Descriptive Analysis of Patients with Gastric Tumors Referred to the Largest Emergency Hospital in Oltenia Region-Romania, Between 2015-2020

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ABSTRACT: Gastric cancer represents the third most frequent cause of death worldwide, with the treatment being impaired also by the fact that patients present in the late stages of disease progression. We have aimed here to evaluate the main clinical and pathological features of all recorded cases of gastric tumor patients presented between January 2015 and December 2020 within the Emergency County Hospital of Craiova. Our retrospective analysis identified a total number of 745 cases, and showed a relative homogenous distribution of the age of the patients / year, with the peak age at presentation of 70-80 years old, and with males having a slightly higher prevalence compared to females. There was no correlation of the number of hospitalization days with the localization of the tumor, but the patients in the age group 60-70 years of age tended to show longer hospitalization times compared to the rest of the age groups. Also, pyloric/antral tumors tended to present at younger ages compared to other localizations, and interestingly, these patients also represented most of the casuistry. Altogether, the distribution of gastric cancer patients’ features did not change significantly in the last 5 years despite treatment advances (especially chemo-and radiotherapy), and the advanced stage of presentation call for a more aggressive detection and increased awareness of the population for this frequent pathology.

KEYWORDS: Gastric cancer, age distribution, anatomical localization, gender distribution, hospitalization time.

Introduction

Gastric cancer (GC) is an aggressive disease that continues to have an increased negative impact on global health [1].

In spite of the general decline in incidence over the past decades, gastric cancer remains the second leading cause of cancer deaths after lung cancer [2].

Risk factors for this disease include age, Helicobacter pylori infection, dietary factors like high salt intake and consumption of processed meat [3].

Consuming fresh fruits and vegetables has been linked to a low risk of cancer [2].

Histologically, approximately 90% of stomach tumors are adenocarcinomas. Most of the remaining 10% are non-Hodgkin’s lymphomas and neuroendocrine tumors.

Other rare malignant primary neoplasms are represented by adenosquamous, squamous and undifferentiated carcinomas.

The rarest tumors are choriocarcinomas, rhabdomyosarcomas, carcinoid tumors and hemangiopericytomas. In association with AIDS we can encounter Kaposi’s Sarcoma [4].

Adenocarcinomas can be subdivided into signet ring-cell carcinoma and undifferentiated carcinoma, according to the World Health Organization guidelines.

Lauren classification distinguishes two main subtypes of gastric cancer: diffuse types and intestinal type (classification is based on microscopic and macroscopic differences) [5].

Epidemiological studies suggest that intestinal types are related to intestinal metaplasia and also chronic atrophic gastritis, whereas diffuse types come from normal gastric mucosa.

The frequency of intestinal and diffuse types is different between countries and continents.

The diffuse type is more common in young people.

Intestinal type prevails in European countries and it affects more often the distal stomach.

A long-standing precancerous lesion precedes sometimes this type in high-risk areas. The surgical treatment is guided by the Lauren’s histological subtype of GCs [6-8].

The incidence of gastric cancer depends on the geographical area and has wide variations. More than half of the new cases are found in developing countries [8,9].
Intestinal type tumors are common in high-risk geographic areas like East Asia, South and Central America and Eastern Europe [10].

A more uniform geographic distribution is observed in diffuse type adenocarcinomas of the stomach [11].

The intestinal type is associated with older age groups and is more frequent in males and black population, whereas the diffuse type is more common in younger individuals and has a more equal male-to-female ratio [10,12,13].

The purpose of our study was to evaluate the main clinical and pathological features of all recorded cases of gastric tumor patients presented within the last 6 years within the largest hospital in Oltenia region, Romania.

**Material and Methods**

The retrospective study was performed on a number of 745 cases of gastric cancer in different stages, the recorded casuistry within the Emergency County Hospital of Craiova between January 2015 to December 2020.

In order to perform the study, we utilized the data from the hospital database.

We included in the study all patients that were diagnosed or hospitalized with gastric cancer regardless of stage and age.

The study was performed after we received the approval of the Ethics Committee of the Emergency County Hospital of Craiova (no. 3519/20.01.2021).

All data was anonymized, and processed respecting and ensuring the complete protection of personal information, according to the present legislation.

Available patients’ data were tabulated in Excel sheets, analyzed and processed in order to make relevant graphs, charts and diagrams regarding the distribution of gastric tumors over different age groups, genders, anatomical localization of the tumor, and the total recorded number of hospitalization days.

The study is observational, retrospective, and did not interfere with the medical care provided to the patients, also it did not require additional tissues or biological samples.

The main criteria for the inclusion in the study were a diagnostic of gastric cancer, regardless of anatomical localization and staging, and hospitalization in the Radiotherapy, Oncology, Gastroenterology, Surgery, or Internal Medicine Departments of the Emergency County Hospital of Craiova.

The main exclusion criteria was the impossibility of collecting clinical or paraclinical data due to incomplete records in the database.

If the patients presented to the hospital only at the emergency department without being hospitalized or treated on polyclinic, they were also excluded from the study.

The aim of this study was to analyse the frequency of gastric cancer in Oltenia, the average age at diagnosis, the frequency according to sex and age group.

The number of hospitalization days was also analyzed, and any putative correlations were sought. Data are represented as absolute values or average±standard deviation (SD).

All analysis was performed in Microsoft Excel, utilizing Student’s t-test and ANOVA (Analysis of Variance) testing for double or multiple comparisons, and calculating the Pearson product-moment correlation coefficient.

A value of p<0.05 was deemed significant for all testings.

**Results**

The study involved patients from Dolj, Vâlcea, Olt, Mehedinți and Teleorman counties, who were diagnosed or hospitalized with gastric cancer, regardless of stage and age, at the Emergency County Hospital of Craiova between January 2015 to December 2020.

The study was performed on a total number of 745 cases of gastric cancer.

Regarding the average age at admission of the patients recorded in each year, we could not find a statistically significant difference between the analysed years (p=0.210) (Figure 1), suggesting a relative homogeneity of the population from where the casuistry emerged.

![Figure 1. Histogram of average age of patients between 2015-2020. Error bars represent SD.](image-url)
Next, we looked for the number of cases grouped per 10 years age intervals (Figure 2), and we noticed that the highest number of cases that were diagnosed with gastric cancer were found in age group 70-80 years, (254 cases representing 34.09% of the total number of cases), followed by patients in the age group 60-70 years (195 cases, 26.17%).

In the age group of 80-90 years there were recorded 140 cases (18.79%), and in the age group of 50-60 years we counted 102 cases (13.69%).

The extremities of the chart with the lowest number of cases were formed by the age group of 40-50 years with only 35 cases (4.69%), followed by patients in age group of 90-100 years with 13 cases (1.74%). The fewest cases were recorded in the age group of 20-30 years with only 2 cases (2 women) and in the age group of 30-40 years with 4 cases (2 women and 2 men) (Figure 3).

Most of the patients with gastric cancer were men (Figure 3). Therefore, it was clear that the pattern of the men's graph dictated the overall shape of the graph for both genders. Regarding the gender distribution of patients, in our study 64.69% were men (482 cases) and 35.31% were women (263 cases). In the age group of 60-70 years of age, gastric cancer was 2.3 times more common in men and in the age group 70-80 years of age (where most of the patients were distributed), gastric tumors were 1.54 times more common in men compared to women.

We did not find any statistically significant difference between the average age at hospitalization between the two genders (p=0.059). In women, the average age at admission was of 71.3±11.7 years, and for men, the average age at admission was of 69.9±11.4 years (Figure 4).

The pathology was significantly more common in men compared to women in all the 5 years analysed. On average, gastric cancer was 1.83 times more common in men compared to women (Figure 5).

The highest discrepancy between the number of men and women was recorded for 2015 (highest difference) and 2020 (the least different values).

By calculation of the average age of men and women during the 6 years of study, we did not find a statistically significant difference between the average ages at hospitalization for the analyzed years. The lowest value of average age was 66.4±11.8 years age for men in 2020 and...
the highest value (74.7±8 years age) was recorded in 2015 in women (Figure 6).

This proved one more time the homogeneity of the population of patients.

Next, we assessed the number of cases for each anatomical region available. Most cases of gastric cancer have been located in the pyloric region for both genders (335 males and 263 females) (Figure 7).

We have next sought to assess the total number of hospitalization days and see if there were any classifiers that would bring any differences. There was no correlation between the age of the patients and the number of days of hospitalization (r=0.004) (Figure 8).

Regarding the average number of days of hospitalization, there were no differences between hospitalization periods grouped by age categories. The graph reflects once more the heterogeneity of the population, from this point of view (Figure 9).

There was however a tendency for the patients in the age groups 60-90 to require more hospitalization days compared to the rest of the age intervals. We did not have the end result of the patients after the hospitalization times, but it can be conceived that increasing age associates with an unfavorable prognostic and survival times.

Figure 6. Gender distribution of patients according to each year of study. Error bars represent SD.

Figure 7. Distribution of cases according to anatomical localization.

Figure 8. Distribution of the number of days of hospitalization according to age.

Regarding the average number of days of hospitalization, there were no differences between hospitalization periods grouped by age categories. The graph reflects once more the heterogeneity of the population, from this point of view (Figure 9).

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Figure 9. Average number of days of hospitalization grouped by age. Error bars represent SD.

There was no statistical difference between the averages number of days of hospitalization according to the anatomical localization of the gastric cancer (Figure 10). Again, there was no statistical difference between the hospitalization times and the primary tumor site, although cardia and gastric fundus seemed to lead to smaller hospitalization times (p>0.05). Despite the relative high number of available cases, the casuistry revealed a marked heterogeneity when considering this classificatory, probably due to different stages and gradings being considered for the same site.

Figure 10. Averages of the days of hospitalization according to the anatomical parts of stomach. Error bars represent SD.
The average age of patients diagnosed with gastric cancer at the antral region (67.52±10.91 years) was significantly lower than the average age of patients diagnosed with gastric cancer located in other areas (p=0.043), and all other anatomical areas had an average value over 78-80 years of age (Figure 11).

After grouping the average number of days of hospitalization by genders, we noticed that there was no significant difference between the two categories. The average number of hospitalization days for women was of 19.27±25.38 days, and for men of 18.91±24.65 days (Figure 12).

There was, again, a huge variability in hospitalization times, explained by the same multiple subfactors that dictate the course of the disease.

There was no correlation between the age of the females and the number of days of hospitalization (r=0.008) (Figure 13).

There was also no correlation between men's age and the number of days spent in the hospital (r=0.001) (Figure 14).

This is linked to the homogenous distribution of hospitalization times for the age group of 60-90 years (Figure 9).

The invasiveness through the mucosae showed that more than half of the tumors had an invasive character (Figure 15), illustrating the fact that most of these patients had been presenting too late during the development of the disease, and screening methods have a low impact on tumor detection.

Discussion

Adenocarcinomas emerge from the glandular epithelia of the mucosa and account for the vast majority of gastric malignancies (about 90%).

The aetiology of GC is diverse, including both environmental and genetic factors playing a major role. Many risk factors, such as age and
gender, cannot be changed, while others, like as smoking and Helicobacter pylori, could be.

The incidence of GC varies considerably between men and women, as well as between countries. Frequency in men is 2-to 3-fold higher than for women. When analyzing countries, East Europe, East Asia and South America have the greatest incidence rates, whereas North America and most regions of Africa have the lowest rates [14].

In most parts of the globe, the incidence of GC has been decreasing [15,16]. But gastric cancer is still a major health concern around the world nowadays. It is the fifth most common tumor in both men and women over the age of 70 in Italy [17].

In our study, we showed that the age group of 70-80 years old was the predominant population from the total number of cases diagnosed with gastric cancer, with 254 cases representing over 34 % of the cases. According to some studies, the average age of stomach cancer patients was of 70.5±4.6 years [18].

The incidence of GC increases with age, with the median age of diagnosis reaching 70 years. Unfortunately, about 10% of stomach carcinomas are discovered in people under the age of 45. After 20-30 years of exposure to carcinogenic compounds, malignancy usually develops [19].

Regarding our study, in women, the average age at admission was of 71.3 years. And for men, the average age at admission was of 69.9 years.

The majority of gastric cancer patients in our studied population were men. In our study, 64.69% of patients were men (482 cases) and 35.31% were women (263 cases).

Cardia GC is about twice as often in Caucasian population as it is in other ethnic groups [20], while non-cardia GC is approximately half as frequent [21].

The link between race and the occurrence of GC appears to be mediated primarily by environmental factors rather than genetic variants. Japan has among the world's highest levels of GC occurrence [19].

After migrating to America, the Japanese maintain relatively high rates in their first generation. After two generations, however, their rates fall and become comparable to those of European-Americans [22].

In our study performed on a number of 745 cases of gastric cancer in different stages from within the largest hospital in the south-east of Romania for a period of 6 years (between 2015-2020) we observed in both genders that the majority of stomach cancer cases have been found in the pyloric area. Helicobacter pylori infection, low socioeconomic level [23], and maybe dietary factors such as limited consumption of fruits and vegetables and excessive intake of salty and smoked food are all risk factors for non-cardia GC [14].

Males had a higher risk of cardia and non-cardia GC than females [20].

The cause for these discrepancies is unclear. Exposure to the environment or work conditions could be a factor. Men, for example, have historically been more prone to smoke tobacco products, despite the fact that increased rates in men appear to remain even in countries where men and women smoke at similar rates [24].

The incidence of GC varies considerably between men and women, as well as between countries. Men's rates are 2-to 3-fold higher than women's (4). When analyzing countries, East Europe, East Asia, and South America have the greatest incidence rates, whereas North America and most regions of Africa have the lowest rates. Furthermore, gender differences could be related to physiological differences. Estrogens may help to prevent the onset of GC. Delaying menopause and increasing fertility in women may reduce the chance of GC, although anti-estrogen medications, on the other hand, may raise the risk [25].

These hormones may protect women from GC during their reproductive years, but their influence fades after menopause, causing women to develop GC in the same way as males, although 10 to 15 years later than their male counterparts [26,27].

In all of the years studied, we noticed that men were considerably more likely than women to develop the disease. Gastric cancer was 1.83 times more common in men than in women, on average.

Around the world, stomach cancer mortality has reduced dramatically during the last few decades [28].

Gastric cancer, on the other hand, has a poor prognosis and a high death rate. This malignancy is the second greatest cause of cancer-related death worldwide, after lung cancer. In general, countries with a greater stomach cancer incidence rate had higher survival rates than those with a smaller incidence rate [29].

This correlation is mostly due to differences in survival rates depending on where the
malignancy is located in the stomach. If compared to tumors in the pyloric antrum, tumors in the gastric cardia had a substantially worse prognosis, with inferior 5-year survival and increased operative death [30].

We observed no significant difference in average ages at admission when we calculated the average age of patients diagnosed with GC from 2015 to 2020 and also there was no statistically significant variation between the two genders' average age at hospitalization. There is no correlation between the age of the females or males and the number of days of hospitalization.

We observed that patients in the age range 70-80 years were the largest number of cases diagnosed with stomach cancer (34.09%), followed by patients in the age group 60-70 years age (26.17%).

The invasiveness through the mucosa showed that more than half of the tumors had an invasive character, indicating that most of these patients had been presenting too late in the disease's progression and the screening approaches have a minimal influence on tumor detection.

Our study had certain limitations. We did not have access to full pathological reports, treatment regimens, survival follow-up of the patients, nor to the data of ambulatory patients. This would have surely decreased the variability and heterogeneity of the patients for most of the classifiers.

Conclusions
To summarize, stomach cancer has a heterogeneous epidemiology and is more common among the elderly, especially men.

In our study, most cases of gastric cancer have been located in the pyloric region in both genders, and have been referred to in advanced stages of the disease, and this calls for a more aggressive detection and increased awareness of the population for this frequent and aggressive pathology.

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Author contributions
Ilona Mihaela Liliac and Mihai Victor Sacerdotianu had equal contributions to this work and thus share first co-authorship.

Conflict of interests
None to declare.

References
1. Carcas LP. Gastric cancer review. J Carcinog, 2014, 13:14.
2. Correa P. Gastric cancer: overview. Gastroenterol Clin North Am, 2013, 42(2):211-217.
3. Smyth EC, Nilsson M, Grabbsch Hi, van Grieken NC, Lordick F. Gastric cancer. Lancet, 2020, 396(10251):635-648.
4. de Martel C, Forman D, Plummer M. Gastric cancer: epidemiology and risk factors. Gastroenterol Clin North Am, 2013, 42(2):219-240.
5. Qiu MZ, Cai MY, Zhang DS, Wang ZZ, Wang DS, Li YH, Xu RH. Clinicopathological characteristics and prognostic analysis of Lauren classification in gastric adenocarcinoma in China. J Transl Med, 2013, 11:58.
6. Ribeiro MM, Sarmento JA, Sobrinho Simoes MA, Bastos J. Prognostic significance of Lauren and Ming classifications and other pathological parameters in gastric carcinoma. Cancer, 1981, 47(4):780-784.
7. Ahn HS, Lee HJ, Hahn S, Kim WH, Lee KU, Sano T, Edge SB, Yang HK. Evaluation of the seventh American Joint Committee on Cancer/International Union Against Cancer Classification of gastric adenocarcinoma in comparison with the sixth classification. Cancer, 2010, 116(24):5592-5598.
8. Sitarz R, Skierucha M, Melko J, Offerhaus GJA, Maciejewski R, Polkowski WP. Gastric cancer: epidemiology, prevention, classification, and treatment. Cancer Manag Res, 2018, 10:239-248.
9. Stock M, Otto F. Gene deregulation in gastric cancer. Gene, 2005, 360(1):1-19.
10. Crew KD, Neugut AI. Epidemiology of gastric cancer. World J Gastroenterol, 2006, 12(3):354-362.
11. Munoz N, Correa P, Cuello C, Duque E. Histologic types of gastric carcinoma in high- and low-risk areas. Int J Cancer, 1968, 3(6):809-818.
12. Lauren P. The Two Histological Main Types of Gastric Carcinoma: Diffuse and So-Called Intestinal-Type Carcinoma. An Attempt at a Histological Classification. Acta Pathol Microbiol Scand, 1965, 64:31-49.
13. Correa P, Sasano N, Stemmermann GN, Haenszel W. Pathology of gastric carcinoma in Japanese populations: comparisons between Miyagi prefecture, Japan, and Hawaii. J Natl Cancer Inst, 1973, 51(5):1449-1459.
14. Karimi P, Islami F, Anandasabapathy S, Freedman ND, Kamangar F. Gastric cancer: descriptive epidemiology, risk factors, screening, and prevention. Cancer Epidemiol Biomarkers Prev, 2014, 23(5):700-713.
15. Kamangar F, Dores GM, Anderson WF. Patterns of cancer incidence, mortality, and prevalence across five continents: defining priorities to reduce cancer disparities in different geographic regions of the world. J Clin Oncol, 2006, 24(14):2137-2150.
16. Bosetti C, Bertuccio P, Malvezzi M, Levi F, Chatenoud L, Negri E, La Vecchia C. Cancer mortality in Europe, 2005-2009, and an overview of trends since 1980. Ann Oncol, 2013, 24(10):2657-2671.
17. Cavatorta O, Scida S, Miraglia C, Barchi A, Nouvenne A, Leandro G, Meschi T, De’ Angelis GL, Di Mario F. Epidemiology of gastric cancer and risk factors. Acta Biomed, 2018, 89(8-S):82-87.
18. Lee SR, Kim HO, Yoo CH. Impact of chronologic age in the elderly with gastric cancer. J Korean Surg Soc, 2012, 82(4):211-218.
19. Machlowska J, Baj J, Sitarz M, Maciejewski R, Sitarz R. Gastric Cancer: Epidemiology, Risk Factors, Classification, Genomic Characteristics and Treatment Strategies. Int J Mol Sci, 2020, 21(11)
20. Brown LM, Devesa SS. Epidemiologic trends in esophageal and gastric cancer in the United States. Surg Oncol Clin N Am, 2002, 11(2):235-256.
21. El-Serag HB, Mason AC, Petersen N, Key CR. Epidemiological differences between adenocarcinoma of the oesophagus and adenocarcinoma of the gastric cardia in the USA. Gut, 2002, 50(3):368-372.
22. Maskarinec G, Noh JJ. The effect of migration on cancer incidence among Japanese in Hawaii. Ethn Dis, 2004, 14(3):431-439.
23. Camargo MC, Kim WH, Chiaravalli AM, Kim KM, Corvalan AH, Matsuo K, Yu J, Sung JJ, Herrera-Goepfert R, Meneses-Gonzalez F, Kijima Y, Natsugoe S, Liao LM, Lisowska J, Kim S, Hu N, Gonzalez CA, Yatabe Y, Koriyama C, Hewitt SM, Akiba S, Gulley ML, Taylor PR, Rabkin CS. Improved survival of gastric cancer with tumour Epstein-Barr virus positivity: an international pooled analysis. Gut, 2014, 63(2):236-243.
24. Freedman ND, Derakhshan MH, Abnet CC, Schatzkin A, Hollenbeck AR, McColl KE. Male predominance of upper gastrointestinal adenocarcinoma cannot be explained by differences in tobacco smoking in men versus women. Eur J Cancer, 2010, 46(13):2473-2478.
25. Derakhshan MH, Lipot S, Paul J, Brown IL, Morrison D, McColl KE. Oesophageal and gastric intestinal-type adenocarcinomas show the same male predominance due to a 17 year delayed development in females. Gut, 2009, 58(1):16-23.
26. Sipponen P, Correa P. Delayed rise in incidence of gastric cancer in females results in unique sex ratio (M/F) pattern: etiologic hypothesis. Gastric Cancer, 2002, 5(4):213-219.
27. Camargo MC, Goto Y, Zabaleta J, Morgan DR, Correa P, Rabkin CS. Sex hormones, hormonal interventions, and gastric cancer risk: a meta-analysis. Cancer Epidemiol Biomarkers Prev, 2012, 21(1):20-38.
28. Jemal A, Thomas A, Murray T, Thun M. Cancer statistics, 2002. CA Cancer J Clin, 2002, 52(1):23-47.
29. Verdecchia A, Corazziari I, Gatta G, Lisi D, Faiivre J, Forman D, Group EW. Explaining gastric cancer survival differences among European countries. Int J Cancer, 2004, 109(5):737-741.
30. Asplund J, Kauppila JH, Mattsson F, Lagergren J. Survival Trends in Gastric Adenocarcinoma: A Population-Based Study in Sweden. Ann Surg Oncol, 2018, 25(9):2693-2702.