ORIGINAL ARTICLE

Survival and prognostic factors among hospitalized pancreatic cancer patients in Northwestern Iran

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Background: Pancreatic cancer (PC) is associated with a poor prognosis, with various modifiable risk factors affecting the survival of patients. Our aim was to evaluate the survival rate and the prognostic factors influencing survival in PC patients in northwestern Iran. **Materials and Methods:** All the PC patients admitted to the Imam Reza Hospital of Tabriz, Iran, from 2016 to 2020, were enrolled in this study. The survival rate and time were calculated, and the risk factors related to survival were evaluated by Cox regressions. The data were analyzed using the Cox proportional hazards model using STATA software. **Results:** Of 110 patients, 12-, 24-, 36-, and 48-month survival rates were 29.1%, 19.8%, 14.1%, and 8.5%, respectively, with the median survival time of seven months. The mean age was 65.5 years. The results showed that a higher age (hazard ratio [HR] [95% confidence interval (CI)] = 2.04 [1.20–3.46]), lower education (1.72 [1.03–2.89]), delayed diagnosis (1.03 [1.02–1.05]), hypertension (1.53 [1.01–2.31]), concomitant heart disorders (2.67 [1.50–4.74]), COPD (4.23 [1.01–17.69]), consanguineous marriage (1.59 [1.01–2.50]), and the presence of icterus complications (adjusted HR = 3.64 [1.56–8.49]) were directly associated with a worse survival. On the contrary, radiotherapy (0.10 [0.01–0.85]), chemotherapy (0.57 [0.36–0.89]), and surgical therapy (AHR = 0.48 [0.23–0.99]) were directly related to a good prognosis. **Conclusion:** Surgery, chemotherapy, and radiotherapy were the best predictors of survival in PC patients. Moreover, it seems that resolving jaundice can improve survival in these patients. It seems that increasing social awareness, treating underlying diseases, and employing an appropriate therapeutic method may promise a better outlook, improve the survival rate of patients, and reduce PC risk.

Key words: Pancreatic cancer, prognosis, survival

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INTRODUCTION

Pancreatic cancer (PC) is a lethal disease[1] causing more than 250,000 deaths each year. It is the eighth most common cause of cancer-related death worldwide and the fourth most common cancer in the world.[2] Iran ranks 11th among Asian countries in terms of PC mortality.[3] In parallel with an increase in the incidence of PC in developed countries, the incidence of this disease is also on the rise in developing and less-developed countries due to lifestyle changes. The incidence rate of PC is lower in Asians than in Caucasians and Africans.[4]

The etiology of this cancer is unknown, but various studies show that smoking, coffee consumption, and alcohol abuse may be associated with the risk of PC.[5] This cancer is also associated with advanced age, so that around 80% of patients belong to the age group

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of 60–80 years.[6] The diagnosis of this disease is generally established at final stages.[7]

The prognosis of PC is poor, with a 5-year survival rate of 1.5% to 17.4%.[8] In European countries, following the implementation of national cancer programs, the survival of PC patients started to rise[9] under the influence of various factors.[10] Studies have shown a higher 5-year survival for females than males with PC.[11] Race, lifestyle, concomitant underlying diseases, and treatment methods are among other important prognostic factors influencing the survival of PC patients.[5] Delayed diagnosis is probably the most important prognostic factor, and indeed most patients with PC remain asymptomatic until progression to advanced stages.[6] Standard treatments for PC include surgery and chemotherapy, as well as radiotherapy for some PC patients.[12]

Considering that PC is one of deadliest cancer, and the fact that its incidence is rising in developing countries, we aimed to study the survival rate of hospitalized Iranian PC patients and determine the risk factors associated with the survival of these patients in the northwest of Iran.

MATERIALS AND METHODS

Study population

This study was a survival analysis performed on hospitalized PC patients in the Turkish Azeri population living in northwestern Iran.[13]

The patients were recruited by the census sampling method. The data of the patients admitted to Imam Reza Hospital of Tabriz, as a medical training and research facility and the referral center in northwestern Iran), were gathered from April 2016 to April 2020. The hospital is affiliated with Tabriz University of Medical Sciences.

Clinical manifestations, laboratory tests, ultrasonography, ERCP, and contrast-enhanced computed tomography (CT) were used to diagnose PC and determine the necessary indications for surgery.[14] Abdominal masses, ascites, prominent weight loss, hepatic or distant metastases, as well as metastasis to distant lymph nodes, large veins, and upper mesenteric, hepatic, or celiac arteries were considered as contraindications for pancreatic surgery. On the other hand, indications for surgery included metastasis to the duodenum, stomach, colon, lymph nodes in the field of surgery, small arterial and small arteries and veins, as well as advanced age.[15]

The inclusion criteria for the current study were (i) the registration of PC patients from 2016 to 2020, (ii) the existence of contact numbers in the medical records, (iii) the definitive diagnosis based on the pathology results, (iv) the existence of sufficient information in the medical records, and (v) the patient's cooperation.

Study questionnaire

A questionnaire was designed according to published previous studies. For this purpose, a pilot study was also performed, and brainstorming ideas and experts' opinions were considered. The questionnaire consisted of demographic characteristics, clinical information, and the outcomes affecting the survival of PC patients. To assess the validity and reliability of the questionnaire, the content validity and test–retest methods were used, delivering a coefficient of 85%.

Data collection

Two medical students (A. E and KH. A) were trained how to complete the questionnaire using patients' medical records, or through phone calls, or when patients or their families were referred to the hospital. Pathological reports available at the hospital's pathology laboratory and medical records were reviewed again by professors (AK. T and V. L) to confirm PC diagnosis.

The patients were followed up until the end of August 2020 by phone calls (every 20 days) to record the survival rate. Survival time for living and deceased patients was considered from the diagnosis to either the end of the follow-up or death, respectively.

Statistical analysis

Statistical analysis was conducted by STATA software (ver. 15) (StataCorp, College Station, Texas, USA). The data were presented using mean (Standard deviation), median (min-max), and frequency (percent/rate/proportion). Survival time was expressed as median (0.95% confidence interval [CI]) in months. The Kaplan–Meier method was used to estimate the survival rates. Cox proportional hazards (PHs) regression analysis was conducted to determine the relationship between PC risk factors with death hazard by estimating the hazard ratio (HR) and 95% CI. In the multivariable analysis, a backward elimination strategy with $P < 0.05$ was utilized. Adjustments were made for age category, sex, employment status, and education level for the probable risk factors, including history of hypertension, diabetes, cerebrovascular accidents, myocardial infarction, blood pressure, heart disease, consanguineous marriage, family history of cancer, and other risk factors [Table 1]. We have followed exactly the same scenario stated by the reviewer; however, those variables which were not significant in the multivariable analysis were removed as per our selection of the multivariable backward strategy. The survival time for living and deceased patients was considered from the time

Table 1: Comparison basic and clinical characteristics of died and survived patients with pancreatic cancer (*n*=110)

Variables	Alive (*n*=18; 16.4%), *n* (%)	Dead (*n*=92; 83.6%), *n* (%)	*P*
Sex			
Male	9 (50)	63 (88.5)	0.13
Female	9 (50)	29 (31.5)	
Education			
Diploma and under diploma	9 (50)	74 (80.4)	0.006
Upper diploma	9 (50)	18 (19.6)	
Job			
Unemployed/housewife	9 (50)	36 (1.1)	0.36
Agriculture	1 (5.6)	24 (39.1)	
Self employed	4 (22.2)	12 (26.1)	
Governmental	4 (22.2)	19 (20.7)	
Cigarette			
Yes	1 (5.6)	30 (32.60	0.95
No	17 (94.4)	62 (67.4)	
Alcohol			
Yes	11 (61.1)	11 (12)	0.42
No	7 (38.9)	81 (88)	
Underling diseases			
Yes	11 (61.1)	67 (72.8)	0.31
No	7 (38.9)	25 (27.2)	
Diabetes mellitus			
Yes	5 (27.8)	34 (37)	0.45
No	13 (72.2)	58 (63)	
Hypertension			
Yes	5 (27.8)	46 (50)	0.08
No	13 (72.2)	46 (50)	
Heart disorders			
Yes	0	15 (16.3)	0.06
No	18 (100)	77 (83.7)	
COPD			
Yes	0	2 (2.2)	0.69
No	18 (100)	90 (97.8)	
IBD			
Yes	1 (5.6)	3 (3.3)	0.51
No	17 (94.4)	89 (96.7)	
CVA			
Yes	0	3 (3.3)	0.58
No	18 (100)	89 (96.7)	
Other diseases			
Yes	4 (22.2)	11 (12)	0.24
No	14 (77.8)	81 (88)	
Parent's family history of marriage			
Yes	4 (22.2)	28 (30.4)	0.48
No	14 (77.8)	64 (69.6)	
Family history of cancer			
Yes	4 (22.2)	30 (32.6)	0.38
No	14 (77.8)	62 (67.4)	
Metastasis			
Yes	6 (33.3)	40 (43.5)	0.42
No	12 (66.7)	52 (56.5)	
Metastasis to nondigestive tract			
Yes	4 (22.2)	14 (15.2)	0.46
No	14 (77.8)	78 (84.8)	
Metastasis to digestive tract			
Yes	2 (11.1)	35 (38)	0.027
No	16 (88.9)	57 (62)	

Contd...

Table 1: Contd...

Variables	Alive (*n*=18; 16.4%), *n* (%)	Dead (*n*=92; 83.6%), *n* (%)	*P*
Surgical methods			
Surgical	12 (66.7)	20 (21.7)	<0.001
Block	2 (11.1)	7 (7.6)	
Stant	1 (5.6)	41 (44.6)	
None	3 (16.7)	24 (26.1)	
Radiotherapy			
Yes	2 (11.1)	11 (12.4)	0.89
No	16 (88.9)	77 (86.5)	
Chemotherapy			
Yes	9 (50)	30 (34.1)	0.2
No	9 (50)	58 (65.9)	
Pain			
Yes	18 (100)	76 (82.6)	0.056
No	0	16 (17.4)	
Lose weight			
Yes	6 (33.3)	20 (21.7)	0.29
No	12 (66.7)	72 (78.3)	
Icterus			
Yes	8 (44.4)	52 (56.5)	0.34
No	10 (55.6)	40 (43.5)	
Other symptoms			
Yes	3 (16.7)	12 (13)	0.68
No	15 (83.3)	80 (87)	
Complications			
Yes	9 (50)	27 (29.3)	0.08
No	9 (50)	65 (70.7)	
Icterus			
Yes	1 (5.6)	11 (12)	0.42
No	17 (94.4)	81 (88)	
Anorexia			
Yes	4 (22.2)	10 (10.9)	0.18
No	14 (77.8)	82 (89.1)	
Abdominal and back pain			
Yes	4 (22.2)	6 (6.5)	0.034
No	14 (77.8)	86 (93.5)	
Weakness			
Yes	2 (11.1)	5 (5.4)	0.36
No	16 (88.9)	87 (94.6)	
Vomiting or diarrhea			
Yes	3 (16.7)	11 (12)	0.58
No	15 (83.3)	81 (88)	
Other complications			
Yes	2 (11.1)	7 (7.6)	0.62
No	16 (88.9)	85 (92.4)	
Place			
Head	11 (84.6)	51 (92.7)	0.42
Body	2 (15.4)	3 (5.5)	
Tail	0	1 (1.8)	
Age (years)			
Mean±SD	55.5±8.74	67.49±10.97	<0.001
Median (minimum-maximum)	53.50 (41-72)	68 (42-91)	
Duration of hospitalization (days)			
Mean±SD	11.38±9.39	8.44±7.61	0.26
Median (minimum-maximum)	6 (2-28)	6 (0-30)	
The time of ciggare usage (years)			
Mean±SD	4.44±2.27	6.25±11.75	0.90
Median (minimum-maximum)	0 (0-20)	0 (0-58)	

In all items were considered alive/dead. SD=Standard deviation; COPD=Chronic obstructive pulmonary disease; IBD=Inflammatory bowel disease; CVA=Cerebrovascular accident

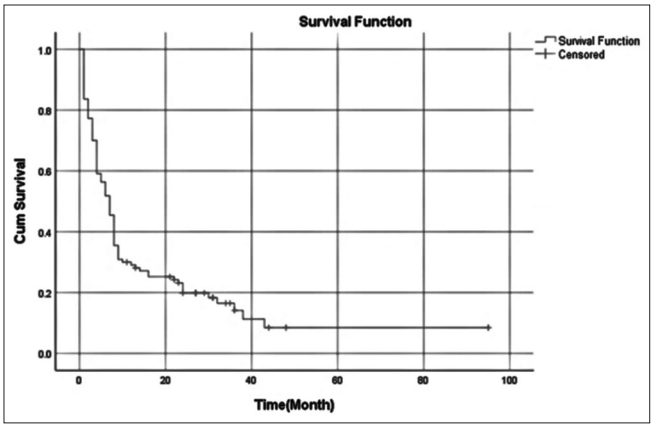

Figure 1: Kaplan–Meier overall survival probabilities in patients with pancreatic cancer

of diagnosis to either the last follow-up (as the censor) or death (as the event), respectively.

The time to the event was specific for each patient and was used along with the event indicator as the main outcomes in Cox regression.

The PH assumption was assessed by the Shoenfield residuals' test, indicating that the assumption was satisfied in the global test ($P = 0.085$) and all individual tests ($P > 0.05$ for all). Variables with $P \leq 0.1$ or 0.2 in univariate regression and variables with $P < 0.05$ in multivariable regression were assessed. All the analyses were carried out by a professor in biostatistics according to the guideline provided by Klein and Moeschberger.[16]

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Deputy of Research of Tabriz University of Medical Sciences (TBZMED. REC.2019.697). Data collection was performed after the approval of the deputy. Written informed consent was obtained from the patients or their families.

RESULTS

Initially, 148 patients were enrolled, of whom 31 and 17 patients were excluded due to incomplete records and no response to phone calls, respectively. Finally, 110 patients were included in the study.

Participants' profiles

The mean age of the patients, mean age at diagnosis, mean smoking duration, and median hospitalization duration were 65.5 ± 11.5 years, 64.4 ± 11.8 years, 6.0 years (min-max: 0–58), and 6.0 days (min-max: 3.0-12.5), respectively.

Most patients had low education and suffered from concomitant underlying diseases. Totally, 32.7% of the patients were smokers, with a median of 7.0 cigarettes per day (25% percentile-75% percentile: 3.0–14.3). Consanguineous marriage and a family history of cancer were observed in more than 30% of the patients. Nearly half of the patients had metastasis, especially to the digestive tract. Liver metastasis was recorded in 12.7% of the cases. Most patients had adenocarcinoma in the head (56.4%) of the pancreas and received nonpharmacological treatments. In 54.5% of the cases, icterus was observed, which decreased to 10.9% after the treatments. Icterus also developed after multiple metastases (50%), chemotherapy-induced liver toxicity (35.5%), and failure to respond to treatments [Table 1].

Results on the event (death)

The survival rates of 12-, 24-, 36-, and 48-month were seen in 29.1%, 19.8%, 14.1%, and 8.5% for patients, respectively, with an 83.6% death rate according to the Kaplan–Meier method. The median survival time was seven months (percentile 25–percentile 75: 22–3 months [5% CI: 5.7–8.3]). Overall, 92 out of 110 patients (83.6%) died at the end of the follow-up.

In the survival curve, a steep descent (i.e., a sharp slope) from 1.0 to about 0.3 was observed in the survival duration after the first 12 months of diagnosis, which reduced (from 0.3 to about 0.1) from 12th to about 48th month. A flat survival line was seen afterward until the end of the study.

Results of univariate cox regression

Kaplan-Meier overall survival probabilities in patients with pancreatic cancer [Figure 1]. Considering demographic characteristics, a higher age and a lower education level were significantly associated with the mortality rate ($P < 0.05$).

Regarding clinical variables, a positive history of diabetes, hypertension, heart disorders, COPD, and consanguineous marriage were directly and significantly related to a poor prognosis ($P < 0.05$ for all). Radiotherapy, chemotherapy, and surgical therapy were directly and significantly associated with a favorable prognosis [$P < 0.05$ for all, Table 2]. We reflected the reference categories in Table 1; however, it is completely customary to remove the reference categories in binary predictors in order to be concise. In addition, we reflect the comparison category in Tables 2 and 3 for binary variables.

Results of multivariate cox regression

Based on the results of multivariable analysis, a lower education level [Figure 2] and icterus were independently and directly related to death hazard. Furthermore, surgery and chemotherapy were inversely and significantly associated with the death HR of ($P < 0.05$ for all) [Table 3].

Furthermore, the likelihood ratio (LR) test showed a significant role for the demographic and clinical variables entered into the model (LR Chi-square = 64.4, df = 45 (Akaike information criterion = 638.7) and $P = 0.030$).

Table 2: Results of univariate Cox regression model for predictors of death in patients with pancreatic cancer

Variables	Category	*B*	SE	HR	95.0% CI for HR		*P*
					Lower	Upper	
Diabetes mellitus	Yes						
Age cat (years)							0.029[#]
	<60	Referent					
	60–70	0.489	0.269	1.631	0.962	2.764	0.069
	70+	0.711	0.270	2.035	1.199	3.455	0.008
Ciggrete time (years)							0.413[#]
	Not smoking	Referent					
	1–10	0.072	0.593	1.074	0.336	3.434	0.904
	10+	0.567	0.379	1.763	0.839	3.703	0.135
Duration cat							0.936[#]
	<4	Referent					
	4–10	0.073	0.261	1.076	0.645	1.795	0.780
	10+	−0.022	0.279	0.979	0.566	1.692	0.938
Age at diagnosis		0.03	0.009	1.03	1.02	1.05	<0.001
Sex	Male	0.168	0.227	1.183	0.758	1.845	0.459
Education	Diploma and under diploma	0.544	0.264	1.724	1.028	2.890	0.039
Job							0.436[#]
	Unemployed/housewife	−0.205	0.289	0.815	0.462	1.436	0.479
	Agriculture	0.185	0.308	1.203	0.657	2.201	0.550
	Self employed	−0.443	0.375	0.642	0.308	1.340	0.238
	Governmental	Referent					
Cigarette	Yes	0.026	0.223	1.026	0.663	1.588	0.907
Alcohol	Yes	0.606	0.326	1.834	0.968	3.473	0.063
Underling diseases	Yes	0.238	0.235	1.268	0.800	2.012	0.312
Diabetes mellitus	Yes	−0.047	0.216	0.954	0.624	1.458	0.828
Hypertension	Yes	0.425	0.211	1.530	1.011	2.314	0.044
Heart disorders	Yes	0.980	0.294	2.666	1.499	4.739	0.001
COPD	Yes	1.441	0.731	4.225	1.009	17.694	0.049
IBD	Yes	−0.261	0.588	0.770	0.243	2.441	0.658
Biliary disorders	Yes	−0.671	0.588	0.511	0.161	1.619	0.254
CVA	Yes	0.919	0.593	2.506	0.783	8.019	0.122
Other diseases	Yes	−0.275	0.322	0.760	0.404	1.428	0.394
Parent's family history of marriage	Yes	0.463	0.231	1.590	1.010	2.501	0.045
Family history of cancer	Yes	−0.012	0.223	0.988	0.639	1.530	0.958
Clinical presentations							
Pain	Yes	−0.507	0.279	0.603	0.349	1.041	0.069
Lose weight	Yes	−0.277	0.254	0.758	0.460	1.248	0.276
Icterus	Yes	0.070	0.210	1.072	0.710	1.620	0.740
Other symptoms	Yes	−0.094	0.311	0.910	0.495	1.673	0.761
Metastasis	Yes	0.078	0.211	1.081	0.715	1.634	0.712
Metastasis to nondigestive tract	Yes	−0.300	0.291	0.741	0.419	1.310	0.302
Metastasis to digestive tract	Yes	0.413	0.216	1.512	0.990	2.309	0.05
Treatment							0.001[#]
	Surgical	−0.962	0.307	0.382	0.209	0.698	0.002
	Blocking	−0.493	0.434	0.611	0.261	1.430	0.256
	Stenting	0.103	0.260	1.109	0.666	1.848	0.692
Radiotherapy	Yes	−2.266	1.074	0.104	0.013	0.851	0.035
Chemotherapy	Yes	−0.565	0.229	0.568	0.363	0.890	0.013
Complications							
Icterus	Yes	0.278	0.323	1.321	0.702	2.486	0.388
Anorexia	Yes	−0.304	0.336	0.738	0.382	1.426	0.366
Abdominal and back pain	Yes	−0.652	0.428	0.521	0.225	1.206	0.128
Weakness	Yes	−0.160	0.461	0.852	0.345	2.103	0.728
Vomiting or diarrhea	Yes	−0.244	0.322	0.784	0.417	1.472	0.449
Other complications	Yes	−0.267	0.395	0.765	0.353	1.662	0.499
Place	HEAD	−0.393	1.016	0.675	0.092	4.942	0.699

[#]Overall *P*. HR=Hazard ratio; CI=Confidence interval; SE=Standard error; Age cat=Age categorized; Ciggrete time=Duration of smoking (years); Duration cat=Duration categorized; COPD=Chronic obstructive pulmonary disease; IBD=Inflammatory bowel disease; CVA=Cerebrovascular accident

Table 3: Results of backward likelihood ratio cox regression model for predictors of death in patients with pancreatic cancer

Variables	Category	*B*	SE	HR	95.0% CI for HR		*P*
					Lower	Upper	
Education	Diploma and under diploma	0.624	0.300	1.867	1.036	3.364	0.038
Treatment							<0.001[#]
	Surgical	−0.736	0.370	0.479	0.232	0.988	0.046
	Blocking	−0.082	0.485	0.921	0.356	2.381	0.865
	Stenting	0.518	0.349	1.678	0.847	3.327	0.138
	Drug	Referent					
Chemotherapy	Yes	−0.519	0.248	0.595	0.366	0.967	0.036
Complication of icterus	Yes	1.292	0.432	3.639	1.560	8.493	0.003

[#]Overall *P*. HR=Hazard ratio; CI=Confidence interval; SE=Standard error

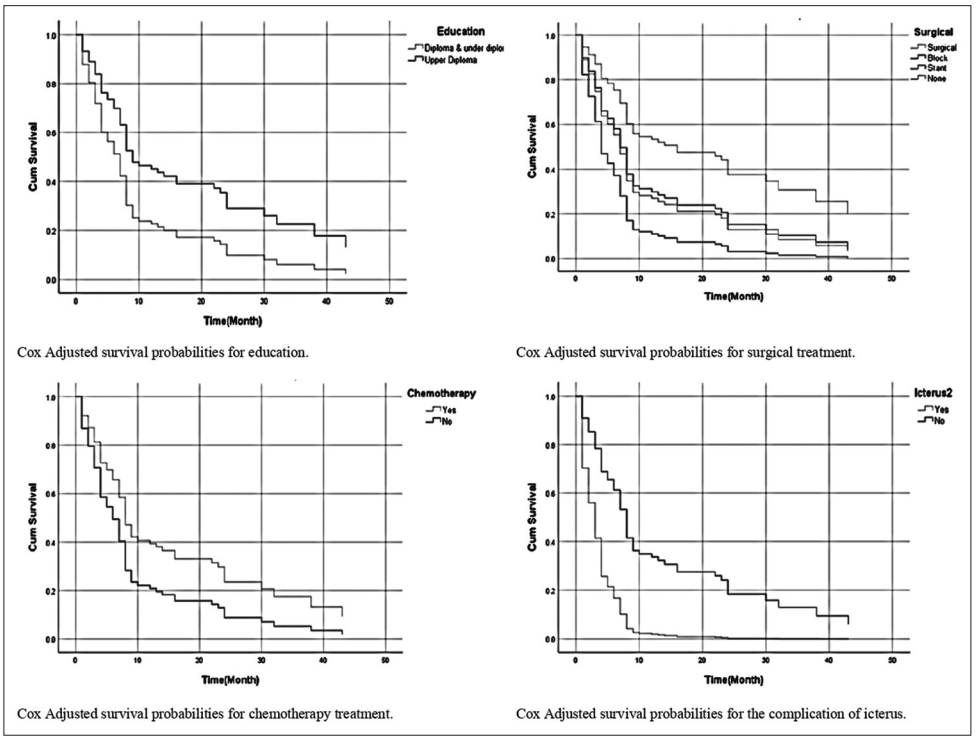

Figure 2: Cox-adjusted survival probabilities for a number of variables in patients with pancreatic cancer

The comparison of basic and clinical characteristics of died and survived patients with PC is shown in Table 1. These results indicated that the mortality risk was higher in patients with lower education, metastasis to digestive tract and patients treated with non-surgical medical procedures.

DISCUSSION

This was a survival analysis performed on the patients hospitalized due to PC in northwestern Iran. The mean age of the patients was 65.5 years, and most of them were male. Overall, 85% of the patients died during the study and most of the patients had low education and suffered from underlying diseases. In a study by Gong *et al.*, on patients with PC, the median age was 70 years, and the male-to-female ratio was approximately 1.1. Most of the tumors in the recent study were located in the pancreas head, and 11% of patients underwent surgical resection while 21% received either radiotherapy or chemotherapy.[17]

In another study conducted by Eloubeidi *et al.*, more than 90% of PC patients had either adenocarcinoma or carcinoma in the head of the pancreas with, a male-to-female ratio of 1:1. Furthermore, 13% of patients had a positive family history of malignancy, and 74% died during the follow-up.[1]

The results of the above-mentioned studies were similar to ours; however, we noticed relatively higher values in terms of the number of patients, family history of cancer, and the number of the patients who underwent tumor surgical resection. A higher male-to-female ratio may be due to the

higher rates of smoking and alcohol abuse among men. We also observed a tendency toward consanguineous marriage among our patients, which may explain the higher rate of family history of cancer.

In the present study, 12-, 24-, 36-, and 48-month survival rates were observed in 29.1%, 19.8%, 14.1%, and 8.5% of the patients, respectively.

Various studies have reported different survival rates in patients with PC. In a study by Zakaria *et al*., 1-, 3-, and 5-year survival rates were reported in 74.5%, 38.7%, and 23.4% of PC patients, respectively.[18] In another study, 1-year survival rate was reported 15%.[17] According to the data from 29 European countries, the prognosis of PC patients was poor with the 1-year survival rate of 26%[6] and the 5-year survival rate varying from 6% to 25% with a median survival of 3–20 months.[17,19-21] The survival rates reported for PC patients in European countries were better than ours, which may be due to their more sophisticated diagnostic and therapeutic methods.[17,19-21] However, many other factors could influence on survival in PC patients. In general, the incidence of PC is lower in Asian populations who may also experience a longer survival in comparison with non-Hispanic whites.[17,22]

The results of the current study showed that various factors such as a higher age, lower education level, delayed diagnosis, simultaneously suffering from either diabetes, hypertension, heart disorders or COPD, consanguineous marriage, and metastasis to the digestive tract were directly associated with a poor prognosis. On the other hand, a history of radiotherapy, chemotherapy, or surgery was independently related to a good prognosis.

According to the findings of other studies, smoking, alcohol consumption, older age, overweight, diabetes, a family history of cancer, the presence of concomitant underlying diseases, delayed or no treatment, and *Helicobacter pylori* infection have been related to a poor prognosis in patients with PC. Furthermore, surgery, radiation therapy, and chemotherapy have been associated with a better survival in these patients.[1,23]

Age is an independent predictor of prognosis in PC patients. This can be explained by the fact that younger people may have fewer underlying diseases and better tolerate extensive surgeries than older patients.[6,17]

Moreover, an early diagnosis can confer a good prognosis due to the early request or start of treatments, as well as the probable premalignant nature of tumors at initial phases.[24]

In the study of Li *et al*., PC was not associated with favorable outcomes even after surgery, radiotherapy, or chemotherapy. Recent evidence suggests that in most cases of PC, specific signaling pathways are suddenly activated, leading to disease progression and widespread metastasis.[25] Accordingly, genetic factors can play roles as prognostic factors, predicting the outcome and survival of PC patients, and therefore they can be effective in disease management and treatment.[10] In our study, we highlighted the role of consanguineous marriage not only in PC incidence but also in the survival of patients, highlighting the importance of genetic signatures. It is also worth mentioning that consanguineous marriage is a common phenomenon among west Asian populations, including Iranians.[13]

Although alcohol abuse is a known risk factor for acute and chronic pancreatitis, available data are not sufficient to support its role as an independent risk factor for PC.[9]

A study observed that diabetes predicted a poor survival in patients with PC.[26] Other studies have also confirmed this issue. In addition, hypertension has been noted as another factor affecting the survival of PC patients.[27] A weak association was reported between some chronic infections such as *H. pylori* and the PC prognosis.[9] In this study, *H. pylori* infection was seen in 20% of our patients, which was the third most common underlying condition after hypertension and heart diseases.

In our study, metastasis was negatively associated with the PC prognosis. In line, liver metastasis was reported to predict a poor prognosis in PC patients.[8]

We also observed that PC patients with metastasis to the gastrointestinal tract and liver were at a higher risk for death.

Treatment strategies are also assumed to significantly affect PC prognosis.[5] Early treatment prolonged the survival of PC patients even those diagnosed at advanced phases.[2] Surgery and radiotherapy have been recommended as standard treatments for PC.

A combination of surgery and radiotherapy improved survival better than radiotherapy alone.

Pancreatic tumors appear to be more sensitive to chemotherapy than other solid tumors. In fact, chemotherapy could improve the survival of CP patients, especially if used before surgery.

The use of a combination of therapies is beneficial for improving the survival of patients and reducing the side effects of treatments.[28,29] In one study performed on patients with PC, the median survival after 13 years of follow-up was longer in those who underwent surgical resection.[2]

In the current study, icterus was reported in 54% of the patients and nearly 56% of the patients had a pancreatic head tumor. The clinical features of PC depend on the size and location of tumors, as well as the presence or absence of metastases. Icterus has been reported in most studies as a result of the obstruction or compression of the bile duct due to a PC tumor. Consistently, it was reported that more than two-third of PC tumors appeared in the pancreas head, and jaundice was noticed as a continuous complication due to the obstruction of bile ducts.[30] Hence, our results were in concordance with those of the mentioned studies. Remarkably, we observed that icterus decreased to 11% after treatment, and it predicted a significantly poor survival in PC patients. Our study also showed that icterus was a poor prognostic factor, so the elimination of this complication is essential for long-term survival in PC patients.

CONCLUSION

PC is an age-associated lethal disease with a soaring incidence rate in the elderly. Although the disease has a poor prognosis, our results showed that the survival of PC patients could be extended by identifying and adjusting prognostic factors.

First, appropriate therapeutic measures are needed to be delivered to patients, and surgery, chemotherapy, and radiotherapy were the best predictors of survival in PC patients. Hence, timely use of these therapeutic methods and optimizing them can prolong patients' survival. Moreover, it seems that resolving jaundice can improve survival in these patients. In addition, it is needed to increase public awareness (for example by training packages) to encourage people for significant changes in their lifestyles, such as quitting smoking, doing exercises, and eating safe foods. It seems that screening the relatives of PC patients can be effective in detecting the disease at a younger age and improving patients' survival.

Limitation

The main limitation of this study was the lack of access to all PC patients diagnosed at the study period, which led to a small sample size over 4 years.

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Conflicts of interest

There are no conflicts of interest.

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