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Comparison of Prognostic Significance of Nodal Staging between Old (4th Edition) and New (5th Edition) UICC TNM Classification for Gastric Carcinoma

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Abstract. The description of nodal staging for gastric cancer was changed in the new fifth edition of the International Union Against Cancer (UICC) TNM classification from the anatomic sites of metastatic lymph nodes to the number of metastatic lymph nodes, as pN1 is metastasis in 1 to 6 lymph nodes, pN2 is in 7 to 15 lymph nodes, and pN3 is in 16 or more lymph nodes. The purpose of this study was to investigate the prognostic significance of the new staging system based on the number of metastatic lymph nodes compared to the old staging system by anatomic site. From 1987 to 1994 a total of 2108 patients who underwent potentially curative resections with D2 or D3 lymph node dissection and with 15 or more lymph nodes retrieved were studied retrospectively. Lymph node metastases were found in 1018 patients (48.3%). A mean of 37.9 lymph nodes were retrieved per patient, and a mean of 7.2 lymph nodes were invaded by tumor cells. We found that the new nodal staging based on the number of metastatic lymph nodes closely correlated with the depth of cancer invasion and with the old nodal staging based on the anatomic site of the metastatic nodes, with statistical significance. The 5-year survival rates after gastrectomy decreased significantly by increasing the extent of the pN classification in both nodal staging methods. In a subgroup analysis of survivals between the old and new nodal staging, the new classification showed more homogeneous survival at the same stage than the old one. With a multivariate analysis of prognostic factors, including the old and new nodal staging, the depth of invasion and the new nodal stage were the most significant prognostic factors, followed by the old nodal stage. Our data suggested that the new nodal staging based on the number of metastatic lymph nodes is not only a reliable and objective method for nodal classification, but it is also a significant prognostic determinant for gastric cancer that can be used in practice.

Gastric cancer is still the most common cause of death from cancer in Korea despite the improved prognosis as a result of early diagnosis, radical operation, and the development of adjuvant therapy. The extent of lymph node metastasis and depth of invasion are the two most important prognostic factors in gastric cancer without distant metastasis [1]. The TNM system has become the principal method for assessing the extent of disease and determining the prognosis of cancer patients. Progress in the treatment of gastric cancer required the objectivity and unification of the TNM system for tumor classification, and there had been many attempts to unify and improve the TNM system through a series of international meetings. The TNM Committee of the International Union Against Cancer (UICC) and the American Joint Committee on Cancer (AJCC) had been working toward similar objectives that have now culminated in a uniform classification for gastric cancer [2, 3]. In the fourth edition of the UICC TNM classification [2], nodal involvement is classified into pN0, pN1, and pN2, based on the site of the metastasis in relation to the primary tumor. The current Japanese classification of lymph node metastasis describes four groups (N1–N4) which are based on the anatomic localization of the lymph nodes [4]. These nodal staging methods based on the sites of the metastatic lymph nodes had some problems, such as complexity and subjectivity, as well as discrepancies in classification, that made comparative analysis on a worldwide base difficult. To overcome these difficulties in the classification of lymph node metastasis, the fifth edition of the UICC TNM classification was published in 1997 with a substantial change for the pN staging of gastric cancer based on the number of metastatic lymph nodes [5]. In this study, the relation between the number of metastatic lymph nodes and survival was evaluated retrospectively to clarify the effectiveness and prognostic significance of the new UICC nodal staging.

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Patients and Methods

We reviewed the records of 2603 patients with gastric adenocarcinoma who underwent gastrectomy at the Department of Surgery, Yonsei University College of Medicine between 1987 and 1994. For accurate pN staging, patients who underwent palliative resection (R1, R2 according to the UICC rules) were excluded because the prognosis of these patients was not influenced by lymph node status. Patients with gastric remnant cancer or fewer than 15 lymph nodes retrieved and who underwent D1 lymph node dissection were excluded because these cases could possibly have been inadequately staged. The old UICC classification classified only pN1 and pN2 categories. Therefore patients with distant lymph node metastasis (periportal, retropancreatic, mesenteric, mesocolic, and paraaortic nodes) were also excluded from this study. Finally, a total of 2108 patients were entered in the study. Among them, lymph node metastases were found in 1018 patients (48.3%), and their pN staging was classified according to the old and the new UICC rules for comparative study. The detailed clinicopathologic features according to lymph node metastasis are listed in Table 1.

The levels of dissected lymph nodes were verified by surgeons

Table 1. Clinicopathologic features of 2108 patients according to lymph node metastasis.

Parameter	No. of patients (%) Lymph node (−) (n = 1090)	Lymph node (+) (n = 1018)	p
Age (years)			0.001
≤60	727 (66.7)	623 (61.2)	
>60	363 (33.3)	395 (38.8)	
Sex			NS
Male	722 (66.2)	676 (66.4)	
Female	368 (33.8)	342 (33.6)	
Location of tumor			0.052
Lower third	551 (50.6)	496 (48.7)	
Middle third	422 (38.7)	362 (35.5)	
Upper third	111 (10.2)	133 (13.1)	
Entire	6 (0.6)	27 (2.7)	
Tumor size (cm)			0.000
<5	708 (65.0)	297 (29.3)	
5–10	322 (29.5)	557 (55.0)	
>10	60 (5.5)	159 (15.7)	
Depth of invasion[a]			0.000
pT1	613 (56.2)	84 (8.3)	
pT2	238 (21.8)	246 (24.2)	
pT3	221 (20.8)	628 (61.7)	
pT4	18 (1.7)	60 (5.9)	
Nodal status[a]			
pN0	1090 (100)	—	
pN1	—	592 (58.2)	
pN2	—	426 (41.8)	
UICC TNM stage[a]			0.000
I	844 (77.4)	69 (6.8)	
II	229 (21.0)	169 (16.6)	
III	17 (1.6)	731 (71.8)	
IV	0 (0.0)	49 (4.8)	
Type of resection			0.000
Subtotal	882 (80.9)	713 (70.0)	
Total	208 (19.1)	305 (30.0)	
Lymph node dissection			NS
D2	195 (17.9)	190 (18.7)	
D3	895 (82.1)	828 (81.3)	

Numbers in parentheses are percents.
[a]By 4th edition of UICC TNM staging.

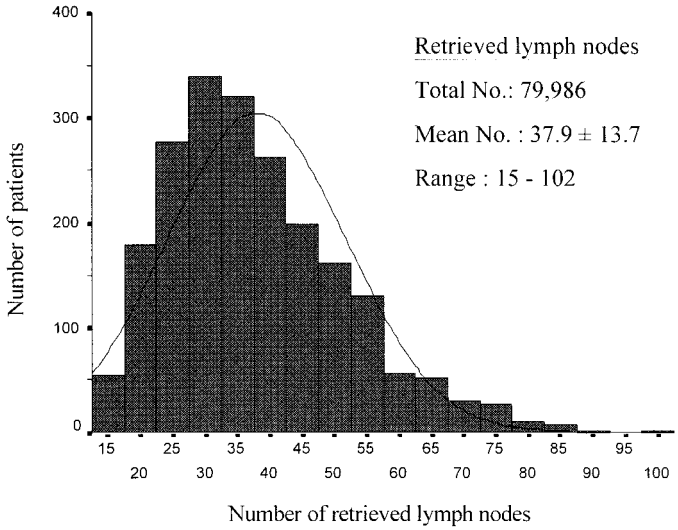

Fig. 1. Histogram showing the numerical distribution of retrieved lymph nodes. The curved line is the normal distribution curve of this histogram.

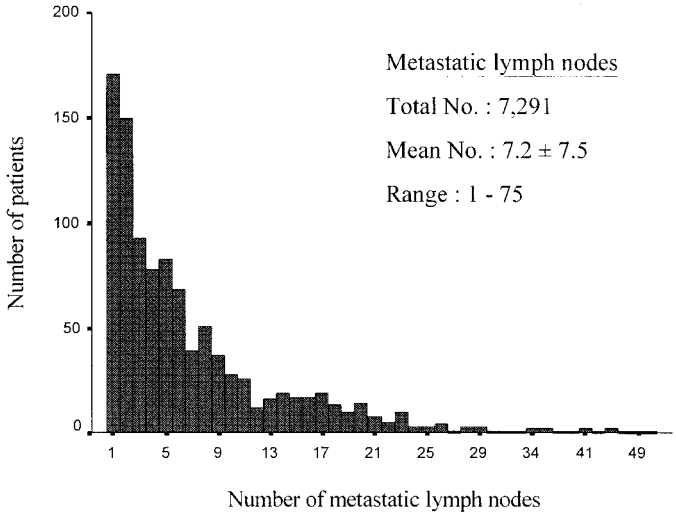

Fig. 2. Bar chart showing the numeric distribution of metastatic lymph nodes.

from the excised specimens, and all retrieved lymph nodes were examined for metastasis by light microscopy after being stained with hematoxylin and eosin. All patients were followed up closely until August 31, 1997; the median follow-up period was 48 months (range 1–121 months). At the time of the last follow-up, 65 patients (3.1%) were subsequently lost to follow-up, and 522 patients (24.8%) had died. The lost cases and deaths from any other cause than gastric cancer were treated as censored data for the analysis of survival rates.

Survival rates were calculated by the Kaplan-Meier method, excluding 16 patients who died of postoperative complications; the differences were analyzed by log-rank test. The correlation between pT and pN was analyzed using the Spearman correlation coefficient. Multivariate analysis was performed using Cox's proportional hazard model. The accepted level of significance was $p < 0.05$.

Results

For the 2108 patients, the mean number of retrieved lymph nodes was 37.9 ± 13.7 (range 15–102) per patient, and the mean number of metastatic lymph nodes was 7.2 ± 7.5 (range 1–75) in 1018 patients with lymph node metastasis (Figs. 1, 2). As shown in Table 1, the lymph node-positive group was older, had a larger tumor size, and had a more advanced pT and TNM stage than the lymph node-negative group. Regarding the operative procedures, total gastrectomy was more often performed in the lymph node-positive group, but there was no difference in the extent of lymph node dissection between the two groups. The most prevailing procedure in our hospital was D3 lymph node dissection, and the number of retrieved lymph nodes increased as the extent of lymph node dissection increased (Table 2).

Correlation between Depth of Invasion and Nodal Stage

The extent of metastatic lymph nodes in the old nodal staging and the number of metastatic lymph nodes in the new nodal staging

Table 2. Number of patients and retrieved lymph nodes according to the extent of lymph node dissection in 2108 patients who underwent potentially curative resection.

Extent of node dissection	Patients No. (%)	No. of retrieved nodes (mean ± SD)
D2	385 (18.3)	32.8 ± 11.5
D3	1723 (81.7)	39.1 ± 13.9

Table 3. Correlation between depth of invasion and old nodal staging according to anatomic site of metastatic lymph nodes.

Depth of invasion*	No. of patients (%) according to old staging* pN0	pN1	pN2
pT1: m (n = 363)	350 (96.4)	12 (3.3)	1 (0.3)
pT1: sm (n = 334)	263 (78.7)	57 (17.1)	14 (4.2)
pT2 (n = 484)	238 (49.2)	154 (31.8)	92 (19.0)
pT3 (n = 849)	221 (26.0)	348 (41.0)	280 (33.0)
pT4 (n = 78)	18 (23.1)	21 (26.9)	39 (50.0)

Numbers in parentheses are percents. m: mucosal; sm: submucosal.
*Correlation coefficient = 0.53 ($p < 0.001$).

increased with the depth of cancer invasion. Significant correlations were observed between both nodal stagings and the depth of cancer invasion ($p < 0.001$). The correlation coefficient for pT/pN was 0.53 for the old staging and 0.54 for the new staging (Tables 3, 4). The mean number of metastatic lymph nodes was 0 in mucosal lesion, 0.6 ± 1.5 in submucosal lesion, 2.6 ± 4.4 in pT2, 6.2 ± 7.9 in pT3, and 7.4 ± 8.1 in pT4 lesion (Table 4).

Correlation between Old and New Nodal Staging

Table 5 shows the relation between the two groups of the old pN and three groups of the new pN classification. Among 592 patients classified as old pN1, 485 patients (81.9%) were classified as new pN1, and the remaining 107 patients were up-staged as pN2 (15.4%) and as pN3 (2.7%), respectively. In 426 patients classified as old pN2, the stage migration was more noticeable: same-staged in 161 patients (37.8%), down-staged in 151 patients (35.4%), and up-staged in 114 patients (26.8%). The old nodal stage according to the localization of lymph node was significantly correlated with the new nodal stage according to the number of metastatic lymph nodes (correlation coefficient 0.49, $p < 0.001$). The mean number of metastatic lymph nodes was 4.1 ± 3.8 in old pN1 and 11.4 ± 9.2 in old pN2 (Table 5).

Survival Rates According to Old and New Nodal Staging

The overall 5-year survival rate of 2108 patients was 72.4%. The 5-year survival rate was 88.7% for patients without lymph node metastasis, and it decreased significantly as the extent of lymph node metastasis increased ($p < 0.001$). The 5-year survival rates for patients involving pN1 and pN2 according to the old staging were 67.9% and 37.8%, respectively, and the rates for patients according to the new staging were 69.3% in pN1, 40.1% in pN2, and 16.3% in pN3 (Table 6). Table 6 also shows the survival rates of all subdivided groups between the old and new nodal staging. Within the old pN1 and pN2 classification, distinctly different survival was noted according to the number of metastatic lymph nodes: The survival discrepancies were 54.9% in pN1 and 37.1% in pN2. In contrast, the new pN classification showed more homogeneous survival according to the localization of metastatic lymph nodes: The survival discrepancies were 21.3% in pN1, 0.1% in pN2, and 3.5% in pN3.

Multivariate Analysis

Multivariate analysis was performed to determine the independent prognostic factors among age, depth of cancer invasion, new nodal stage, tumor size, and histologic and gross types that were found by univariate analysis to be significantly associated with survival. The new nodal stage was the most significant prognostic factor (RR 1.81, $p < 0.0001$), followed by depth of invasion (RR 1.63, $p < 0.0001$). When multivariate analysis was performed including the old and new nodal stage, the best prognostic determinant was depth of invasion and new nodal staging (RR 1.59, $p < 0.0001$) followed by the old nodal staging (RR 1.52, $p < 0.0001$) (Table 7).

Discussion

The controversy over the value of extended lymph node dissection for treatment of gastric cancer is still under debate. Whereas Japanese surgeons claim that the superior survival rates in their series are due to extended lymph node dissection (D2 resection) [6, 7], many Western surgeons believe that lymph nodes are still indicators rather than governors of disease and that extended lymph node dissection merely improves the accuracy of tumor staging [8].

The number of retrieved lymph nodes is correlated with the results of the pN classification. With an increasing number of retrieved nodes, a higher frequency of lymph node-positive cases is found. Therefore the number of retrieved lymph nodes reflects the reliability of the pN classification [9]. Wagner et al. [10] recommended that surgeons obtain an average of at least 27 lymph nodes with D2 resection and 43 lymph nodes with D3 resection. Siewert et al. [11] reported that removal of 26 or more lymph nodes was defined as radical lymph node dissection, and removal of fewer than 26 nodes was defined as a standard lymph node dissection, corresponding to the Japanese D1 procedure. The prevalence of lymph node metastases was not dependent on the number of removed lymph nodes, provided 15 or more nodes were removed [8, 10]. In the *UICC TNM Supplement 1993,* the number of examined lymph nodes adequate for staging and ordinarily included in regional lymphadenectomies is 15 or more in gastric cancer. These numbers are considered to be the minimum needed for adequate staging, not the standard level for quality assurance of lymph node surgery [9].

In this study we excluded the patients with fewer than 15 lymph nodes retrieved and obtained a mean of 37.9 lymph nodes. The overall 5-year survival rate of 2603 patients who underwent gastric resection from 1987 to 1994 at our hospital was 66.5%, which was much better than that in Western hospitals. We believe that the possible explanations for this survival discrepancy may be the routine extended lymph node dissection performed since the early 1980s and the relatively high proportion (29%) of patients with early gastric cancer [12]. Regarding the extent of lymph node dissection, D3 resection was the most prevailing procedure in our hospital because operative morbidity and mortality were not

Table 4. Correlation between depth of invasion and new nodal staging according to the number of metastatic lymph nodes.

Depth of invasion*	No. of patients (%) according to new staging*				No. of metastatic lymph nodes (mean ± SD)
	pN0	pN1	pN2	pN3	
pT1: m	350 (96.4)	13 (3.6)	—	—	0
pT1: sm	263 (78.7)	62 (18.6)	9 (2.7)	—	0.6 ± 1.5
pT2	238 (49.2)	182 (37.6)	50 (10.3)	14 (2.9)	2.6 ± 4.4
pT3	221 (26.0)	348 (41.0)	178 (21.0)	102 (12.0)	6.2 ± 7.9
pT4	18 (23.1)	31 (39.7)	15 (19.2)	14 (17.9)	7.4 ± 8.1

Numbers in parentheses are percents.
*Correlation coefficient = 0.54 ($p < 0.001$).

Table 5. Correlation between old and new nodal staging.

Old staging*	No. of patients by new staging*			No. of metastatic lymph nodes (mean ± SD)
	pN1 ($n = 636$)	pN2 ($n = 252$)	pN3 ($n = 130$)	
pN1 ($n = 592$)	485 (81.9%)	91 (15.4%)	16 (2.7%)	4.1 ± 3.8
pN2 ($n = 426$)	151 (35.4%)	161 (37.8%)	114 (26.8%)	11.4 ± 9.2

*Correlation coefficient = 0.49 ($p < 0.001$).

Table 6. 5-Year survival rates according to old and new nodal staging.

Old staging	Survival rate (%), new staging			
	pN1	pN2	pN3	Subtotal
pN1	74.4	40.1	19.5	67.9
pN2	53.1	40.0	16.0	37.8
Subtotal	69.3	40.1	16.3	55.1*

*Five-year survival rate for patients with lymph node metastasis.

Table 7. Multivariate analysis in 2108 patients with gastric cancer including the old and new nodal staging.

Covariate	Coefficient	SE	RR	95% CI	p
Depth of invasion	0.46	0.09	1.59	1.33–1.89	0
New nodal stage	0.46	0.07	1.59	1.37–1.84	0
Old nodal stage	0.42	0.12	1.52	1.20–1.91	0
Age	0.16	0.04	1.17	1.07–1.28	0.005
Tumor size	0.04	0.08	1.04	0.88–1.22	0.570
Gross type	0.09	0.07	1.09	0.96–1.17	0.190
Histologic type	0.06	0.05	1.06	0.96–1.17	0.220

SE: standard error; RR: relative risk; CI: confidence interval.

different between D2 and D3 resection. On the other hand, D1 resection was performed with limited indications, such as early mucosal lesions or far-advanced lesions with high operative risk.

According to the rules of the Japanese Research Society for Gastric Cancer [4], the gastric lymph node stations are numbered 1 to 16 and are subsequently grouped into four lymph node levels, designated N1 to N4. In 1987 the UICC proposed a new stage classification to accommodate the development in surgical procedures according to surveys in Japan and the United States; the nodal staging was also based on the anatomic site of involved nodes considering the distance from the primary tumor [2]. The survival rate after resection of gastric cancer was closely related to the extent of lymph node metastasis. Maruyama et al. [13] reported that a limited spread to perigastric nodes correlated with better survival rates than deposits around the left gastric artery, common hepatic artery, celiac axis, or splenic artery (stations 7–11), with the poorest prognosis being associated with metastasis in the hepatoduodenal ligament, behind the pancreas head, at the root of the mesentery, and along the aorta (stations 12–16). Noguchi et al. [14] reported 5-year survival rates in patients with metastases involving N0, N1, N2, and N3 levels as 85%, 60%, 25%, and 11%, respectively.

These figures were similar to our data, the body of which was large enough to provide information regarding survival rates in the presence of metastasis to individual node stations. However, these classifications are too complicated to be used routinely because it is difficult for a surgeon to define the accurate anatomic site of the lymph nodes during node dissection. It is also difficult for a surgeon to group the lymph nodes on an en bloc dissected specimen and inform the pathologist of the location of the nodes. Therefore simpler, more objective staging of lymph node metastasis has been suggested.

In breast and colorectal cancer, the number of metastatic lymph nodes has been recognized as a significant prognostic factor [15, 16]. For gastric cancer, the number of metastatic lymph nodes has also been reported to be a significant prognostic indicator [17–26]. However, opinions differ as to the relative importance of the total number versus the anatomic level of the metastatic lymph nodes. Isozaki et al. [24] reported that the long-term outcome was affected by the extent of lymph node involvement but was not significantly affected by the number of metastatic lymph nodes. On the other hand, Makino et al. [25] considered that the prognosis varies in patients with N1 lymph node metastasis according to the number of metastatic lymph nodes, and Ichikura et al. [26] suggested that the number of metastatic lymph nodes has a more adverse effect on the survival of patients with gastric cancer than the anatomic level of involved nodes.

In 1996 data of the German Gastric Cancer Study were presented to the TNM/Prognostic System Committee of the UICC. These data were a contribution to the formulation of changes in the new 5th edition of the UICC TNM classification in 1997, and the nodal staging was changed substantially based on the number of metastatic nodes. Roder et al. [27] suggested that

this new pN classification based on the number of metastatic lymph nodes allows an estimation of prognosis that is superior to that using the old classification and can be applied without methodologic problems.

Conclusions

In this study the relationship between the number of metastatic lymph nodes, the depth of invasion, the old nodal stage, and survival rates were examined to evaluate the prognostic significance of the new nodal staging classification. We found that this new nodal staging system based on the number of metastatic lymph nodes closely correlated with the depth of cancer invasion and the old nodal staging system based on the anatomic sites of metastatic lymph nodes, with statistical significance. In the survival analysis based on the extent of lymph node metastasis, both nodal classifications showed significant survival differences as increasing with the N number. Using multivariate analysis, we found that the new nodal staging was the most important prognostic factor, followed by the depth of invasion. Another multivariate analysis that included the old and new nodal staging showed that the two methods of nodal staging had almost the same predicting power for the prognosis of patients with gastric cancer. However, at the same nodal stage, the new pN classification showed more homogeneous survival according to the localization of metastatic lymph nodes than survival differences in the old pN classification based on the number of metastatic lymph nodes.

The new N classification based on the number of metastatic lymph nodes is therefore a simpler, more objective method of nodal staging than the old system based on their anatomic site, and it is a significant prognostic factor with predicting power similar to that of the old pN classification. In addition, we believe that if the number of metastatic lymph nodes can be used in practice as a new nodal staging method, D2 or more lymph node dissection should be performed as a surgical quality control of adequate lymphadenectomy.

Résumé

Dans la cinquième édition de la classification TNM de UICC (Union Internationale Contre le Cancer), la modalité descriptive de l'envahissement ganglionnaire des cancers gastriques a changé: desormais, ce n'est plus le site anatomique des métastases ganglionnaires mais le nombre de métastases ganglionnaires qui entrent en ligne de compte: pN1 veut dire entre 1 et 6 ganglions envahis, pN2 entre 7 et 15, et pN3, 16 ganglions ou plus. Le but de cette étude a été d'examiner la signification pronostique de cette nouvelle classification basée sur le nombre de ganglions envahis comparée au système ancien basé sur les sites anatomiques. Entre 1987 et 1994, 2108 patients qui ont eu une résection potentiellement curative avec une lymphadénectomie D2 ou D3 et plus de 15 ganglions ont été étudiés de façon rétrospective. On a trouvé des métastases ganglionnaires chez 1018 patients (48.3%). On a enlevé une moyenne de 37.9 ganglions par patient et parmi ceux-ci, 7.2 ganglions en moyenne étaient envahis par des cellules tumorales à l'examen histologique. Nous avons trouvé que le nouveau système de classification basé sur le nombre de ganglions envahis corrélait étroitement et statistiquement significativement avec la profondeur d'envahissement et également avec le staging ganglionnaire ancien basé sur le site anatomique des ganglions métastatiques. La survie à cinq ans après gastrectomie a diminué de façon significative en augmentant l'étendue de la classification pN dans les deux systèmes de classifications ganglionnaires. Dans l'analyse de sous-groupe concernant la survie comparant les deux systèmes, le nouveau et l'ancien, la classification nouvelle a montré que la survie était plus homogène que dans la classificiaton ancienne, pour un même stade de maladie. En analyse multivariée des facteurs pronostiques, comprenant les classifications ancienne et nouvelle, la profondeur d'envahissement, et le stade ganglionnaire nouveau étaient des facteurs pronostiques les plus significatifs, suivi du stade ancien. Nos résultats suggèrent que la nouvelle classification ganglionnaire tenant compte du nombre de ganglions envahis n'est aps suelemnt fiable mais aussi un déterminant pronostique significatif pour le cancer gastrique qui peut être utilisé en pratique courante.

Resumen

La 5ª edición de la Unión Internacional contra el Cáncer (UICC), la estadificación glanglionar para clasificar la extensión y gravedad del cáncer gástrico ha clarificado la antigua clasificación TNM, en el sentido de que la N, no se refiere solo a la localización de las metástasis linfáticas sino también a su número. Así, pN1 indica la existencia de metástasis en uno a seis ganglios; pN2 en 7 a 15 y pN3 en 16 o más adenopatias. El presente trabajo trata de averiguar la significación pronóstica de esta nueva clasificación, basada en el número de metástasis ganglionares, frente a la estadificación antigua fundamentada en la localización anatómica. Se estudiaron retrospectivamente 2.108 pacientes, que entre 1987 y 1994 fueron sometidos a una resección gástrica, potencialmente curativa, con linfadenectomía D2 o D3 en las que se extirparon 15 o más ganglios linfáticos. Se encontraron metátasis ganglionares en 1.018 pacientes (48,3%). Se extirparon un promedio de 37,9 ganglios por paciente, de los que 7,2 por término medio, estaban invadidos por células tumorales. Demostramos que la nueva estadificación glanglionar, basada en el número de ganglios linfáticos afectados, se correlaciona con el grado de invasión neoplásica, al igual que ocurría con la vieja estadificación basada en la localización anatómica de las metástasis ganglionares. Tras una gastrectomía, la tasa de supervivencia a los cinco años disminuyó significativamente al aumetar la gravedad del N con ambas clasificaciones. Analizando la supervivencia por subgrupos entre el nuevo y viejo método de estadificación se observa que, dentro del mismo estadio, si se utiliza el nuevo método, la supervicencia es más homogénea. El análisis multivariante de factores prónosticos, incluyendo la nueva y la vieja estadificación ganglionar, demuestra que el grado de invasión y la nueva estadificación pN, constituyen los factores pronósticos más significativos. Nuestros hallazgos sugieren que la nueva estadificación ganglionar, basada en el número de ganglios linfáticos metastatizados, es no sólo un proceder fidedigno y objetivo para la estadificación ganglionar sino que también es un factor determinante en el pronóstico del cáncer gástrico. Por ello, aconsejamos su utilización.

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References

1. Maruyama, K.: The most important prognostic factors for gastric cancer patients. Scand. J. Gastroenterol. *22*:63, 1987
2. Hermanek, P., Sobin, L.H., editors: TNM Classification of Malignant Tumors (4th ed.). International Union Against Cancer (UICC). Berlin, Springer, 1987, pp. 43–46
3. Beahrs, O.H., Henson, D.E., Hutter, R.V.P., Kennedy, B.J., editors: Manual for Staging of Cancer (4th ed.). American Joint Committee on Cancer (AJCC). Philadelphia, Lippincott, 1992, pp. 63–67
4. Nishi, M., Omori, Y., Miwa, K., editors: Japanese Classification of Gastric Carcinoma (1st English ed.). Japanese Research Society for Gastric Cancer (JRSGC). Tokyo, Kanehara, 1995, pp. 6–11
5. Sobin, L.H., Wittekind, C.H., editors: TNM Classification of Malignant Tumors (5th ed.). International Union Against Cancer (UICC). New York, Wiley, 1997, pp. 59–62
6. Maruyama, K., Okabayashi, K., Kinoshita, T.: Progress in gastric cancer surgery and its limits of radicality. World J. Surg. *11*:418, 1987
7. Nakamura, K., Ueyama, T., Yao, T., Xuan, Z.X., Ambe, K., Adachi, Y.: Pathology and prognosis of gastric carcinoma: findings in 10,000 patients who underwent primary gastrectomy. Cancer *70*:1030, 1992
8. Roder, J.D., Bonenkamp, J.J., Craven, J., van de Velde, C.J.H., Sasako, M., Böttcher, K., Stein, H.J.: Lymphadenectomy for gastric cancer in clinical trials: update. World J. Surg. *19*:546, 1995
9. Hermanek, P.: pTNM and residual tumor classification: problems of assessment and prognostic significance. World J. Surg. *19*:184, 1995
10. Wagner, P.K., Ramaswamy, A., Rüchoff, J., Schmitz-Moormann, P., Rothmund, M.: Lymph node counts in the upper abdomen: anatomical basis for lymphadenectomy in gastric cancer. Br. J. Surg. *78*:825, 1991
11. Siewert, J.R., Böttcher, K., Roder, J.D., Busch, R., Hermanek, P., Meyer, H.J.: Prognostic relevance of systemic lymph node dissection in gastric carcinoma: German Gastric Carcinoma Study Group. Br. J. Surg. *80*:1015, 1993
12. Noh, S.H., Yoo, C.H., Kim, Y.I., Kim, C.B., Min, J.S., Lee, K.S.: Results after gastrectomy of 2603 patients with gastric cancer: analysis of survival rate and prognostic factor. J. Korean Surg. Soc. *55*:206 1998 (in Korean)
13. Maruyama, K., Gunven, P., Okabayashi, K., Sasako, M., Kinoshita, T.: Lymph node metastases of gastric cancer: general patterns in 1931 patients. Ann. Surg. *210*:596, 1989
14. Noguchi, Y., Imada, T., Matsumoto, A., Coit, D.G., Brennan, M.F.: Radical surgery for gastric cancer: a review of the Japanese experience. Cancer *64*:2053, 1989
15. Fisher, B., Bauer, M., Wickerham, D.L.: Relation of number of positive axillary nodes to the prognosis of patients with primary breast cancer: an NSABP update. Cancer *52*:1551, 1983
16. Spratt, J.S., Jr., Spjut, H.J.: Prevalence and prognosis of individual clinical and pathological variables associated with colorectal carcinoma. Cancer *20*:1976, 1967
17. Haruyama, K.: Quantitative statistical studies on lymph node metastasis of gastric carcinoma, with reference to its relationship with primary lesion and prognosis. J. Jpn. Surg. Soc. *82*:612, 1981
18. Shiu, M.H., Perrotti, M., Brennan, M.F.: Adenocarcinoma of the stomach: a multivariate analysis of clinical, pathologic and treatment factors. Hepatogastroenterology *36*:7, 1989
19. Msika, S., Chastang, C., Houry, S., Lacaine, F., Huguier, M.: Lymph node involvement as the only prognostic factor in curative resected gastric carcinoma: a multivariate analysis. World J. Surg. *13*:118, 1989
20. Jaene, J., Meyer, H.J., Maschek, H., Geerlings, H., Bruns, E., Pichlmayr, R.: Lymphadenectomy in gastric carcinoma: a prospective and prognostic study. Arch. Surg. *127*:290, 1992
21. Okusa, T., Nakane, Y., Boku, T., Takada, H., Yamamura, M., Hioki, K., Yamamoto, M.: Quantitative analysis of nodal involvement with respect to survival rate after curative gastrectomy for carcinoma. Surg. Gynecol. Obstet. *170*:488, 1990
22. Lee, W.J., Lee, P.H., Yue, S.C., Chang, K.C., Wei, T.C., Chen, K.M.: Lymph node metastasis in gastric cancer: significance of positive number. Oncology *52*:45, 1995
23. Wu, C.W., Hsieh, M.C., Lo, S.S., Tsay, S.H., Lui, W.Y., P'eng, F.K.: Relation of the number of positive lymph nodes to the prognosis of patients with primary gastric adenocarcinoma. Gut *38*:525, 1996
24. Isozaki, H., Okajima, K., Kawashima, Y., Yamada, S., Nakata, E., Nishimura, J.: Prognostic value of the number of metastatic lymph nodes in gastric cancer with radical surgery. J. Surg. Oncol. *53*:247, 1993
25. Makino, M., Moriwaki, S., Yonekawa, M., Oota, M., Kimura, O., Kaibara, N.: Prognostic significance of the number of metastatic lymph nodes in patients with gastric cancer. J. Surg. Oncol. *47*:12, 1991
26. Ichikura, T., Tomimatsu, S., Okusa, Y., Uefuji, K., Tamakuma, S.: Comparison of the prognostic significance between the number of metastatic lymph nodes and nodal stage based on their location in patients with gastric cancer. J. Clin. Oncol. *11*:1894, 1993
27. Roder, J.D., Böttcher, K., Busch, R., Wittekind, C., Hermanek, P., Siewert, J.R., for the German Gastric Cancer Study Group: Classification of regional lymph node metastasis from gastric cancer. Cancer *82*:621, 1998

Invited Commentary

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For gastric carcinoma resected for cure (R0), lymphatic spread is one of the most relevant prognostic factors. Although the preoperative imaging technique for the assessment of the T category have markedly improved in recent years, the preoperative determination of lymph node metastasis is still unreliable. Therefore the classification of lymphatic spread on the resected gastric specimen is decisive when estimating the prognosis of the individual patient and analyzing international treatment results.

Chang Hak Yoo and colleages have compared the prognostic significance of nodal staging between the old (4th edition) and new (5th edition) UICC TNM classification for gastric carcinoma. They analyzed 2108 patients after an R0 resection for gastric cancer. Patients with gastric remnent cancer, patients with distant lymph nodes metastasis, patients with a D1 lymph node dissection, and patients with fewer than 15 lymph nodes in the resected specimen were excluded from the study.

The authors found that the new nodal staging (UICC/AJCC 1997) based on the number of metastatic lymph nodes was closely correlated with the depth of cancer invasion and with the old nodal staging (UICC/AJCC 1992) based on the anatomic site of the metastatic nodes with statistical significance. In addition, the new lymph node classification showed more homogeneous survival at the same stage than the old one.

In their patient population the authors have treated more than 300 patients per year. These large numbers are a prerequisite for large studies such as this, especially when a standardized treatment protocol and a standardized analysis of a resected specimen exists. This is surely true for the patient population reported here.

A reliable, reproducible description of the pattern of lymphatic spread in gastric carcinoma was first provided by the Japanese Research Society for Gastric Cancer. The current Japanese classification of lymphatic spread describes four groups (N1–N4)

based on the anatomic localization of the lymph nodes in relation to the localization of the primary tumor. There is currently no doubt that these basic studies of the lymphatic spread of gastric carcinoma and the techniques of systematic lymphadenectomy based on them resulted in marked improvement of the prognosis for the patient with gastric carcinoma. However, due to discrepancies in the classification, particularly regarding lymphatic spread, comparable worldwide data on the results of the management of gastric carcinoma are not available.

The 1992 UICC and AJCC classification of regional lymph node metastasis is based on the site of the metastasis in relation to the primary tumor. The surgical technique of en bloc resection for gastric carcinoma with shrinkage of the specimen due to fixation in formalin can make it impossible for the pathologist to discriminate pN1 and pN2. The matter is further complicated by the fact that the individual lymph node stations in Japan are classified by the surgeon and sent to the pathologist in separate, individually labeled containers, whereas in the Western world the anatomic localization of lymph node metastasis at many institutions is determined by the pathologist based on the formalin-fixed en bloc resected specimen. To overcome these difficulties in the classification of regional lymph node metastasis, in 1997 the UICC and AJCC changed the N classification. This classification is now based on the number of involved lymph nodes only, and their localization is no longer taken into account. The prognostic significance of the number of lymph nodes involved was investigated in several studies. These studies, however, showed a marked variation in the cutoff points for the classification of lymph node metastasis. These discrepancies can be explained by small patient populations, differences in the selection of patients, differences in the definitions of patients with regional lymph node metastasis or distant metastasis, and differences in the histopathologic methods of the lymph node examination.

The current study is based on patients with uniformly diagnosed disease, standardized surgical resection technique, standardized histopathologic evaluation of the specimens, and uniform description of the anatomic extent of lymph node metastasis. The data analysis was limited to patients who had an R0 resection and those who had lymph node metastasis only at stations 1 to 11; patients with more distant lymph node metastasis were not included. This study convincingly underlines the reliability of the new UICC/AJCC TNM classification for assessing gastric cancer.