International Surgery Journal
Bazine A et al. Int Surg J. 2018 May;5(5):1628-1632
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: http://dx.doi.org/10.18203/2349-2902.isj20181389

Original Research Article

Pancreatic ductal adenocarcinoma in a Moroccan population: analysis of six years experience

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Received: 09 March 2018
Accepted: 19 March 2018

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ABSTRACT

Background: Few studies have been done to investigate pancreatic cancer in Morocco. Therefore, the aim of our study was to describe the epidemiological, clinical and therapeutic features of pancreatic ductal adenocarcinoma in Moroccan population.
Methods: Author retrospectively reviewed the medical data of pancreatic ductal adenocarcinoma patients presented to the Medical Oncology Department of the Military Hospital Moulay Ismail in Meknes, Morocco, from January 2011 to December 2016.
Results: The study included 67 cases of pancreatic ductal adenocarcinoma. The mean age of patients was 61.24±10.35 years. Male/female ratio was 3.2/1. 20.9% of patients were cigarette smokers, 10.5% alcoholics. 23.9% diabetics, 3.0% with a positive family history of pancreatic cancer and 25.4% with a family history of diabetes mellitus. The main symptoms for consultation were weight loss (68.6%), abdominal pain (64.2%), jaundice (53.7%) and vomiting (25.4%). The tumour was located to the pancreatic head in 71.6% of cases. Stage IV disease was the most common stage representing 47.8% of patients. Biliary and duodenal stent placements were respectively performed in 10.4% and 3.0% of patients. 23.9% of patients underwent curative surgery, 7.5% had palliative surgery and 86.6% received chemotherapy. The median overall survival for the entire cohort was 9.3 months (95% CI 7.2-12.1 months) with a median follow-up of 9.7 months (2-63 months).
Conclusions: The data on pancreatic ductal adenocarcinoma in Moroccan population are similar to the epidemiologic literature data. With multimodality treatments, the results in terms of survival benefit seem to be similar to those in Asian and Caucasian populations.

Keywords: Diagnosis, Epidemiology, Pancreatic neoplasm, Therapeutics

INTRODUCTION

Pancreatic cancer is fatal cancer with the annual death rate nearly approximates its incidence.[1] It is the 12th most frequent cancer worldwide with 338 000 new cases and the 7th most common cause of cancer death in the world with 331 000 deaths per year in both sexes in 2012.[2,3] Pancreatic ductal adenocarcinoma (PDAC) is the most common malignancy of the pancreas. It accounts for about 90% of pancreatic cancers.[4,5] In Morocco, according to cancer register of Casablanca 2008-2012, which represents 10% of Moroccan population, it is the

17th most common cancer with a standardized incidence ratio of 1.4 per 100 000 people.[6]

To the best of our knowledge, few studies have been done to investigate pancreatic cancer in Morocco.[7-10] Therefore, the aim of our study was to describe the epidemiological, clinical and therapeutic features of PDAC in Moroccan population.

METHODS

Author retrospectively reviewed the medical data of PDAC patients presented to the Medical Oncology Department of the Military Hospital Moulay Ismail in Meknes, Morocco, from January 2011 to December 2016. Only the patients with histopathologically proven PDAC were recruited into the study. Other histological types, such as neuroendocrine, pseudo-papillary, acinar cell, serous, mucinous and intraductal carcinomas were excluded.

Epidemiological data included age, sex, body mass index (BMI), alcohol consumption, smoking status, family history of cancer, diabetes mellitus, and history of chronic pancreatitis. Tumor features were also recorded including the presenting symptoms, the site in the pancreas, the histologic grade, the serum tumor markers, and the extension of the disease according to TNM (tumor/node/metastasis) classification adopted by the AJCC (American Joint Committee on Cancer), 7th edition.[11] Data on endoscopic, surgical, oncological and supportive therapy performed were also reported. Overall survival (OS) was calculated from the date of histological diagnosis to date of death for any cause or last follow up visit.

Statistical analysis was performed using Epi Info version 7.2. Quantitative data were expressed as means±standard deviation (SD) or median values with range while qualitative data were expressed as numbers with percentages. The survival analysis was generated using the Kaplan-Meier method. *P*-values <0.05 were considered statistically significant.

The study was approved by the Ethical Committee of the Military Hospital Moulay Ismail in Meknes in Morocco and the confidentiality of data was maintained throughout the study.

RESULTS

From January 2011 to December 2016, 67 patients were diagnosed with PDAC at the Medical Oncology Department of the Military Hospital Moulay Ismail in Meknes, Morocco. The mean age of patients was 61.24±10.35 years with extremes ranging from 38 years to 89 years. There were 51 males (76%) and 16 females (24%). Male/female ratio was 3.2/1. Socio-demographic characteristics are summarized in table 1.

Table 1 illustrates also the frequency of well-known risk factors related to PDAC. 16.4% of cases were overweight, 9.0% were obese and 3.0% were very obese. While no female alcoholics or smokers were reported in our study, 20.9% of male patients were cigarette smokers and 10.5% were alcoholics. The proportion of PDAC patients with diabetes mellitus was 23.9%, and 68.8% of them were type 2 diabetics. 3.0% of patients had a positive family history of pancreatic cancer and 25.4% had a family history of diabetes mellitus. No previous history of chronic pancreatitis was found.

Table 1: Epidemiological characteristics of patients.

Characteristic	No. of patients	Percentage
Total of patients	67	100
Age		
Median	61.24 ± 10.35	
Range	38-89	
Sex		
Male	51	76
Female	16	24
Body mass index		
Normal	48	71.6
Overweight	11	16.4
Obese	6	9.0
Very obese	2	3.0
Smoking history		
Yes (only males)	14	20.9
No	53	79.1
Alcohol history		
Yes (only males)	7	10.5
No	60	89.5
Diabetes mellitus		
Yes	16	23.9
No	51	76.1
Family history of diabetes mellitus		
Yes	17	25.4
No	50	74.6
Family history of pancreatic cancer		
Yes	2	3.0
No	65	97.0

The main symptoms for consultation were weight loss (68.6%) and abdominal pain (64.2%), followed by jaundice (53.7%) and vomiting (25.4%). Other less common symptoms included gastrointestinal hemorrhage (6.0%), diarrhea (3.0%), steatorrhea (3.0%) and fever (3.0%) (Table 2).

The tumor was located to the pancreatic head in the majority of cases (71.6%), while 18.0% of patients had cancer located in the tail and only 10.4% of patients in the body of the pancreas. Histological examinations revealed 52.2% of well-differentiated PADC, 32.8% of moderately differentiated PADC, and 15.0% of poorly differentiated PADC. Cancer antigen 19-9 (CA19-9) and carcinoembryonic antigen (CEA) were elevated in 64.2% and 52.2% of patients respectively.

Table 2: Tumor characteristics.

Characteristic	No. of patients	Percentage
Presenting symptoms		
Weight loss	46	68.6
Abdominal pain	43	64.2
Jaundice	36	53.7
Vomiting	17	25.4
Site of primary tumour		
Head	48	71.6
Body	7	10.4
Tail	12	18.0
Histologic grade		
Well-differentiated PDAC	35	52.2
Moderately differentiated PDAC	22	32.8
Poorly differentiated PDAC	10	15.0
CA 19-9		
Normal	24	35.8
Elevated	43	64.2
CEA		
Normal	32	47.8
Elevated	35	52.2
Tumour stage		
I	3	4.5
II	10	14.9
III	22	32.8
IV	32	47.8

19.4% of patients had localized resectable disease at presentation (stages I-II). 32.8% of patients presented with locally advanced, unresectable disease (stage III) and 47.8% of patients had metastatic disease (stage IV). Metastases sites included the liver in 44 patients (65.7%), the peritoneum in 25 patients (37.3%), the lungs in 14 patients (20.9%), the lymph nodes in 12 patients (17.9%), and other rare sites in 4 patients (6.0%) (Table 2).

Biliary stent placement during endoscopic retrograde cholangiopancreatography was reported in 7 patients (10.4%) (4 cases with metallic stents and 3 cases with plastic stents). Duodenal stent implantation for duodenal obstruction was performed in only 2 cases (3.0%). 23.9% of patients underwent curative surgery including 11 cases of duodeno-pancreatectomy cephalic, 3 cases of left spleno-pancreatectomy, and 2 cases of total pancreatectomy. Palliative surgical treatment was performed in 5 patients (7.5%) (3 cases of the enteral bypass and 2 cases of the biliary bypass). 86.6% of patients received chemotherapy as an adjuvant (17.9%), palliative (64.2%) or neo-adjuvant (4.5%) treatment. The two most common regimens were single-agent gemcitabine in 32 patients (47.8%) and gemcitabine + oxaliplatin in 15 patients (22.4%). Only one patient (1.5%) received concurrent chemoradiation with 5FU for a locally advanced disease. 11.9% of patients had symptomatic treatment only. All patients benefited from supportive care for nutrition and pain (Table 3).

Table 3: Treatment modalities.

Modality	No. of patients	Percentage
Biliary stent placement	7	10.4
Metallic stent	4	5.9
Plastic stent	3	4.5
Duodenal stent placement	2	3.0
Curative surgery	16	23.9
Duodeno-pancreatectomy cephalic	11	16.4
Left spleno-pancreatectomy	3	4.5
Total pancreatectomy	2	3.0
Palliative surgery	5	7.5
Enteral bypass	3	4.5
Biliary bypass	2	3.0
Chemotherapy	58	86.6
Neo-adjuvant	3	4.5
Adjuvant	12	17.9
Palliative	43	64.2
Concurrent chemoradiation	1	1.5
Only Symptomatic treatment	8	11.9
Supportive care	67	100

The median OS for the entire cohort was 9.3 months (95% CI 7.2-12.1 months) with a median follow-up of 9.7 months (2-63 months). The median OS for the patients with locally resectable disease was 32.9 months (95% CI 29.4-39.7 months), as compared with a median OS of 11.3 months (95% CI 9.2-14.9 months) for those with locally advanced, unresectable disease and a median of 6.6 months (95% CI 5.3-9.2 months) for those with metastatic disease.

DISCUSSION

Current work is one of the few studies of PDAC conducted in Morocco. We reported 67 new cases from January 2011 to December 2016, with an incidence of 11.2 cases each year. The incidence of pancreatic cancer varies substantially across regions of the world. The age-standardized rate (ASR) incidence for pancreatic cancer in 2012 was highest in Northern America (7.4/100000) and Western Europe (7.3/100000), followed by other regions in Europe and Australia/New Zealand (6.5/100000). The lowest rates (1.0/100000) were observed in South-Central Asia and most of Africa. These wide variations in incidence rates of pancreatic cancer in different parts of the world have been attributed to exposure to known or suspected risk factors which can be grouped as either environmental and host factors. The environmental factors may be modifiable while the most host factors are non-modifiable.[12-14] Modifiable risk factors include obesity, smoking, and alcohol. Risk factors that are not modifiable include age, gender, diabetes mellitus, family history of pancreatic cancer and

chronic pancreatitis.[15-21] Generally, the characteristics of our patients were mostly similar to that reported in the literature. The mean age of our patients was 61.24 years, which is similar to that observed in other studies.[22-28] However, other literature data reported higher average age (67-77 years).[29-32] In accordance with the results of other studies, the patients were predominantly males. This is due to, at least in part, increased cigarette smoking and alcohol consumption in males.[33-36] The results showed that the proportion of PDAC patients with diabetes mellitus was 23.9%, which is comparable to that reported by several authors.[1,22,28]

Similar to the findings of other studies, the presenting symptoms for PDAC were dominated in our series by weight loss (68.6%), abdominal pain (64.2%) and jaundice (53.7%).[27,36,37] Present study showed that the tumor was located to the pancreatic head in the majority of cases (71.6%), This was in accordance with the results reported in the literature.[22,25,28] As for many other cancers in Morocco, we noted that the majority of our patients presented with locally advanced or metastatic disease. This confirms the late presentation of PDAC and agrees with the finding of other studies.[27-29]

Treatment modalities of PDAC include surgery, chemotherapy, radiation therapy, and palliative care. Treatment options are selected depending on the disease's stage and the patient's condition in a multidisciplinary approach.[38] Only 23.9% of the patients underwent radical surgery, which is similar to other series.[23,36,37] On the other hand, 20.9% of patients underwent palliation with biliary stent placement (10.4%) for biliary obstruction, duodenal stent implantation (3.0%) for duodenal obstruction and palliative surgery (7.5%) with enteral or biliary bypass. Although FOLFIRINOX has shown significant survival benefit than gemcitabine in selected patients with metastatic pancreatic cancer, Gemcitabine was the most commonly used chemotherapy in our cohort.[39] This is due to increased risk of febrile neutropenia, gastrointestinal toxicities, sensory neuropathy and fatigue with FOLFORINOX. Therefore, its use is constrained to patients aged 75 years or younger with good performance status and without significant risk of cholangitis or cholestasis.[38,39] To improve quality of life, all patients benefited from supportive care for nutrition and pain.

Despite the advancement in research over the last two decades, PDAC remains a fatal malignancy with an overall 5-year survival of 5% for all stages combined.[40] Our study also showed a very poor prognosis of PDAC with a median OS of 9.3 months for the entire cohort.

CONCLUSION

The data on PDAC in Moroccan population are similar to the epidemiologic literature data. With multimodality treatments, the results in terms of survival benefit seem to be similar to those in Asian and Caucasian populations. Further larger-scale prospective studies are recommended to analyze the epidemiological, clinical and therapeutic features of this disease in the Northern Africa region.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Bazine A, Fetohi M, Tores M, Tanz R, Tahiri ME, Choho A, Ichou M. Pancreatic ductal adenocarcinoma in a Moroccan population: analysis of six years experience. Int Surg J 2018;5:1628-32.