Proposed Modification of Nodal Staging as an Alternative to the Seventh Edition of the American Joint Committee on Cancer Tumor-Node-Metastasis Staging System Improves the Prognostic Prediction in the Resected Esophageal Squamous-Cell Carcinoma

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Introduction: The 7th American Joint Committee on Cancer (AJCC) tumor-node-metastasis staging system for esophageal cancer defined N classification based on the number of metastatic lymph nodes (LNs). However, this classification might neglect the extent of LNs metastasis. This study aimed to revise N classification based on the extent of LNs metastasis and propose a modification to the current AJCC staging system for better representing the prognostic characteristics of Chinese esophageal squamous-cell carcinoma (ESCC).

Methods: We retrospectively reviewed 1993 ESCC patients who underwent curative resection. The proposed N categories based on the number of LNs metastasis stations were compared with the current staging system by univariate and multivariate Cox regression analyses. Homogeneity, discriminatory ability, and monotonicity of gradients of two staging systems were compared using likelihood ratio χ^2 statistics and Akaike information criterion calculations.

Results: The survival differences were not significant for N2 versus N3 category ($p = 0.231$) and stages IIIB versus IIIC ($p = 0.713$) based on the 7th AJCC staging system. When the modified staging system was adopted, the survival difference for N2 versus N3 and IIIB versus IIIC could be well discriminated. Statistical analysis showed that the modified staging system had higher likelihood ratio χ^2 scores and smaller Akaike information criterion values than the 7th AJCC staging system, which represented the optimum prognostic stratification.

Conclusions: The modified staging system with the revised N categories based on the number of LNs metastasis stations better predicts the survival of Chinese ESCC population than the 7th AJCC staging system. Further studies are required to confirm this result.

Key Words: Esophageal squamous-cell carcinoma, Lymph nodes metastasis stations, Prognosis, 7th American Joint Committee on Cancer staging system.

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Cancer staging system is commonly used to unify clinicopathological classification, guide treatment decision making, evaluate prognosis, and compare treatment results from different institutions.[1] Many studies have previously suggested that the number of metastatic lymph nodes (LNs) is the most important independent prognostic factor in esophageal cancer.[2–12] The 7th version of the American Joint Committee on Cancer (AJCC) staging system for esophageal cancer, in which Nodal (N) categories are based on the number of metastatic LNs, is more reliable than before.[13–15] However, this classification might have neglected the extent of LNs metastasis, an even more important factor in predicting prognosis.[16] Moreover, the exact number of metastatic LNs is sometimes difficult to evaluate, when an enlarged LN is actually the coalescence of multiple positive LNs or when a single enlarged LN becomes broken during surgical dissection. Moreover, it was reported by several studies that the 7th edition of the AJCC staging system cannot satisfactorily distinguish the prognosis among different risk groups of patients with resected esophageal carcinoma, especially between N2 and N3 and between IIIB and IIIC.[16,17]

The current AJCC staging system for esophageal cancer used global data from 4627 patients.[1] However, esophageal squamous-cell carcinoma (ESCC) patients only constitute 39.6% of the database (1834 of 4627) used to elaborate the 7th AJCC staging system for esophageal cancer.[18] The most common pathological type of esophageal cancer in China is squamous-cell carcinoma type, which accounts for more than 90% of cases.[19] We believe that more data from Chinese patients are essential to validate the N categories in the current staging system for ESCC.

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In this retrospective study, we present data from a large cohorts of Chinese patients in a single institution and aimed to revise N staging based on the extent of LNs metastasis and propose a modification to the current AJCC staging system in order to better represent the prognostic characteristics of ESCC after radical esophagectomy in Chinese population.

METHODS

Patients Selection

This study was undertaken according to the Declaration of Helsinki at the Third Affiliated Hospital of Soochow University with the approval of the ethics committee at our institution, which waived the requirement for written informed consent of individual patients owing to the retrospective nature of this study. None of stage IV patients according to the 7th edition tumor-node-metastasis (TNM) system was included because all the patients enrolled in this study underwent radical resection and had no distant metastasis. A total of 1993 resectable ESCC patients who underwent radical esophagectomy at our institution were retrospectively reviewed from January 2002 to December 2011. Among 1993 patients, 672 patients with either preoperative or postoperative radiotherapy and/or chemotherapy were excluded to eliminate the influence of adjuvant and neoadjuvant treatment. Then, 339 patients with less than 12 LN examined or supraclavicular LN involved were also excluded, as they were regarded as nonregional LN metastasis or insufficient LN dissection according to the suggestion of AJCC.[20] In the remaining 982 ESCC patients, 65 patients were excluded because of incomplete resection and/or perioperative death and/or lost to follow-up. Finally, 917 patients were included into this study. Clinical data, including age, gender, tumor location, staging, pathology, and survival outcomes, were collected. Description of the LNs (number of involved LNs and LNs metastatic station) was also recorded.

Surgery

All patients who were conformed to be resectable ESCC without distant metastasis by clinical and experimental examination received radical surgical resection of a transthoracic en-bloc esophagectomy with mediastinal and abdominal two-field lymphadenectomies. Mediastinal lymphadenectomies were performed to include subcarinal, left and right bronchial, lower posterior mediastinum, pulmonary ligament, and paraesophageal and thoracic duct nodes. Abdominal lymphadenectomies were performed to include the paracardial, lesser curvature, left gastric, common hepatic, celiac, and splenic nodes. The paratracheal and recurrent laryngeal nerve LNs were also dissected. Cervical lymphadenectomy was only performed in case of suspicious cervical lymphadenopathy. Each resected node group was labeled by the operator.

Staging

Tumor staging was performed according to the 7th AJCC staging system for ESCC.[20] According to Casson's LN drainage map, LN metastasis station (LMS) was grouped and shown in Table 1.[21] Four revised N categories (r-N: r-N0, 0 station; r-N1, 1 station; r-N2, 2 stations; r-N3, more than 2 stations) were classified by the number of LMS in this study. To compare the 7th edition AJCC TNM staging system, a modified TNM staging system with the revised N category based on the number of LMS was proposed as seven prognostically homogeneous classes of patients just as the 7th AJCC staging system (IA; IB; IIA; IIB; IIIA; IIIB; IIIC).

TABLE 1. The Station and Name of Regional LN Drainage for Esophageal Cancer

Station[a]	Name	Station	Name
2R	Right upper paratracheal nodes	9	Pulmonary ligament nodes
2L	Left upper paratracheal nodes	10R	Right tracheobronchial nodes
3P	Posterior mediastinal nodes	10L	Left tracheobronchial nodes
4R	Right lower paratracheal nodes	15	Diaphragmatic nodes
4L	Left lower paratracheal nodes	16	Paracardial nodes
5	Aortopulmonary nodes	17	Left gastric nodes
6	Anterior mediastinal nodes	18	Common hepatic nodes
7	Subcarinal nodes	19	Splenic nodes
8M	Middle paraesophageal LNs	20	Celiac node

[a]Supraclavicular lymph node was not included because of being regarded as nonregional LN metastasis.
LN, lymph node.

Follow-Up

All patients were followed up every 3 months for the first 2 years, every 6-month intervals until 5 years, and then annually. All patients underwent clinical, laboratory, imaging, and endoscopy examination for assessing recurrence or metastasis. The last follow-up of survivors was conducted at the end of July 2014. All patients were followed up by phone calls and regular mail. The observation time in this study was the interval from the date of surgical resection to death or last follow-up. Surviving patients were censored on the day of the last contact.

Statistical Analysis

Optimal cutoff values for the number of LMS (which were 0, 1, and 2 station in our series) were determined using X-tile software (http://www.tissuearray.org/rimmlab).[22] All statistical analyses were performed using SPSS 13.0 software (SPSS, Inc., Chicago, IL). Survival was calculated using the Kaplan–Meier method, and the log-rank test was used to assess differences in survival between groups. In multivariate analysis, forward stepwise regression analysis was carried out with a Cox proportional hazards model. The likelihood ratio χ^2 test related to the Cox regression model was used for measuring the homogeneity. To compare prognostic systems with different staging system, the Akaike information criterion (AIC) value was applied to measure the discriminatory ability of each prognostic model.[23] AIC was defined as follows: AIC = –2 log maximum likelihood + 2 × (the number of parameters in the model). A smaller AIC value indicates a better model for predicting outcome. p Value less than 0.05 from the two-sided test was considered to be statistically significant.

RESULTS

Patients and Clinicopathological Characteristics

Among the 917 patients enrolled in this study, 690 (75.2%) were male patients, and 227 (24.8%) were female patients. The median age of the patients at surgery was 60 years (range, 37–85 yr). Four hundred thirty-four patients (47.3%) had LN metastasis. Most tumors originated from the mid esophagus (65.6%). The overall 5-year survival rate for all patients was 44.5%, and 406 patients were alive when the follow-up was completed. Detailed patients characteristics and pathologic variables are summarized in Table 2.

Survival Analyses

In univariate analysis, age, gender, tumor differentiation, pT category, pN category, and r-pN (based on the number of LMS) category were found to be significant prognostic factors (Table 2). In our study, the pN and r-pN classifications were highly correlated. Therefore, two separate multivariate models, one with pN and the other with r-pN, were run to avoid problems with the presence of multicollinearity. In multivariate analysis, pT category, pN category, and r-pN were independent prognostic factors (Table 3).

The 5-year survival rates according to the different pN and r-pN categories were shown in Figure 1. The Kaplan–Meier plots showed a good discriminatory ability in both pN and r-pN categories, except for pN2 versus pN3 in N category ($p = 0.231$) (Fig. 1*A* and *B*). The 5-year survival rates of pN0, pN1, pN2, and pN3 patients were 61.0%, 31.6%, 17.3%, and 9.5%, respectively ($p < 0.001$). The 5-year survival rates of r-pN0, r-pN1, r-pN2, and r-pN3 patients were 61.0%, 33.5%, 21.9%, and 8.3%, respectively ($p < 0.001$). Pair comparison of adjacent subgroups for LN status showed improvement in separation of r-pN2 versus r-pN3 by the revised staging ($p < 0.001$), compared with LN status by the current 7th N-staging classification.

By analyzing all the seven substages in the 7th AJCC staging system, there are significant survival differences among seven groups ($p < 0.001$; Fig. 1*C*). However, we found that stages IIIB and IIIC had similar survival curves between ($p = 0.713$; Fig. 1*C*). In the subsequent analysis, we modified the current staging system using our redefined N category without any other alteration to the 7th AJCC staging system. Overall survival among seven subgroups is significantly different ($p < 0.001$), and the survival curves between stages IIIB and IIIC in the modified AJCC staging system could be easily distinguished ($p = 0.011$; Fig. 1*D*).

To evaluate the utility of the N categories for predicting survival in different pathologic T categories, we performed stratified analysis in the T2 and T3 subgroups based on the 7th AJCC TNM staging system in the entire cohort of patients. We only included the cases with T2 and T3 disease for subgroup analysis because the number of Tis-T1 ($n = 43$) and T4 ($n = 12$) subgroups with LNs involved was too small to be further studied in stratified analysis. In the T2 subgroup, there were no differences in survival between patients with pathological N2 and N3 stages ($p = 0.301$; Fig. 2*A*). A similar result was also observed in the T3 subgroup ($p = 0.477$; Fig. 2*B*).

TABLE 2. Patient Demographics and Results of Univariate Analysis for Overall Survival ($n = 917$)

	n (%)	Median Survival (mo)	5-Yr Survival (%)	*p*
Age, yr				0.029
≤60	462 (50.4%)	50	46.7	
>60	455 (49.6%)	34	42.4	
Gender				0.027
Male	690 (75.2%)	39.2	42.6	
Female	227 (24.8%)	70	50.4	
Location				0.750
Proximal esophagus	59 (6.4%)	34	48.9	
Mid esophagus	601 (65.6%)	40	43.1	
Distal esophagus	257 (28%)	50	46.8	
Differentiation				<0.001
Well	48 (5.2%)	Not reached	80.5	
Moderately	451 (49.2%)	58.4	49.9	
Poorly	418 (45.6%)	29	34.7	
T stage				<0.001
Tis-T1	210 (22.9%)	Not reached	73.1	
T2	235 (25.6%)	82.7	52.3	
T3	460 (50.2%)	25	28.5	
T4	12 (1.3%)	13	16.7	
N stage				<0.001
pN0	483 (52.7%)	110	61.0	
pN1	270 (29.4%)	29	31.6	
pN2	122 (13.3%)	17	17.3	
pN3	42 (4.6%)	13	9.5	
Revised N stage				<0.001
r-pN0	483 (52.7%)	110	61.0	
r-pN1	236 (25.7%)	32	33.5	
r-pN2	107 (11.7%)	22	21.9	
r-pN3	91 (9.9%)	13	8.3	
7th AJCC staging				<0.001
0 + IA	40 (4.4%)	Not reached	92.4	
IB	130 (14.2%)	Not reached	76.1	
IIA	82 (8.9%)	75	55.4	
IIB	330 (36%)	52	47.4	
IIIA	191 (20.8%)	24	26.3	
IIIB	92 (10%)	16	13.9	
IIIC	52 (5.7%)	14	11.2	
Modified staging				<0.001
0 + IA	40 (4.4%)	Not reached	92.4	
IB	130 (14.2%)	Not reached	76.1	
IIA	82 (8.9%)	75	55.4	
IIB	319 (34.8%)	55	48.4	
IIIA	171 (18.6%)	26	27.7	
IIIB	75 (8.2%)	21	18.9	
IIIC	100 (10.9%)	13	8.3	

AJCC, American Joint Committee on Cancer.

To evaluate the utility of the revised N categories in predicting survival, similar subgroups analyses were conducted based on the modified AJCC staging system with the revised

TABLE 3. Cox Multivariate Regression Analyses for the Influence of Clinicopathological Characteristics on Overall Survival in Patients with ESCC (n = 917)

Variables	Hazard Ratio	p	95% CI
Multivariate model with 7th AJCC			
Age	1.273	0.007	1.067–1.517
Gender	1.126	0.283	0.906–1.400
Location (baseline, proximal esophagus)		0.376	
Mid esophagus	0.825	0.307	0.570–1.194
Distal esophagus	0.761	0.173	0.513–1.127
Differentiation (baseline, well)		0.004	
Moderately	1.918	0.060	0.973–3.780
Poorly	2.411	0.011	1.222–4.758
7th AJCC T (baseline, Tis-T1)		<0.001	
T2	1.613	0.003	1.171–2.221
T3	2.564	<0.001	1.920–3.424
T4	3.722	<0.001	1.872–7.401
7th AJCC N (baseline, N0)		<0.001	
pN1	1.656	<0.001	1.338–2.050
pN2	2.678	<0.001	2.070–3.465
pN3	3.832	<0.001	2.673–5.494
Multivariate model with modified staging system			
Age	1.269	0.008	1.065–1.511
Gender	1.113	0.336	0.895–1.384
Location (baseline, proximal esophagus)		0.461	
Mid esophagus	0.818	0.284	0.565–1.182
Distal esophagus	0.779	0.214	0.526–1.154
Differentiation (baseline, well)		0.005	
Moderately	1.923	0.059	0.975–3.794
Poorly	2.388	0.012	1.209–4.716
7th AJCC T (baseline, T1)		<0.001	
T2	1.572	0.006	1.141–2.168
T3	2.476	<0.001	1.850–3.315
T4	3.908	<0.001	1.964–7.777
Revised N (baseline, N0)		<0.001	
r-pN1	1.606	<0.001	1.286–2.005
r-pN2	2.235	<0.001	1.702–2.936
r-pN3	3.604	<0.001	2.734–4.749

ESCC, esophageal squamous-cell carcinoma; CI, confidence interval; AJCC, American Joint Committee on Cancer.

N categories. In the T2 subgroup, survival could be distinguished between patients with r-pN2 and r-pN3 in the entire cohort of patients (p = 0.04; Fig. 3*A*). The survival between patients with r-pN2 and r-pN3 stages can also be distinguished in the T3 subgroup (p = 0.018; Fig. 3*B*).

The proportion of patients who migrated between stages when the modified AJCC staging system was applied was summarized in Table 4. There were no changes observed in ESCC stage 0-IA, IB, and IIA, but significant changes were observed in ESCC stage IIB and III. From the 7th AJCC staging system to the modified AJCC staging system, 31.3% of the patients with LNs metastasis (136 of 434) in the entire cohort change their AJCC stage, with major changes including IIIA migrating to IIIB and IIIB migrating to IIIC.

The performance between the 7th AJCC and the modified staging systems, as well as between the 7th N staging and the revised N staging defined according to the number of LMS, was assessed by likelihood ratio χ^2 and the AIC tests (Table 5). Compared with the 7th AJCC staging system, the modified staging system had better homogeneity (higher likelihood ratio χ^2 score, 248.5 versus 225). Furthermore, in our study, the modified staging system had a smaller AIC value (6307.3 versus 6322.4), representing an optimum prognostic stratification.

DISCUSSION

The reasonable staging system should abide by the following basic principles. First, subgroups with the different T, N, and M combinations in the same stage should have the similar survival (the uniform of risk). Second, there should be a different survival rate between each stage (the difference of risk). Third, there is higher predictive value for survival according to the staging system (the predictability of survival).

LN metastasis is the most important independent prognostic factor affecting long-term survival in patients with esophageal cancer after curative resection. Some studies, which attempted to validate the 7th nodal staging, reported that this nodal classification enabled risk stratification for overall survival after surgery and was an independent predictor of survival in esophageal cancer.[14,17] Despite the current 7th AJCC staging for esophageal cancer provides a great improvement over previous editions with the N category by stratifying patients based on the different numbers of LNs involved, several studies have found no significant differences in prognosis between pN2 and pN3 patients. Chen et al.[24] retrospectively reviewed 2011 Chinese ESCC patients who underwent surgical resection alone and reported that the survival differences were not significant between pN2 and pN3 categories. Yamasaki et al.[15] also investigated the significance of 7th edition of the Union for International Cancer Control-TNM staging system on differentiating the survival of 665 ESCC patients after esophagectomy and found that there were no significant differences in survival between patients with pN2 and pN3. Another study by Xu et al.[16] reported that the N category based on the 7th AJCC staging system was not satisfactory because of similar prognosis in ESCC between patients with pN2 and pN3.

Moreover, Hsu et al.[13] and other investigators have demonstrated that not only pN2 versus pN3 but also stage IIIB versus IIIC showed no significant difference in the survival of patients with ESCC.[25] In this study, we also showed that no significant differences was observed in the survival between pN2 and pN3 patients according to 7th edition AJCC staging system (p = 0.231). Similar result was also found in the survival between IIIB and IIIC patients according to 7th AJCC staging system (p = 0.713). All of these data were assembled from Asian patients with ESCC. The reasons for the difference in survival between ESCC patients from Asia and predominantly adenocarcinoma patients from the Worldwide Esophageal Cancer Collaboration need to be further investigated.

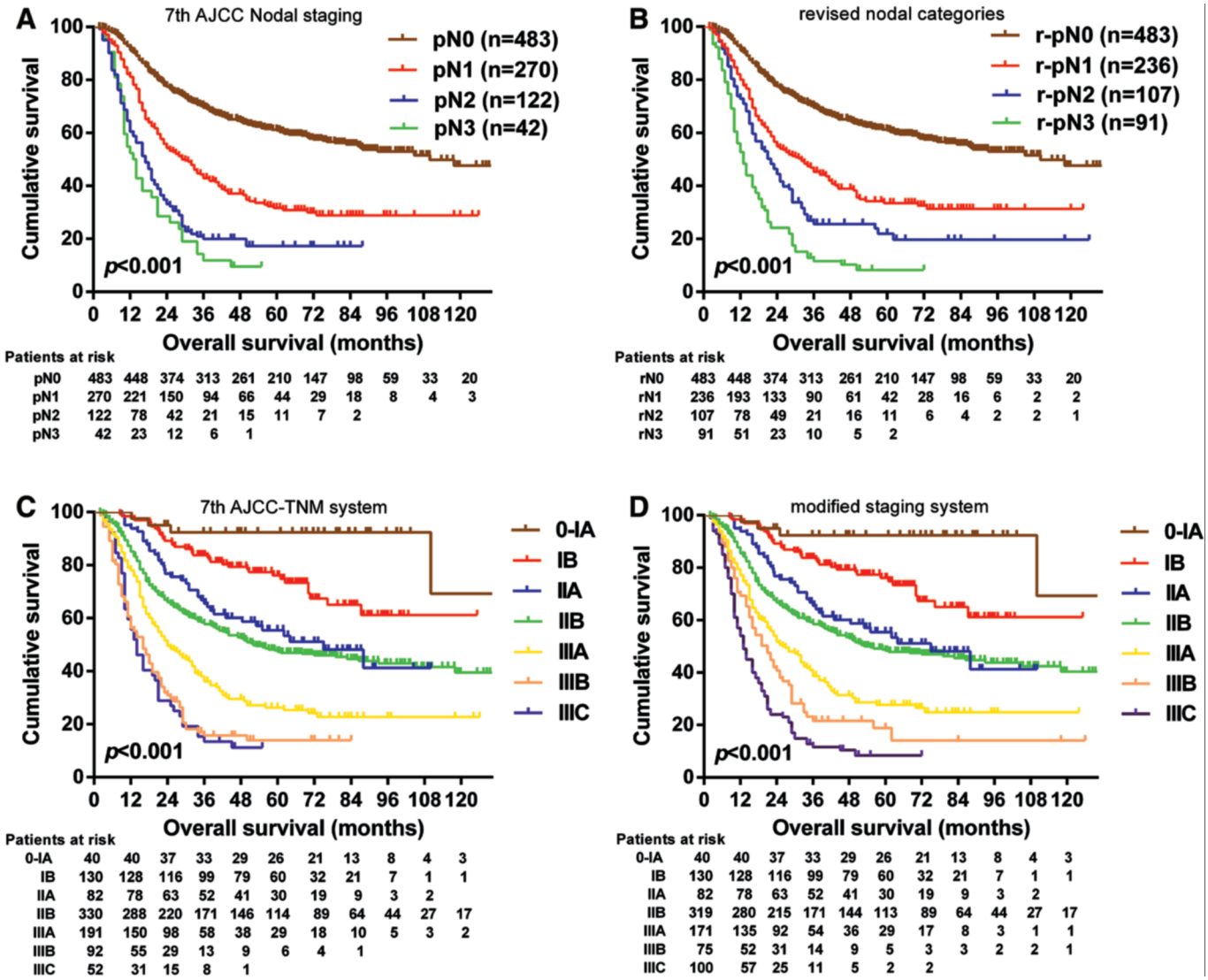

FIGURE 1. Kaplan–Meier survival curves for patients stratified by according to the 7th American Joint Committee on Cancer (AJCC) nodal categories (*A*), revised N categories based on the number of lymph node metastasis station (*B*), the 7th AJCC-TNM staging system (*C*), and modified staging system with the revised N categories based on the number of lymph node metastasis station (*D*). TNM, tumor-node-metastasis.

N category according to the 7th edition of AJCC staging system only considers the number of LN metastasis and does not take into account the extent of LN metastasis. Logically, given the same number of involved LNs, the prognosis might differ between the patients with metastatic LNs clustered in one anatomic LN station and those with metastatic LNs distributed to more than two LN stations. Therefore, this study was carried out to evaluate the performance of new N category and the modified AJCC staging system based on the number of LMS. The revised N category covered both extent-dependent staging and numerically based classification. To the best of our knowledge, this is the first study to assess the prognostic difference value of the number of LMS in ESCC patients by making comparisons with 7th N staging. Furthermore, our results demonstrated that N category based on the number of LMS was an independent prognostic predictor for long-term survival in Chinese patients with ESCC and could make better stratification for the ESCC patients with different prognosis compared with the 7th nodal staging. Because the pathologic T category is a well-established independent prognostic factor, we evaluated the survival differences between groups with different nodal stage for different T classification. Significant differences in survival were observed in pT2 and pT3 subgroups between patients with the different revised N categories, whereas with the N categories based on the 7th AJCC staging system, no significant difference between N2 and N3 was found in pT2 and pT3 subgroups. With the revised N categories applied to modify the existing AJCC staging system, we found that survival curves stratified according to the modified staging system did not overlap, which is in contrast to the curves of the 7th AJCC staging system (i.e., stage IIIB and IIIC). Furthermore, comparison of the current nodal

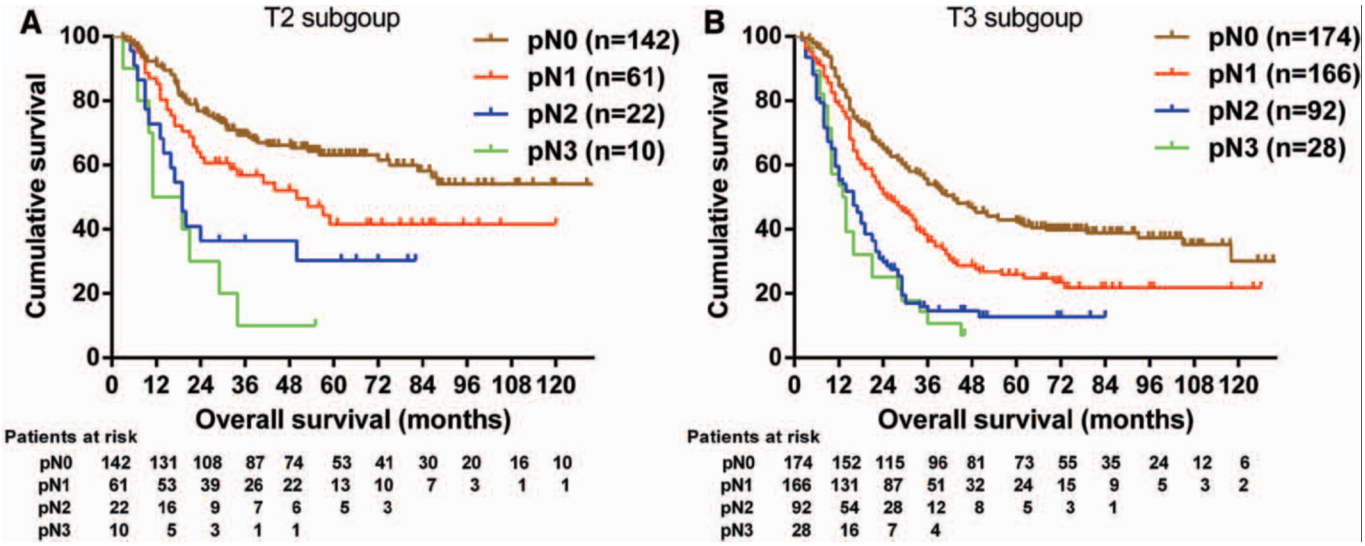

FIGURE 2. *A,* Survival curves for T2 patients stratified by the 7th American Joint Committee on Cancer (AJCC) nodal categories ($n = 235$; among four categories, $p < 0.001$; pN2 versus pN3, $p = 0.301$). *B,* Survival curves for T3 patients stratified by 7th AJCC nodal categories ($n = 460$; among four categories, $p < 0.001$; pN2 versus pN3, $p = 0.477$).

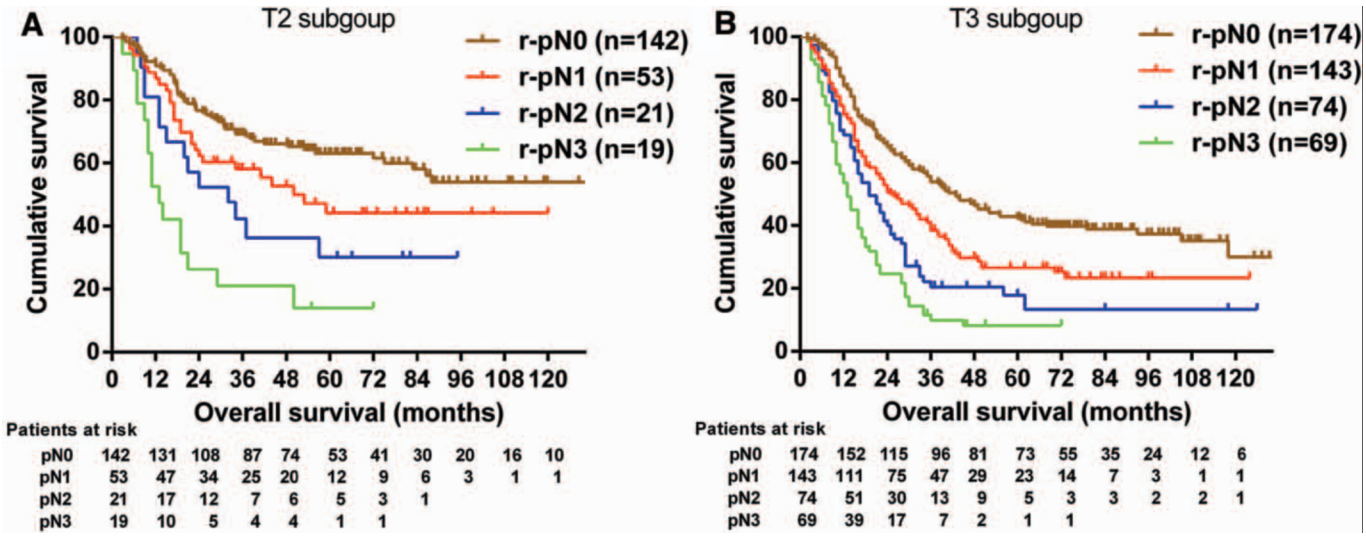

FIGURE 3. *A,* Survival curves for T2 patients stratified by the revised nodal categories based on the number of lymph node metastasis station ($n = 235$; among four categories, $p < 0.001$; r-pN2 versus r-pN3, $p = 0.04$). *B,* Survival curves for T3 patients stratified by the revised nodal categories ($n = 460$; among four categories, $p < 0.001$; r-pN2 versus r-pN3, $p = 0.018$).

staging to the proposed staging system revealed that the modified staging system has better performance than the 7th AJCC staging system in terms of homogeneity, discriminatory, and prognostic stratification because of higher likelihood ratio χ^2 and lower AIC in Cox regression models.

Previous studies have redefined N categories based on the number of LNs metastasis fields (LMF) and evaluated the significance of LMF number on the prognosis of esophageal cancer.[16,26,27] In these studies, LMF were defined as neck, chest, and abdomen field. Both these studies showed that further stratification according to the number of LMF can effectively discriminate between LN-positive patients. However, the performance of the modified staging systems based on the revised N categories was not evaluated, which may be due to the inhomogeneity of gradients in patients stratified by the number of LMF (i.e., few patients grouped to the three field). Despite the abovementioned limitation, the results in these studies hinted to us that the extent of LN metastasis, rather than the number alone, might be a better nodal staging method. In this study, we demonstrated that the modified staging system with the revised N categories based on the number of LMS stratified the prognosis of ESCC patients more accurately than the 7th AJCC staging system.

Despite of the advantages of revised N stage applied in the prediction of survival, we recognize that there are some limitations in this study that have to be considered in the interpretation of these results. First, the relatively small patient numbers

TABLE 4. Cross Table of Staging for 917 ESCC Patients According to the 7th AJCC-TNM Staging System and the Modified Staging System with the Revised N Category Based on the Number of LMS

		Revised TNM Staging						
		0-IA	IB	IIA	IIB	IIIA	IIIB	IIIC
7th AJCC TNM staging	0-IA	40	0	0	0	0	0	0
	IB	0	130	0	0	0	0	0
	IIA	0	0	82	0	0	0	0
	IIB	0	0	0	311	19	0	0
	IIIA	0	0	0	7	136	35	13
	IIIB	0	0	0	0	13	37	42
	IIIC	0	0	0	1	3	3	45

ESCC, esophageal squamous-cell carcinoma; AJCC, American Joint Committee on Cancer; TNM, tumor-node-metastasis; LMS, lymph node metastasis station.

TABLE 5. Comparison of the Performance of the 7th AJCC Staging System and the Modified Staging System with the Revised N Category Based on the Number of LMS

Model	Figure	Subgroups	LR χ^2	AIC Value[a]
AJCC 7th edition N staging	Figure 1*A*	pN0, pN1, pN2, pN3	184.5	6376.8
Revised N staging	Figure 1*B*	r-pN0, r-pN1, r-pN2, r-pN3	198.5	6368.4
AJCC 7th edition TNM	Figure 1*C*	0-IA, IB, IIA, IIB, IIIA, IIIB, IIIC	225.0	6322.4
Revised AJCC 7th edition TNM	Figure 1*D*	0-IA, IB, IIA, IIB, IIIA, IIIB, IIIC	248.5	6307.3

[a]A lower Akaike information criterion value represents a better discriminatory model.
AJCC, American Joint Committee on Cancer; LMS, lymph node metastasis station; AIC, Akaike information criteria; LR, likelihood ratio; TNM, tumor-node-metastasis.

in some subgroups, especially in the T2 subgroup, may limit statistical power. Second limitation is the retrospective nature of this study. A multicenter collaborative study with a large cohort would be required to substantiate the result. However, it is worth to mention that the patients enrolled in this study from single institution underwent highly uniform surgical procedures, pathological examination, and follow-up throughout the whole study period. Third, most of patients in this underwent mediastinal and abdominal two-field lymphadenectomy without cervical lymphadenectomy. Three-field lymphadenectomy could provide more accurate pathologic N stage. However, several studies evaluated the prognostic role of three-field lymphadenectomy for ESCC patients and suggested that the addition of cervical nodal dissection did not provide a survival benefit.[28–30] Moreover, extensive lymphadenectomy is not free of additional risks of complications and may reduce postoperative recover and quality of life.[31,32] Therefore, more extensive lymphadenectomy should be balanced against the risk of postoperative complications. Finally, as this study is focused on ESCC, our proposed modification for AJCC staging system cannot be directly applied in esophageal adenocarcinoma. In the future, the staging system needs to be classified separately according to the histopathological cell type, for example, ESCC and esophageal adenocarcinoma.

CONCLUSIONS

In conclusion, we suggest that N categories of ESCC based on the number of LMS, considering both the number and the extent of LNs metastasis, could provide a better basis for distinguishing subgroups of patients with different prognosis after radical esophagectomy compared with 7th nodal staging based on the number of metastatic LNs alone. Further validation on a multicenter, large data set is warranted, especially when defining the next edition of the AJCC staging system for esophageal cancer.

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