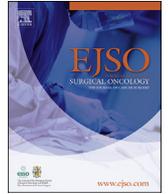




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Survival comparison in gastric cancer patients between 7th and 8th edition of the AJCC TNM staging system: The first western single center experience



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ABSTRACT

Background: The objective of this study was to compare the 7th and the 8th edition of American Joint Committee on Cancer staging system (AJCC TNM) in terms of better stratification in our gastric cancer resected patients.

Methods and materials: A retrospective analysis of a single western center series was made. Patients who underwent surgery from January 2004 to December 2016 were enrolled in the study. We compared survival rates across patients classified according to the 7th and the 8th AJCC TNM staging system.

Results: Among 295 patients we observed 9.8% stage migration according the 8th edition. Of these 2.1% and 7.9% of patients showed respectively a higher and a lower stage.

5 years Overall Survival (5Y-OS) according to the 8th edition for stage IIIB and IIIC were 32% versus 9% showing a better stratification compared to the 7th edition in which 5Y-OS were respectively 26% versus 22%.

Conclusion: Restaging system seems to improve survival rate discrimination in particular comparing stage IIIB and stage IIIC; whereas in stage IIIA this is not so clear.

More studies are necessary to confirm these data.

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Background

Gastric cancer is one of the worst neoplasms in terms of mortality and prognosis being the second leading cause of cancer related death worldwide [1].

Gastric cancer staging system according to American Joint Committee on Cancer staging system (AJCC TNM) has changed over the years reaching its recent 8th edition. Several changes have been made in this last edition, which has been implemented since January 2017 [2]; first of all a tumor, the epicenter of which is within 2 cm of the oesophagogastric junction and also extends into the oesophagus, is classified and staged using the oesophageal scheme. Cancers involving the oesophagogastric junction (OGJ) whose epicenter is within the proximal 2 cm of the cardia (Siewert types I/II) are to be staged as oesophageal. Cancers whose epicenter

is more than 2 cm distal from the OGJ will be staged using the Stomach Cancer TNM and Stage even if the OGJ is involved.

Secondly there are no changes in the definitions of the T, N and M categories.

Pathological classification N3 is subdivided into N3a (7–15 positive lymph nodes) and N3b (≥ 16 positive lymph nodes). Although this subgrouping was included in the 7th edition, it was not applied to pathological staging. However, in the 8th edition, N3 subgrouping has been applied to pathological staging. This resulted in important changes in pathological staging.

The objective of our study was to compare the 7th and the 8th edition of AJCC TNM to analyze the different survival rate of discrimination in resected gastric cancer patients in a Western center, considering that there is literature from Eastern experience.

Patients and methods

This is a single center retrospective study, of data that were prospectively collected and stored in a database. Patients who underwent surgery for gastric cancer in our department from

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January 2004 to December 2016 were enrolled in the study. All the patients sign a written consent form for anonymous acquisition of data.

Exclusion criteria were: [1] tumors other than adenocarcinoma; [2] tumors involving the cardia (Siewert I and II); [3] palliative procedures; [4] explorative procedures.

Patients were staged according to both the 7th and the 8th American Joint Committee on Cancer staging system TNM editions.

A total of 295 patients were thus enrolled in the study. Of these 192 (65.1%) male and 103 (34.9%) female with a mean age of 71.67 ± 11.14 .

Patients' characteristics including information on: demographic parameters, pathological tumor type and survival rates are shown in [Table 1](#).

The same experienced surgeons performed all the surgical procedures consistently in routinely performed D2 gastric resection.

The postoperative follow-up schedule in our institution was as follows: patients were required to undergo laboratory examinations including complete blood count and blood chemistry every 3 months; abdominal computed tomography (CT) scans, tumor marker evaluation and endoscopy were carried out every 6 months, for the first 2 years. After 2 years (i.e., from the 3rd to the 5th year), we carried out laboratory examinations, abdominal CT scans, esophagogastroduodenoscopy, and tumor markers evaluations every 6 months. Annual follow-up assessments were carried out for another 5 years or until the death of the patient.

Patients' records/information were anonymized and deidentified prior to analysis, so that an approval by the Ethic Committee was not necessary.

Table 1
Univariate analysis of clinicopathologic factors for 5-year survival rate; * the missing patients were treated either for linitis or for stump tumor.

Factor	Number	5Y-OS	P value
Age			
<65	82	47%	
>65	213	30%	0.04
Gender			
Male	192	34%	
Female	103	48%	0.03
Tumor location*			
Upper	48	28.7%	
Middle	91	55%	
Lower	140	32%	0.003
Lauren Type			
Intestinal	173	40%	
Diffuse	92	32%	
Mixed	30	47%	n.s
N stage (7th)			
0	109	67.4%	
1	37	32.2%	
2	49	38.3%	
3	100	9.2%	<0.001
N stage (8th)			
0	109	67.4%	
1	37	32.2%	
2	49	38.3%	
3a	61	14.8%	
3b	39	4.8%	<0.001
TNM stage (7th)			
IIIA	30	29.3%	
IIIB	32	21.1%	
IIIC	28	25.9%	n.s.
TNM STAGE (8 TH)			
IIIA	37	25.3%	
IIIB	35	33%	
IIIC	18	9.9%	

Statistical analyses

Statistical analyses were conducted using Graph Pad PRISM 7.0 and Med Calc softwares. Differences between groups were tested with a Chi-square test or T unpaired student. Survival rates were calculated using the Kaplan–Meier method, and prognostic factors and survival curves were compared using the log-rank test. Overall Survival (OS) was defined as the time from surgery either to death or to the last follow-up.

A *P*-value <0.05 was deemed to be statistically significant.

Results

According to the AJCC 7th edition, our patients were distributed as follows:

Stage Ia (n = 55; 18.6%), stage Ib (n = 19; 6.4%), stage IIa (n = 20; 6.8%); stage IIb (n = 40; 13.6%), stage IIIa (n = 30; 10.2%), stage IIIb (n = 32; 10.8%), stage IIIc (n = 28; 9.5%), stage IV (n = 71; 24.1%).

According to the AJCC 8th edition stage distribution was the following:

Stage Ia (n = 55; 18.6%), stage Ib (n = 19 6.4%), stage IIa (n = 20; 6.8%); stage IIb (n = 40; 13.6%), stage IIIa (n = 37; 12.5%), stage IIIb (n = 35; 11.9%), stage IIIc (n = 18; 6.1%), stage IV (n = 71; 24.1%).

We observed 9.8% stage migration. Of these 2.1% and 7.9% of patients showed respectively a higher and a lower stage ([Table 2](#)).

Median Overall Survival of the entire series was 30 months as shown in [Fig. 1](#) with a respectively five (5Y-OS) and ten (10Y-OS) years overall survival of 37.5% and 24.1% respectively. Survival according to the different TNM editions are shown in [Fig. 2](#).

The 5y-OS observed with the 7th edition of the AJCC TNM staging system were as follows: Stage I: 69.8%; Stage II: 51.6%; Stage IIIA: 27.7%, Stage IIIB 22.4%, Stage IIIC: 26%, Stage IV: 4.5% (*p* < 0.001).

According to the 8th edition, the 5Y-OS were as follow: Stage I: 69.8%; Stage II: 51.6%; Stage IIIA: 25.9%, Stage IIIB: 32.7%, Stage IIIC: 9.8%, Stage IV: 4.5% (*p* < 0.001).

Sub-classification of stages

According to the 7th edition of the AJCC TNM staging system, similar 5-year overall survival rates were noted in stage IIIB (22,4%) and IIIC (26%) patient groups. We used the Kaplan Meier method to analyze the differences in survival rates between these groups. There was no significant difference between these 2 groups (*P* > 0.05).

According to the 8th edition of the AJCC TNM staging system, the 5-year overall survival rates for the patients with stages IIIB and IIIC were 32.7% and 9,8%, respectively. This result suggested improved survival discrimination (*P* < 0.001). The Kaplan–Meier plot showed a good discriminatory ability among stage IIIB through stage IIIC, according to the 8th edition of the AJCC TNM staging system.

Discussion

The last 8th edition gastric cancer staging brought fundamental innovations for both gastric cancer staging and EGJ cancer definition [3].

The TNM classification system is the most important tool for tumor treatment planning and for assessing oncological patient's prognosis [4,5].

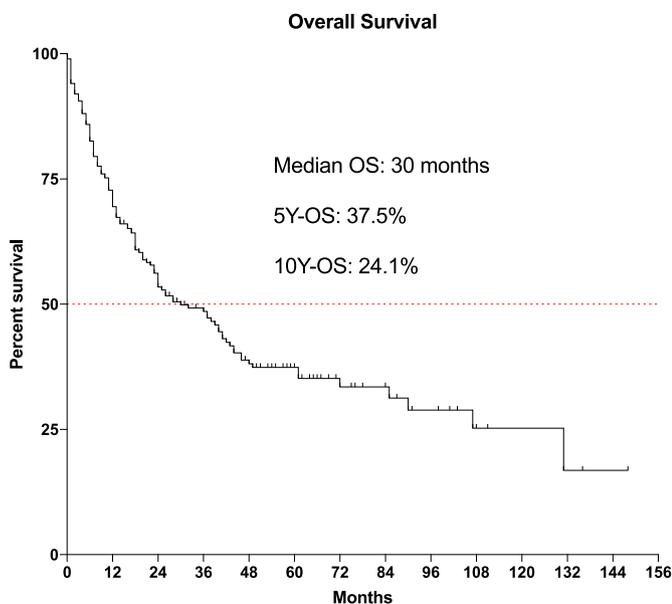
It's well known that the most intensive prognostic indicator of gastric cancer is lymphonodal status involvement [6] and the new TNM staging system stresses its role.

In contrast, to the 7th edition [7], both (PN3a and PN3b)

Table 2

Patients stages' distribution and migration according to TNM 7th and 8th.

Stage	TNM 7 th	TNM 8 th	P
I:			
• A	55	55	N.S
• B	19	19	
II			
• A	20	20	N.S
• B	40	40	
III			
• A	30	37	P < 0.05
• B	32	35	
• C	28	18	
IV	71	71	N.S

**Fig. 1.** Overall Survival of the entire series.

subgroups are an important discriminant of the pathologic staging in the 8th edition.

This revision resulted in a final redistribution of pathological stages (Fig. 2).

Surgical resection remains the main and unique choice of treatment for gastric cancer.

Currently, despite advances made in oncological treatment strategies over past decades, the prognosis for advanced gastric cancer stages as stage III remains poor [8].

In our region, where gastric cancer has a very high incidence, the majority of patients are diagnosed at middle or advanced stages, leading to a limited overall survival rates when compared with

eastern countries where there are successful program for early detection.

Therefore, we decided to focus on stage III, which accounts for a high proportion of patients considering our entire gastric cancer practice.

In our study similar 5-year overall survival rates were observed between stages IIIB and IIIC patients, on classification according to the 7th edition of the AJCC staging system.

Restaging these two groups, according to the 8th edition criteria, we recognized a clear survival difference.

This signifies that the new 8th edition of the AJCC staging system provides more useful stratification of pathological TNM staging than the 7th edition.

According to our survival analysis, the 8th TNM edition is more accurate in predicting prognosis for stage III gastric cancer than the 7th edition.

Looking the restaged survival curves for stage IIIC and IV appear similar; this is not unexpected because we only included resected patients. If we had enrolled stage IV patients who did not undergo surgery, probably there would have been a more evident separation between the stage IIIC and IV.

According to the 7th staging edition stage IIIC patients showed an overestimated survival compared to stage IV.

Similar results have been reported by KIM S.G. et al. [3] showing stage migration in 6.4% (n = 355) of the patients. Wherein, 3.5% (n = 192) and 2.9% (n = 158) of patients showed a higher and lower stage respectively.

According to the 8th edition of the AJCC TNM staging criteria, the 5-year overall survival rates of his patients with stage IIIB and IIIC showed a significant difference (40.8% vs. 20.2%, P < 0.001) whereas no significant differences in the 5-year overall survival rates were observed according to the 7th edition criteria (37.6% vs. 33.2%, P = 0.381).

In contrast to our results, Lu Ju [9] et al. showed that the eighth TNM edition might not provide significantly better accuracy in predicting the prognosis of stage III GC. The performance of the eighth edition did not reveal significant improvement compared to

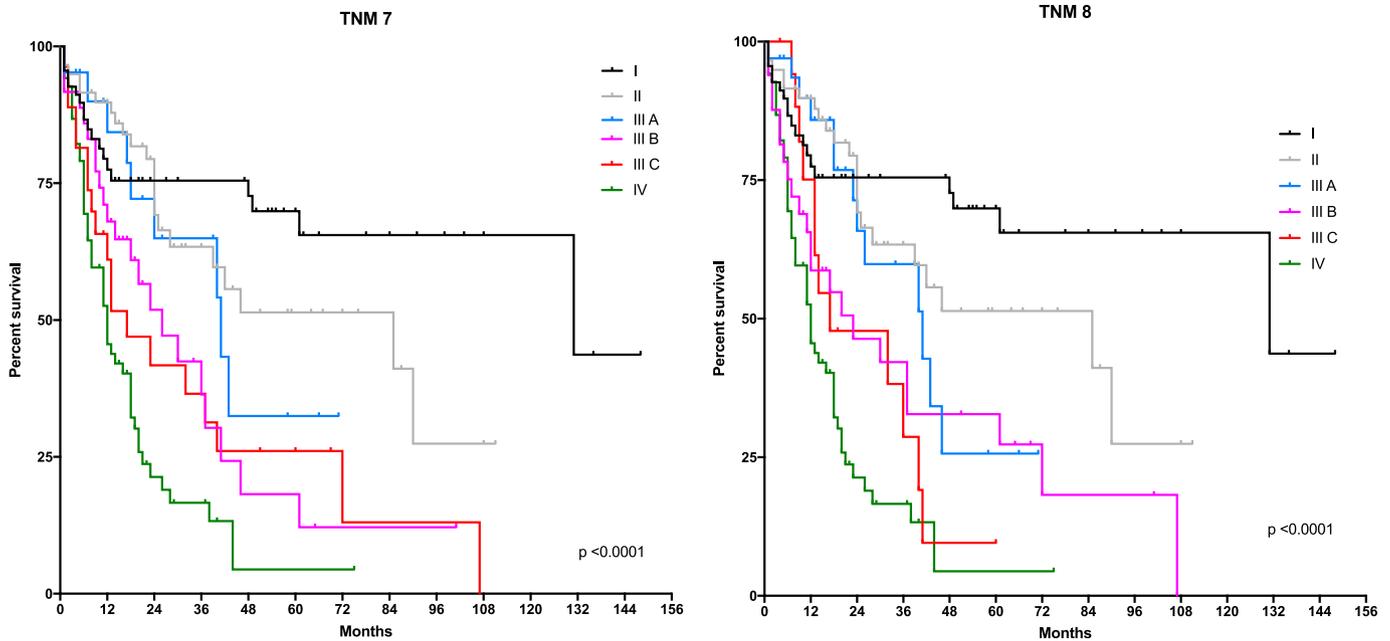


Fig. 2. Overall Survival according to 7th TNM edition and 8th TNM edition respectively.

the seventh edition analyzing the Concordance Index [10] (c-index 0.625 vs. c-index 0.616, $p = 0.085$).

We can conclude that this is the first western study to analyze the 8th TNM stage redistribution and according to our data appears to be a valid pathological classification.

In our opinion this latest TNM edition provides surgeons with understanding that having greater than 15 positive lymph nodes confers even worse prognosis than 7–15 positive nodes and provides an impetus to examine more than 15 nodes during surgical lymphadenectomy to obtain a more definite gastric cancer patients prognosis.

TNM staging is widely accepted for decisions relating to adequate oncological cancer treatment. The accurate staging of cancer patients reveals the progression of a disease, the risk of recurrence and survival outcomes determinations, which have a significant influence on treatment planning made by a multidisciplinary team.

Moreover we strongly believe that other variables such as histological and molecular phenotypes could be considered to stage patients with gastric cancer. Thus, progress will be achieved by combining the TNM classification system with molecular tools.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejso.2018.12.010>.

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