Original Article

Delayed diagnosis of pancreatic cancer reported as more common in a population of North African young adults

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Background: Pancreatic cancer is one of the most challenging tumor entities worldwide, characterized as a highly aggressive disease with dismal overall prognosis and an incidence rate equaling mortality rate.

Objective: In order to have an update about pancreatic cancer incidence and evolution in North Africa, we conducted an epidemiological analytical retrospective study at the level of three Algerian regions: Sidi-bel-Abbes, Oran and Tlemcen along the last eight years [2006-2013].

Methods: We performed a retrospective hospital-based study in which we analyzed the records of 160 pancreatic cancer patients registered, evaluated and treated in a Northern African region; at the level of hospital centers of the three western Algerian regions from 2006 to 2013.

Results: Along the period of study, 160 patients were diagnosed with pancreatic cancer; with a mean age of 66.2 years, and a sex ratio of 1.65; other parameters such as a medical history smoking and alcoholism history, tumor site; histological type as well as the stage of diagnosis were also enrolled in the study. Our statistical analyses reported a very significant correlation between patients who belonged to the age group of 21-40 years and the advanced stage of diagnosis (basing on TNM classification) with P=0.02.

Conclusions: Pancreatic cancer is increasingly diagnosed in young adults at an advanced stage in North African regions.

Keywords: Pancreatic cancer; young adults; delayed diagnosis; North Africa

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Introduction

Pancreatic cancer is one of the most challenging tumor entities worldwide, characterized as a highly aggressive disease with dismal overall prognosis and an incidence rate equaling mortality rate (1,2). Less developed regions have low rates of pancreatic cancer (2.4), it is relatively rare in Africa and Asia (3,4). However and despite all medical research efforts; it ranks as the fourth deadliest cancer in the United States after cancers of the lung, colon, and breast. In 2013, an estimated 45,220 newly diagnosed of pancreatic cancer and 38,460 deaths were expected in the US (5).

The main reason could be the difficulty of its diagnosis since no specific cost-effective screening tests can easily and reliably find early-stage pancreatic cancer in people who have no symptoms of the disease. This means it is often not found until later stages when the cancer can no longer be removed with surgery and has spread from the pancreas to other parts of the body (6). In fact, the Surveillance, Epidemiology, and End Results (SEER) database also shows that for every 12.2 patients diagnosed per 100,000, 10.9 will die from pancreatic cancer, despite the best efforts of researchers and clinicians to improve survival outcomes in patients (7).

In order to have an update about pancreatic incidence and evolution in western Algeria, we conducted an epidemiological analytical retrospective study at the level of three western Algerian regions: Sidi-bel-Abbes, Oran and

Tlemcen along the the last 8 years [2006-2013].

Patients and methods

The population

This hospital based study was carried out respectively at the level of Surgery Departments of the University Hospitals of Sidi-bel-Abbes and Tlemcen as well as the Pathology Department of the Military Hospital of Oran (HMRUO) where patients' data were collected routinely. In the current epidemiological retrospective study we analyzed patients' records basing on different parameters such as: age, gender, medical history, smoking history, as well as TNM histopathological classification. A total sample of 160 patients aged between 16-96 years was diagnosed with pancreatic cancer between 2006 and 2013.

The statistical analysis

Concerning the statistical analytical study, the raw data were summarized using rates and cross-tabulations. Associations between categorical parameters were tested using Pearson's chi-squared test (χ^2) test. Results were presented using P value; the level of its significance was limited by the rate of 5%. All data were processed and analyzed via SPSS 20.0 (Statistical Package for the Social Sciences, IBM Corporation; Chicago, IL, USA. August 2011).

Results

Of 160 patient records were included in our survey, 105 (65.6%) were male and 55 (34.8%) were female. There was an overall male predominance with the male to female ratio of 1.9 (*Table 1*). The median age at the diagnosis was 62.2 with a minimum age of 16 years and maximum of 96 years.

More than the half of our patients were aged between 61-80 years old (57.5%) followed respectively by the age groups of 41-60 (21.2%), the more than 80 (13.7%); 21-40 (6.87%) and finally patients aged less than 20 (0.62%) (*Table 1*).

The site of the tumor was in the head of the pancreas in 90% of cases, in the body of the pancreas in 5.62% of cases, and in the tail of the pancreas in 4.3% of cases (*Table 1*).

The proportion of patients with a history of cigarette smoking was 32.5%; all the smokers were male patients; similar results were also reported for history of alcohol; where only males were alcoholics (20.6%) (*Table 1*).

Table 1 Patients medical features

Characteristics	Number of cases	Percentage (%)
Sex (n=160)		
Male	105	65.62
Female	55	34.38
Sex ratio	–	1.9
Age (years)		
<20	1	0.62
21-40	11	
41-60	34	21.25
61-80	92	57.5
>80	22	13.75
Smoking history		
Male smoker	52	32.5
Female smoker	0	0
Male non-smoker	24	15
Female non-smoker	55	34.38
Not mentioned	29	18.12
Alcohol history		
Alcoholism (only males)	33	20.6
Not mentioned	52	32.5
Symptoms and signs		
Jaundice	148	92.5
Abdominal pain	152	95
Right hypocondrium pain	145	90.6
Vomiting and nausea	138	86.3
Weight loss	140	87.5
Dark urine	102	63.75
Pruritus	105	65.6
Tumour site		
Head of the pancreas	144	90
Body of the pancreas	9	5.63
Tail of the pancreas	7	4.37
Histopathology		
Well differentiated adenocarcinoma	72	45
Moderately differentiated adenocarcinoma	33	20.62
Poorly to moderately differentiated adenocarcinoma	30	18.75
Infiltrant adenocarcinoma	10	6.25
Poorly differentiated carcinoma	7	4.37
Non differentiated carcinoma	5	3.12
Not mentioned	3	1.89

Table 1 illustrates as well the following histological types: 20% moderately differentiated adenocarcinomas; 45% well differentiated adenocarcinomas; 6% infiltrant adenocarcinomas; 3% non-differentiated carcinomas; 4% poorly differentiated carcinomas and 18% poorly to moderately differentiated adenocarcinomas.

The majority of our patients complained from the following symptoms: abdominal pain (95%); jaundice (92%); right hypocondrium pain (90%); vomiting and nausea (86%); weight loss (87%); dark urine (63%); pruritus (65%); acholic stools (57%) (*Table 1*).

Table 2 demonstrates the most common diseases recorded in medical history of our studied population which were respectively: high blood pressure (20.6%); type 2 diabetes (15%) and type 1 diabetes (13%).

Table 2 Patients' medical history

Medical history	Number of cases	Percentage (%)
High blood pressure	33	20.6
Males	20	12.5
Females	13	8.1
Type 1 diabetes	22	13.7
Males	16	10
Females	6	3.7
Type 2 diabetes	25	15.6
Males	16	10
Females	9	5.6
Nothing to report	80	50
Males	53	33.1
Females	27	16.8

Table 3 illustrates the different proportions of diagnosis stages of our patients. A total of 26.2% were diagnosed at M1 stage; followed respectively by T4 stage (21.8%); T3 (21.2%); T2 (13.2%); N1 (10.6%); T1 (4.3%) and Tis (1.8%).

In order to deepen our investigation, we performed a statistical analytical study by which we studied possible association between patient's age group and the stage of diagnosis (TNM classification) via Pearson's chi-squared test. Our statistical analyses reported a significant association between patients aged between 21-40 years and the stage of diagnosis with P=0.02 i.e., (P>0.05); however any significant association was reported between the other age groups and the stage of diagnosis (*Table 3*).

Discussion

The present survey is one of the very few surveys who studied the profile of pancreatic cancer in North Africa in general and Algeria in particular.

With a sex-ratio of 1.9 our investigation confirmed once more that men are more likely to develop pancreatic cancer than women. These results matched with many other previous investigations as those of Schiffman *et al.* (8).

Our results showed that 32% of our patients were cigarette smokers, and 20% were alcoholics; which could represent a risk factor for developing a pancreatic cancer since several published reports showed that smokers had about a 2-fold increased risk, compared to nonsmokers (9,10).

We noticed also that most of our patients complained from Jaundice; right hypochondrium pain and abdominal pain; which proves that pancreatic cancer is a silent disease, as reported in many other findings stated that pancreatic cancer symptoms do not manifest early and initial symptoms

Table 3 Association between age and TNM histopathological classification

Characteristics	Tis (%)	T1 (%)	T2 (%)	T3 (%)	T4 (%)	N1 (%)	M1 (%)	P value
Age (years)								
<20	–	0	0	0	0	0	1 (0.6)	–
21-40	–	0	1 (0.6)	3 (1.9)	2 (1.25)	1 (0.6)	4 (2.5)	0.027
41-60	1 (0.6)	1 (0.6)	6 (3.7)	7 (4.3)	5 (3.1)	6 (3.7)	8 (5.0)	0.928
61-80	1 (0.6)	3 (1.9)	12 (7.5)	21 (13.1)	21 (13.1)	9 (5.6)	25 (15.6)	0.733
>80	1 (0.6)	3 (1.9)	3 (1.9)	3 (1.9)	7 (4.3)	1 (0.6)	4 (2.5)	0.521
Total	3 (1.8)	7 (4.3)	22 (13.7)	34 (21.2)	35 (21.8)	17 (10.6)	42 (26.2)	

P, statistical significance.

are often nonspecific (11). Concerning tumors' location, most of them were located in the head of the pancreas (90%), followed respectively by cancer of the neck and the tail of the pancreas which represented a tiny minority. The study of Kalser *et al.* demonstrated as well that more than two thirds of pancreatic cancers occur in the head of the pancreas (12).

Diabetes mellitus was associated and pointed in several investigations as possible risk factor for pancreatic cancer (10); which concord to our findings since 30% of our studied population presented type 1 and type 2 of diabetes (*Table 2*).

Our survey demonstrated an increasing frequency of pancreatic cancer with the advanced age of patients since most of them were aged between 61 and 80 years old, these results agree with those of Shibata's *et al.* who concluded that this could be due to the dietary habits of the patients (13).

In the other hand; the current investigation confirmed indeed the rarity of pancreatic cancer in young adults; since only 7% of our population suffered from it, which agrees with the results of Perez *et al.* who found that the incidence of identified pancreatic carcinomas in patients under the age of 30 was only about 0.46/million (14). Same conclusion for Lüttges *et al.* who evaluated the incidence of pancreatic ductal adenocarcinomas in patients aged of 40 years old and was approximately equal to 0.3%, and the incidence in patients aged of 20 years was only about 0.1% (15).

However, despite the low rate of our patients (7%) belonging to that young age group; 36.36% of them were diagnosed at M1 stage which represented the majority. Concordant with our results those of Brand *et al.* who found that pancreatic cancer is increasingly diagnosed in the younger at an advanced stage (16). Berry *et al.* stated that nearly 50% of patients aged between 16 and 54 with pancreatic cancer are more likely than those who are older to be diagnosed at a stage when the disease is incurable, because of poor awareness, misdiagnosis and care delays (17).

Some authors confirm that pancreatic cancer is frequently diagnosed at an advanced stage, possibly because of the tumor biology showing an aggressive behavior and symptoms often being non-specific mainly in the young (18); Gulliford *et al.* reported as well that patients with some less common cancers such as pancreatic cancer were more likely to require three visits or more to their primary care physician before they were referred to a specialist (19). What we have to emphasis as well is the status of Algeria as a third world country, thus it's undeniable that lack of healthcare centers, high prices of drugs, cancer therapies, medical checkups as well as the low socioeconomic level of Algerian citizen are all major factors which may have a direct impact on that fatal disease survival chances.

Since most of our patients had pancreatic adenocarcinomas (*Table 1*) presented in late stage at the time of diagnosis; their prognosis was pretty poor; with a 1-year survival rate of 20% and a 5-year survival rate of less than 5%: as explained the survey of Kuvshinoff *et al.* (20). The only hope of long-term survival is if curative resection can be undertaken; however, since pancreatic cancer patients seldom exhibit disease-specific symptoms until late in the course of the disease, very few patients (<15-20%) have resectable disease by the time the diagnosis is made (21,22). While complete surgical resection may lead to long-term survival in approximately 25% of patients, only 15% are actually resectable (20).

It is therefore essential to distinguish all kinds of tumor from other pancreatic neoplasms particularly adenocarcinoma for which the prognosis is extremely poor as stated above (23). Surgery for pancreatic cancer is probably the most demanding and risky operative procedure in abdominal surgery (24). Nevertheless the huge lack of pathology laboratories and cancer research centers in Algeria and third world countries have a main negative impact on the precision and quality of the diagnosis.

Seelig *et al.* reported that in a young patient with advanced disease, resection may give a weak but valuable increase of survival. In fact, metastatic pancreatic cancer could become overt when the point of no return has already been passed as it could be the case in the presence of positive interaortocaval lymph nodes, or metastatic cancer will be detected during operation despite negative imaging results preoperatively (25). Picozzi *et al.* affirmed that despite R0 resection, long-term survival does not exceed 25% even in the most experienced pancreatic centers may prove that carcinoma of the pancreas is a systemic disease. Further improvement of survival can only be achieved by adjuvant treatment (26).

Our survey showed clearly that young adults who suffered from pancreatic cancer in general; and cancer of the head of pancreas in particular; are unfortunately diagnosed at a very late stage in Western Algeria; when the likelihood of recovery is poor and patients have no other choice than to accept their ongoing symptoms.

Conclusions

Young adults are often seen to be healthier than older ones. Lack of awareness, socio-cultural habits and carelessness

could be fatal for patients who suffer from pancreatic cancer; awareness should be increased among healthcare professionals and mainly among third world countries' citizen. The earlier the diagnosis is made, the better are chances for the patient's survival.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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