Preliminary Results Regarding the New Changes in the 7th AJCC/UICC Staging System of Gastric Carcinomas

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Objective: The aim of the 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 about the new staging system.
Methods: We analyzed data obtained retrospectively from 134 hospitalized patients diagnosed with gastric carcinomas, who underwent surgery at the Surgery Clinic of the Emergency County Hospital of Tîrgu Mureș, 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. For statistical analysis we used GraphPad InStat software.
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, become pN3 in the new system. Some of pN1 cases turned into pN2 in the new system (p=0.004). The 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

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 years survival rate is about 50% [3].

The 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.

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].

The present study aims at highlighting the importance of changes brought about by the 7th TNM staging of AJCC/UICC introduced in 2010, in order to achieve a better postoperative staging. The changes brought about by the 7th staging system as compared to the 6th staging system are listed in the Table I.

This study presents the preliminary results of the benefic effects brought by the new TNM stadialization. The data concerning the clinical importance of this new TNM stadialization in relation with the survival are still being processed and evaluated.

Methods

One-hundred thirty-four patients who underwent surgical intervention between 2008–2010 were enrolled in an observational retrospective study. On every case open surgery was performed to remove the gastric tumor.

In all cases, formalin-fixed embedded tissues were used. Sections were dewaxed and were stained with Hematoxylin-Eosin.

In every case we analyzed the histological type and grade of the tumor. These parameters were correlated with the patients' age and gender.

We should mention that 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

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

Variable	6th edition of the AJCC [6]	7th edition of the AJCC [5]
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
pT3	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

Table II. Structure of the study group based on the tumor size

ST TNM	Tumor size <5cm	Tumor size 5–10cm	Tumor size >10cm
ST 0–I	61.53%	23.07%	15.40%
ST II	53.57%	32.15%	14.28%
ST III A	46.66%	46.66%	6.68%
B	27.27%	50%	22.73%
C	27.77%	41.68%	30.55%
ST IV	10%	40%	50%

was conducted with the chi-square test. The level of significance was set at $p<0.05$.

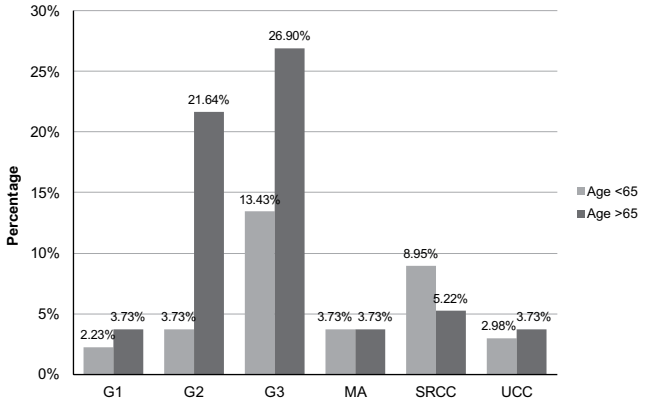

Fig. 1. Structure of the study group based on age and histological type

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

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 for females was 68 years (minimum 23, maximum 86), and for males it was 70 years (minimum 23, maximum 87).

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 cell carcinomas, and 6.71% undifferentiated carcinomas. There was no significant correlation between 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

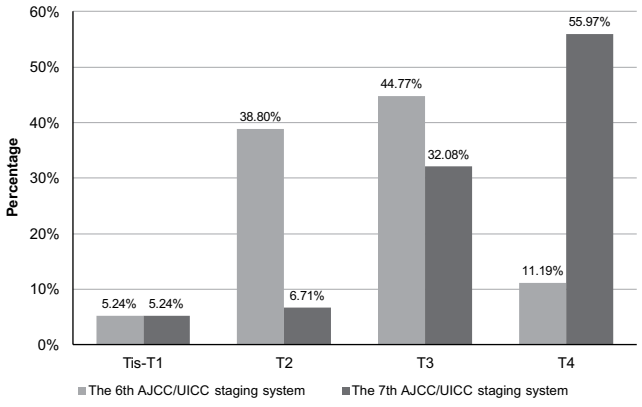

Fig. 2. Structure of the study group based on the depth of tumor invasion (pT) in both 6th and 7th AJCC/UICC staging systems

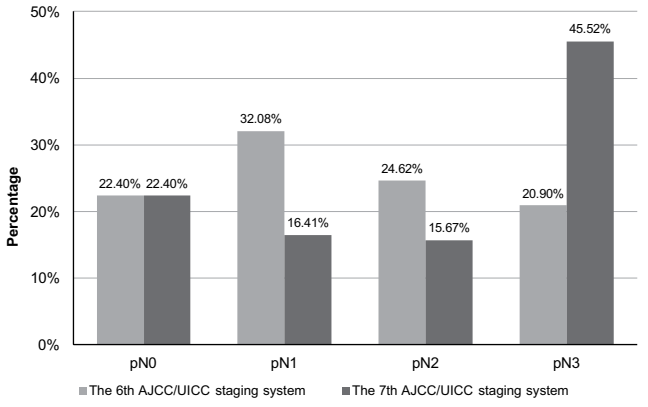

Fig. 3. Structure of the study group based on the number of lymph node metastases (pN) in both 6th and 7th AJCC/UICC staging system

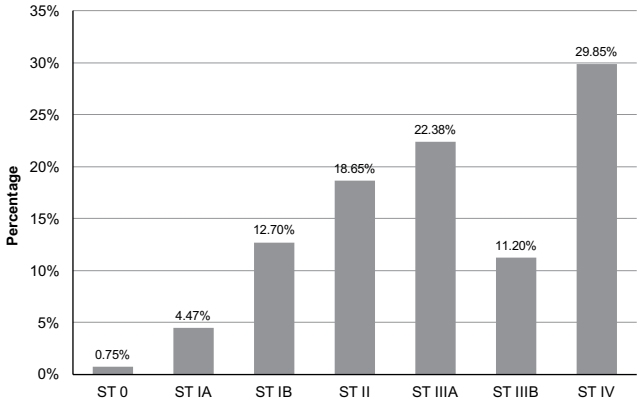

Fig. 4. The grouping staging of the cases according on the 6th AJCC/UICC staging system

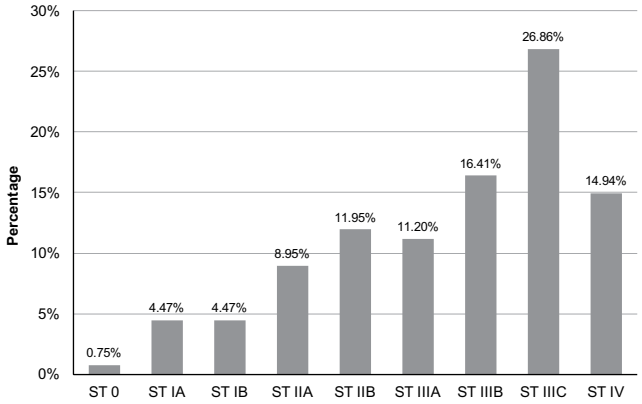

Fig. 5. The grouping staging of the cases according on the 7th AJCC/UICC staging systems

case of younger patients signet ring cell carcinoma (8.95%) was more frequent (Fig. 1).

All the patients included in the study, underwent through a surgical intervention in order to remove the gastric tumor, as follows: 51 (38.05%) cases underwent through a total gastrectomy, and 83 cases (61.95%) through a partial gastrectomy.

Concerning the lesion location, the most common tumor site was the gastric body (60.46%), followed by the antrum (35.07%) and then pangastric cancer (linitis plastica) (4.47%).

Regarding the tumor size, it can be observed (Table II) that the most voluminous tumors are found in the advanced staged cases, respective in stages IIIB, IIIC and IV, according to the 7th AJCC/UICC staging system.

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% ($p<0.0001$) (Fig. 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 al cases classified as pN2 in the old staging system, become pN3 in the new system (Fig. 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%) (Fig. 4, 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 classification, based on clasical pathological parameteres is essential in establishing a proper postoperative stadialization and the adequate therapeutic protocol [7].

Out of the total number of gastric cancer cases admitted to and investigated at the Emergency County 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 gender ratio was M/F=2.11, in line with bibliographical data [1].

We noted a predominance of adenocarcinomas (71.66%) over other carcinomas (28.34%) but it was not proved a statistically significant correlation between gender of the patients and 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 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 of the cases framed in stage IV according to the 6th classification downstage to stage III, according to the new classification. Several studies showed that these patients have a better surviving rate comparing to those who remaind in stage IV [7].

Subdivision of stage IV gastric cancer into IVa and IVb, according to the 7th classification, offers a better accuracy in establishing the prognosis for the patients framed in stage IV [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.

Several studies pointed out that the pN parameter, evaluated according to the 6th TNM classification should not be used as a prognostic factor in gastric cancer. There were even found similar surviving rates for the patients framed as pN2 and pN3 according to the 6th stadialization [7,9].

In 2010, Jingzu Deng and co. showed that the pN parameter, evaluated according to the 7th TNM classification is a useful prognostic factor in patients with gastric cancer and curative resection [10].

These results are supported to Ueno and colleagues' theory according to the prognostic value of a TMN classification is better with the major differences between the surviving rates of the patients framed in different stages and with the minor differences between the surviving rates of the patients framed in the same stage [7,11].

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.

Acknowledgements

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