

Original Article



Comparison of the Differences in Survival Rates between the 7th and 8th Editions of the AJCC TNM Staging System for Gastric Adenocarcinoma: a Single-Institution Study of 5,507 Patients in Korea

Sung Geun Kim , Ho Seok Seo, Han Hong Lee, Kyo Yong Song, Cho Hyun Park

Division of Gastrointestinal Surgery, Department of Surgery, The Catholic University of Korea School of Medicine, Seoul, Korea



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Correspondence to

Cho Hyun Park

Division of Gastrointestinal Surgery,
Department of General Surgery, The Catholic
University of Korea School of Medicine, Seoul
St. Mary's Hospital, 222 Banpo-daero, Seocho-
gu, Seoul 06591, Korea.

Tel: +82-2-2258-2876

Fax: +82-2-595-2822

E-mail: chpark@catholic.ac.kr

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ORCID iDs

Sung Geun Kim

<https://orcid.org/0000-0002-3087-9728>

Author Contributions

Conceptualization: P.C.H.; Data curation:
K.S.G.; Formal analysis: K.S.G.; Investigation:
S.H.S.; Methodology: L.H.H.; Project
administration: S.K.Y.; Resources: P.J.H.;

ABSTRACT

Purpose: The aims of this study were to compare the 7th and 8th editions of the American Joint Committee on Cancer (AJCC) staging manuals on tumor, node, and metastasis (TNM) staging systems and to evaluate whether the 8th edition represents a better refinement of the 7th staging system, when applied for the classification of gastric cancers.

Materials and Methods: A total of 5,507 gastric cancer patients, who underwent treatment from January 1989 to December 2013 at a single institute, were included. We compared patient survival rates across the disease groups classified according to the 7th and 8th editions of the AJCC TNM staging systems.

Results: Stage migration was observed in 6.4% (n=355) of the patients. Of these, 3.5% (n=192) and 2.9% (n=158) of patients showed a higher stage and lower stage, respectively. According to the 8th edition of the AJCC TNM staging criteria, the 5-year overall survival rates of the 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%, $P=0.381$).

Conclusions: Restaging stage III cancers according to the 8th edition of the AJCC TNM classification criteria improved survival rate discrimination, particularly, in institutes where the stage III patients were not distinctly categorized.

Keywords: Stomach neoplasms; 8th edition; American Joint Committee on Cancer; Survival; Prognosis

INTRODUCTION

Gastric cancer is the 4th most common occurring malignant tumor with over 1 million people diagnosed with this cancer each year; it is the 2nd leading cause of cancer-related death worldwide [1]. The incidence of gastric cancer is particularly high in eastern Asia [2].

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

In Korea, gastric cancer is the most frequently diagnosed cancer in men and the 4th most common cancer in women. In 2013, nearly 30,000 new cases of gastric cancer were reported, constituting approximately 13.4% of all diagnosed cancers [3,4].

The tumor, node, and metastasis (TNM) staging system has been widely used as a method for staging gastric cancer patients and is considered the most important reference in multimodal treatment. TNM classification of the American Joint Committee on Cancer (AJCC) has been used for gastric cancer staging worldwide. Since 2010, the 7th edition of the AJCC TNM staging system has been used for staging gastric cancer [5]. In October 2016, the new 8th edition of the AJCC TNM staging manual was published and this new TNM system has been implemented since January 2017 [6].

Compared to the 7th edition, in the 8th edition, there are several changes in gastric cancer staging. The anatomic boundary between the esophagus and the stomach has been redefined in the 8th AJCC edition. Tumors involving the esophagogastric junction (EGJ) with the tumor epicenter no more than 2 cm into the proximal stomach are classified as esophageal cancers. EGJ tumors with their epicenter located greater than 2 cm into the proximal stomach are classified as stomach cancer.

In 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 changes in pathological staging. For example, T2N3M0, which was earlier stage IIIA as per the 7th edition, was now classified as both T2N3aM0, stage IIIA and T2N3bM0, stage IIIB.

The aims of this study were to compare staging between the 7th and 8th editions of the AJCC TNM staging manuals and to evaluate whether the 8th AJCC classification for gastric cancer represents a better refinement of the 7th edition of the AJCC TNM staging system.

MATERIALS AND METHODS

Patients

Between January 1989 and January 2013, the medical records of 5,615 newly diagnosed gastric adenocarcinoma patients, who received treatment at St. Mary's Hospital, Seoul were analyzed retrospectively. Siewert's types II and III cancer cases were not included in this study. A total of 109 patients (1.9%) were excluded from the study because of missing baseline characteristics. Finally, 5,507 patients were enrolled in this study. Curative resection was performed in 4,948 patients (89.8%), palliative gastrectomy in 52 (0.9%), exploratory laparotomy in 111 (2%), and bypass surgery in 59 (2.8%). For early gastric cancer, D1+ dissection and more was performed. For advanced gastric cancer patients, D2 lymph node dissection was performed, except in those where curative resection was not possible. No patient received adjuvant radiotherapy or neoadjuvant chemotherapy.

Postoperative follow-up schedule

The postoperative follow-up schedule in our institution was as follows: patients had 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 marker evaluations every 6 months. Annual follow-up assessments were carried out for another 5 years or until the death of the patient.

Statistical analysis

All patients were restaged using the 8th edition of the AJCC pathological staging system for survival analysis. Survival analysis was performed using the Kaplan-Meier method, and univariate analysis was performed using the log-rank test. For patients who remained alive, data were censored at the date of the last visit to the outpatient department. All statistical analysis was performed using SPSS 18.0 statistical software (SPSS Inc., Chicago, IL, USA). $P < 0.05$ was considered a statistically significant difference.

The Institutional Review Board of the Catholic University of Korea approved this study (KC17RESI0281).

RESULTS

Patients and characteristics

The median age of the 5,507 patients was 59 years (range=18–92 years) of which 3,682 patients (66.9%) were men and 1,825 patients (33.1%) were women. Approximately 2,682 patients (48.7%) had early gastric cancer. The median follow-up time was 50 months (range=3.0–299.0 months). The overall survival for the entire group of patients was 55.6%, with a median survival of 74.6 months. The characteristics of the patients are summarized in **Table 1**.

Stage distribution and migration

Using staging with the AJCC 7th edition, our patients were distributed as follows: stage IA (n=2,383, 43.3%), stage IB (n=733, 13.3%), stage IIA (n=503, 9.1%), stage IIB (n=395, 7.2%), stage IIIA (n=424, 7.7%), stage IIIB (n=375, 6.8%), stage IIIC (n=197, 3.6%), and stage IV (n=497, 9.0%). On using the AJCC 8th edition, the distribution of patients changed from stage IIB to IIIC, resulting in a patient distribution as follows: stage IIB (n=394, 7.2%), stage IIIA (n=418, 7.6%), stage IIIB (n=355, 6.4%), and stage IIIC (n=224, 4.1%) (**Table 1**).

On analysis, 5,157 of 5,507 patients (93.6%) had the same stage in both AJCC 7th and 8th pathological classification systems. Stage migration was observed in 6.4% of patients. A total of 192 patients (3.5%) showed a higher stage (the stage according to the 8th edition classification was higher than that according to the 7th staging system) and 158 patients (2.9%) showed a lower stage.

Five-year overall survival

The 5-year overall survival rates obtained with the 7th edition of the AJCC TNM staging system were as follows: stage IA (94.7%), stage IB (89.9%), stage IIA (80.7%), stage IIB (72.6%), stage IIIA (52.7%), stage IIIB (37.6%), stage IIIC (33.2%), and stage IV (8.8%) ($P < 0.001$, **Fig. 1A**). According to the 8th edition of the AJCC TNM staging system, the 5-year overall survival rates were as follows: stage IA (94.7%), stage IB (89.9%), stage IIA (80.7%), stage IIB (72.5%), stage IIIA (58.4%), stage IIIB (40.8%), stage IIIC (20.2%), and stage IV (8.8%) ($P < 0.001$, **Fig. 1B**).

Comparison of the 7th and 8th Edition of AJCC Staging System for Gastric Cancer

Table 1. Demographics and pathological variables in 5,507 gastric cancer patients

Characteristics	Frequency
Sex	
Male	3,682 (66.9)
Female	1,825 (33.1)
Age (median age: 59 yr)	
≤59	2,869 (52.0)
≥60	2,648 (48.0)
M stage	
M0	5,010 (91.0)
M1	497 (9.0)
The 7th AJCC TNM classification	
IA	2,383 (43.3)
IB	733 (13.3)
IIA	503 (9.1)
IIB	395 (7.2)
IIIA	424 (7.7)
IIIB	375 (6.8)
IIIC	197 (3.6)
IV	497 (9.0)
The 8th AJCC TNM classification	
IA	2,383 (43.3)
IB	733 (13.3)
IIA	503 (9.1)
IIB	394 (7.2)
IIIA	418 (7.6)
IIIB	355 (6.4)
IIIC	224 (4.1)
IV	497 (9.0)

Values are presented as number (%).

AJCC = American Joint Committee on Cancer; TNM = tumor, node, and metastasis.

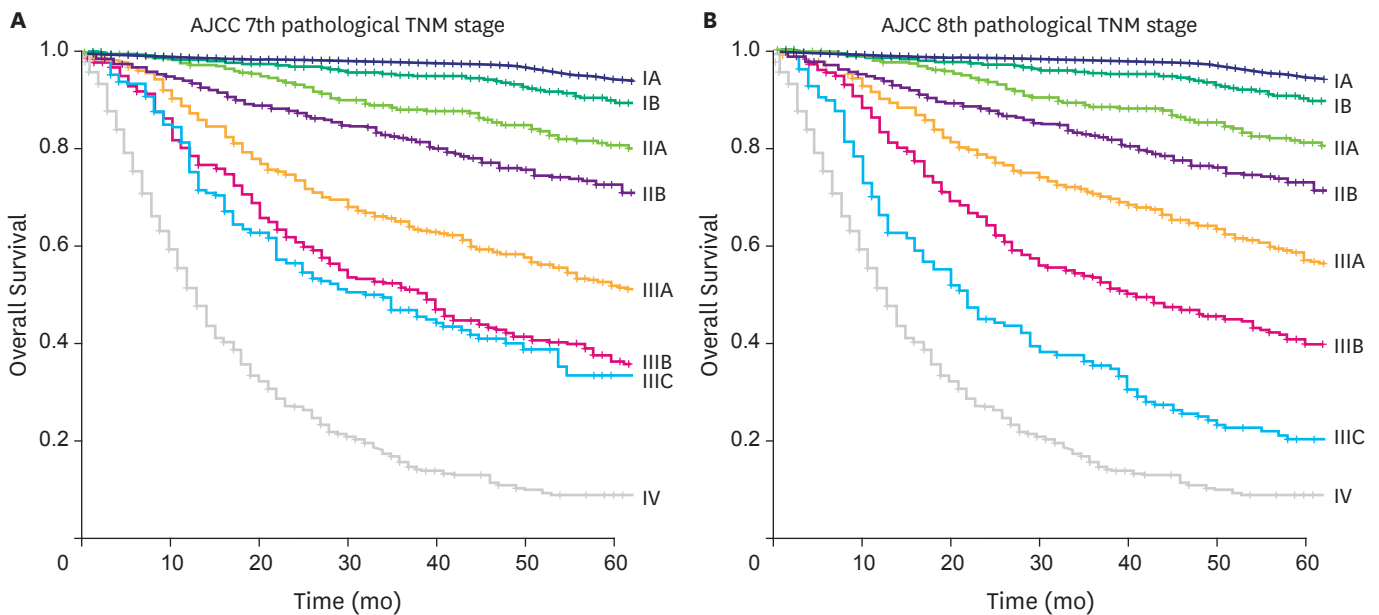


Fig. 1. (A) 5-year overall survival of patients with gastric cancer (AJCC 7th edition). (B) 5-year overall survival of patients with gastric cancer (AJCC 8th edition). AJCC = American Joint Committee on Cancer; TNM = tumor, lymph node, metastasis.

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 (37.6%) and IIIC (33.2%) 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 ($P=0.381$). 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 40.8% and 20.2%, 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. The 5-year overall survival rates were significantly different between the 184 stage IIIB (T3N3aM0) patients and 122 stage IIIC (T3N3bM0) patients using the 8th edition of the AJCC TNM staging system ($P<0.001$), who are from the 306 patients in the same 7th stage IIIB, 42.9% and 19.7%, respectively.

DISCUSSION

According to the 7th edition of the AJCC TNM grading system, tumors arising at the EGJ, or arising in the stomach 5 cm or less from the EGJ and crossing the EGJ, are staged using the TNM system for esophageal carcinoma [7]. In the 8th edition, the anatomic boundary between the esophagus and the stomach was redefined. Tumors involving the EGJ with the tumor epicenter no more than 2 cm into the proximal stomach are classified as esophageal cancers. EGJ cancers with their epicenter located greater than 2 cm into the proximal stomach are classified as stomach cancer. In this study, Siewert's types II and III cancer cases were already excluded because these cases were excluded in the 7th edition of the AJCC TNM staging system.

The TNM classification system is the most important tool for treatment planning in oncology and for assessing the patient's prognosis. It also has utility in determining the extent of disease, providing guidance for treatment planning, and predicting outcomes [8-10]. Besides the depth of primary tumor invasion, the most intensive prognostic indicator of gastric cancer is the status of lymph node involvement [11,12]. Although the pN3 group was subdivided into pN3a and pN3b in the 7th edition of the AJCC TNM staging system, neither of the subgroup was an individual determinant of the pathologic TNM staging. However, both groups are individual determinants of the pathologic TNM staging in the 8th edition [6].

This revision resulted in the redistribution of subgroups of stages (**Fig. 2**). T1N3M0 was stage IIB in the 7th edition of the AJCC TNM staging system. However, N3 was subdivided into N3a and N3b. T1N3aM0 is still in stage IIB but T1N3bM0 shifted to stage IIIB. T2N3M0 is subdivided into T2N3aM0 (stage IIB) and T2N3bM0 (stage IIIA). T3N3M0 also is subdivided into T3N3aM0 (stage IIIB) and T3N3bM0 (stage IIIC). Some groups were downstaged. T4aN2M0 and T4bN0M0, which were stage IIIB in the 7th edition of the AJCC TNM staging system, have now been classified as stage IIIA. T4bN2M0, which was stage IIIC in the 7th edition, is now stage IIIB in the 8th edition of the AJCC staging system. T4aN3M0 is now subdivided into T4bN3aM0 (stage IIIC) and T4bN3bM0 (stage IIIB).

Qiu et al. [13] compared the 6th and 7th editions of the AJCC staging system for gastric cancer. Stage migration was observed in 37.2% of patients, with 25.9% of patients showing a higher stage and 11.3% showing a lower stage. In another study, the stage migration rate increased to 60% [14]. In Korea, Jung et al. [15] reported that upstaging was observed in 26.4% and downstaging in 6.1% patients according to the 7th edition of the AJCC pathological TNM staging system compared to the 6th edition. In our study, stage migration

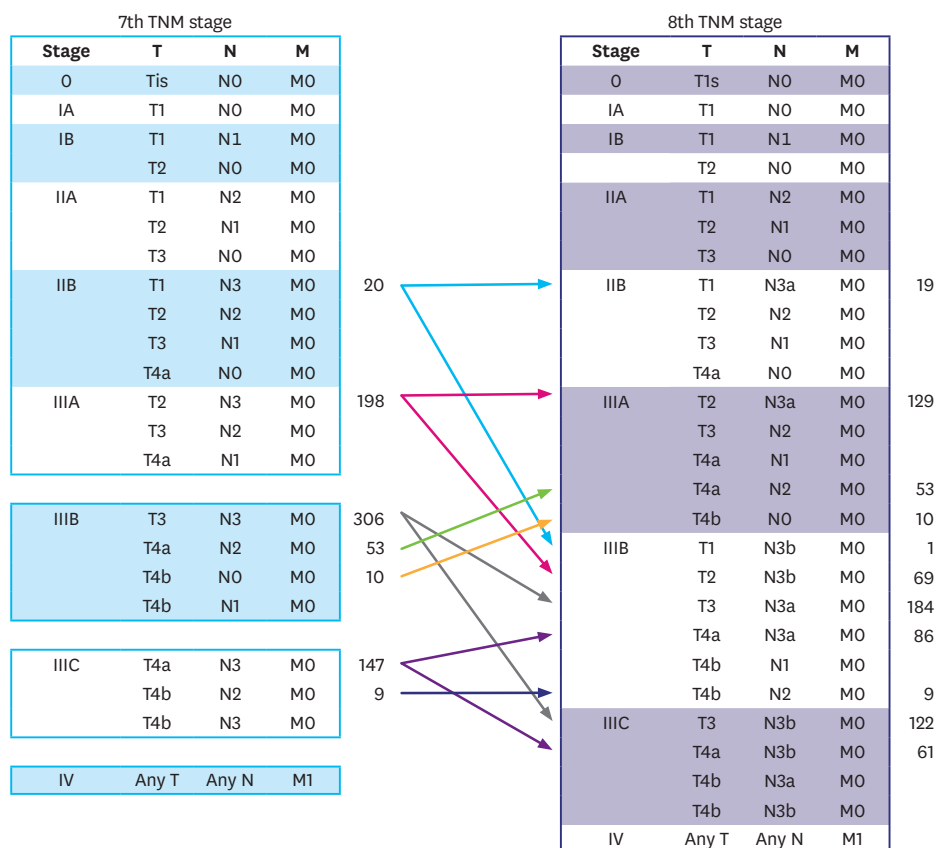


Fig. 2. The number of patients migrated in the 8th edition of the AJCC staging system for gastric cancer in each stage from 7th edition. AJCC = American Joint Committee on Cancer; TNM = tumor, node, and metastasis.

was observed in 6.4% of patients. Of these, 3.5% of patients showed a higher stage and 2.9% of patients showed a lower stage. This result shows that the impact of the revised pathological staging system, from the 7th to the 8th edition, is relatively smaller as compared to the change from the 6th to the 7th edition.

There have been some reports that in gastric cancers, the 7th edition staging system does not adequately categorize the tumor's biologic potential and the patient's prognosis [14,15]. Kikuchi et al. [16] reported no significant differences between consecutive stages (IIB and IIIA, IIIC and IV) and that the survival curves of stages IIB and IIIC almost overlapped with those of stages IIIA and IV, respectively, in the 7th edition of the AJCC TNM classification system. Wang et al. [8] reported similar survival curves between stages IB and IIA (P=0.261).

Since the publication of the 7th edition of the AJCC TNM staging system, there have been unceasing concerns about stage groupings of gastric cancer. Jung et al. [15] suggested some modification to overcome some of the drawbacks. They proposed a hybrid staging system consisting of a combination of the 7th edition pathological T and the 6th edition pathological N classifications. In addition, Warneke et al. [14] proposed the Kiel proposal of stage grouping of gastric cancer. Sano et al. [17] proposed a new stage grouping based on data of 25,411 patients from 59 institutions in 15 countries. They showed that patients with pN3a and pN3b had distinct prognosis irrespective of regional differences.

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. It would be a unique condition of our institution. Restaging these 2 groups, according to the 8th edition criteria, improved survival differences. This signifies that the new 8th edition of the AJCC staging system has a better-stratified distribution of pathological TNM staging than the 7th edition.

We obtained our sample population from a single institution. Surgical procedures, study design for follow-up, and administration of adjuvant chemotherapy were conducted in a highly systematic manner during the course of the study. A relatively small proportion of patients were restaged according to the 8th edition of the AJCC TNM staging system in comparison to the changes in restaging from the 6th to the 7th edition. Stage migration occurred in 6.4% of patients. A total of 3.5% of patients showed a higher stage and 2.9% of patients showed a lower stage. For the patients with stages IIIB and IIIC, the 8th edition of the AJCC TNM staging system provided a stratified distribution. In conclusion, restaging stage III cancers according to the 8th edition of the AJCC TNM classification criteria improved survival discrimination in institutes where the survival rates of the stage III group were not distinctly categorized.

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