Is the 7th TNM Edition Suitable for Biological Predictor in Early Gastric Cancer?

Da Hyun Jung

Department of Medicine

The Graduate School, Yonsei University

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Directed by Professor Jie-Hyun Kim

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Thesis Supervisor : Jie-Hyun Kim

[Thesis Committee : Yong Chan Lee]

[Thesis Committee : Kyung A Lee]

The Graduate School
Yonsei University

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ABSTRACT

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Department of Medicine
The Graduate School, Yonsei University

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OBJECTIVES: The previous node classification of the TNM staging system has been clear and reliable in advanced gastric cancer; however, its clinical and prognostic value in early gastric cancer (EGC) has been less definitive. In January 2010, the TNM staging system was revised. Thus, the aim of this study was to assess the suitability of the revised node staging system for the prediction of the clinical behavior of EGC.

METHODS: Between January 2005 and December 2008, 1845 patients were diagnosed with EGC and underwent surgery at Severance and Gangnam Severance Hospital. Clinicopathological characteristics were analyzed with comparisons between the sixth and seventh TNM staging systems for EGC.

RESULTS: According to the seventh staging system, 49 (2.7%) patients were upstaged to IIA from IB based on the sixth staging system. When comparing stage IB with IIA upstaged based on the seventh staging system, poorly differentiation, signet ring cell, diffuse, and undifferentiated histological types,

perineural invasion, larger size, and younger age were more significantly associated with stage IIA than with IB. Clinicopathological factors were compared between N0/N1 and N2/N3 subgroups based on both the sixth and seventh staging systems. In mucosal cancer, larger size and lymphovascular invasion (LVI) were more significantly associated with the N2/N3 subgroup based on the sixth and seventh staging systems. However, younger age, diffuse and undifferentiated histological types were more significantly associated with the N2/N3 subgroup just based on the seventh staging system. In submucosal cancer, LVI was more significantly associated with the N2/N3 subgroup according to the sixth and seventh staging systems. However, larger size, poorly differentiation, signet ring cell, diffuse, and undifferentiated histological types, PNI, and deeper submucosal invasion were more significantly associated with the N2/N3 subgroup just based on the seventh staging system.

CONCLUSIONS: Upstaging in EGC based on the revised TNM staging system reflects more aggressive biological behavior of the cancer. The new seventh AJCC TNM staging system may be informative in the prediction of the biological behavior of EGC as well as prognosis and survival.

Key words : seventh edition of the american joint committee on cancer TNM staging system, early gastric cancer, biologic behavior

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I. INTRODUCTION

The TNM staging system has been an effective tool with which to predict clinical behaviors, such as the prognosis and survival rate of cancer. In January 1, 2010, the TNM staging system of the American Joint Committee on Cancer/International Union against Cancer Classification (AJCC/UICC) was revised. The seventh TNM staging system classified more minutely for the primary tumor (T) and regional lymph node metastasis (N) than the sixth TNM staging system. In the seventh staging system, previous subgroups pT2a (muscularis propria), pT2b (subserosa), and pT3 (serosa) were newly classified as pT2 (muscularis propria), pT3 (subserosa), and pT4a (serosa) [1]. In particular, the node classification was revised in the seventh TNM staging system, focusing on early gastric cancer (EGC). The previous node classification was clear and reliable in advanced gastric cancer; however, its

clinical and prognostic value in EGC was less definitive [2]. Thus, in the seventh staging system, the previous subgroup pN1 (1–6 involved lymph nodes [LNs]) was divided into pN1 (1–2 involved LNs) and pN2 (3–6 involved LNs), and the previous subgroups pN2 (7–15 involved LNs) and pN3 (> 15 involved LNs) were taken together into pN3 group (> 6 involved LNs).

Thus, the aim of this study was to assess the suitability of the revised node-staging for predicting clinical behavior in EGC by comparison of clinicopathological characteristics between the seventh and sixth TNM staging systems for EGC.

II. MATERIALS AND METHODS

1. *Study population*

In total, 1942 patients were diagnosed with EGC and underwent surgery at Severance and Gangnam Severance Hospital from January 2005 to December 2008. For analysis, we excluded patients who underwent surgery after endoscopic resection and patients who underwent prior chemotherapy. Of the 1942 patients, 97 were excluded and 1845 patients were included.

2. *Study details*

Patients were evaluated in terms of general informations, such as age,

gender, surgical methods, and follow-up information. Additionally, the location, gross appearance, ulcer existence, surrounding mucosal characteristics, and pathological factors, such as histological classifications (WHO, Lauren, and Japanese), size of tumor, depth of invasion, lymphovascular invasion (LVI), and perineural invasion (PNI), of EGC were included. The depth of submucosal invasion of the cancer cells into the upper third, middle third, and lower third of the submucosa was classified as SM1, SM2, and SM3, respectively. Invasion was measured at the deepest point of the penetration of cancer cells. Tumor locations were categorized by the longitudinal axis and cross-sectional circumference of the stomach. That is, the longitudinal axis of the stomach was divided into three sections (the upper third contained the fundus, cardia, and upper body; the middle third contained the mid-body, lower body, and angle; and the lower third contained the antrum and pylorus), and the cross-sectional circumference was divided into four sections (lesser curvature, posterior wall, greater curvature, and anterior wall). Investigation was performed by retrospectively reviewing medical records.

We compared stages IB and IIA upstaged based on the seventh TNM in terms of the clinicopathologic characteristics. We also stratified into N0/N1 and N2/N3 subgroups (lower and higher lymph node metastasis groups, respectively). Further, we compared the clinicopathologic characteristics of N0/N1 and N2/N3 subgroups based on the sixth and seventh staging systems in the same T stage.

3. *Statistical analysis*

The chi-square test and Fisher's exact test were used to evaluate associations among various categorical variables, and the *t*-test was used for non-categorical variables. Survival time was measured from the date of diagnosis to the date of the most recent follow-up visit or date of death, and we used the Kaplan–Meier method to analyze survival outcomes. A *P*-value of < 0.05 was to indicate statistical significance. All analyses were performed using the SPSS software (ver. 12.0; SPSS Inc., Chicago, IL).

III. RESULTS

Table 1 shows the distribution of subjects based on the TNM staging system. According to the sixth TNM staging system, the proportions of N0, N1, N2, and N3 were 89.8%, 8.9%, 1.1%, and 0.2%, respectively. According to the seventh TNM staging system, the proportions of N0, N1, N2, and N3 were 89.8%, 6.2%, 2.7%, and 1.2%, respectively. N1 stage in the sixth staging system was divided into N1 and N2 in the seventh staging system. Thus, 49 (2.7%) patients were upstaged to IIA from IB, and 3 (0.16%) patients were downstaged to IIB from IV, based on the seventh TNM staging system. Demographic features of 1845 patients are shown in **Table 2**. The mean age of the patients was 56.9±11.4 years, and the male-to-female ratio was 1.9:1.

Table 1. The Distribution of Subjects based on TNM Staging System

6th TNM staging (n, %)	**N0 (IA)**	**N1 (IB)***	**N2 (II)**	**N3 (IV)**
T1	1658 (89.8)	164 (8.9)	20 (1.1)	3 (0.2)
7th TNM staging (n, %)	**N0 (IA)**	**N1 (IB)***	**N2 (IIA)***	**N3 (IIB)**
T1	1658 (89.8)	115 (6.2)	49 (2.7)	23 (1.2)

***** N1 stage in the 6th staging was divided into N1 and N2 in the 7th staging system. 2.7% patients were upstaged to IIA from IB based on the 7th TNM staging

We compared stage IB with IIA upstaged based on the seventh TNM staging system in terms of clinicopathological characteristics to investigate whether upstaging from stage IB to stage IIA, based on the seventh TNM staging system for EGC, was reasonable. The comparison between stage IB and IIA upstaged based on the seventh TNM staging system is shown in **Table 3**. Histological types, such as poorly differentiated, signet ring cell, diffuse, and undifferentiated type, PNI, larger size, and younger age were more significantly associated with stage IIA than with stage IB ($P < 0.05$).

Table 2. The Clinicopathologic Characteristics of Subjects

Characteristics	Number of patients (n, %)
Gender	
Male	1202 (65.1)
Female	643 (34.9)
Age (yr)	
≤ 40	172 (9.3)
> 40	1673 (90.7)
Tumor location	
Upper	176 (9.5)
Middle	191 (10.4)
Lower	1478 (80.1)
Gross type	
Elevated	306 (16.6)
Flat	528 (28.6)
Depressed	1011 (54.8)
WHO classification	
Adenocarcinoma, well differentiated	418 (22.7)
Adenocarcinoma, moderate differentiated	527 (28.6)
Adenocarcinoma, poorly differentiated	363 (19.7)
Signet ring cell carcinoma	522 (28.3)
Mucinous cell carcinoma	15 (0.8)
Lauren classification	
Intestinal	820 (44.4)
Diffuse	659 (35.7)
Mixed	100 (5.4)
Japanese classification	
Differentiated	945 (54.2)
Undifferentiated	900 (48.8)
Tumor diameter (mm)	
< 20	589 (31.9)
≥ 20	1253 (67.9)
Depth of invasion	
Mucosa	1000 (54.2)
Submucosa	845 (45.8)
Number	
Single	55 (3.0)
Multiple	1790 (97.0)
Lymphovascular invasion	
Absence	1632 (88.5)
Presence	213 (11.5)
Perineural invasion	
Absence	1803 (97.7)
Presence	42 (2.3)

Table 3. Comparison of the Clinicopathologic Findings in Stage IB and IIA upstage on the 7th Staging System

Characteristics	IB (N=115) (n, %)	IIA (N=49) (n, %)	*P*-value
Age (yr, mean±SD)	58.3±11.5	54.4±11.4	**0.012**
Gender			0.743
Male	72 (62.6)	32 (65.3)	
Female	43 (37.4)	17 (34.7)	
Gross type			0.355
Elevated	28 (24.3)	7 (14.3)	
Flat	21 (18.3)	10 (20.4)	
Depressed	66 (57.4)	32 (65.3)	
WHO classification			**0.003**
Adenocarcinoma, well differentiated	10 (8.7)	2 (4.1)	
Adenocarcinoma, moderate differentiated	54 (47.0)	12 (24.5)	
Adenocarcinoma, poorly differentiated	35 (30.4)	18 (36.7)	
Signet ring cell carcinoma	14 (12.2)	17 (34.7)	
Mucinous cell carcinoma	2 (1.7)	0 (0.0)	
Lauren classification			**0.007**
Intestinal	55 (47.8)	13 (26.5)	
Diffuse	27 (23.5)	21 (42.9)	
Mixed	10 (8.7)	9 (18.4)	
Japanese classification			**0.001**
Differentiated	64 (55.7)	14 (28.6)	
Undifferentiated	51 (44.3)	35 (71.4)	
Depth of invasion			0.950
Mucosa	16 (13.9)	7 (14.3)	
Submucosa	99 (86.1)	42 (85.7)	
Lymphovascular invasion			0.109
Absence	65 (56.5)	21 (42.9)	
Presence	50 (43.5)	28 (57.1)	
Perineural invasion			**0.014**
Absence	113 (98.3)	44 (89.8)	
Presence	2 (1.7)	5 (10.2)	
Tumor diameter (mm, mean±SD)	33.2 ± 18.1	37.3 ± 19.3	**0.016**

We also compared the N0/N1 and N2/N3 subgroups based on the sixth and seventh staging systems in the same T stage. In mucosal cancer (T1a), larger

size and LVI were more significantly associated with the N2/N3 subgroup based on the sixth staging system (**Table 4**). However, according to the seventh staging system, larger size, diffuse, undifferentiated types, LVI, and younger age were more significantly associated with the N2/N3 subgroup (**Table 4**). That is, the clinicopathologic features associated with aggressive biological behavior in gastric cancer were more readily detected in the seventh than in the sixth staging system. In submucosal cancer (T1b), female and LVI were more significantly associated with the N2/N3 subgroup according to the sixth staging system (**Table 5**). However, according to the seventh staging system, larger size, histological types such as poorly differentiated, signet ring cell, diffuse, and undifferentiated, LVI, PNI, and deeper submucosal invasion were more significantly associated with the N2/N3 subgroup according to the seventh staging system (**Table 5**). As with mucosal cancer, aggressive clinicopathologic characteristics were more readily detected in the seventh than in the sixth staging system for submucosal cancer.

The 3-year cumulative survival rate was not significantly different between the N0/N1 and N2/N3 subgroups according to both the sixth and seventh TNM staging systems for mucosal cancer (data not shown). However, the 3-year cumulative survival rate of the N2/N3 subgroup was significantly lower than that of the N0/N1 subgroup, according to both the sixth and seventh TNM staging systems for submucosal cancer (**Fig. 1, 2**).

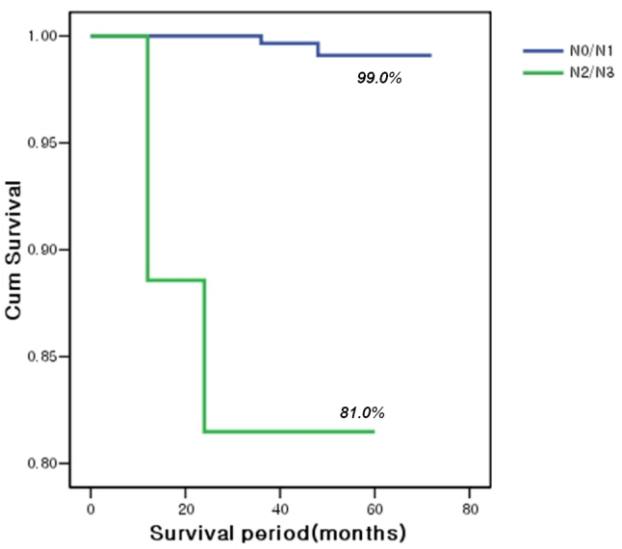

Figure 1. The 3-year cumulative survival rate of N0/N1 and N2/N3 subgroups according to the 6th staging in submucosal cancer ($P < .001$).

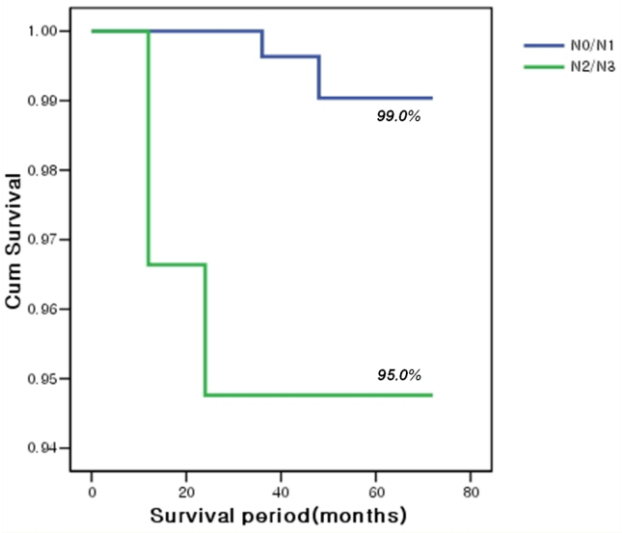

Figure 2. The 3-year cumulative survival rate of N0/N1 and N2/N3 subgroups according to the 7th staging in submucosal cancer ($P < .001$).

Table 4. Comparison of the Clinicopathologic Findings as Node staging on the 6th and 7th Stages in Mucosal cancer (T1a)

	6th staging			7th staging		
	N0/N1 (N=997) (n, %)	**N2/N3(N=3) (n, %)**	***P* -value**	**N0/N1 (N=990) (n, %)**	**N2/N3 (N=10) (n, %)**	***P* -value**
Tumor diameter (mm, mean ± SD)	24.0 ± 15.9	28.3 ± 14.4	**0.001**	23.9 ± 15.9	31.5 ± 11.6	**0.047**
Age (yr, mean ± SD)	55.5 ± 11.4	45.0 ± 12.0	0.173	55.6 ± 11.4	42.6 ± 6.9	**0.029**
Lauren classification			0.243			**<0.001**
Intestinal	402 (40.3)	0 (0.0)		402 (40.6)	0 (0.0)	
Diffuse	416 (41.7)	3 (100.0)		413 (41.7)	6 (60.0)	
Mixed	45 (4.5)	0 (0.0)		42 (4.2)	3 (30.0)	
Japanese classification			0.099			**0.017**
Differentiated	475 (47.6)	0 (0.0)		474 (47.9)	1 (10.0)	
Undifferentiated	522 (52.4)	3 (100.0)		516 (52.1)	9 (90.0)	
Lymphovascular invasion			**<0.001**			**<0.001**
Absence	984 (98.7)	2 (66.7)		978 (98.8)	8 (80.0)	
Presence	13 (1.3)	1 (33.3)		12 (1.2)	2 (20.0)	

Table 5. Comparison of the Clinicopathologic Findings as Node staging on the 6th and 7th Stages in Submucosal cancer (T1b)

	6th staging			7th staging		
	N0/N1 (N=824) (n, %)	**N2/N3 (N=20) (n, %)**	***P*-value**	**N0/N1 (N=782) (n, %)**	**N2/N3 (N=62) (n,%)**	***P*-value**
Gender			**0.029**			0.418
Male	561 (68.1)	9 (45.0)		531 (67.9)	39 (62.9)	
Female	263 (31.9)	11 (55.0)		251(32.1)	23 (37.1)	
Tumor diameter (mm, mean ± SD)	29.0 ± 15.8	38.0 ± 21.1	0.074	28.6 ± 15.4	38.0 ± 20.4	**0.006**
WHO classification			0.156			**0.036**
Adenocarcinoma,well differentiated	148 (18.0)	1 (5.0)		146 (18.7)	3 (4.8)	
Adenocarcinoma,moderate differentiated	310 (37.6)	11 (55.0)		299 (38.2)	22 (35.5)	
Adenocarcinoma, poorly differentiated	205 (24.9)	6 (30.0)		189 (24.2)	22 (35.5)	
Signet ring cell carcinoma	147 (17.8)	1 (5.0)		134 (17.1)	14 (22.6)	
Mucinous cell carcinoma	14 (1.7)	1 (5.0)		14 (1.8)	1 (1.6)	
Lauren classification			0.085			**0.013**
Intestinal	410 (49.8)	8 (40.0)		397 (50.8)	21 (33.9)	
Diffuse	236 (28.6)	3 (15.0)		218 (27.9)	21 (33.9)	
Mixed	52 (6.3)	3 (15.0)		46 (5.9)	9 (14.5)	
Japanese classification			0.694			**0.011**
Differentiated	458 (55.6)	12 (60.0)		445 (56.9)	25 (40.3)	
Undifferentiated	366 (44.4)	8 (40.0)		337 (43.1)	37 (59.7)	
Depth of invasion			0.052			**0.026**
SM1	197 (26.5)	2 (11.1)		192 (27.2)	7 (12.7)	
SM2	184 (24.7)	2 (11.1)		174 (24.6)	12 (21.8)	
SM3	363 (48.8)	14 (77.8)		341 (48.2)	36 (65.5)	
Lymphovascular invasion			**<0.001**			**<0.001**
Absence	640 (77.7)	5 (25.0)		625 (79.9)	20 (32.3)	
Presence	184 (22.3)	15 (75.0)		157 (20.1)	42 (67.7)	
Perineural invasion			0.296			**0.018**
Absence	784 (95.1)	18 (90.0)		747 (95.5)	55 (88.7)	
Presence	40 (4.9)	2 (10.0)		35 (4.5)	7 (11.3)	

IV. DISCUSSION

Cancer staging is a key factor that defines prognosis and determines appropriate treatment. Additionally, accurate staging is essential in evaluating the results of treatments and clinical trials, and to exchange information regarding cancer incidence and outcomes between treatment and research centers [1]. The TNM staging system has been an informative tool for the prediction of prognosis and survival. Therefore, the staging system was revised by stages to be more sensitive in the prognostic evaluation and to reflect better overall survival rates.

The fifth and sixth TNM staging systems classified N stage by the number of metastatic LNs rather than by the LN location [3-5]. The previous node-staging system, which was based on numbers of metastatic LNs, has proven clear and reliable in advanced gastric cancer. However, the superiority of the previous node classification was not sustained in EGC [6, 7].

Some investigators reported that the overall survival of EGC patients with a subdivided number of metastatic LNs differed in the same N stage of the previous fifth and sixth TNM staging systems [2, 8]. Others proposed that the N ratio, which is the ratio between metastatic and examined LNs, has been a reliable prognostic factor in EGC [9-12]. Thus, the seventh TNM staging system adopted a more detailed classification, such as N1 (1–2 involved LNs) and N2 (3–6 involved LNs). To date, several studies have reported the usefulness and validation of the seventh TNM staging system for gastric cancer [13-15]. *Ahn et*

al. reported that the revised seventh TNM staging system for gastric cancer better categorized grouping than the sixth TNM staging system for 5-year survival rates, especially between T2 and T3 tumors and N1 and N2 tumors [4].

Studies that analyzed the seventh TNM staging system have focused on the prediction of survival rates and prognosis in gastric cancer. According to these studies, the seventh TNM staging system might more accurately predict the prognosis and survival rates in gastric cancer. However, these studies simply investigated survival rates at each stage of gastric cancer. Thus, it may be insufficient to validate the revised TNM staging system focusing on node staging in EGC. Therefore, we sought to assess the revised node-staging system focused on EGC in the seventh TNM staging system, based on an investigation of clinicopathologic factors of patients whose stage was changed by the revised node staging in the seventh TNM system.

In the present study, younger age, histological type, LVI, PNI, and depth of invasion were significantly different in patients whose stage was changed by the revised node staging in the seventh TNM staging. Generally among host factors, younger age has been associated with aggressive progression and behavior of gastric cancer. Furthermore, in terms of lesion factors, histological types, such as poorly differentiated adenocarcinoma, diffuse, and undifferentiated types, LVI, PNI, and deeper invasion of cancer cells have been widely presumed to reflect aggressive biological behavior. Thus, clinicians have determined indications for local treatments or minimally

invasive surgery in EGC after consideration of histological type or the other factors stated above. Our study showed that the revised TNM staging system could more accurately detect such aggressive clinicopathological factors than the previous TNM staging system for EGC.

Our study has some limitations. We only analyzed the 3-year cumulative survival rate. The overall survival rate of each stage was not significantly different between the sixth and seventh TNM staging systems. Reasons for this may include the short follow-up duration and the fact that our study was focused on EGC. The reason that we analyzed data from 2005 is that we aimed to investigate the clinicopathological characteristics focusing on EGC, so a detailed depth of SM invasion was necessary as one of the variables. However, pathologists officially reported the detailed depth of invasion such as SM1, SM2, and SM3 in Korea from 2005.

V. CONCLUSION

In conclusion, upstaging of EGC, based on the revised TNM staging system, reflects the more aggressive biological behavior of this cancer. Although the TNM staging system has been proposed to better predict the clinical behavior for prognosis and survival rather than the biological behavior of cancer, the new seventh AJCC TNM staging system may be informative in predicting the biological behavior of EGC as well as the prognosis and survival.

REFERENCES

1. Edge SB, Byrd DR, Compton CC. AJCC Cancer Staging Handbook. 7th ed. New York: Springer-Verlag; 2010.
2. Huang BJ, Zheng XY, Wang ZN, Wang MX, Dong YL, Zhao B, et al. Prognostic Significance of the Number of Metastatic Lymph Nodes: Is UICC/TNM Node Classification Perfectly Suitable for Early Gastric Cancer? Ann Surg Oncol 2009;16:61-7.
3. Ichikura T, Tomimatsu S, Uefuji K, Kimura M, Uchida T, Morita D, et al. Evaluation of the New American Joint Committee on Cancer/International Union against cancer classification of lymph node metastasis from gastric carcinoma in comparison with the Japanese classification. Cancer 1999;86:553-8.
4. Ahn HS, Lee HJ, Hahn S, Kim WH, Lee KU, Sano T, 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. Roder JD, Bottcher K, Busch R, Wittekind C, Hermanek P, Siewert JR. Classification of regional lymph node metastasis from gastric carcinoma. German Gastric Cancer Study Group. Cancer 1998;82:621-31.

6. Hermanek P. The superiority of the new International Union Against Cancer and American Joint Committee on Cancer TNM staging of gastric carcinoma. Cancer 2000;88:1763-5.

7. Celen O, Yildirim E, Gulben K, Berberoglu U. Prediction of survival in gastric carcinoma related to lymph node grading by the new American Joint Committee on Cancer/Union International Contre le Cancer System or the Japanese system. Eur J Surg Suppl 2003:33-9.

8. Roviello F, Rossi S, Marrelli D, Pedrazzani C, Corso G, Vindigni C, et al. Number of lymph node metastases and its prognostic significance in early gastric cancer: a multicenter Italian study. J Surg Oncol 2006;94:275-80; discussion 4.

9. Marchet A, Mocellin S, Ambrosi A, de Manzoni G, Di Leo A, Marrelli D, et al. The prognostic value of N-ratio in patients with gastric cancer: validation in a large, multicenter series. Eur J Surg Oncol 2008;34:159-65.

10. Cheong JH, Hyung WJ, Shen JG, Song C, Kim J, Choi SH, et al. The N ratio predicts recurrence and poor prognosis in patients with node-positive early gastric cancer. Ann Surg Oncol 2006;13:377-85.

11. Sianesi M, Bezer L, Del Rio P, Dell'Abate P, Iapichino G, Soliani P, et al. The Node Ratio as Prognostic Factor after Curative Resection for Gastric Cancer. Journal of Gastrointestinal Surgery 2010;14:614-9.

12. Bando E, Yonemura Y, Taniguchi K, Fushida S, Fujimura T, Miwa K. Outcome of ratio of lymph node metastasis in gastric carcinoma. Ann Surg Oncol 2002;9:775-84.

13. Jung H, Lee HH, Song KY, Jeon HM, Park CH. Validation of the seventh edition of the american joint committee on cancer TNM staging system for gastric cancer. Cancer 2011.

14. Deng J, Liang H, Sun D, Wang D, Pan Y. Suitability of 7th UICC N stage for predicting the overall survival of gastric cancer patients after curative resection in China. Ann Surg Oncol 2010;17:1259-66.

15. Washington K. 7th edition of the AJCC cancer staging manual: stomach. Ann Surg Oncol 2010;17:3077-9.

ABSTRACT(IN KOREAN)

조기 위암에서 개정된 TNM 병기의 생물학적 예측 인자로서 의미

<지도교수 김지현>

연세대학교 대학원 의학과

정다현

목적: 이전의 TNM N 병기는 진행성 위암에서 더 명확하고 신뢰성 있는 것으로 알려져 있었으나, 조기위암에서 예측인자로서의 의미는 명확하지 않았다. 2010년 1월, TNM 병기가 개정되었고 조기 위암에서 예측인자로서 개정된 N 병기의 의미에 대해서 알아보고자 하였다.

방법: 2005년 1월부터 2008년 12월까지 신촌세브란스병원과 강남세브란스병원에서 조기 위암을 진단 받고 수술 받은 1845명의 환자를 대상으로 하였다. 임상조직학적 특성에 대해 6번째와 7번째 TNM 병기를 비교하여 분석하였다.

결과: 7번째 병기에 따르면, 49 (2.7%) 명의 환자가 6번째 병기의 IB에서 7번째 병기의 IIA로 바뀌었다. 7번째 병기에서 IB환자와 IIA환자를 비교하였을 때, 통계적으로 유의하게 분화도가 나쁘거나, 반지

세포암, 미만성, 크기가 큰 경우, 젊은 나이, 신경 침윤이 많은 경우 IIA 병기와 연관성이 있었다. N0/N1과 N2/N3로 나누어 임상조직학적 특성을 비교하였을 때, 점막암에서는 6번째와 7번째 병기에서 모두 크기가 크거나 림프혈관침윤이 많은 경우 통계학적으로 유의하게 N2/N3 그룹과 연관성이 있었다. 그러나, 젊은 나이, 미만성이거나 미분화 조직학적 특성을 가진 경우 7번째 병기에서만 통계학적으로 유의하게 N2/N3 그룹과 연관성이 있었다. 점막하층암에서는 림프혈관 침윤이 있는 경우 통계학적으로 유의하게 6번째와 7번째 병기 모두에서 N2/N3 그룹과 연관성이 있었다. 그러나, 크기가 큰 경우, 반지 세포암, 미만성, 미분화암, 신경 침윤이 있거나, 점막하층의 침윤 깊이가 깊을수록 통계학적으로 유의하게 7번째 병기에서만 N2/N3 그룹과 연관성이 있었다.

결론: 조기 위암에서 개정된 TNM 병기에 의해 병기가 올라간 경우 공격적인 임상 양상을 더 잘 반영하였다. 새로운 7번째 AJCC TNM 병기는 조기위암에서 예후와 생존율뿐만 아니라 생물학적 예측 인자로서도 유용할 것으로 보인다.

핵심단어 : 7번째 TNM 병기, 조기 위암, 생물학적 양상