

Ongoing problems concerning 7th TNM Staging System and Proposals for 8th TNM Staging System of Gastric Cancer

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Abstract

Because of different prognosis of gastric cancer patients with the same T and N stages, the impossibility of N3 staging in patients with fewer than 15 removed lymph nodes, and the presence of stage migration phenomenon, the 6th edition TNM Staging System for gastric cancer was updated to the 7th edition TNM staging system in 2009. Despite some opposing views, the superiority of the 7th edition TNM staging system compared to the 6th has been demonstrated in many studies. However, there are doubts about the 7th edition that it will reduce the stage migration phenomenon. The most important problem about the 7th TNM staging system is regarding subgroups N3a and N3b. The separation of N3 stage as N3a and N3b does not contribute to the TNM staging system. In conclusion, separate usage of N3a and N3b subgroups in the TNM staging system should be considered in the creation phase of the 8th edition.

The tumor node metastasis (TNM) staging system is considered as the gold standard for staging gastric cancer as well as staging of other types of cancer. Because of different prognosis of gastric cancer patients with the same T and N stages, the impossibility of N3 staging in patients with fewer than 15 removed lymph nodes, and the presence of stage migration phenomenon, the 6th Edition American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC) TNM Staging System for gastric cancer was updated to the 7th Edition UICC/AJCC TNM Staging System in 2009. In the 7th edition TNM staging system there are several major changes in T, N, and TNM staging systems (Tables I and II). In the 7th edition TNM staging system, greater than or equal to seven metastatic lymph nodes were classified as N3 stage. Furthermore, the component of stage IV including M0 was removed and I1C was added to the TNM staging system with the components of T4aN3M0, T4bN2M0, and T4bN3M0. In addition, positive peritoneal cytology (CY+) was assessed as M 1 (stage IV) in the 7th edition TNM staging system. Moreover, gastroesophageal junc-

tion (GEJ) tumours such as Siewert type I and II were classified as oesophageal cancer, and Siewert III type tumors were classified as gastric cancers. All of these changes were thought to be effective in the evaluation of clinicopathological data and in minimising the stage migration phenomenon [1].

Despite some opposing views, the superiority of the 7th edition compared to the 6th has been demonstrated in many studies [2–4]. However, there are doubts about the 7th edition that it will reduce the stage migration phenomenon [5]. Therefore, the search for alternatives to the TNM staging system and proposals for modification of the system continues. One of them is a hypothetical classification based on the ratio between metastatic and examined lymph nodes (N-ratio). Because both positive lymph nodes and examined nodes are its main components, it has been suggested that the N-ratio staging system is effective in precluding stage migration and determining the prognosis, and it can be used instead of N-staging [6, 7].

Another important point about the 7th edition TNM staging system is regarding subgroups N3a and N3b.

Table I. The comparison of T and N stages in 6th edition and 7th edition TNM staging systems

6 th edition UICC/AJC TNM Staging System (2002)	7 th edition UICC/AJCC TNM Staging System (2009)
T1	T1a – lamina propria, muscularis mucosa
T1	T1b – submucosa
T2a	T2 – muscularis propria
T2b	T3 – subserosa
T3	T4a – serosa invasion
T4	T4b – adjacent organ invasion
N1	N1 (1–2 lymph node metastasis)
N1	N2 (3–6 lymph node metastasis)
N2	N3a (7–15 lymph node metastasis)
N3	N3b (16 and more lymph node metastasis)

Table II. The comparison of 6th edition and 7th edition TNM staging system

6 th edition UICC/AJC TNM Staging System (2002)		7 th edition UICC/AJCC TNM Staging System (2009)	
Stage	TNM	Stage	TNM
0	TisN0M0	0	TisN0M0
IA	T1N0M0	IA	T1N0M0
IB	T1N1M0, T2N0M0	IB	T2N0M0, T1N1M0
II	T1N2M0, T2N1M0, T3N0M0	IIA	T3N0M0, T2N1M0, T1N2M0
IIIA	T2N2M0, T3N1M0, T4N0M0	IIB	T4aN0M0, T3N1M0, T2N2M0, T1N3M0
IIIB	T3N2M0	IIIA	T4aN1M0, T3N2M0, T2N3M0
IV (with M0)	T1-3N3M0, T4N1-3M0	IIIB	T4bN0M0, T4bN1M0, T4aN2M0, T3N3M0
IV (with M1)	Any T, any N, M1	IIIC	T4bN2M0, T4bN3M0, T4aN3M0
		IV	Any T, any N, M1

Although T4a and T4b stages correspond to different stages in the 7th edition TNM staging system, separated concepts of N3a and N3b stages correspond to relevant stages as the only N stage as N3. In this case, the separation of N3 stage as N3a and N3b does not contribute to the TNM staging system. Yeh *et al.* [8] evaluated 884 N3 positive patients for N3a and N3b subtypes, clinico-pathological findings, and surgical outcomes. The findings of this study showed that the survival of: a) T1-3N3aM0 patients is similar to stage IIIB patients, b) T1-3N3bM0 patients is similar to stage III C patients, c) T4aN3bM0 patients is lower than stage IIIC and higher than stage IV patients, and d) T4bN3bM0 patients is similar to stage IV patients. Based on these findings, the authors suggested modification of the 7th edition TNM staging system to classify T1-3N3aM0 as stage

IIIB, T1-3N3bM0 as stage IIIC, T4aN3bM0 as stage IIID, and T4bN3bM0 as stage IV. In a study of Ahn *et al.* [4] including 9998 gastric cancer patients, the researchers announced the superiority of the 7th TNM staging system over the 6th TNM staging system in terms of prognosis, especially for T2/T3 and N1/N2 tumours, but they indicated that further studies are needed for N3a and N3b subclassification.

Most recently, Sano *et al.* [9] published the results of the International Gastric Cancer Association (IGCA) Project study. Fifteen countries and 53 institutions participated in the study. The clinical and pathological data of 25,441 patients who underwent curative gastrectomy between 2000 and 2004 were evaluated retrospectively. Of the participating patients, 84.8% were from Japan and South Korea. N3a and N3b sub-

groups had different results in terms of 5-year survival rate. The authors suggested a new staging system (IGCA Proposal Staging System) for gastric cancer and Siewert type II-III EGJ tumours evaluating N3a and N3b subtypes separately. There are significant differences in the proposed staging system, especially in stage III subgroups. According to these results, the authors have noted the availability of the IGCA proposal staging system's advantages compared to AJCC7 for both gastric and Siewert type II, and III EGJ tumours. They also suggested its usage for forthcoming TNM staging system of gastric cancer.

In conclusion, separate usage of N3a and N3b subgroups in the TNM staging system should be considered in the creation phase of the 8th edition TNM staging system. In that case, however, evaluation failure of N3b sub-classification should occur in patients with fewer than 15 lymph nodes examined. We think this problem can be solved by acceptance of the suggestion "25 lymph nodes should be removed for extended lymphadenectomy" of the German Gastric Cancer Group [10] or the usage of a hypothetical N-ratio staging system.

Conflict of interest

The authors declare no conflict of interest.

References

1. Sobin LH, Gospodarowicz MK (eds.). International Union Against Cancer (UICC) TNM Classification of Malignant Tumours (ed. 7). Wiley-Blackwell, Oxford 2009.
2. Marano L, Boccardi V, Braccio B, et al. Comparison of the 6th and 7th editions of the AJCC/UICC TNM staging system for gastric cancer focusing on the "N" parameter-related survival: the mono institutional NodUs Italian study. *World J Surg Oncol* 2015; 13: 215.
3. Hayashi T, Yoshikawa T, Bonam K, et al. The superiority of the seventh edition of the TNM classification depends on the overall survival of the patient cohort: comparative analysis of the sixth and seventh TNM editions in patients with gastric cancer from Japan and the United Kingdom. *Cancer* 2013; 119: 1330-7.
4. Ahn HS, Lee HJ, Hahn S, et al. 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: 5592-8.
5. Kim CY, Yang DH. Adjustment of N stages of gastric cancer by the ratio between the metastatic and examined lymph nodes. *Ann Surg Oncol* 2009; 16: 1868-74.
6. Ilhan E, Zengel B, Simsek H, et al. Can the ratio of metastatic to examined lymph nodes (N ratio) be used as an independent prognostic factor in patients with gastric cancer? Is hypothetical TRM (tumor-ratio-metastasis) staging system an alternative to TNM (tumor-node-metastasis) staging system? *Prz Gastroenterol* 2013; 8: 247-56.
7. Son T, Hyung WJ, Lee JH, et al. Clinical implication of an insufficient number of examined lymph nodes after curative resection for gastric cancer. *Cancer* 2012; 118: 4687-93.
8. Yeh CN, Wang SY, Hsu JT, et al. N3 subclassification incorporated into the final pathologic staging of gastric cancer: a modified system based on current AJCC staging. *Medicine (Baltimore)* 2015; 94: e575.
9. Sano T, Coit DG, Kim HH, et al. Proposal of a new stage grouping of gastric cancer for TNM classification: International Gastric Cancer Association staging project. *Gastric Cancer* 2016 Feb 20 [Epub ahead of print].
10. Siewert JR, Böttcher K, Stein H, et al. Relevant prognostic factors in gastric cancer: ten-year results of the German Gastric Cancer Study. *Ann Surg* 1998; 228: 449-61.

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