

Gastric Cancer In Young Patients Under The Age Of 45 Years : Clinico-Pathological Features

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Abstract :

Introduction : The incidence rate of gastric cancer (GC) in young patients is increasing , with worse clinical features . Our aim was to investigate the clinico-pathological aspects of GC in young patients .

Methods : We conducted a descriptive retrospective study conducted in the Department of Gastroenterology unit B, Ibn Sina teaching hospital in Rabat, Morocco during the period from January 2005 to December 2019. 164 patients with GC were enrolled . Out of these, GC in young patient was diagnosed in 31 cases.

Results : Young patients represent (under the age of 45 year old) 18 % . the main symptom was alteration in general condition (87%). The predominant aspect in the endoscopy was the burgeoning ulcer tumor and in histology it was the intestinal type of adenocarcinoma (90.32%) . Diffuse type of adenocarcinoma was found in only 3 patients (9.7%). 24 patients (76,5 %) have been diagnosed in a metastatic stage .

Conclusion : GC in young population is mainly distinguished by pathologically poor prognostic factors . An endoscopy screening system is of paramount importance for an early diagnosis to be able to provide curative care.

Key word : Gastric– Cancer -Adenocarcinoma .

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I. Introduction :

Gastric cancer (GC) is a major public health issue . Globally it accounts for 989,600 new cases and 738,000 deaths annually , it's the second most frequent cause of cancer-related death ; in that way it is a major public health issue in spite of decreasing trends in its incidence and mortality[1] . Over the last decade the incidence rate of gastric cancer in young patients has a trend towards a gradual increase , beside clinical observation has suggested that they have a far worse prognosis than their counterparts . Studies also indicate that the carcinogenesis process develops within years, though , the recorded medical history usually does not exceed one year, indicating an extensive asymptomatic period [2]. This is why many questions about the molecular and biological conditions and the early diagnosis and treatment of CG on a young population remain relevant. Our aim was to investigate the clinico-pathological features of GC in young patients and to determine whether very young patients with gastric adenocarcinoma have a more severe form of the disease .

II. Methods :

This is a single institution , retrospective study conducted in the Department of Gastroenterology unit B, Ibn Sina teaching hospital in Rabat, Morocco during the period from January 2005 to December 2019. 164 patients with GC were enrolled . Out of these, Gastric cancer in young patient (defined as younger than 45 years of age) was diagnosed in 31 cases. The patient's gender, age, familial cancer history , clinical manifestations were recorded . The location of the tumour was assigned to one of four regions: the upper, middle or lower third of stomach , or in the whole stomach. Histological type of tumor , stage of the disease , and operative outcomes of these patients were also obtained from the retrospective database .

III. Results :

In the observed group of gastric cancer patients , young patients represent 18 % , female to male ratio was 1.41. No one of the patient had an oncological history .

Table 1 shows prevalence of symptoms reported by patients : 27 patients (87%) presented with alteration in general condition , 26 patients (86.09%) presented with a gastric pain , 17 (58.1 %) patient had a clinical profil of gastric obstruction and vomiting , 10 patients with hetametesis , when 7 patients had only anemia (22.58%).

Physical examination found an abdominal mass in 9 (29%) patients, ascites in 5 (16.1%) patients and sentinel node in 3 (9.7%) patients.

The endoscopic finding shows that the predominant aspect was the burgeoning ulcer tumor. It was located in the middle third of stomach in 15 (48.38%) patients, in the lower third in 11 (35.48%) patients, in the upper third in 3 (9.67%) patients and in the whole stomach in 2 (6.45%).

The predominant histology form found was intestinal type of adenocarcinoma in 28 patients (90.32%): 44.14% poorly differentiated, 28.33% moderately differentiated and 17.85% well differentiated. Diffuse type of adenocarcinoma was found in only 3 patients (9.7%). 24 patients (76.5%) have been diagnosed in a metastatic stage. Therefore, they were candidate for palliative (76%) treatment, when only 7 (24%) patients have undertaken a curative treatment (**Figure 1**). Shows that patients with curative treatment had different types of surgical treatment, out of these 2 (33.3%) had Subtotal gastrectomy, 5 (66.6%) had total gastrectomy. (**Figure 2**)

IV. Discussion :

In spite of a decrease in frequency, GC is the fifth common cancer around the world. Morocco is considered as a low incidence area such as other African countries [3]. Though, it remains one of the most common malignancies of the gastrointestinal tract.

Most of the GC patients have advanced age, with a mean age approximately from 50 to 60 years. In the literature, there is a wide variation of the percentage of young patient with GC ranging from 2 to 15% [4,5,6,7]. In our study we found a higher rate: 18% of patients were under age 45 years. It should be noted that the cut-off of young patients is arbitrarily defined depending on the studies; in the latter reports; young patients are considered under the age of 40, when in ours we have included subjects between 40 and 45 years old too.

A notable feature in the young group is the predominance of women, rather than men. We indeed found a female-to-male ratio of 1.14:1 (18% of female). Similar findings were observed in other reports: In the study by Chung and al, female patient proportion was 75% in patients under age 30 years [8]. In other series, the number of females is either similar or higher than males and the male-to-female ratio ranges from 0.64 to 1.6 [9]. The causes of this gender distinction are currently unknown; therefore two possible theories are postulated. First, we know that environmental factors: smoking, infections, and dietary habits are risk factors of GC in elderly [10]. The exposition of males to these environmental carcinogens is more frequent than woman but the phenomena of carcinogenesis are long, so they result in cancer at an advanced age [11]. Second, epidemiologic data suggest that the predominance of females is due the harmful role of estrogens: in fact, a higher percentages of estrogen receptor-positive cells in young females and in patients with poorly differentiated GC have been reported [6]. Several studies have shown that the presence of the latter receptor is associated with poor survival in young patients with gastric carcinoma [12]. Though the relationship between gender hormones and the prognosis of GC is still controversial. Further studies are paramount to determine whether gender affects prognosis in young population.

The disease was symptomatic in all patient in the current study which is also consistent with the literature findings [6, 14, 15, 16]. Such an observation, along with several other studies, emphasize the importance of early detection by upper endoscopy in patients presenting with alarm symptoms despite their age, specially in areas with relatively high incidences of gastric cancer.

GC predominates globally in the distal third of the stomach [12]. In our study, tumors was essentially located in the middle third of stomach in 15 (48.38%) patients and in the lower third in 11 (35.48%) patients, which is consistent with other literature finding [16].

The data we herein reported and those of several other series suggest that GC in younger patients has an increased likelihood of an aggressive form. In Fact, a delay in diagnosis have been reported in young patient with GG in comparison with the elderly [17]. As a result there is a high rates of nodal and distant metastases at diagnosis. In the some context, "Surveillance, Epidemiology and End Results (SEER)" database, showed that 53% of patients under age 45 years are diagnosed in the metastatic stage of the disease [18].

Santoro et al, reported a percentage of 49% of metastatic stage in patients under age of 45 years [2]. In the some way, the study carried out by Smith and al have shown that patients aged <35 years compared with those aged >35 years, have a greater incidence of invasion of adjacent organs (74% vs 29%) and distant metastasis (81% vs 50%) [19]. In our study, this proportion was 76.5%.

Despite those findings Eguchi et al. reported that 52.7% of their young patients had early stage carcinoma [14]. As well as Lee et al, in a study including 54 Korean patients aged under 40 years no differences were found with regard to TNM stage or tumor size [20]. It may be explain by the fact that the latter studies have been carried out in Asian countries; where there is an effective screening program of GC.

Another aspect of the aggressiveness of gastric cancer in young subjects is the histological form of the disease. We found that poorly differentiated adenocarcinoma was the most common (44.14%) in young patients with gastric carcinoma, 3 patients had a diffuse type of Adenocarcinoma. Other studies have reported similar

results [12]. The diffuse type of gastric adenocarcinoma is believed to be less common than intestinal type in elderly patient, it is more known to affect young patients [2].

Data gathered so far have proved that intestinal type cancers develop as a result of chronic atrophic gastritis and subsequent intestinal metaplasia, mostly associated with chronic *Helicobacter pylori*. That can explain the decrease in the incidence of distal-type GC over the last two decades with the improvement and effectiveness of therapies for *H. pylori*. It is common in the distal stomach of patients in advanced age in high-risk populations, though, it also affects young adults with an incidence ranging from 15 to 32 per cent [21].

Young patients also have been shown to have a high incidence of the *cagA*-positive genotype of *Helicobacter pylori* infection; that is known to be more virulent than infection by the other bacterial strains, and which is more associated with the cascade of carcinogenesis leading to GC [19].

In other hand the diffuse type of gastric adenocarcinoma may be familial and dependent on an autosomal dominant, incomplete penetrance pattern of genetic inheritance [22].

No one of our patient had a family history of GC as it has been reported for other groups of young patients. In contrast Ramos and al., [18] showed that 16.9% of their young patients had a family history of gastric cancer [13].

Genetic factors constitute another important features in the young group, but only about 8–10% of cases may be related to a family history of gastric cancer [23]. Hereditary GC is associated to a constitutional mutation of the *CDH1* gene (encoding the cellular adhesion molecule E-cadherin). It is in about one-third of affected families and manifests phenotypically as linitis plastica [22]. As young patients in our study were significantly more affected with the intestinal type of adenocarcinoma, the implication of a genetic would be unlikely.

Curative resection is associated with long-term survival for GC patients. Some analysis have indicated that younger patients undergoing curative resection have a better prognosis [23]. In patients with distal gastric cancer, subtotal gastrectomy remains the procedure of choice. Therefore we do not have enough data about the risk of recurrent cancer of the gastric stump; mainly in a young population with a longer life expectancy [2]. Unfortunately; in younger patients, a reduced possibility of curative surgery is reported: resection was possible in 58% of patient in the study by Smith BR [19]. And only in 50% in the study carried out by Manzoor A. Dhobi and al [24]. We found a lower proportion; only 24% of patients undergo a curative surgery, the disease was discovered at an advanced stage.

V. Conclusion

In this study we have demonstrated that although Gastric cancer often occur in advanced ages, it may be diagnosed in young patients. It is distinguished by a female predominance, pathologically poor prognostic factors such as diffuse type, and a diagnosis in more advanced stages.

Thus, we conclude to on the extreme aggressiveness of gastric cancer in younger patients. An endoscopy screening system is of paramount importance for an early diagnosis to makes these young patients candidate for curative care. Further studies are needed to investigate the different genetic pathways, in order to provide tools for prevention and screening.

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Tables and Figures :

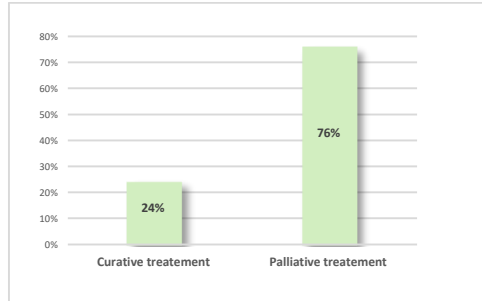


Figure 1

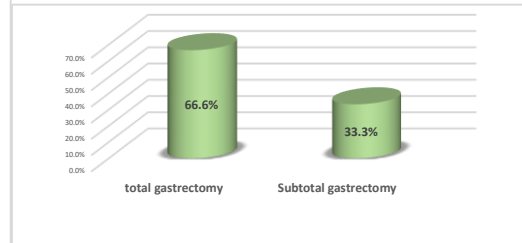


Figure 2

Population of young patients with GC	n (%)
Alteration of general conditions	27 (87)
Gastric pain	26 (86.09)
Vomitting	17 (58.1)
Bleeding	10 (31)
Anemia	7 (22.58).
Abdominal mass	9 (29)
Ascities	5 (16.1)
Troisier sign	3 (9.7)