RESEARCH ARTICLE

The New Changes in the 7th AJCC/UICC Staging System of Gastric Carcinomas

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Objective: The aim of this study was to analyze in parallel the 6th and the newest 7th AJJCC/UICC (American Joint Committee on Cancer/ International Union Against Cancer) staging system in order to highlight changes brought by the new staging system.

Methods: We analyzed data obtained retrospectively from 134 hospitalized patients diagnosed with gastric carcinomas, who underwent surgery at the Surgery Clinics of the County Emergency Clinical Hospital of Tirgu Mureş, Romania between 2008–2010. The data have been obtained from histopathology reports, and the analyzed parameters were the following: age, gender and pTNM staging. For all cases included in the study restaging was performed according to the 7th AJJCC/UICC staging system.

Results: 71.66% of cases were adenocarcinomas, 7.46% mucinous adenocarcinoma, 14.17% signet ring cell carcinoma, and 6.71% undifferentiated carcinoma. The signet ring cell carcinomas predominated before 65 years of age (p = 0.003). Compared to the 6th staging system, in the new system pT2 percentages decreased significantly from 38.8% to 6.71%, and pT4 increases from 11.19% to 55.97% (p < 0.0001). The pN3 cases increased from 20.9% to 45.52%, because all cases classified as pN2 in the old staging system, became pN3 in the new system. Some of the pN1 cases turned into pN2 in the new system (p = 0.004). Stage IV cases also decreased from 29.85% to 14.94%, due to regrouping of stage III.

Conclusions: There are significant changes between the two staging systems. The new staging system aims to achieve a better postoperative follow-up.

Keywords: gastric cancer, 6th AJJCC/UICC staging system, 7th AJJCC/UICC staging system

Received: 27 April 2012

Introduction

Gastric cancer is one of the most frequent gastrointestinal tumors, and represents the second cause of cancer death worldwide, although global incidence is declining [1].

It is known that most of gastric cancer patients are diagnosed in advanced stages, due to unspecific symptoms, and also to late reporting of patients to the physician [2]. Surgery is the only option providing substantial improvement of survival in cases with early diagnosis, but even in patients diagnosed with early stages, the 5-year survival rate is about 50% [3]. Patients with advanced stages of gastric cancer can benefit from palliative care or neoadjuvant chemotherapy. Thus, accurate quantification of tumor stage is an extremely important aspect in establishing the subsequent treatment protocol for the patient.

The stage of the disease also represents one of the most important prognostic factors of gastric cancer; therefore TNM staging has the main role in establishing the treatment protocol [4]. In 2010 the 7th TNM staging of gastric carcinomas has been introduced by the American Joint Committee on Cancer (AJCC) and International Union Against Cancer (UICC) [5].

Correspondence to: Ioana Hălmaciu E-mail: anca_halmaciu@yahoo.com The present study aims to highlight the importance of changes brought by the 7th TNM staging of AJCC/UICC, in order to achieve a better postoperative staging. The changes brought by the 7th staging system compared to the 6th staging system are listed in Table I [5,6].

Methods

One-hundred forty-three patients who underwent surgical intervention during 2008–2010 were enrolled in the study. Open surgery was performed in each case to remove the gastric tumor. In all cases, formalin-fixed embedded tissues were used. Sections were dewaxed and were stained with Hematoxylin-Eosin.

We analyzed the histological type and grade of the tumor. These parameters were correlated with the patients' age and gender. Only carcinomas of the stomach were included in our study. Lymphomas, carcinoid tumors and gastrointestinal stromal tumors were excluded.

We analyzed in parallel the 6th and 7th AJCC/UICC staging systems [5,6] in order to underline the clinical significance of the new staging of gastric carcinomas.

Data was collected with Microsoft Excel, and analyzed with GraphPad InStat software. Categorical data analysis was conducted with the chi-square test. The level of significance was set at p < 0.05.

Table I. The 7th vs. 6^{th} edition of pTNM classification of gastric carcinomas

Variable	6 th edition of the AJCC	7 th edition of the AJCC
pTis	carcinoma in situ	carcinoma in situ
pT1	invasion of mucosa or submucosa	same features
pT2	invasion of muscularis propria or subserosa	invasion only in muscularis propria
рТ3	tumor penetrates serosa (visceral peritoneum) without invasion of adjacent structures	tumor penetrates subserosal connective tissue without invasion of visceral pritoneum or adjacent structures
pT4a	tumor invades adjacent structures	tumor penetrates serosa (visceral peritoneum)
pT4b	-	invasion of the adjacent structures
pN1	1–6 lymph nodes with metastases	1–2 lymph nodes with metastases
pN2	7–15 lymph nodes with metastases	3–6 lymph nodes with metastases
pN3	>15 lymph nodes with metastases	>6 lymph nodes with metastases
Stage 0	TisN0M0	same features
Stage IA	T1N0M0	same features
Stage IB	T1N1M0, T2N0M0	same features
Stage II A	T1N2M0, T2N1M0, T3N0M0	same features
Stage II B	-	T1N3M0, T2N2M0, T3N1M0, T4aN0M0
Stage IIIA	T2N2M0, T3N1M0, T4N0M0	T3N2M0, T2N3M0, T4aN1M0
Stage IIIB	T3N2M0,	T4aN2M0, T3N3M0, T4bN0–1M0
Stage IIIC	-	T4bN2M0, T4bN3M0, T4aN3M0
Stage IV	T4N1–3M0, T1–3N3M0, AnyT AnyN M1	AnyT AnyN M1

Results

Clinico-pathological features

Analysis of the study group revealed that most of the cases were males (67.88%), and only 32.12% were females. The male/female ratio was about 2.11.

Mean age was 68 years for females (range 23–86 years), and 70 years for males (range 23–87 years).

Distribution of cases based of histological type was as follows: 5.96% well differentiated adenocarcinomas (G1), 25.37% moderately differentiated adenocarcinomas (G2), 40.33% poorly differentiated adenocarcinomas (G3), 7.46% mucinous adenocarcinomas, 14.17% signet ring







Fig. 1. Structure of the study group based on age and histological type.

G1 = well differentiated adenocarcinoma; G2 = moderately differentiated adenocarcinoma; G3 = poorly differentiated adenocarcinoma, MA = mucinoUs adenocarcinoma, SRCC = signet ring cell carcinoma, UCC = undifferentiated carcinoma.

cell carcinomas, and 6.71% undifferentiated carcinomas. There was no significant correlation between the gender of the patients and histological type (p = 0.2008).

There was a statistically significant correlation between age and histological type of gastric carcinomas (p = 0.003). We noted an increase in the frequency of moderately differentiated adenocarcinoma (21.64%) and poorly differentiated adenocarcinoma (26.9%) over 65 years of age. In case of younger patients signet ring cell carcinoma (8.95%) was more frequent (Figure 1).

Staging systems

The present study revealed a statistically significant correlation between the depths of infiltration of the primary tumor (pT) evaluated according to the 6th AJCC/UICC staging system, and those evaluated with the 7th AJCC/UICC staging system (p <0.0001).

We noted that pT2 decreased significantly from 38.8% to 6.71%, and pT4 increased from 11.19% to 55.97% (p <0.0001) (Figure 2).

Analyzing the number of invaded regional lymph nodes (pN) according to the two staging systems we also noted a statistically significant correlation (p = 0.004).

We noted that pN3 increased significantly from 20.9% to 45.52%, because all cases classified as pN2 in the old



Fig. 3. Structure of the study group based on the number of lymph node metastases (pN) in both 6th and 7th AJCC/UICC staging system



Fig. 4. The grouping staging of the cases according on the $6^{\rm th}$ AJCC/UICC staging system

staging system became pN3 in the new system (Figure 3). A large number of pN1 cases from the old staging system turned into pN2 in the new system.

Regarding the grouping stages, we observed an obvious decrease in the number of cases classified as stage IV (29.85%) in the old staging system, compared to the new system (14.94%) (Figures 4 and 5). This is due to the fact that most of the cases classified as stage IV in the old staging system were reclassified into stages IIIB, IIIC, IIIA in the new system. Likewise, cases classified in the old system as stage IIIA were redistributed into stages IIB and IIIB in the new system.

Discussion

The TNM staging system takes into consideration the most basic parameters of cancer, and it determines the extent of the disease, providing guidance for treatment planning, and predicting outcome [7].

Out of the total number of gastric cancer cases admitted to and investigated at the County Emergency Clinical Hospital of Tîrgu Mureş, Romania, 134 cases were included in the study, all being gastric carcinomas.

Preponderance of gastric tumors in males was obvious; in our study the male/female ratio was 2.11, in line with bibliographical data [1].

We noted a predominance of adenocarcinomas (71.66%) over other carcinomas (28.34%) but there was no statistically significant correlation between the gender of the patients and the histological type of the tumor.

G1 and G2 adenocarcinomas were more frequently after 65 years of age, and an increase in frequency of signet ring cell carcinoma in younger patients was observed. These data correspond to those reported by other authors [1].

Regarding the tumor staging, we should mention again that in the old system pT4 referred to tumor invasion into adjacent structures, while in the new staging system pT4 is subdivided into T4a (tumor invasion into serosa) and T4b (tumor invasion into adjacent structures) [5]. Practically, pT3 of the old system now corresponds to pT4a. Thus, cases classified into pT3 (44.77%) are labeled as pT4 (55.97%) in the new system. This explains the large number of pT4 (55.97%) cases of the new staging system versus



Fig. 5. The grouping staging of the cases according on the 7^{th} AJCC/UICC staging system

the small number of pT4 (11.19%) cases of the old system.

Similarly, the ratio of pT2 cases of the old system (38.8%) decreases significantly to 6.71% in the new system. This is due to the following: in the old system pT2 referred to tumor invasion into the muscularis propria or subserosa, while in the new staging system pT2 represents only muscularis propria invasion, while subserosa invasion is classified as pT3 [5,6]. Thus, T2b of the old system becomes pT3, and pT2a turns into T2.

The most recent studies did not demonstrate significant differences between survival of cases classified as pT2 and pT3 in the new system [7].

Some researchers reported that patients with stage IV gastric cancer as classified by the 6th edition system could be divided into two subgroups. Patients downstaged to stage III in the 7th edition system had better prognosis than those who remained in stage IV. Even if these patients were divided into three substages (stage IIIB, IIIC, IV) they still had different prognoses. Subdivision of stage IV gastric cancer into IVa and IVb may help predict the outcome of patients with stage IV gastric cancer as classified by the 6th edition system [7,8].

Details of pN classification based on the number of metastatic lymph nodes were also changed. N1 of the old staging system has been divided into N1 and N2, while N2 and N3 are classified as N3 in the new system [5].

Our study analyzed the number of regional metastatic lymph nodes according to the two staging systems, and noted a statistically significant correlation. All cases classified as pN2 (24.62%) in the old staging system were reclassified as pN3 (45.52%). pN1 (32.08%) cases became pN1 (16.41%) and pN2 (15.67%) in the new system.

Many studies demonstrated that N stage of the 6^{th} edition system was not suitable for prognostic prediction in clinical analysis, because of the inappropriate cut-offs of that stage. In a study performed on 308 gastric cancer cases with therapeutic resection, classified by the 6^{th} edition system, Deng et al. established that the most appropriate cutoffs of metastatic lymph nodes are 0, 1–4, 5–8, and 9 [9]. In several multicenter retrospective studies performed on 652 resected early gastric cancer cases classified by the 6^{th} edition system, Roviello et al. found that the 10-year survival rate in early gastric cancer patients was 92% for patients with negative nodes, 82% for patients with 1–3 positive nodes, 73% for 4–6 positive nodes, and 27% for 6 positive nodes [10]. In accordance with Deng et al. [9] N2 and N3 patients in their study using the 6th edition system had similar survival [11]. The studies mentioned above demonstrated that in the 6th AJCC/UICC edition N stage reflected less accurately patient prognosis.

According to the theory mentioned by Ueno et al., the criteria for evaluating the performance of the staging systems were as follows: (1) homogeneity within subgroups, (2) discriminatory ability between different groups, and (3) monotonicity of gradients demonstrated in the association between stages and survival rates [12]. In the 6th edition staging system, the survival rate of the six substages had significant differences, while in the 7th edition system, the discriminatory ability between the eight substages appeared more powerful. Thus, the 7th edition UICC TNM staging system is superior to the 6th edition system in terms of homogeneity, discriminatory, and monotonicity of gradients [7].

Conclusion

The present study highlighted significant differences between the two staging systems. The new system aims at a better tumor staging, and a better accuracy in evaluating prognosis and strategies for adjuvant therapy.

The pTNM grading system seems to remain the key element of the treatment protocol of gastric cancer patients.

Acknowledgement

This work was partially supported by the Romanian National University Research Council (CNCSIS), Ministry of Education and Research, projects frame: PN II – PD, no. 504/2010 and by the Sectoral Operational Programme Human Resources Development, financed from the European Social Fund and by the Romanian Government under the contract number POSDRU/89/1.5/S/60782.

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