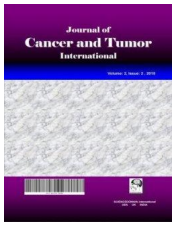

Journal of Cancer and Tumor International

7(3): 1-7, 2018; Article no.JCTI.31933
ISSN: 2454-7360

Exocrine Pancreatic Cancer: A Clinico-epidemiologic Study

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Authors' contributions

This work was carried out in collaboration between all authors. Authors HAEH, HAW and WA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author SR managed the analyses of the study. Author WE managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JCTI/2018/31933
Editor(s):
(1) Rafael Roesler, Cancer Research Laboratory, University Hospital Research Center, Federal University of Rio Grande do Sul, Brazil.
(2) Bing Yan, Department of Oncology, Hainan Branch of PLA General Hospital, China.
(3) Giulio Tarro, Professor, Foundation T. & L. de Beaumont Bonelli for Cancer Research, Napoli, Italy.
Reviewers:
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(5) Hideyuki Konishi, Kyoto Prefectural University of Medicine Graduate School of Medicine, Japan.
Complete Peer review History: http://www.sciencedomain.org/review-history/23886

Original Research Article

Received 5th January 2017
Accepted 12th March 2018
Published 30th March 2018

ABSTRACT

Background: Incidence of pancreatic cancer is relatively low compared to other types of cancer but had the lowest survival rate of all cancers.
Objective: To describe clinical-epidemiological features of pancreatic cancer patients recorded in our region and assessed its different prognostic factors.
Materials and Methods: The medical records of patients with pancreatic cancer attended to Clinical Oncology, and Nuclear Medicine department and Oncology centre between 2005-2014 were reviewed.
Results: This retrospective study included 380 patients with exocrine pancreatic cancer. Median age was 56 years with male predominance (65%). The most predominant histologic type was adenocarcinoma with grade III in 55% of patients. Tumours were located at the head of the

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pancreas were 75.5%, followed by the body (20.8%). Most patients presented with metastatic disease (57.9%). The pain was the most common presenting symptom (63.9%), while jaundice was found in 47.4% of patients. 23.7% of patients were smokers and 19.7% suffered from diabetes mellitus. 1-year survival rate was 28%. On multivariate analysis; we found significant lower survival rate with male gender (P=0.004), high-grade disease (P=0.002), older age (P=0.001), PC located in tail and body (P=0.006), high level of CA19-9(> 37U/L) (P=0.001), and metastatic cases (P=0.003).

Conclusion: This study is a clinical-epidemiologic survey of pancreatic cancer in our locality. However, because of its relatively small number of patients and retrospective nature; larger prospective studies are needed to study the epidemiologic and genetic basis of pancreatic cancer in our region.

Keywords: Pancreatic cancer; exocrine; chemotherapy; gemcitabine.

1. INTRODUCTION

The incidence of pancreatic cancer (PC) is relatively low compared to other types of cancer in 2012 is 2.4% worldwide [1]. In men, PC is the 11th most common cancer while the 9th in women and it is the 4th leading cause of cancer death in both sexes in the United States [2]. PC had the lowest survival rate of all cancers at both 1-year and 5 and ten years [3]. 94% of patients with PC die within five years of diagnosis, and 74% die within the first year [4]. This is attributed to the difficult diagnosis of PC in early stages; as at first presentation 52% of patients have distant metastasis and 26% have local spread disease [5]. Although PC can affect both exocrine and endocrine pancreas, 99% of tumours are exocrine [6]. Their many studies with variable results were conducted to identify prognostic factors of PC [7-9]. This study was conducted to describe clinical-epidemiological features of PC patients recorded in our region and assess different prognostic factors of PC.

2. MATERIALS AND METHODS

This study included all patients with pancreatic cancers presented to our department. The medical records of patients with PC attended to Clinical Oncology and Nuclear Medicine department and Oncology centre between 2005-2014 were reviewed. Patients with secondary malignancy were excluded. The study was approved by the Medical Ethics Committee.

Collected data included age, gender, grade, histology, site, stage and presenting symptoms of the disease. Risk factors for PC as diabetes mellitus, smoking, family history of PC and hypertension were also reviewed.

Overall survival was defined as the period between the date of diagnosis and date of death or last follow-up.

Variable prognostic factors for PC such as age, gender, site, grade, stage, site of the disease and CA19.9 were assessed for their significance through multivariate analysis.

2.1 Statistical Methods

The statistical package (SPSS version 15) was used. Data were expressed as number and percentage; Chi-square test was used for comparison of categorical variables, Kaplan-Meier test was used for survival function.

3. RESULTS

This retrospective study included 380 patients with exocrine PC. Their characteristics are shown in the Table 1. Median age was 56years with male predominance (65%). The most predominant histologic type was adenocarcinoma with grade III in 55% of patients. Tumours were located at the head of the pancreas in most of the cases (75.5%), where tumours of the body presented in (20.8%). Most patients were presented with metastatic disease (57.9%). The pain was the most common presenting symptom (63.9%), while jaundice was found in 47.4% of patients. 23.7% of patients were smokers and 19.7% suffered from diabetes mellitus. Pancreatitis was recorded in a small percent of cases (8%) that is one of the disadvantages of retrospective nature of the study.

Chemotherapy was administered in 35% of patients. Gemcitabine was the most common agent used (77%) followed by cisplatin (15%), and capecitabine (8%).

1-year survival rate was 28% (Fig. 1) with a median survival time of 7 months (95% CI: 5.961-8.039).

On multivariate analysis we found significant lower survival rate with male gender (P=0.004), high-grade disease (P=0.002), older age (P=0.001), PC located in tail and body (P=0.006), high level of CA19-9(> 37U/L) (P=0.001), and metastatic cases (P=0.003) Table 2.

Table 1. Demographic data of studied patients

Character	N0	%
Age		
Median 56(38-70)y		
≤60y	228	60
>60y	152	40
Gender		
Male	247	65
Female	133	35
Site		
Head	287	75.5
Body	79	20.8
Tail	14	3.7
Grade		
I	78	20.5
II	93	24.5
III	209	55
Pathological type		
Adenocarcinoma	364	95.8
Others	16	4.2
Disease presentation		
Resectable	35	9.2
Locally advanced	125	32.9
Metastatic	220	57.9
Risk factors		
Diabetes mellitus	75	19.7
Smoking	90	23.7
Hypertension	45	11.9
Family history	33	8.6
CA19.9		
≤37U/L	130	34.2
>37U/L	250	65.8
Presenting symptoms		
Pain	243	63.9
Jaundice	180	47.4
Vomiting	142	37.4
Weight loss	118	31
Anorexia	64	16.8

4. DISCUSSION

PC is considered a major health problem due to associated high mortality rates [10]. In our study, the 1-year survival rate was 28%. This lower survival rate can be explained by the late diagnosis of the disease as it remains asymptomatic for a long period due to the anatomic deeper site of the pancreas, this advanced stage of diagnosis make therapeutic approach has a low rate of success [11]. The majority of our patients were presented with metastatic disease (58%).

Table 2. Multivariate analysis of variables affecting survival

Variables	No. (%)	P
Age		
≤60 year	180(79%)	0.001
>60 year	70(46%)	
Gender		
Male	140(56.5%)	0.004
Female	100(75%)	
The site of the tumour		
Head	170(59%)	0.006
Body and Tail	40(43%)	
Grade		
III	160(76.5%)	0.0002
I-II	100(58.5%)	
Metastasis		
No	110(68.8%)	0.0003
Yes	110(50%)	
CA 19-9		
≤37 U/L	110(84.6%)	0.001
>37 U/L	150(60%)	

In the present study, median age was 56 years which is lower than that reported in both Saudi Arabia (63 y) [12] and the United States (72 y) [13], this may be due to overall younger population pool in Egypt or different biology of cancer. However, studies reported that incidence of PC increase with advancing age with a steep increase after the age of 50 y [14-16].

We found male predominance for PC, that is confirmed in other studies [17-19]. This higher rate in males can be explained by increase tobacco smoking and more prevalence of diabetes mellitus in males than females above the age of 25 [20].

Our results revealed that about two-thirds of PC occurred at the head of the pancreas that matches with other studies [21,22].

We found that adenocarcinoma was the most recorded histologic type that is by the literature [2,15].

It was reported that tobacco smoke contains about 69 chemicals can cause cancer as Arsenic, Cadmium, Nickel, Ethylene oxide [23] and the tobacco-specific nitrosamines NNK and NNN. So cigarette smokers are at higher risk for

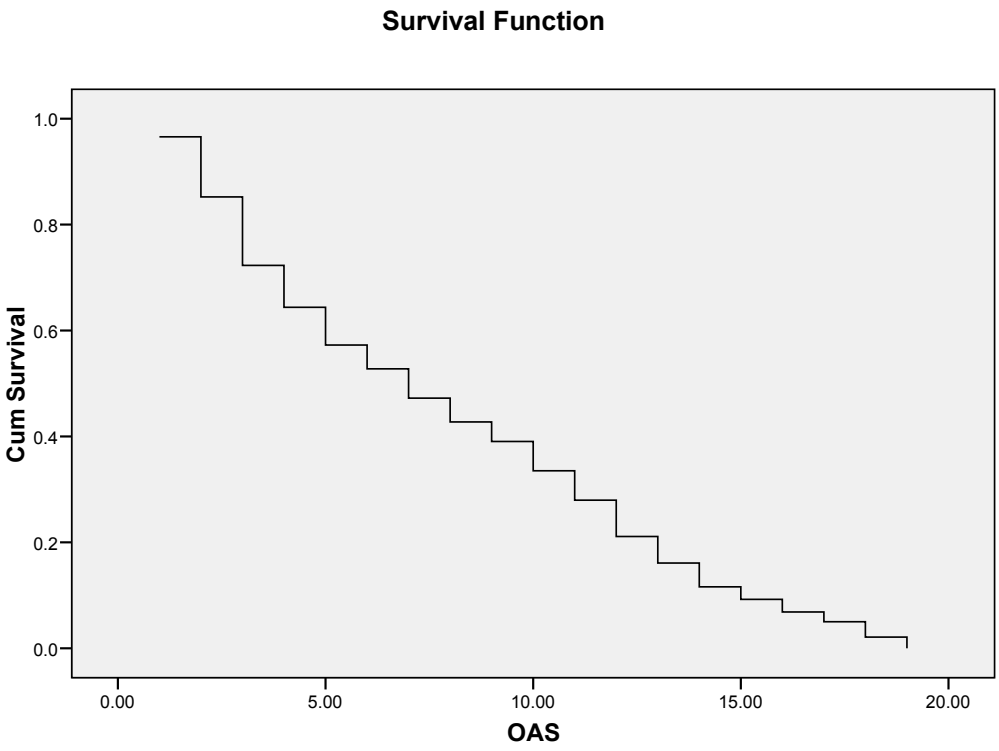

Fig. 1. Overall survival (OAS) among studied patients

developing PC compared with the non-smokers and this risk increases with increasing amount of pack-year smoked [24]. However, cessation of smoking may reduce this risk [25]. In our study, 24% of our patients were smokers. The other correlation found was the one between PC and diabetes mellitus and this result agrees with other studies [26-29]. This relation can be explained by the theory that hyperinsulinemia favours the occurrence of PC as insulin has not only metabolic effect but also has a mitogenic one [30]. Also, insulin-mediated mitogenesis can be stimulated by some medications used for the treatment of diabetes mellitus [31,32].

Most of our patients presented with abdominal pain followed by jaundice; this can prolong the interval between the onset of symptoms and the treatment as reported in the literature [33].

We found that age and stage of the disease are significant prognostic factors for survival that is supported by other studies [7,9]. Elevated CA 19-9 was found to be associated with an advanced stage, so this can explain the correlation between its high level and poorer survival as reported by Hartwig W et al. [34]. This is similar to our finding.

In our study, a pancreatic tumour located in the body had a poorer survival. It was reported that pancreatic tumours of the body have a higher risk of 11% mortality compared to the cephalic region with a higher degree of metastasis [21].

Among variable prognostic factors, authors report histologic grade as a significant predictor of survival [35-37]. This made Elton et al. devised a cytologic grading system for biopsy specimens obtained by endoscopic ultrasound-guided fine needle aspiration in patients with PC to help prediction of survival [38]. One possible aetiology of poorer survival in males than females is the presence of lower grade tumours in females [39,40].

Our study had some limitations like relatively small number of patients and retrospective nature.

As pancreatic cancer is genetically very complex with a high diversity of mutations, early diagnosis with the new protein markers may lead to early intervention and better prognosis [41]. Molecular markers are important not only because they can offer a better understanding of clinical outcome, but also because it can guide the research for

new molecular-based therapies Germline mutations of p16INK4A/p14ARF locus is a characteristic genetic alteration observed in >80% of PC. This locus encodes for two related, and partially overlapping, suppressor genes. Several studies confirmed the role of p16 expression as a prognostic factor in PDAC [42,43].

In particular, a lower survival has been observed in patients with p16 mutations or hypermethylation.

5. CONCLUSION

Our study is a clinical-epidemiologic survey of pancreatic cancer in our locality. However, because of its relatively small number of patients and retrospective nature; larger prospective studies are needed to study the epidemiologic and genetic basis of pancreatic cancer in our region. This study investigated the association between clinicopathological parameters, treatment selection, and laboratory tests data with the prognosis of patients with pancreatic cancer and so; can guide future clinical practice in the management of pancreatic cancer patients. However, studies of molecular prognostic factors are needed to help choice of proper treatment.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history/23886