Research Article

Epidemiology, Diagnosis and Management of Pancreatic Cancer in 4 Hospitals in Yaoundé And Douala (Cameroon)

Jean Paul Engbang[1,2*], Christian Beugheum Chasim[3], Franck Moise Abenelang[1], Marcelin Ngowe Ngowe[1,4]

[1]Faculty of Medicine and Pharmaceutical Sciences, The University of Douala, Douala-Cameroon

[2]Douala Laquintinie Hospital, Douala-Cameroon

[3]Douala General Hospital, Douala-Cameroon

[4]Faculty of Medicine and Biomedical Sciences, The University de Yaounde I, Yaoundé-Cameroon

[*]**Corresponding Author:** Jean Paul Engbang, Faculty of Medicine and Pharmaceutical Sciences, The University of Douala, Douala-Cameroon

Abstract

Introduction: Pancreatic cancer is a public health problem because of its poor prognosis. Most of the factors related to the prognosis of this cancer are negative and pessimistic. Therefore, our work is to estimate the overall survival of our patients and to establish the prognostic factors associated to survival.

Materials and Methods: This was a cohort study with retrospective data collection method, carried out from January 1, 2010 to December 31, 2019 i.e. a period of 10 years. The research took place in General hospitals of Yaounde and Douala; at Yaounde University Teaching Hospital and at Laquintinie. We obtained ethical clearance from the Institutional Review Board of the University of Douala. We included records of patients with pancreatic cancer of at least 12 months follow-up after diagnosis.

Results: We had a total of 94 cases of pancreatic cancer during our study. Mean age at diagnosis was 56.5 ±12.3 years, the most represented age group was 50-59 years (48.9%), with sex ratio of 1.6 in favor of men. Median consultation time was 6 months. The

most common stage of diagnosis was stage IV of the TNM classification.

Conclusion: At the end of our study, it appeared that survival associated to pancreatic cancer remains low, in fact the median overall survival was 25 months. All prognostic factors found in our study were factors of poor prognosis which were: consultation time >3 months; high serum creatinine level and the occurrence of metastases.

Keywords: Pancreatic cancer; Prognostic factors; Survival; Therapy; Cameroon

1. Introduction

Cancer refers to an uncontrolled proliferation of abnormal cells [1]. These cells can metastasize through the blood or lymphatic route [2]. In 2018 global mortality from all cancers, for all ages and for both sexes was around ten million deaths; after lung cancer (18.2%), digestive cancers, in particular colorectal (9.2%) and gastric (8.2%) cancers are the major causes of death across the world [3]. Pancreatic cancer was responsible for four hundred and fifty-nine thousand new cases and nearly four hundred and fifty thousand deaths in 2018, ranking it the 7th leading cause of cancer death in the world and justifying the challenge it represents today [4], becoming in recent years a real global health problem [5, 6]. Indeed, in North America the mortality associated with pancreatic cancer was 6.5/100,000 inhabitants, classifying it as the 3rd cause of death in the United States [7]. In France, mortality was higher (7.3%) in women [8]. According to the WHO, by 2030, five hundred thousand new cases are expected in developing countries, this also means that at least four hundred and eighty thousand deaths from this cancer are predicted [5]. In Africa, a study shows

that the mortality is 7% and is higher than the incidence [9]. Moreover, according to the WHO, in Africa in 2018, sixteen thousand new cases of pancreatic cancer were noted against fifteen thousand five hundred deaths [3]. The prevalence of pancreatic cancer is 0.7% with a death rate associated with pancreatic cancer of 87% during hospitalization in Togo [10]. Cholestatic jaundice, abdominal pain and deteriotion of general condition are the most frequent complaints of patients [10]. The most widely used surgical treatment is a palliative surgery (bilio-digestive bypass) versus curative surgery (Cephalic Duodenopancreatectomy and Splenopancreatectomy) [11]. Concerning chemotherapy, gemcitabine, folfirinox and capecitabine are the chemotherapy molecules in mono or poly chemotherapy [11, 12]. In Cameroon, this cancer has a prevalence of 1.16% of cancers for survival below 5% [13-15]. Very few studies concerning the different aspects of pancreatic cancer management have been carried out in Cameroon, which is why we thought of doing this multicenter study on this subject.

2. Materials and Methods

This was a retrospective descriptive study of histologically proven malignant tumors of pancreas, diagnosed from January 1, 2010 to December 31, 2019. The research took place in departments of surgery, gastro-enterology and oncology of General hospitals of Yaounde and Douala; at Yaounde University Teaching Hospital and at Laquintinie. Patients for whom the diagnosis was confirmed by histology were included in the study. We collected, from register of those departements, socio-demographic, clinical, paraclinical, therapeutic data and those relating to the evolution of patients operated on for gastric pathologies. All these data entered in a

pre-tested data sheet. Data were registered and processed using Statistical Package for Social Sciences (SPSS) software version 23.0.

3. Results

3.1 Epidemiological characteristics and medical history

As shown in table 1, our studied population had a mean age at diagnosis of 56.5±12.3 years with extremes ranging from 17 to 87 years. Patients aged between 50 and 59 years were the most represented at 48.9% (46 cases).

Men were in the majority. We had 58 men (62%) for a sex ratio of 1.6.

Patients were mostly alcohol and tobacco users at 71.3% and 52.1%, respectively. While familial diabetes returned to first position at 46.8% among family history.

Variable	N	%
Age		
Oct-19	1	1.1
20-29	1	1.1
30-39	4	4.3
40-49	9	9.6
50-59	46	48.9
60-69	23	24.5
70-79	4	4.3
≥80	6	6.4
Gender		
Male	58	61.7
Female	36	38.3
Comorbidities		
Diabetes	30	31.9
Chronic pancreatitis	9	9.6
Pancreatic tumor	3	3.2
Acute pancreatitis	8	8.5
Chronic hepatopathy	10	10.6
Other cancer	2	2.1
Hemoglobin electrophoresis	4	4.3
Hemoglobin electrophoresis	4	4.3
Family history		
Diabetes	29	30.9
Chronic pancreatitis	5	5.3
Pancreatic cancer	3	3.2
Breast cancer	10	10.6
Ovarian cancer	3	3.2
Colorectal cancer	12	12.8
Toxicological history		

Alcoholic intake	67	71.3
Smoking history	49	52.1

Table 1: General characteristics and medical history of patients

3.2 Clinical signs

The frequent reasons for consultation were cholestatic jaundice and abdominal pain represented at 78.8% (74 cases) each (table 2). The patients seen in consultation mainly presented the grade IV deterioration in general condition according to the WHO classification; or 47.9% (45 cases) of the patients examined. Overweight patients accounted for 42.6% (40 patients) of the sample (table 2). About 4 out of 5 patients presented with scleral jaundice on physical examination. And almost 1 in 4 patients presented with edema during physical examination.

Symptoms/Signs	n	%
Functional signs		
Cholestatic jaundice	74	78.8
Abdominal pains	74	78.8
Weight loss	35	37.2
Vomiting	35	37.2
Constipation	29	30.9
Diarrhea	3	3.2
Abdominal bloating	5	5.3
Leg swelling	2	2.1
General signs		
WHO general condition		
AGC stade 0	11	11.7
AGC stade I	10	10.6
AGC stade II	14	14.9
AGC stade III	14	14.9
AGC stade IV	45	47.9
Température		
Normothermy	84	89.4
Hyperthermia (T°≥37,8°C)	10	10.6
Physical signs		
Sclera		
Icterics	74	78.7
Anicteric	20	21.3
Presence of abdominal mass	**23**	**24.5**
Edemato-ascitic signs	**22**	**23.4**
Lower limb(s)	12	12.8
Ascites	1	1.1
Ascites + lower limb(s)	8	8.5
Hydrops	1	1.1

AGC-Alteration of General Condition

Table 2: Symptoms and physical signs of the study population.

3.3 Paraclinical signs

3.3.1 Biological data: According to table 3, CA 19-9 was achieved in 48 patients (51.1% of the sample), came back high in 39 of them (81.3%). Of the 20 (21.3% of the sample) patients for whom lipase results were available, 10 had a high rate (50.0%).7 out of 10 patients had high amylasemia. Sixteen patients (17.0% of the sample) achieving total bilirubin, all of them had predominantly conjugated hyper bilirubinemia. We found that 87 (92.5% of the sample) patients had kidney workup and 31 of them had high creatinine. Of the 91 (96.8% of the sample) patients who achieved the rhesus blood group, just below 30% of these were of O blood group and were the most represented in our study; on the other hand, all were rhesus positive.

Variables	Effective (n=94)	Percentage (%)
Tumor marker		
CA 19-9	**48**	**51.1**
≥ 37 UI/ml	39	81.3
ACE	**7**	**7.4**
> 5 µg/l	3	42.9
AFP	**6**	**6.4**
≥ 10 ng/ml	1	16.7
Enzymes		
Lipasemia	**20**	**21.3**
> 60 UI/L	10	50
Amylasemia	**10**	**10.6**
> 45 UI/l	7	70
Hepatic check		
Total bilirubin	**16**	**17.0**
> 12 mg/l	16	100
Direct bilirubin	**16**	**17.0**
> 2 mg/l	16	100
Renal check	**87**	**92.5%**
Urea		
> 0.45 g/l	10	11.5
Creatinine		
> 13 mg/l	31	35.6
Hepatic cytolysis	**78**	**82.9**
Presence	68	87.2
Absence	10	12.8
Nutrionation assessment		

Albumin	10	10.6
< 40 g/l	2	20
≥ 40 g/l	8	80
ABO blood group	**91**	**96.8**
O	27	29.6
A	21	23.1
B	21	23.1
AB	22	24.2
Rhesus	**91**	
+	91	100

ACE: Carcinoembryonic Antigen; AFP: Alpha Foeto-Protein; CA 19-9: Carbohydrate Antigen 19-9

Table 3: Distribution of patients according to biological signs

3.4. Imaging signs

3.4.1. Diagnostic radiological workup: Abdominal ultrasound was the first-line examination and in 47 patients (50.0%), it revealed a mass most often located at the cephalo-isthmic level (43 cases; 91.5%). While the CT scan found a pancreatic abdominal mass in 45 patients (47.8%), it identified a cephalo-isthmic mass in 8 out of 10 patients (table 4).

In total, the tumor was usually localized in just over 4 out of 5 patients at the cephalo-isthmic level of the pancreas.

The majority (46.7% of patients with ductal dilation) presented with diffuse dilation of the bilio-pancreatic ducts.

Variables		Effective (n=94)	Percentages (%)
Localization of pancreatic mass			
Abdominal ultrasound (n=47)	Céphalo-isthmic	43	91.5
	Corporealocaudal	4	8.5
Abdominal CT scan (n=45)	Céphalo-isthmic	36	80.0
	Corporealocaudal	9	20.0
MRI (n=2)	Céphalo-isthmic	1	50
	Corporealocaudal	1	50
Ductal dilations (n=75)	Choledochus	6	8.0
	Secondary biliary tree	2	2.6
	Wirsung	1	1.3
	Santorini	0	0
	CA	12	16.0
	CAW	14	18.7
	CAWS	35	46.7
	Other combination	5	6.7

MRI: Magnetic Resonance Imaging; CA: Choledochus + secondary biliary tree; CAW : CA + Wirsung ; CAWS :

CAW + Santorini

Table 4: Distribution of patients according to diagnostical imaging results.

3.5 Extension assessment and staging

As represented in table 5, metastases were present in 65 patients (nearly 7 out of 10) in our sample and were predominantly lymph node (n = 63; 96.9%). CT revealed metastasis in 57.6% (37 cases) of our sample. MRI was rarely performed. We could only find the charts of 5 patients in whom the results of the chest x-ray were available, and these showed interstitial lung disease (3 cases) and were normal in 2. The most common TNM stage at diagnosis is stage IV in 51.1% (48 cases).

Variables		Effective (n=94)	Percentages (%)
Presence of métastases		65	69.2
Ultrasound (n=26)	Ganglionic	26	100
	Hépatic	10	38.5
	Pulmonary	0	0
CT TAP (n=37)	Ganglionic	37	100
	Hépatic	22	59.4
	Pulmonary	16	43.2
MRI TAP (n=2)	Ganglionic	2	100
	Hépatic	1	50
	Pulmonary	1	50
Stade TNM			
Stade IA		15	16
Stade IB		10	10.6
Stade IIA		4	1.1
Stade IIB		12	12.8
Stade III		5	3.2
Stade IV		48	51.1

TAP: Thoraco-Abdomino-Pelvic

Table 5: Distribution according to extension assessment and staging

3.6 Histopathology

Analysis of the surgical specimen was performed in 75 patients (79.5%). The most common histologic type is pancreatic ductal adenocarcinoma at 80.7% (78 cases). Low-grade differentiation of the tumor was most often seen in 59 patients (75.6%). In the end, the histological diagnosis was made in 78 patients (82.9%). In our patients under 30 years of age we were not able to objectify the histologic type asserting pancreatic cancer.

Variables	Effectifs (n=94)	Pourcentages (%)

Sample		
Surgical specimen	75	79.8
Histological type		
Pancreatic ductal adenocarcinoma	63	84
Acini carcinoma	1	1.3
Acini cystadenocarcinoma	2	2.7
Pancreatoblastoma	8	10.7
Solid pseudo papillary tumor	1	1.3
Degree of differentiation	75	79.8
Undifferentiated	13	17.3
Low grade differentiation	58	77.3
Well differentiated	4	5.3

Table 6: Distribution according to histopathology

3.7 Treatment

3.7.1 Types of treatment: The most commonly performed surgical procedure was bilio-digestive bypass in almost 4 out of 5 of those who had surgery.

Gemcitabine monotherapy was the most widely used (32 patients; 43.2%) as chemotherapy in our study (table 7).

Variables	Effective (n=94)	Percentages (%)
Surgical treatment	**87**	**92.6**
Cephalic duodenopancreatectomy	12	13.8
Left splenopancreatectomy	6	6.9
Median pancreatectomy	0	0
Total pancreatectomy	0	0
Bilio-digestive bypass	69	79.3
Medical treatment	**74**	**78.7**
Exclusive gemcitabine	32	43.2
Gemcitabine+Erlotinib	4	5.4
Gemcitabine+oxaliplatin	8	10.8
Gemcitabine+Cysplatin	1	1.4
Folfirinox	25	33.8
Gemcitabine+ Paclitaxel	13	17.6

Table 7: Distribution according to treatment modalities

3.7.2 Treatment according to stage: As shown in table 8, Bilio-digestive derivation associated with chemotherapy (most often exclusive gemcitabine in 29 patients) was most often adopted as a management protocol (46 cases, 51.1%) for patients with stage IV cancer.

Therapies	Stage	Effective (n=94)	Percentages (%)
Exlusive excisional surgery	IA	4	4.3
Resection + adjuvant chemotherapy	IA	2	2.1
	IB	1	1.1
	IIB	5	5.3
Neoadjuvant chemotherapy + excision	IB	2	2.1
	IIB	4	4.3
BDD + Chemotherapy	IA	6	6.4
	IB	4	4.3
	IIA	1	1.1
	IIB	3	3.2
	III	3	3.2
	IV	46	48.9
Exlusive BDD	IA	4	4.3
	IB	2	2.1
Exlusive chemotherapy	IV	7	7.4

BDD: Bilio-Digestive Derivation

Table 8: Types of treatment according to stage

3.8 Evolution

3.8.1 Response to therapy: We have 10 patients (10.6% of the sample) who had good control of the progression of their pancreatic cancer after a median follow-up time of 18 months and more. We initially had 63 patients (67.0%) with lymph node involvement and 48 patients (51.1%) with distant metastases at the time of diagnosis (table 9)

Variables	Effective (n=94)	Percentages (%)
Situation before the treatment		
Invaded lymph nodes	65	69.1
Distant metastases	48	51.1
After the treatment (t≥12moths)		
Full remission	10	10.6
Locoregional recurrences	12	12.7
Secondary metastases	21	22.3

Table 9: Distribution according to the response to the treatment.

3.9 Locoregional invasion after treatment

The median occurrence time of locoregional recurrence was 13.1 months. The lymph nodes of the celiac plexus were most often affected. Chemotherapy was most often used in case of recurrence and as a first-line (table 10).

Variables	Modalities	Effective (n=12)	Percentages (%)
Occurrence delay	12 months	7	58.3
	18 months	3	25.0
	24 months	1	8.3
	30 months	1	8.3
Occurrence site	Mesenteric lymph nodes	3	25.0
	Celiac lymph nodes	8	66.7
	Other lymph nodes	1	8.3
Treatment initiated	Abstention	3	25.0
	Chemotherapy	9	75.0

Table 10: Distribution according to the occurrence of locoregional metastatases.

3.10 Occurrence of distant metastases after the treatment

The median time to secondary onset of metastases was 12.7 months. Most often they occurred in the liver or simultaneously in the liver and lungs (8 cases; 38.1% each).

Exlusive chemotherapy gemcitabine or folfirinox was often used for cases of metastasis. In addition, we have a patient lost to follow-up after 18 months of follow-up.

Variables	Modalités	Effectifs (n=21)	Pourcentages (%)
Occurrence delay	12 months	14	66.7
	18 months	6	28.6
	24 months	1	4.7
Occurrence site	Liver	8	38.1
	Lungs	5	23.8
	Liver + Lungs	8	38.1
	Other	0	0
Treatment initiated	Lost view	1	4.7
	Chemotherapy	20	95.3

Table 11: Occurrence of distant metastatases after therapy

3.11 Complications

As shown in table 12, the main complications of pancreatic cancer were diabetes (in 76.6%) and compression of the main bile duct (63.8%).

Gastroparesis was the most common surgical complication (5.3%), while chemotherapy mainly induced renal toxicity (14.9%).

Variables	Effective (n=94)	Percentages (%)
Complications related to the disease	**82**	**87.2**
Acute pancreatitis	13	13.8
Pseudo cyst of the pancreas	3	3.2

Compression of the bile ducts	60	63.8
Exocrine pancreatis insufficiency	25	26.6
Diabetes/hyperglycemia	72	76.6
Infections	10	13.5
Induced immunosuppression	3	3.2
Thromboembolism	3	3.2
Surgical complications	**10**	**10.6**
Gastro paresis	5	5,3
Pancreatic fistula	1	1.1
Gastrointestinal bleeding	2	2.1
Abscess of the abdominal wall	2	2.1
Complications of chemotherapy	**28**	**29.8**
Renal toxicity	14	14.9

Table 12: Distribution according to occurrence of complications

4. Discussion

The mean age at diagnosis was 56.5 ± 12.3 years, with extremes ranging from 17 to 87 years. Ntagirabiri et al in Burundi in 2012 had an average age of 50.3 years [16]. In Burkina Faso, Koura et al who found in 2020 an average of 56.4 years [17] while in Algeria, Sellam et al in 2015 who found an average of 62.2 years [18]. These data confirm that pancreatic cancer is said to be "age-dependent" with the elderly as a preferential target.

Our study finds that the sex ratio is 1.6 in favor of men. These findings are similar to those of Rawla et al in the United States in 2019, who found a sex ratio of 1.5 [7]; and Bouvier et al. in France in 2017 who found a sex ratio of 1.4 [19]. These data confirm that males are the most affected by pancreatic cancer.

According to our study, patients with average socioeconomic status are the most affected, followed by those with an affluent standard of living. This does not agree with the results of the study conducted by Bryere et al in France in 2019, which found a higher incidence in patients with a very low standard of living rather than in the less poor [20]. And neither does it agree with the data of Ouédraogo S et al. in 2018 which found that digestive cancers in general (including pancreatic cancer) had as a target population patients with less than 1 US dollar of daily income (defining the socioeconomic level of patients in their study) [6]. Our findings could be explained by the fact that people at a low (or even very low) socioeconomic level are hardly diagnosed with pancreatic cancer because they do not have enough means to go to the hospital at the onset of symptoms.

During our study, we found a median consultation time of around 6 months with extremes ranging from 0 to 52 months. While most of our patients coming to consult were already at the metastasis stage, in our study we found a median time to onset of metastases of 0 days. Our consultation time is similar to that found by Alegbeyele et al in Nigeria in 2019, who found a median consultation time of 25 weeks, or around 6 months [21]. This is because in Cameroon, we first resort to traditional therapies as a first-line treatment. Patients won't get to the hospital until when the later have not been effective, thus the delay in diagnosis and the diagnosis at a late stage (metastasis stage).

In our personal study, patients consuming alcohol were the most represented (71.3%), followed by patients consuming tobacco (52.1%). El Fatihi in his research in Morocco in 2019 found that diabetes (29.6%) and tobacco (26.1%) were the most frequent [11], while El Mir found that tobacco was the most important risk factor and attributed to it was 20% of pancreatic tumors [12]. We can justify that because in Cameroon alcohol consumption begins at an early age and is taken disorderly in large quantities. If alcohol has not yet demonstrated its role in the genesis of pancreatic cancer; it can in the long run lead to chronic pancreatitis and even according to the study by Mandengue et al. [22] alcohol is associated with obesity which are both (chronic pancreatitis and obesity) risk factors establishing the occurrence of pancreatic cancer.

We found that cholestatic jaundice and abdominal pain (78% each) were the most frequent complaints of patients, followed by vomiting and weight loss (37.2% each). Zertiti S found in 2018 in Morocco that the most frequent signs were jaundice (81%), abdominal pain (78%) and pruritus (38%) [23]. Aaouidi in 2019, still in Morocco, found that abdominal pain was the most frequent complaint (60%), followed by vomiting and jaundice (20% each) [24]. While Bouglouga O et al instead found in 2015 a deterioration of the general condition (97%), abdominal pain (87%) and jaundice (80%) as being the frequent reasons for consultation [10]. The most frequent signs are similar. We could explain it by the fact that in general the tumor is localized at the level of the head of the pancreas; which will therefore combine signs such as jaundice, pruritus, abdominal pain or a change in general condition, weight loss and vomiting.

We discovered that the majority of patients (56.4%) were diagnosed with stage IV pancreatic cancer against 26.6% for stage I. Sellam, et al in their study found 26.2% of cases were diagnosed at stage M1, followed respectively by stages T4 (21.8%) and T3 (21.2%); on the other hand Aomari et al found 80% of patients with visceral metastatic extension [18, 25]. We can cite three reasons for this: the insidious or silent evolutionary nature of pancreatic cancer; the nonspecific nature of its clinical expression, which from the outset did not lead to making this diagnosis; and finally we can say that the patient generally comes to the hospital long after the revelation of the disease for various reasons such as lack of financial means or simple negligence.

The most widely used surgical treatment during our study was palliative surgery, in particular bilio-digestive bypass (79%) versus curative surgery, which represented 21% (Cephalic Duodenopancreatectomy at 14% and Splenopancreatectomy at 7%). El Fatihi had also found that 31% of his patients underwent palliative surgery (choledoco-duodenal diversion with cholecystectomy, duodeno-jejunal diversion, gastro-jejunal and bilio-digestive diversion...) against 21% who had undergone surgery for curative purposes (DPC, SPG) [11]. Meanwhile El Mir in his research found rather that palliative surgery (bilio-digestive bypass) was 31% against curative surgery at 57.9% (CPD with lymph node dissection) [12]. We could justify our data by the fact that in our study, the majority of our patients were diagnosed with stage IV cancer. Stage IV is that of distant metastases and contraindicates any tumor resection; therefore the only possible alternative is palliative surgery, including bilio-digestive bypass.

Gemcitabine was the chemotherapy molecule most

used in mono (42.3%) or poly chemotherapy in our study, followed by Folfirinox (33%). El Mir also found that Gemcitabine is more used for neo-adjuvant chemotherapy and in combination with Capecitabine in case of adjuvant chemotherapy [12]. El Fatihi finds similar data concerning Gemcitabine, which is very often used in pancreatic cancer in combination or alone [11]. Gemcitabine would therefore still be widely used to date and more often preferred to other molecules in monotherapy or in combination, probably because Gemcitabine had better median overall survival and better progression-free survival compared to survival associated with other molecules; when used in combination, there is a survival gain of several months or even years.

5. Conclusion

The mean age at diagnosis of our patients with pancreatic cancer was 56.5 ± 12.3 years and the male sex was predominant with a sex ratio of 1.6. The frequent risk factor in our study was 71.3% alcohol consumption; the most frequent functional signs were cholestatic jaundice and abdominal pain at 78.8% each. The diagnosis was most often made at stage IV of the TNM classification in 56.4% of cases and the most common histologic type was pancreatic ductal adenocarcinoma in 67.0% of cases. In 79% of cases a bilio-digestive diversion was performed among those who had undergone a surgical intervention; while gemcitabine was used more in our study. The most common cancer-related complication was diabetes (76.6%); nearly 3 out of 4 patients had died.

References

1.   Bennet JC, Plum F, Gill GN, Kokko JP, Mandell GL, Ockner RK et al. Cecil traité de médecine interne. Paris: éditions Flammarion. 20 (1997): 1004.

2.   Hubert S, Abastado JP. Les étapes précoces du processus métastatique. Médecine/Sciences 30 (2014): 378-384.

3.   Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Pineros M et al. Cancer today. WHO: Cancer data base No 15. IARC publication (2018).

4.   Ferlay J, Partensky C. Le cancer du pancréas est un fardeau préoccupant à l'échelle mondiale. Médecine des maladies métaboliques 13 (2019): 288-292.

5.   Ferlay J, Partensky C. L'augmentation inquiétante de l'incidence et de la mortalité du cancer du pancréas à l'échelle mondiale. Bulletin de l'académie de médecine 201 (2017): 227-235.

6.   Ouédraogo S, Ouédraogo S, Kambire JL, Zoungrana SL, Bambara B, Traore MT et al. Profil épidémiologique, Clinique, histologique et thérapeutique des cancers digestifs primitifs dans les régions du Nord et Est du Burkina Faso. Bulletin du cancer 105 (2018): 1119-1125.

7.   Rawla P, Sunkara T, Gadopoti V. Epidémiology of pancréatic cancer: Global trend, etiology and risk factors. World Journal oncology 10 (2019): 10-27.

8.   Mathieu P, Lepoutre A, Cariou M, Billot-Grasset A, Chatignoux E. Estimations régionales et départementales d'incidence et de mortalité par cancer en France, 2007-2016. Registres du réseau Francim (2018): 163.

9.   Bray F, Ferlay J, Soerjomataram I, Siegel R, Torre L, Jemal A et al. Global Cancer Statistics: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. Cancer Journal for Clinicians 68 (2018): 394-424.

10.   BougLouga O, Lawson-Ananissoh LM, Bagny A, Kaaga L, Redah D. Cancer du pancréas: études épidémiologique et clinique, et prise en charge

dans le service d'hépato-gastro-entérologie du CHU Campus de Lomé (Togo). Médecine et Sante Tropicales 25 (2015): 323-326.

11. El Fatihi M. Le cancer du pancréas: Prise en charge thérapeutique expérience du centre hospitalier universitaire Mohamed VI de Marrakech. Thèse de médecine No 190. Maroc: Université Cadi Ayyad (2019).

12. El Mir S. Le cancer de la tête du pancréas : aspects épidémiologique, clinique, thérapeutique et pronostic à propos de 19 cas au service de chirurgie générale et oncologie digestive A- CHU d'Oujda. Thèse de médecine No 105. Maroc : Université Sidi Mohammed Ben Abdellah (2017).

13. Ndjitoyap NEC, Mbakop A, Tzeuton C, Guemne TA, Fewou A, Abondo A. Cancer du pancréas: étude épidémiologique et anatomo-clinique (résultats préliminaires). Médecine d'Afrique Noire 37 (1990): 112-113.

14. Zeitoun JD, Chryssostalis A, Lefevre J. Hépato-gastro-entérologie. Paris: Editions Vernazobres-Grego. 6 (2017): 247.

15. Bellesoeur A, Cabel L, Hutt E, Moustarhfir M. Cancérologie module 10. Paris: Editions Vernazobres-Grego. 5 (2013): 261-262.

16. Ntagirabiri R, Niyonkuru S, Karayuba R, Ndayisaba G, Marerwa G. Cancer du pancréas au Burundi, expérience du CHU de Kamenge. Journal Africain d'hépato gastroentérologie 6 (2012): 312-314.

17. Koura M, Napon-Zongo PD, Some OR, Belemsigri D, Zoure N, Ouattara ZD et al. Le cancer du pancréas au Centre Hospitalier Universitaire Souro SANOU de Bobo Diolasso (Burkina Faso): Aspects épidémiologiques, Diagnostiques et Thérapeutiques. The Journal of Medicine and Biomedical sciences 21 (2020): 95-99.

18. Sellam F, Harir N, Khaled MB, Mrabent MN, Salah R, Diaf M, Moulesshoul S. Aspects épidémiologiques et histopronostiques du cancer pancréatique au niveau de l'Ouest Algérien à propos de 160 cas. Journal Africain d'Hépato-gastro-entérologie 9 (2015): 76-79.

19. Defossez G, Le Guyader-Peyrou S, Uhry Z, Grosclaude P, Remontet L, Colonna M, et al. Estimations nationales de l'incidence et de la mortalité par cancer en France métropolitaine entre 1990 et 2018. Registres des cancers du réseau Francim 1 (2019): 1-372.

20. Bryere J, Tron L, Menvielle G, Launoy G. French Network of Cancer Registries (FRANCIM). The respective parts of incidence and lethality in socioeconomic differencies in cancer mortality. An analysis of the French Network of Cancer Registries (FRANCIM) data. International Journal for equity in health 18 (2019): 11.

21. Alegbeyele BJ, Afolabi AO. Clinicopathologic pattern and outcome of management of pancreatic carcinoma in Ibadan, Nigeria. Sudan Journal of Medical Sciences 14 (2019): 172-187.

22. Mandengue SH, Bita Fouda AA, Epacka Ewane M, Moumbe Tamba M, Kollo B. Epidémiologie de l'obésité en milieu estudiantin à Douala, Cameroun. Médecine et santé tropicale. 25 (2015): 386-391.

23. Zertiti S. Apport de l'écho-endoscopie dans les cancers du pancréas. Thèse de Médecine No 99. Maroc: Université de Mohammed V-Rabat (2018).

24. Aaouidi Z. Les tumeurs du pancréas chez l'enfant (à propos de 5cas). Thèse de médecine No 215. Maroc: Université de Mohammed V-Rabat (2019).

25. Aomari A, Firwana M, Rahaoui A, Bakkali M, Afifi R, Essaid EA. Pancreas cancer: epidemiologicals, clinicals, morphologicals aspects,

and therapeutic modalities. Resultof a moroccan
university center. Annales des Sciences de la Santé 13
(2017): 13-22.