JMS 2020;3 (2):13-17
UDC:616.33-006.6-092(497.7)

DEMOGRAPHIC AND PATHOLOGICAL CHARACTERISTICS OF GASTRIC CARCINOMAS – A Three-Year Single Center Experience

Ognjenovic Ljubomir[1], Sumkovski A[1], Trajkovski G[1], Bushinoska J[2], Nikolova D[3], Hadzi-Mancev D[1], Dzambaz D[1]

[1]University Clinic for Abdominal Surgery, [2]University Clinic for Anesthesiology, Reanimation and Intensive Care, [3]University Clinic for Gastroenterohepatology, Faculty of Medicine, University "Ss.Cyril and Methodius", Skopje, Republic of North Macedonia

Abstract

Introduction: Despite the decline in incidence and mortality rate in recent years, gastric carcinoma (GC) remains one of the leading causes of cancer-related deaths worldwide, especially in developing countries.

The aim of this study was to present the clinical and pathological characteristics of gastric carcinomas in patients from R. North Macedonia.

Material and methods: One hundred and forty-nine patients with gastric carcinoma were included in the study. Sixty-one patients underwent subtotal gastric resection with lymphadenectomy, and 88 patients underwent total gastrectomy with lymphadenectomy. Tumor localization, TNM classification, grade and stage were determined for each patient. The parameters of the TNM classification (AJCC Cancer Staging 2017) were obtained from the archived histopathological reports of the Institute of Pathology in Skopje, and for the clinical stage patients' files from the University Clinic for Abdominal Surgery in Skopje were used.

Results**:**The most common intragastric location of gastric carcinomas was cardia in 61 (40.94%) patients, followed by antral/pyloric carcinoma location in 51 (34.23%) patients and corpus location in 37 (24.83%) patients. According to the T status (local tumor growth), more than half of the examined patients 84 (56.38%) were in T4 status of the disease. Presence of positive regional lymph nodes was detected in 113 (75.84) patients, and negative in 36 (24.16%) patients. The majority of patients that comprised the analyzed group - 81 (54.36%) had a poor differentiated gastric carcinoma, and 88 (59.06%) were in Stage III of the disease.

Keywords: gastric carcinoma, TNM stage, grade, T status

Introduction

Despite the decline in incidence and mortality rate in recent years, gastric carcinoma (GC) remains one of the leading causes of cancer-related deaths worldwide, especially in developing countries. Having in mind the fact that even in developed countries primary detection of GC is in the nonresectable stage of the disease, the systemic therapy is the main option for treatment that can only prolong the duration of survival [1-4]. The survival rate of patients with GC is still low in spite of the numerous surgical techniques and development of supplementary preoperative, neoadjuvant and adjuvant protocols for chemotherapy, as a consequence of which the medical treatment of patients in advanced stage of gastric carcinoma demands novel therapeutic possibilities [1-6].

The aim of this study was to present the clinical and pathological characteristics of gastric carcinomas in the Macedonian population.

Material and methods

One hundred and forty-nine patients with gastric carcinoma surgically treated at the University Clinic for Abdominal Surgery in Skopje were included in the study. The operative material was analyzed at the Institute of Pathology, Faculty of Medicine in Skopje. Before the surgical treatment, an imaging technique procedure, gastroscopy and preoperative evaluation were made. For every patient, a standard surgical procedure, according to the tumor localization with loco-regional and systemic lymphadenectomy was performed. Sixty-one patients underwent subtotal gastric resection with lymphadenectomy, and 88 patients underwent total gastrectomy with lymphadenectomy. Following the surgical treatment, a substitution therapy in the postoperative period was applied, using different solutions. The substitution therapy included correction of electrolyte disbalance with electrolyte solutions, correction of anemia with transfusion, correction of

hypoproteinemia with plasma and pure albumin solution, correction of coagulation factors deficiency with fresh frozen plasma, and if necessary, antibiotic therapy. Every patient had a controlled postoperative dietary regime, antithrombotic prophylaxis and controlled analgesia for pain management.

Tumor localization, TNM classification, stage and grade of differentiation were determined for every patient. The parameters of the TNM classification (according to AJCC Cancer Staging 2017) were obtained from the archived histopathological reports of the Institute of Pathology in Skopje, and for the clinical stage, patients' files from the University Clinic for Abdominal Surgery in Skopje were used.

Descriptive statistical methods were used for statistical analysis of data. The rate of the interdependence of the analyzed parameters was obtained with linear correlation. Statistical program SPSS for Windows 19.0 was used.

Results

The analyzed group consisted of 149 patients, with the mean age of 65.19 ± 10.1, 108 (72.48%) of which were female and 41 (27.52%) male. In terms of ethnicity, 114 (76.51%) patients were Macedonians, and 35 (23.49%) were Albanians.

Clinical and histopathological characteristics of the GC are shown in Table 1.

Table 1. Clinical and histopathological characteristics of GC

Variable	**n (%)**
Localization	
Cardia	61 (40.94)
Corpus	37 (24.83)
Antrum/Pylorus	51 (34.23)
T	
1	5 (3.6)
2	19 (12.75)
3	41 (27.52)
4	84 (56.38)
Nodal involment	
Negative	36 (24.16)
Positive	113 (75.84)
Nodal status (TNM classification)	
0	36 (24.16)
1	27 (18.12)
2	30 (20.13)
3	56 (37.58)
Metastases	
No	136 (91.27)
Distant metastasis	13 (8.72)
Gradus	
well differentiated	2.68)
moderately differentiated	64 (42.95)
poorly differentiated	81 (54.36)
Stage	
I	11 (7.38)
II	37 (24.83)
III	88 (59.06)
IV	13 (8.72)

The most common intragastric location of gastric carcinomas was cardia in 61 (40.94%) patients, followed by antral/pyloric carcinoma location in 51 (34.23%) patients and corpus location in

37 (24.83%) patients. According to the T status (local tumor growth), more than half of the examined patients 84 (56.38%) were in T4 status of the disease. Presence of positive regional lymph nodes was detected in 113 (75.84) patients, and negative in 36 (24.16%) patients. More than half of the analyzed patients - 88 (59.06%) were in Stage III of the disease.

The majority of patients that comprised the analyzed group-81(54.36%) had a poor differentiated gastric carcinoma.

Discussion

Gastric cancer is a complex, multifactorial disease that includes various genetic and epigenetic changes in its background [7]. The main method of predicting the outcome of the disease in patients with GC is the clinical pathological stratification used by the TNM classification, and the grade of tumor differentiation is part of this classification. In practice, the emergence of many differences in outcome (using the same classification and stratification, with a completely different outcome) has imposed the need of finding new, more relevant ways for more accurate identification of GC's biological subgroups.

Yasui W *et al*. in 2011 pointed out that GC is largely due to changes in gastric epithelial cells. The process of carcinogenesis remains complex and difficult to understand and is due to additional factors such as microeconomics, inflammation, oxidative stress, and hypoxia [8].

A deeper understanding of the pathogenesis and biological occurrence of GC is essential for the further development of early detection and treatment methods. The discovery of new biomarkers and their application in practice, coupled with traditional methods of diagnosis, stratification, and prognosis, have helped to improve early detection of GC, early care for patients, and appropriate therapy [9]. There are 4 types of biomarkers: diagnostic, predictive, prognostic and therapeutic. Predictive biomarkers are defined as markers that can be used to show the subpopulations of patients who are likely to respond (or not) to a target therapy. The understanding of the molecular basis of neoplasms opened a new era for early detection and early modern treatment of gastric cancer, with the possibility of a higher survival rate. New molecular target therapies are interfering with the various signaling cascades involved in cell proliferation that directly affect tumor survival and differentiation.

TNM classification of gastric carcinoma is the most valuable prognostic factor in patients with this disease. The classification contains the following elements: T- local tumor growth, N - lymph node involvement and M - the distant metastatic spread of the primary disease. The grade of differentiation of a tumor is also part of the classification. However, there is a variable prognosis among patients at the equal stage of the disease. Therefore, a request for finding additional parameters for better identification of biological subgroups is imposed by itself. Biological predictive factors are obtained from genetic process, which is considered to be the key step in the development of gastric carcinoma (HER2, E-cadherin, EGFR, microsatellite instability, changes in few factor expression, including thymidylate synthase, beta-catenin, mucin-Ag, p53, COX-2, matrix metalloproteinases, and receptors for vascular endothelial factor) [10]. Defining the tumor stage is a way to describe where the GC is located, whether and where it has been spread, and whether it has affected another part of the body. With the help of clinical diagnostic tests, the stage of GC can be determined. However, this is not always easy. In order to find the most appropriate way to treat the tumor, and to histologically determine the subtypes based on major morphological components, there are a number of difficulties with the classification of the anatomical localization of the tumor, especially if the GC is located in the upper part of the stomach. This is due to the fact that there is no universal consensus in defining what a gastro-esophageal junction (GES) is, and where the cardia comes from [11]. In this study, the TNM classification proposed by the American Joint Committee on Cancer (AJCC) was used to simplify and base the location of the tumor epicenter and the presence and absence of GES involvement [12].

According to the results of this study, the most common localization of gastric cancer was the cardia (40.94% of patients), which was 6.6% more common than antrum / pylorus and 16.11% than the corpus localization.

According to literature, it can be noticed that in the first half of the last century until the 70's, in most cases the GCs were located in the distal part of the stomach; they were of intestinal type and well differentiated cancers. In the last quarter of the last century, there was an increase in poorly

differentiated, diffusely infiltrated GC. The reason for this increase in malignancy in proximal parties remains unclear. In a study published in Arch Oncol 2004 by Pesic M. *et al*., in 13.33% of cases GC was located in the proximal stomach [13], which is a lower percentage than that obtained in our study. Recent reports in the literature suggest that the incidence of gastric cancer in the proximal regions ranges from 25% to 40% [1,14,15].

The results of this study were based on the TNM assessment as the most important prognostic factor in GC. This classification is based on the stage of depth of involvement with gastric wall carcinoma (T), involvement in the lymph node (N) process, and the presence of distal metastases (M). The analysis of the examined material showed that 56.38% of the patients had gastric cancer with T4 stage. This finding is consistent with the findings presented by several authors.

Positive regional lymph nodes were detected in 113 (75.84%) patients; with N3 stage were56 (37.58%) patients.

Metastatic lesions had 13 (8.72%) patients. These results correlate with the findings reported by other authors [1, 7, 16].

According to the differentiation of the tumor, the majority of respondents had poorly differentiated gastric cancer - 81 (54.36%), while according to the stage, the cancers were most commonly diagnosed in stage III - 88 (59.06%).

In conclusion, the most common intragastric location of GC was cardia (40.94%); more than half of the examined patients (56.38%) were in T4 status of the disease; positive regional lymph nodes were detected in 75.84% of patients; the majority of patients (54.36%) had poor differentiated GC and Stage III of the disease (59.06%).

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