbidities. Surgical complications were three times higher than the general complications in our study which included pancreatic cyst, biliary fistula, surgical site infection, anastomotic leakage, chylous ascites. It is reported that postoperative complications are an independent risk factor for overall survival and affect the long-term outcome of patients due to decreased host immunity against the tumor and a delay in adjuvant chemotherapy (20,21). Therefore, a careful postoperative observation of the patient is of upmost importance because early diagnosis and management of the complications can improve outcome and save life (22).

Limitations

This study is limited by the retrospective nature that affected the selection of the control group. Additionally, exposure to the interventions and outcomes may be difficult to control. We used the same inclusion and exclusion criteria during the data collection period to prevent this disadvantage. Data were obtained from multiple sources including patient files and electronic medical records. The same surgical team performed all interventions. The patient files with insufficient data were excluded.

Other information

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Author's contributions: ŞD and MAC conducted the study, collected the data, and contributed the writing of the manuscript. MAC and ŞD analyzed the study results and contributed the revision of manuscript. MAC and ŞD assisted in analysis data and contributed the writing of the manuscript. SD designed, directed, and reviewed the study.

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Figure 1. Study Flow Diagram

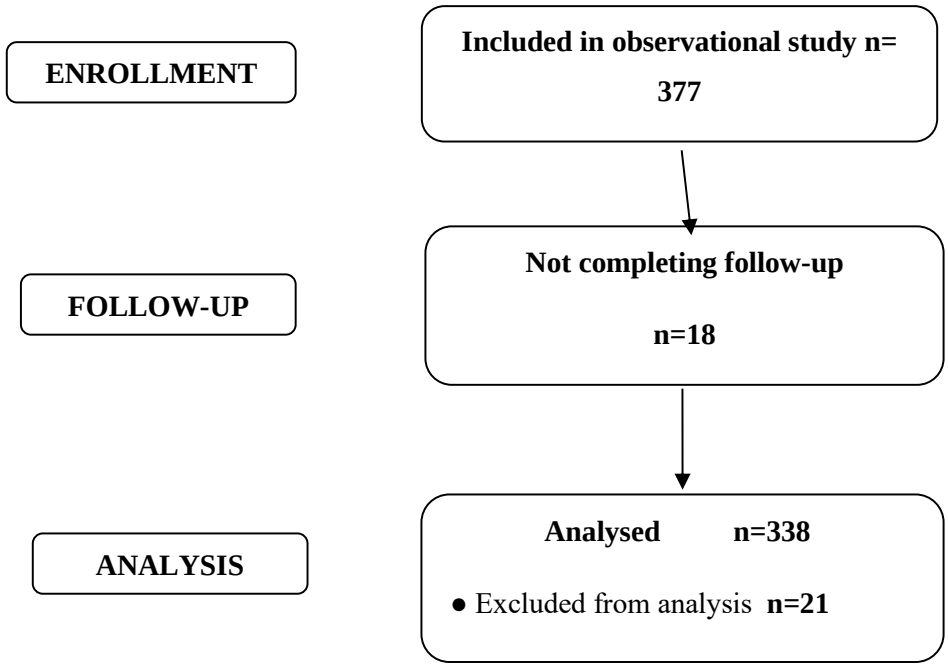

Figure 2. Kaplan-Meier Survival Curves for Primary Pancreatic Malignant Tumors

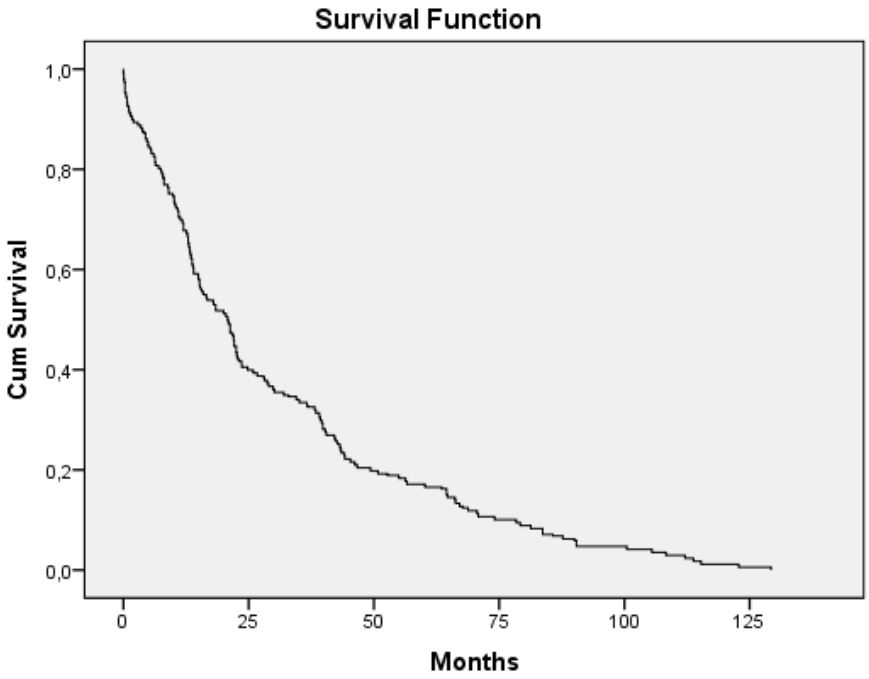

Table 1. Clinicopathologic Features of Pancreatic Tumors

	n	%
Histopathology		
Adenocarcinoma	260	76.9
Neuroendocrine tumor	38	11.2
Solid pseudopapillary neoplasia	17	5.0
Intraductal papillary mucinous neoplasm	12	3.6
Cystic neoplasia	11	3.3
Localization		
Head – neck	150	44.4
Body – tail	92	27.2
Ampulla	89	26.3
Other	7	2.1
Surgery		
Whipple	234	69.2
Distal pancreatectomy	98	29.0
Other	6	1.8
Postoperative complications (yes/no)	115/ 223	34.0 / 66.0
A. Surgical complications	85	25.2
Pancreatic cyst	55	16.3
Biliary fistula	14	4.1
Surgical site infection	12	3.6
Anastomotic leakage	2	0.6
Chylous ascites	2	0.6
B. General complications	30	8.8
Multiorgan failure	10	2.9
Respiratory complications	6	1.7
Hepatic failure	4	1.2
Deterioration in renal function or acute renal failure	4	1.2
Bleeding	2	0.6
Pleural effusion	2	0.6
Cerebrovascular accident	2	0.6

Table 2. Median, 1-Year, 2-Year, and 5-Year Survival Rate of Patients with Primary Pancreatic Malignant Tumors by Histological Subtypes

Relative Survival	Adenocarcinoma	IPMN	pNET	MCN	SPT
Median Overall	24.7	39	45.5	38.1	73.8
1-y OS,%	61.5	83.3	89.5	72.7	88.2
2-y OS,%	32.7	50	65.8	54.5	76.5
5-y OS,%	11.2	17	31.6	18.2	58.8

Overall survival (OS), intraductal papillary mucinous neoplasm (IPMN), pancreatic neuroendocrine tumor (pNET), mucinous cystic neoplasm (MCN), solid pseudopapillary tumor (SPT).