

Epidemiological, clinical, pathological, and therapeutic aspects of gastric cancer in Morocco

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ABSTRACT

Purpose: Gastric cancer is a relatively frequent cancer and has poor prognosis. The present study is the first Moroccan study to investigate the epidemiological, clinical, pathological, therapeutic characteristics, and outcomes of gastric cancer. **Materials and Methods:** We conducted a retrospective study including 154 cases of gastric cancer treated at the National Institute of Oncology between January 2007 and December 2007. **Results:** The mean age at diagnosis was 55 years (18-87 years) and the sex ratio was 2.14. Risk factors were dominated by tobacco use (30.5%) and gastric ulcer (4.5%). The average interval between symptom presentation and consultation was 8.7 months (1-48 months). The clinical symptoms were dominated by epigastric pain (88.7%), vomiting (62.3%), and weight loss (80.5%). Oeso-gastric fibroscopy was performed in all patients and showed an ulcerated aspect in 77.9% of the cases. The location of the tumor was antropyloric in 42.2% of the cases. The most common histology was adenocarcinoma (72.8%), followed by non-Hodgkin lymphoma (22%), gastrointestinal stromal tumors (GIST; 3.2%), and neuroendocrine tumors (NET; 2%). Tumor stage was metastatic in 62% of the cases, locally advanced in 18.5% of the cases, and localized in only 8% of the cases; however, 11.5% of patients were not staged. Also, 46% of the patients with adenocarcinoma ($n = 111$) were not treated, 6.4% received chemotherapy first (non-resectable) (one patient was operated), 20.6% received surgery first followed by adjuvant treatment, 4.5% received chemo-radiotherapy, 5.4% received chemotherapy only, and 27% received palliative chemotherapy. In the sub-group of patients diagnosed with non-Hodgkin lymphoma ($n = 35$), 48.5% received chemotherapy based on Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (CHOP) regimen. In the sub-group diagnosed with GIST ($n = 5$) histology, all cases received surgery first and 2 cases received adjuvant chemotherapy based on doxorubicin. Finally, in the NET ($n = 3$) sub-group, 2 patients received surgery and 1 was not treated. The mean follow-up was 10 months for locally advanced tumors and 7.6 months for metastatic tumor. The overall survival rate at 3 years was not exceeding 20%. **Conclusion:** Clinical and pathological aspects of Moroccan patients are the same of those in developing countries. The majority of our patients were diagnosed at late stages, which explains the poor prognosis of gastric cancers in our population.

Key words: Developing countries, epidemiology, gastric cancer, histology, treatment

INTRODUCTION

Gastric cancer is a relatively common cancer accounting for 8% of the total cases and 10% of total deaths due to

cancer.^[1] Gastrointestinal cancers are unevenly distributed around the world and has undergone significant changes in incidence over time.^[1-7] The highest incidences have been observed in Eastern Asia, Eastern Europe, and South America, and the lowest incidence have been observed in North America and in most parts of Africa.^[1] The most predominant histological type was adenocarcinoma. Most patients were diagnosed at advanced stages of the disease. Surgery is the standard treatment of operable gastric adenocarcinoma. Adjuvant treatments based on radiotherapy and chemotherapy improved loco-regional control rate and overall survival. Chemotherapy remained the only treatment of patients with advanced stages. The

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prognosis of gastric cancer is poor with a five-year survival, not exceeding 15% for all stages combined. The aim of our study was to analyze the epidemiological, clinical, histological, and therapeutic aspects of gastric cancer in Morocco. We have reported here a series of 154 gastric cancers diagnosed during 2007 at the National Institute of Oncology, Rabat, Morocco.

MATERIALS AND METHODS

This is a retrospective study of 154 cases of gastric cancers diagnosed at the National Institute of Oncology in Rabat between January 2007 and December 2007. For each case studied, the information used to the collection of data were demographic information of the patient, date of diagnosis, topography, histological type, and treatment modalities.

- Marital status, age, sex, profession
- Eating habits and toxic habits
- Data from the clinical examination
- Results of additional tests (upper gastro-intestinal endoscopy and histology)
- Surgery report
- Treatments.

Statistical analyses were performed using SPSS version 17 software. Kaplan-Meier method was used to estimate survival of patients. Overall survival was calculated from the pathological diagnosis of gastric cancer to death from any case. The groups of patients were compared using the log-rank test. $P < 0.05$ was considered significant.

RESULTS

Epidemiological data

Frequency

Gastric cancer is the most common gastrointestinal cancer in our cancer center. It represents the fifth most common cancer.

Age

The median age of our patients was 56 years (18-87 years). The study of the distribution of cases by age showed that the incidence of gastric cancer is closely related to age. The first few cases were diagnosed in the interval of age ranged 35-44 years, and the number of cases increased with age. For men, the first peak of frequency was 45-54 years and the second peak was 65-74 years. For women, the peak of frequency was 55-64 years, and then gradually the incidence decreased, as reported in Figure 1.

Gender

As showed in Figure 1, there is a male predominance with a sex ratio of 2.08. The risk of gastric cancer increased in men aged 15-24 years and in women aged 25-34 years [Figure 1].

Risk factors

Risk factors were not mentioned in all cases.

- A history of gastric ulcer was reported in 6.5% of cases [Figure 2]
- Toxic habits included smoking in 47 patients (30.5%) [Figure 2]
- Family history: One patient aged 74 years had family history of gastric cancer; his brother died from gastric adenocarcinoma

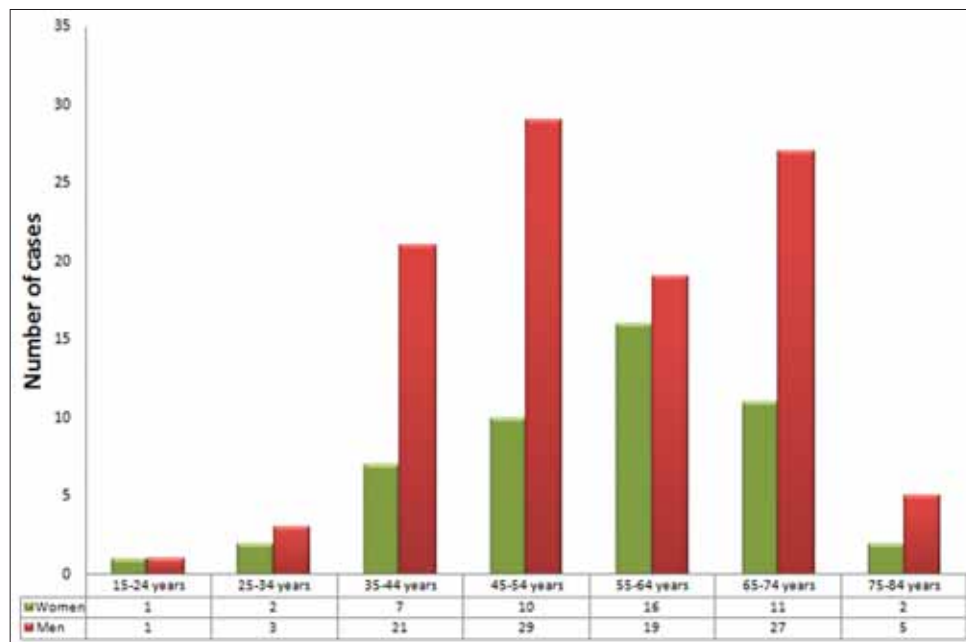


Figure 1: Distribution of gastric cancer according to age and sex

- *Helicobacter pylori* infection (HP): No case of infection with HP was detected before diagnosis, even in patients previously treated for ulcer. The HP infections in our patients were diagnosed at the time of histological study of biopsy specimen. Research was performed in a specimen of 17 patients: HP was present in 12 biopsies (7.8%) (3 with adenocarcinomas, 8 with lymphoma, and 1 with neuroendocrine carcinoma) and was absent in 5 biopsies.
- Diet: Unfortunately, we were not able to identify the diet information from our patients.

Clinico-pathological data

In our series, we found that only 6 patients consulted within 1 month, while the majority of patients consulted after 1 months (range: 1-48 months). The average interval between the first symptom and consultation was 8.7 months. The most predominant clinical symptoms were epigastralgia (88.7%), weight loss (80.5%), and vomiting (62.3%) [Figure 3].

Oeso-gastric endoscopy was performed in all patients and showed an ulcerated aspect in 121 cases (78.5%), infiltrative aspect in 30 cases (19.5%), and plastic linitis in 3 cases (2%).

Topography

Among the 154 gastric cancers, topography of 39 cases (25.3%) was unknown. Among the 115 patients

Signes cliniques	n	%
Epigastralgias	137	88.7%
Weight loss	135	87.6%
Vomiting	96	62.3%
Hematemesis	24	15.6%
General symptoms	14	9%
Epigastric mass	7	4.5%
Ascites	5	3.2%
Dysphagia	15	9.7%
Lymphadenopathy of Troisier	10	6.5%
Hépatomegaly	4	2.6%

Figure 2: Symptoms of gastric cancer

Topography	n	%
Antropyloric	65	42.2%
Fundus	29	18.8%
Cardiale	18	11.7%
Large tuberosity	3	2%
Not defined	39	25.3%

Figure 4: Topography of gastric cancer

in which information about the topography was available, we have highlighted the predominance of antropyloric topography in 65 cases (42.2%), followed by the location at the fundus in 29 cases (18.8%), at the cardia in 16 cases (11.7%), and at the large tuberosity in 3 cases (2%) [Figure 4].

Macroscopic appearance

Most often, the aspect of tumors was ulcerated.

Histological type

Among the 154 cases of gastric cancer, adenocarcinoma is the most common histological type representing 72% of the cases, followed by malignant lymphoma representing 22.8% of the cases. Five patients were diagnosed with gastrointestinal stromal tumors (3.2%) and 3 patients were diagnosed with neuroendocrine carcinoma (2%) [Figure 5].

Staging

The stage was assessed by clinical examination, chest, abdomino-pelvic CT scan, and exploratory laparotomy. Lymph node metastases were the most frequent site of metastases (39 cases, 25%), followed by the liver (22 cases, 14%), the peritoneum (26 cases or 16.8%), and the ovary (1 case) [Figure 6]. Tumors are diagnosed at metastatic disease in 62% of the cases, at locally advanced stage in 18.5%, and at localized stage in 8%. About 11.5% of patients were unstaged. Exploratory laparotomy was performed in 18 cases (11.6%) and showed inoperable tumors (invasion of adjacent organs, peritoneal carcinomatosis, or liver

Median of age (years)	All patients	55
	Adenocarcinoma	55 (Women) 57 (Men)
	Lymphomas	51
	GIST	55
	NET	59
Mal/Femal	N = 104/50	67,5%/32,5 %
Tobacco	N = 47	30.5%
Gastric ulcer	N= 10	6.5%

Figure 3: Epidemiological characteristics

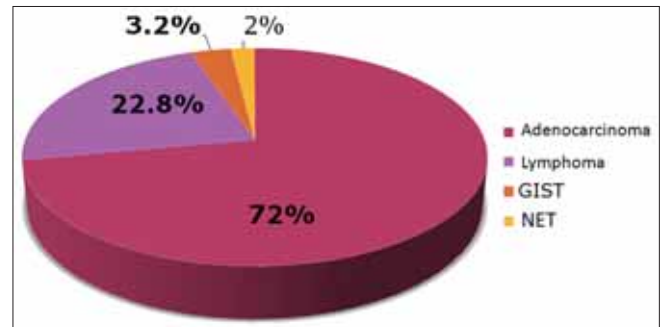


Figure 5: Histological types

metastases). The classification of patients according to histological types is detailed in Figure 7.

Treatment and outcomes

Treatment characteristics were analyzed according to histological type in Figure 8. Forty-six percent of the patients with adenocarcinoma (n = 111) were not treated, 6.4% received primary chemotherapy (inoperable disease), and among them, 1 patient received surgery. About 20.6% of the patients received surgery first, and 9.9% of the cases received adjuvant treatment based on radio-chemotherapy, according to the McDonald protocol in 5% of the cases and chemotherapy alone in 5.4% of the cases. Finally, 27% of patients received palliative chemotherapy. In the sub-group of patients diagnosed with non-Hodgkin lymphoma (n = 35), 48.5% of the cases were treated with Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (CHOP)-based chemotherapy. All patients with GIST (n= 5) received surgery first, among them, 2 received adjuvant chemotherapy based on doxorubicin. Finally, among the 3 patients with neuroendocrine tumor, 2 patients were operated and 1 patient received best supportive care. The mean follow-up was 10 months for locally advanced tumors and 7.6 months for metastatic tumor. The overall survival rate at 3 years for all patients combined was not exceeding 20% [Figure 9]. The main prognostic factor was stage of disease with a significant difference (Log-rank test; P= 0.002).

DISCUSSION

Gastric cancer is a relatively common cancer. It represents the fifth most commonly diagnosed cancer in the world. The incidence of gastric cancer is the subject of considerable geographical variation. It is highest in Eastern Asia.^[1] In Morocco, gastric cancer is the most common gastrointestinal cancer. It represents the fifth most common cancer according to Rabat registry (2005)^[8,9]. The stomach cancer rarely occurs before the age of 40 years. The incidence increased rapidly beyond, with a peak of incidence in the seventh decade. The average

age of our patients was 56 years. The median age of our patients was the same as that reported in Senegal,^[10] but lower than that reported in France (70 years).^[11] In Africa, gastric cancer occurs in relatively young patients because of a shorter life expectancy of African population. In our series, 72% of cases were diagnosed with adenocarcinoma and 22.8% of cases were diagnosed with lymphomas. These proportions are approximately comparable to those reported in Madagascar by Peghini *et al.*, which reported 88% of cases with adenocarcinoma and 7% of cases with lymphoma.^[12] Among the risk factors, dietary factors play an important role in gastric carcinogenesis.^[13] A diet high in salt is associated with an increased risk of gastric cancer.^[14] Nitrites have also been implicated.^[15] Several case-control and cohort studies reported an increased risk of stomach cancer in smoking population,^[16] especially in cases of *H. pylori* infection.^[17] On the other hand, the consumption of tobacco promotes the progression of preneoplastic lesions.^[18] The causality of alcohol consumption in occurrence of stomach cancer has been explored by several studies; however, the relationship between alcohol and gastric cancer was not clearly confirmed.^[19] *H. pylori* has been recognized as an etiological factor in gastric cancer since 1994, as demonstrated by several epidemiological and pathophysiological studies. Several meta-analyses involving large epidemiological studies have shown that the relative risk of gastric cancer is 2-6 times higher in patients harboring *H. pylori* infection as compared with uninfected population.^[20] In our series, *H. pylori* was reported in 8% of cases, history of tobacco use in 30.5% of cases, and history of gastric ulcer in 6.5% of cases. Cancers of the stomach are most often diagnosed in symptomatic patients with advanced disease. It was the case in our series, locally advanced and metastatic stages, III and IV, represented 38.8% and 48.6% of patients with adenocarcinoma, respectively. Early tumors are usually asymptomatic and rarely detected outside of country adopting a screening policy such as Japan. In our series, stages I and II represent only 3.6% and 9%, respectively. Weight loss and epigastralgiias are the most common

	Histology	Number
Peritoneal metastases (n=26)	Adenocarcinoma	20 (16%)
	Lymphoma	4 (11.4%)
	GIST	1 (20%)
	NET	1 (33%)
Liver metastases (n=22)	Adenocarcinoma	18 (16%)
	LMNH	2 (5.7%)
	GIST	1 (20%)
	NET	1 (33%)
Lung metastases (n=17)	Adenocarcinoma	13 (11.7%)
	LMNH	4 (11.4%)
Ovarian metastases	Adenocarcinoma	1 (0.6%)

Figure 6: Metastatic sites according to histology

Hystology	Stage	Number (%)
Adenocarcinoma (n=111)	Stage I	4 (3.6%)
	Stage II	10 (9%)
	Stage III	43 (38.8%)
	Stage IV	54 (48.6%)
Lymphoma (n=35)	Stage IE	1 (2.9%)
	Stage IIE	2 (5.8%)
	Stage IVE	13 (37%)
	Unknown	19 (54.3%)
GIST (n=5)	Stage IV	4 (80%)
	Stage NP	1 (20%)
NET (n=3)	Stage IV	1 (33%)
	Unknown	2 (67%)

Figure 7: Stage of disease according to histology

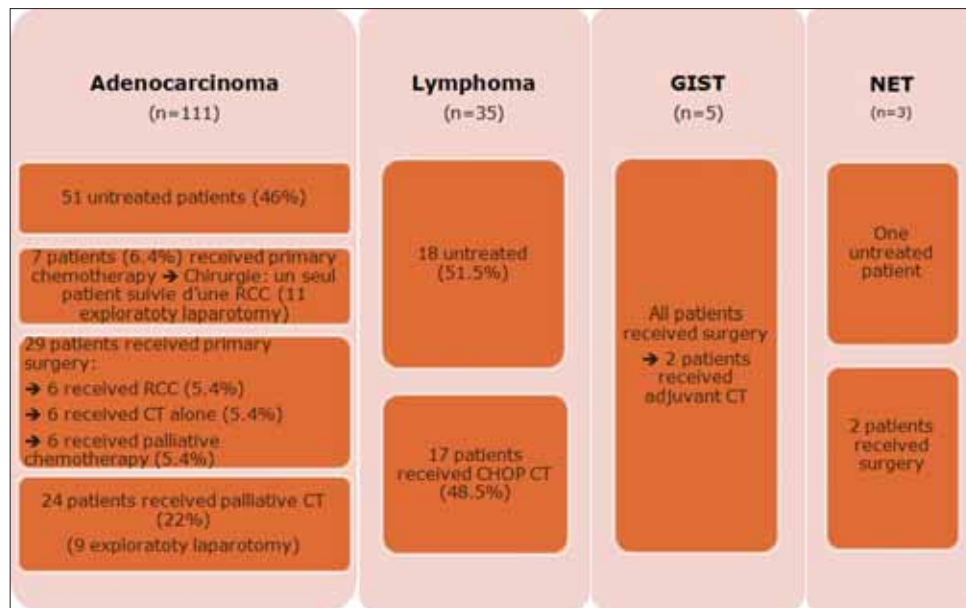


Figure 8: Treatment according to histology

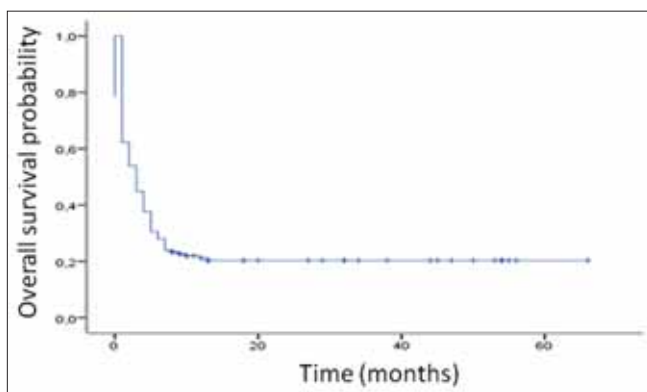


Figure 9: (a) Survival curve of all patients (b) Survival curves according to stages of disease

symptoms at the initial diagnosis. In our study, the most common symptoms were epigastralgiias in 88.7% of cases and weight loss in 80.5% of cases. A history of gastric ulcer was found in about a quarter of cases.^[21] In our series, it was found in 6.5% of cases. Externalized digestive bleeding was found in 20% of cases. The general signs are common in cases of gastric lymphoma. In our series, they were present in 31.4% of lymphomas patients ($n=35$). In clinical practice, the confirmatory diagnosis was based on gastroduodenal endoscopy-associated with biopsies.^[22] Endoscopy was performed for all patients in our series. Tumor may have a polypoid, ulcerated, or infiltrative tumor. Abdominal and pelvic CT scan is the initial step of staging. However, this radiological test tends to underestimate the locoregional extension of disease. Depending on the series, the correlation was 51-67% with cT and pT, 51-73% with cN and pN, and 30-71% with peritoneal carcinomatosis. In our series, the CT scan was performed in 114 cases (74%). Laparoscopy is proposed by some authors as an essential

step of staging before curative resection. This intervention avoids unnecessary laparotomy in up to 38% of patients, especially in the case of peritoneal carcinomatosis or liver metastases.^[23] The standard treatment for patients with operable adenocarcinoma is surgery. Radiotherapy and chemotherapy improve rates of loco-regional control and survival. Adjuvant radio-chemotherapy and peri-operative chemotherapy are two standard of care. Chemotherapy remains the only treatment of advanced disease.

CONCLUSION

In Morocco, gastric cancer is the most common gastrointestinal cancer. It represents the fifth most common cancer in concordance with that in developed countries. Tobacco use is a frequent cause. Our patients diagnosed with gastric cancer were younger and diagnosed at advanced stages. Stomach cancer incidence was about twice as high in males than in females in concordance with global statistics. Adenocarcinoma was the frequent histological type. Prognosis was poor; 3-year survival was not exceeding 20%.

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