Original Article
Prognostic significance of the metastatic lymph node ratio in gastric cancer patients after radical resection

Shugang Yang[1*], Guangwei Zhu[1,2,3*], Hongyan Rao[1*], Yongjian Huang[1], Wei Zheng[1], Jin Hua[1], Jianxin Ye[1,2,3]

[1]Department of Gastrointestinal Surgery 2 Section, The First Hospital Affiliated to Fujian Medical University, Fuzhou, Fujian, China; [2]Key Laboratory of Ministry of Education for Gastrointestinal Cancer, Fujian Medical University, Fuzhou, Fujian, China; [3]Fujian Key Laboratory of Tumor Microbiology, Fujian Medical University, Fuzhou, Fujian, China. *Equal contributors.

Abstract: Objective: Our study aims to investigate the prognostic significance of metastatic lymph nodes ratio (MLR) in gastric cancer patients undergoing radical resection. Methods: 477 patients who were diagnosed with gastric adenocarcinoma with more than 15 lymph nodes dissected by postoperative pathology, undergoing radical gastrectomy were retrospectively analyzed during January 2010 to December 2011. And the clinicopathologic parameters were analyzed to investigate the relationship between the MLR staging and pN staging in assessing the prognosis of gastric cancer patients. Result: The median follow-up time is 53 months, and the overall survival time is 45.5 months on average. The estimated overall 1-year, 3-year and 5-year survival rates were 89.94%, 64.0% and 52.1% respectively. Spearman correlation analysis showed that MLR did not correlate with the inspected number of lymph nodes (P=0.657), whereas pN did (P=0.001). Univariate analysis and Cox multivariate stepwise regression analysis showed that MLR stage, histological type, tumor sites, vascular cancer embolus, lymphatic vessel invasion, pathological stage and tumor size were independent prognostic factors (P < 0.05), while pN classification, invasion depth, differentiation degree, nerve invasion, gross type were not significantly independent prognostic parameters (P > 0.05). In subgroup analysis, the MLR stage showed more homogenous survival than pN classification in pN3 stage (P=0.002), meanwhile, the pN classification showed more homogenous survival than MLR stage in MLR1 stage (P=0.000). ROC curves analysis displayed MLR was consistent with pN on evaluating the diagnostic value of prognosis in gastric cancer patients, whether staging or not (P > 0.05). Conclusions: MLR stage can be regarded as an important supplement to pN category, and the combination of MLR and pN stage will greatly improve gastric lymph stage system.

Keywords: Gastric cancer, metastatic lymph node ratio, metastatic lymph node number, prognosis

Introduction

Gastric cancer is one of common carcinoma of digestive system, with a strong heterogeneity and a poor prognosis. It has a high incidence of the fourth malignancy and a mortality of the second cancer-related disease in the world [1, 2]. It is estimated that approximately 400,000 new cases of gastric carcinomas patients occurred in China accounting for 42% of the world. Gastric cancer has become the third leading cause of death in cancer patients with 300,000 deaths per year in China [3]. Despite new therapeutic approaches emerging continuously, the 5-year survival rate of gastric cancer still has not been improved significantly.

Accurate evaluation of the pathological staging is of paramount importance in judging prognosis and instructing treatment. Currently, there are three main staging systems of gastric cancer in the worldwide, namely the Japanese treatment guideline of gastric carcinoma (version 14) proposed by the Japanese Gastric Cancer Association (JGCA), the tumor, node, metastasis (TNM) classification (version 7) proposed by the International Union for Cancer Control (UICC)/American Joint Committee on Cancer (AJCC) and tumor, Metastasis Lymph node ratio, metastasis (TRM) staging system.

As the most important part of the gastric carcinoma staging system, lymph node staging was

both the focus and controversy of the staging system. It has not been recognized on a universal standard about the optimal metastatic lymph node status assessment in the world.

Although lymph node metastasis is an important prognostic factor in gastric cancer patients with radical resection [4], there remains a controversy on the classification of the metastasis lymph nodes in gastric cancer until the UICC/AJCC released the seventh edition of TNM staging [5]. Then JGCA released the 14th edition of the gastric cancer treatment statute, which made drastic changes in lymph node staging which switched to a new classification based on the number of metastatic lymph nodes (pN classification), and it give up the original classification which was based upon the anatomical location or group of positive nodes [6]. At this point, the two staging systems above come to an agreement on lymph node staging, taking pN as the criteria of lymph node staging.

However, the seventh TNM staging system does not make a specific provision of the number of regional lymph node excision. It only requires that ≥ 15 lymph nodes were detected. If the scope and depth of the radical resection are expanded intraoperatively, more metastasis lymph nodes could detect, which may result in stage migration. In order to ensure the accuracy of the lymph node staging, previous reports suggested that for pN0 classification the number of detected lymph node can be reduced from 15 to 10, for pN1-3 classification, it should be examined at least 20 lymph nodes [7]. And the lymph node staging is more desirable if 30 or more nodes were examined. Some researches have demonstrated that for D1 lymphadenectomy, insufficient lymph node cleaning may result in stage migration, and the calculated incidence of this migration can be up to 10%-15% [8]. Bouvier, AM et al. [9] found that the number of examined lymph nodes is variable which independently influenced the prognosis of TNM Stage I or II gastric carcinoma, and strongly suggests that TNM staging is unreliable, especially for fewer than 10 nodes detection, and the number of examined lymph nodes should be taken as a stratification criterion in clinical trials and an adjustment variable in survival studies. Due to the stage migration of the pN classification, how to assess the metastasis lymph node status precisely and how to overcome the problem of pN in stage migration reasonably demand prompt solution. Therefore scholars have conducted following explorations, but the result is consistent.

In 2002, Inoue K. et al. [10] first proposed the MLR to predict the prognosis of gastric carcinoma, which is the ratio between the number of metastatic and the number of examined lymph nodes. Staging based on MLR is simple, while it gives more precise prognosis information and fewer problems of stage migration.

Researches demonstrated that MLR was an independent prognostic factor on gastric cancer patients, and it has nothing to do with the range and quantity of lymph node cleaning [11-13]. Scholars also have found that MLR has better accuracy, homogeneity and applicability on evaluating the prognosis of gastric cancer patients By, and it can reflect the efficiency of the lymph node cleaning [14-18]. What's more, it still can be used as a simple and effective prognostic indicators when the number of detected lymph nodes is less than 15 [4, 10, 19-21]. Yu CJ, et al. [22] reported that MLR stage can match the pN stage in accuracy of evaluating the survival outcomes of gastric cancer patients, meanwhile, the uniformity and applicability are superior than those of pN stage. Liu H, et al. [23] even demonstrated that MLR stage is a better prognosis indicator of gastric cancer patients undergoing radical surgery when compared with pN category and log odds of positive lymph nodes (LODDS). Xu J, et al. [24] found that neither MLR nor LODDS could reduce the stage migration, the sufficient number of detected lymph nodes is key to ensure an accurate prognosis of gastric cancer patients for D2 resection. Therefore, whether MLR stage has a far greater value than pN category in evaluating the prognosis of gastric cancer is still inconclusive. This research is to explore the relationship between MLR staging and prognosis of patients with gastric cancer and provides guidance for clinical work.

Materials and methods

Patients

Clinicopathologic parameters of 477 gastric cancer patients undergoing radical resection were retrospectively analyzed during January 2010 to December 2011. All the operations were performed by expertise of surgeons specialized in gastrointestinal surgery in The First
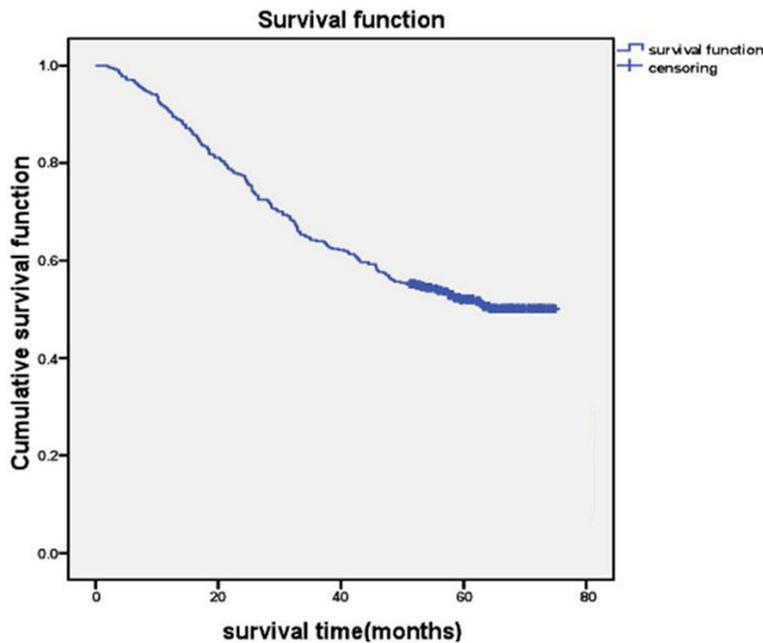
Figure 1. The overall survival rate curve.

Table 1. The correlation between MLR, pN and the number of the examined lymph nodes

Variables	R	P value (2-sided)
pN/examined number of lymph nodes	0.163	0.001*
MLR/examined number of lymph nodes	0.021	0.657

*P < 0.05.

Affiliated Hospital of Fujian Medical University. The following criteria were adopted for patients enrolled in the study: diagnosed with gastric adenocarcinoma by postoperative pathology; undergoing radical surgery (≥ D2 lymph node dissection) and reaching the R0 resection; with integral clinical pathology and follow-up data; at least 15 lymph nodes being examined in a pathological examination; no preoperative radiotherapy and chemotherapy. Our exclusion criteria included: abdominal metastasis; liver, lung and other distant organ metastasis; undergoing Palliative surgery and simple reroute of the gastrointestinal tract; diagnosed with secondary malignancies other than primary gastric carcinoma or a family history of malignancy; less than 1 month postoperative survival or postoperative death of other non-cancer related diseases.

Clinicopathologic analysis

The clinicopathological parameters such as sex, age, tumor sites, tumor size, gross type, histological type, differentiation degree, invasion depth, pathological stage, vascular cancer embolus, nerve invasion, lymphatic vessel invasion, MLR stage, pN category, and survival outcome were collected. The clinicopathologic datas were reviewed and the MLR was calculated by dividing the number of metastatic lymph nodes by the total number of lymph nodes found by histologic examination. All of the patients had undergone Radical surgery (≥ D2 lymph node dissection) according to the Japanese treatment guideline of gastric carcinoma (third English version) by JGCA. All the lymph nodes had been examined by professionals. 444 cases of patients were Followed-up and a total of 11571 lymph nodes had been detected with an average detection number of 26.06±8.97, among which the number of metastasis lymph nodes was 2488 and the metastasis Lymph node ratio was 21.50% on average. According to the 7th edition of the UICC/AJCC TNM staging system, the pN stage was stratified into four groups based on the number of tumor-infiltrated lymph nodes, N0: no positive, N1: 1-2 positive lymph node; N2: 3-6 positive lymph nodes; N3: > 7 positive lymph nodes. In this study four stages of MLR were defined: 0, 0-0.3, 0.3-0.6, > 0.6, which is in reference to Yu J, et al. [25].

Follow-up

All of the Postoperative patients were on a follow-up, which was done by telephone calls, outpatient visits or investigation records. The median follow-up time were 53 months, overall follow-up rate was 93.1% (444/477) and 6.9% (33/477) of patients were lost to follow-up.

Statistical analysis

SPSS 19.0 software (SPSS Inc, Chicago, IL, USA) was used for statistical analysis. The cor-

Table 2. Univariate and multivariate survival analysis results of 444 gastric cancer patients undergoing radical resection

Variables	Number	Univariate analysis			Multivariate analysis		
		5-YSR (%)	X^2 value	P value	HR	(95% CI)	P value
Sex			1.356	0.244			
Male	333	54.0%					
Female	111	46.5%					
Age (year)			0.043	0.836			
≤ 60	234	52.9%					
> 60	210	51.3%					
Location of primary tumor			40.038	0.000*	0.851	0.728-0.995	0.044*
Gastric fundus and cardia	114	42.2%					
Gastric body	133	50.4%					
Gastric antrum	184	62.7%					
≥ Two parts	13	7.70%					
Size of primary tumor (cm)			46.969	0.000*	1.616	1.233-2.239	0.001*
≤ 5	353	58.6%					
> 5	91	26.9%					
Gross type			36.786	0.000*			0.669
Ulcerative type	349	50.9%					
Infiltrative and diffuse infiltrative type	34	26.5%					
Uplift and polyp type	28	50.0%					
Superficial type	33	93.9%					
Histological type			12.717	0.005*	0.029	1.015-1.336	0.029*
Adenocarcinoma simplex	341	55.1%					
Mucous adenocarcinoma	27	46.7%					
Signet ring cell carcinoma	53	45.3 %					
Undifferentiated carcinoma	23	30.4%					
Differentiation degree			32.004	0.000*			0.459
High differentiation	21	81.0%					
Moderately differentiated	121	69.6%					
Low and undifferentiated	302	43.2%					
pT stage			86.309	0.000*			0.639
T1	68	94.1%					
T2	42	83.3%					
T3	103	51.3%			2.636		
T4	231	34.7%					
TNM stage			147.108	0.000*		1.804-3.853	0.000*
I	91	95.6%					
II	89	76.1%			1.543		
III	264	29.2%					
Vascular cancer embolus			83.679	0.000*		1.132-2.102	0.006*
Yes	320	62.8%					
No	124	24.8%					
Nerve invasion			67.626	0.000*	2.517		0.052
Yes	242	68.7%					
No	202	32.2%					
Lymphatic vessel invasion			9.801	0.002*	1.635	1.456-4.351	0.001*
Yes	426	53.4%					
No	18	22.2%					
MRL stage			214.306	0.000*		1.346-1.986	0.000*
MLR0	145	88.0%					
MLR1	166	49.4%					

MLR2	90	21.6%				
MLR3	43	7.0%				
pN stage			199.720	0.000*		0.196
pN0	145	88.0%				
pN1	64	66.5%				
pN2	78	41.9%				
pN3	157	18.5%				

*P < 0.05.

relation between MLR and pN, as well as the total number of the examined lymph nodes were analyzed with the Spearman correlation analysis. The cumulative survival rate was obtained using a Kaplan-Meier Curve, and the differences in cumulative survival rates were compared by the log-rank test. The multivariate prognostic analysis was conducted with the Cox proportional risk regression model. Sub-group analysis adopt the group in each MLR stage was regrouped in accordance with pN stage, and the overall survival differences within groups and among groups were analyzed using the log-rank survival test to compare the homogeneity of the 2 staging methods, and using the same method to regroup the same pN stage with different MLR stages and learn the homogeneity of the 2 staging methods. The accuracy of the prognosis assessment of each staging method was compared using the receiver operating characteristic curve (ROC) and the area under the curve (AUC), and the Z test were used to compare the differences of the AUC among groups. *P* value of < 0.05 (2-sided) was considered statistically significant.

Results

The overall survival time was 45.5 months and the overall survival rate was 51.8%

There are 477 patients altogether with gastric adenocarcinoma were accepted in our study, 444 cases received follow-up, the main age of the patients was 60 years (range from 18 to 90 years) and 111 patients were female, 333 patients were male. The median follow-up time was 53 months (range 2 to 75 months). There were 214 deaths (relapse or metastasis) and 33 cases were lost to follow-up, losing to follow-up rate was 6.92% (33/477). The overall survival time was 45.5 months on average and the overall survival rate was 51.8%. The estimated overall 1-year, 3-year and 5-year survival rates

were 89.94%, 64.0% and 52.1% respectively (**Figure 1**).

MLR rarely effected by the inspected number of lymph nodes than pN, which can make up for the inadequacy of the pN in stage migration

Spearman correlation analysis showed that MLR did not correlate with the inspected number of lymph nodes (r=0.021, P=0.657), and rarely effected by the inspected number of lymph nodes; whereas pN was significantly associated with detected number of lymph nodes (r=0.163, P < 0.01), markedly influenced by the examined number of lymph nodes (**Table 1**).

MLR stage was independent prognostic risk factor while pN classification was not

Among the 444 cases of Follow-up patients, there were 145 cases of MLR0, 166 cases of MLR1, 90 cases of stage MLR2 and 43 cases of MLR3. The results of univariate analysis showed that MLR and pN staging were risky factors for prognosis of patients with gastric cancer (**Table 2**), With MLR and pN stage increasing, postoperative patients with 1, 3, 5-years survival rate significantly reduced (**Figure 2A**, **2B**, respectively). In the subsequent Cox proportional risk regression model, the results showed that MLR stage [hazard ratio (HR)=1.401, P=0.012] was independent prognostic risk factor (P < 0.05), while pN classification (HR=1.376, P=0.005) was not independent, significant prognostic parameter of patients with gastric cancer (**Table 2**).

MLR stage, histological type, tumor sites, vascular cancer embolus, lymphatic vessel invasion, pathological stage and tumor size were independent prognostic factors

Univariate analysis showed that tumor sites, tumor size, gross type, histological type, differ-
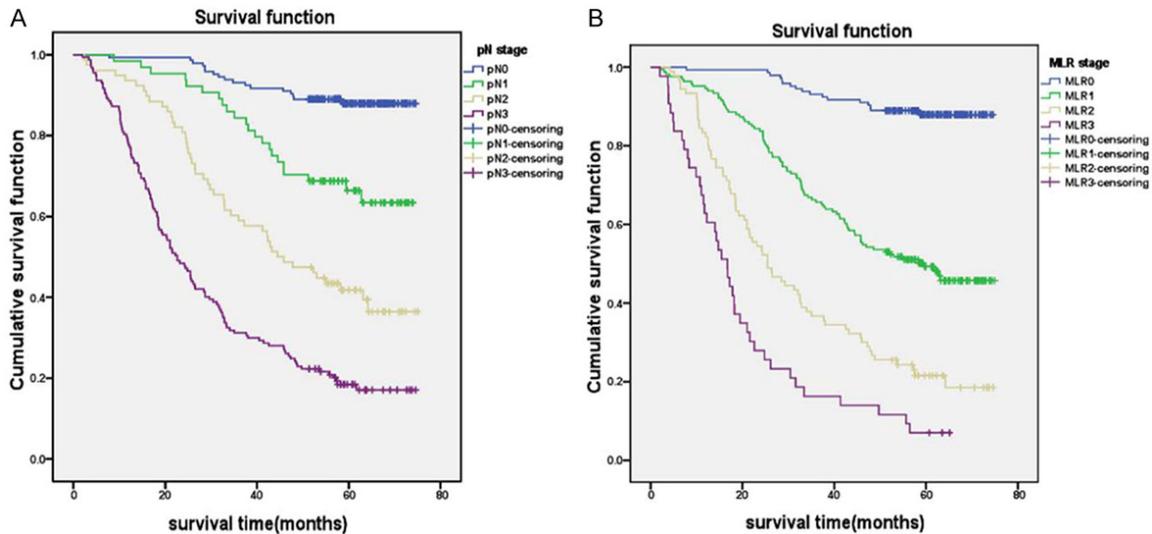
Figure 2. A: The relationship between MLR staging and the prognosis of gastric cancer; B: The relationship between pN staging and the prognosis of gastric cancer.

entiation degree, invasion depth, pathological stage, vascular cancer embolus, nerve invasion, lymphatic vessel invasion, MLR stage and pN stage were risky factors for prognosis of patients with gastric cancer (P < 0.05), but differences in Gender and age did not have statistical significance effect on prognosis (P > 0.05). Cox multivariate regression analysis showed MLR stage, histological type, tumor sites, vascular cancer embolus, lymphatic vessel invasion, pathological stage and tumor size were independent prognostic factors of patients with gastric cancer (P < 0.05), while invasion depth, pN category, differentiation degree, nerve invasion, gross type were not independent, significant prognostic parameters (P > 0.05) (**Table 2**).

The homogeneity of prognostic prediction by subgroup analysis showed that the MLR stage was batter, especially in patients within pN3 stage

The group in each MLR stage was firstly regrouped in accordance with pN to analysis the overall survival rate differences to compare the homogeneity of the MLR stage and pN stage. We found that in MLR1 stage, the different overall survival rate among the pN subgroups were statistically significant (P=0.000); in MLR2 stage, the pN subgroups had no statistically significant difference between the survival rate (P=0.854). Then the subgroups with the same pN category were stratified into different

subgroups by the MLR stage. We noticed that a significantly heterogeneous overall survival was found in patients within pN3 stage (P=0.002), but not in pN2 patients (P=0.077). (The survival curves comparing the homogeneity of MLR and pN stage in patients with MLR1-2 and pN2-3 stages are shown in **Figure 3A-D** respectively). As the staging of the patients in pN0 were the same as MLR0, therefore we did not include the part of the cases in the analysis.

The MLR was consistent with pN on evaluating the diagnostic value of prognosis in patients with gastric cancer

The death of overall patients during 3 and 5-years postoperative and the survival time of them after surgery were used as the gold standard to draw the ROC curve. Respectively it compares the accuracy of the prognosis assessment of the two staging methods of the death undergoing radical resection for gastric cancer patients. The ROC curves analysis displayed whether classified by staging or not, the corresponding AUC for MLR and pN had no statistically significance (P > 0.05). (The ROC curves comparing the accuracy of the prognosis assessment of the MLR and pN classification of the death are shown in **Figure 4A**, **4B** respectively). Hence we speculated that whether classified by staging or not, the MLR was consistent with pN on evaluating the diagnostic value of prognosis in patients with gastric cancer.
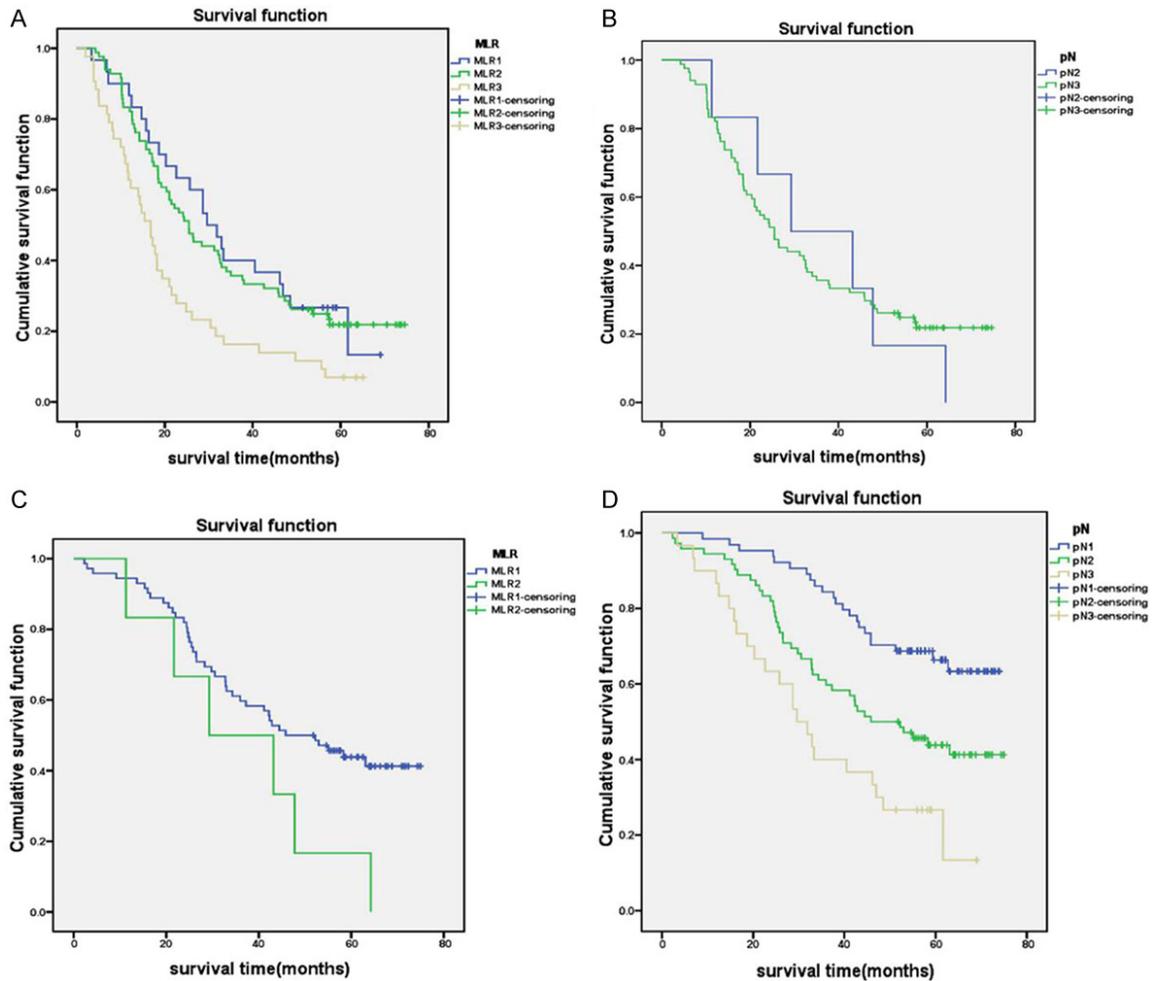
Figure 3. A: With the same MLR stage but different pN stage, in MLR1 stage, the different overall survival rate among the pN subgroups were statistically (P=0.000); B: With the same MLR stage but different pN stage, in MLR2 stage, the pN subgroups had no statistically significant difference between the survival rate (P=0.854); C: For patients in the same pN category but in difference MLR subgroups, (P=0.002) there were no statistically significant difference between the survival rate in pN2 stage (P=0.854); D: For patients in the same pN category but in different MLR subgroups, a statistical significance overall survival was found in patients within pN3 stage (P=0.077).

Discussion

Cheong JH, et al. [26] and Kong SH, et al. [27] prospectively analyzed the correlation between MLR, pN and the inspected number of lymph nodes among 1264 cases of early gastric cancer patients, which demonstrated that pN has associated with the number of inspected lymph nodes, whereas MLR had not, which is consistent with our result. Bando E, et al. [28] prospectively analsized 650 gastric cancer patients with D2 curative gastrectomy. It recognized that the incidence of stage migration was 15% when the pN classification was used, nevertheless, only 7% for MRL staging and they considered that MRL staging may prevent st-age migration. Yu JX, et al. [29] and Liu XW, et al. [30] used variable relation Scatter plot to learn the correlation between MLR, PN and the number of inspected lymph nodes got similar results. Xu J, et al. [24] demonstrated that MLR, pN, and LODDS were susceptible to the number of examined lymph nodes, therefore neither of them could reduce the phenomenon of stage migration , the key to guarantee an exact prognosis of patients underwent D2 radical gastrectomy is a sufficient number of examined nodes. Zha Y, et al. [31] confirmed that the MLR staging system has a preferable power to predict the prognosis even if the the number of inspected lymph node is no more than 15. This study eliminated the case of detected lymph node
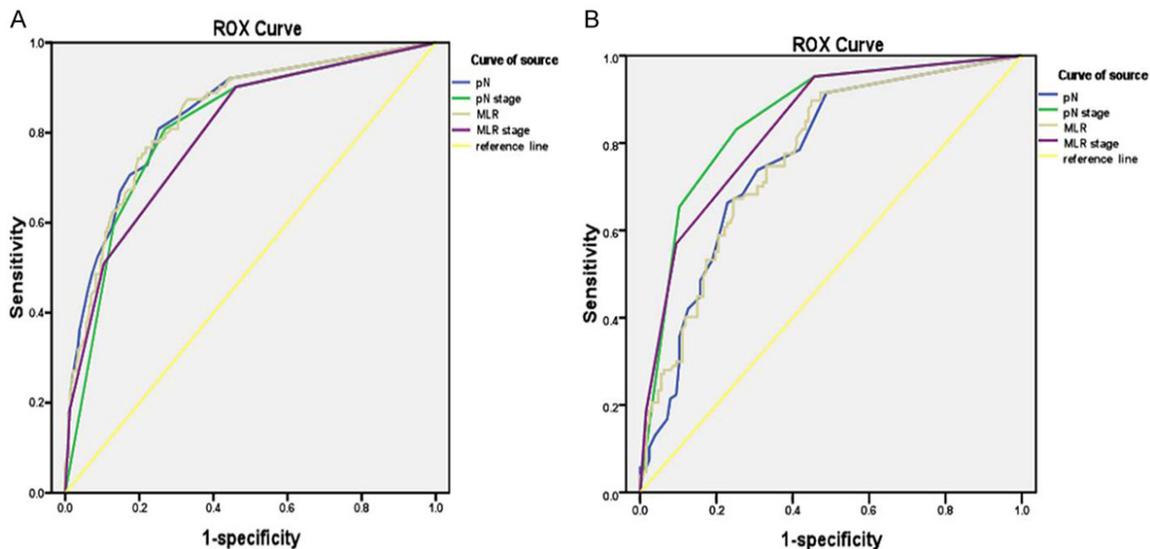
Figure 4. A: The ROC curves and AUC comparing the accuracy of the prognosis forecasting value of the MLR, MLR stage and pN, pN classification ending in death during 3-years postoperative had no significant differences z=0.018, P > 0.05; z=0.051, P > 0.05, respectively; B: The ROC curves and AUC comparing the accuracy of the prognosis forecasting value of the MLR, MLR stage and pN, pN classification ending in death during 5-years postoperative had no statistically significance z=0.009, P > 0.05; z=0.055, P > 0.05, respectively.

number less than 15 and the sample size is less.

Our results demonstrated that MLR stage can evaluate the survival of patients with gastric cancer preferably. When MLR stage increased, postoperative patients with 1, 3, 5-years survival rate significantly reduced. Liu C, et al. [32] in the study of pN/MLR redistribution of the log-rank test confirmed that a statistical significant difference of 5-year survival rate was found in patients within pN3 stage. Whereas when each MLR stage was re-grouped in accordance with pN stage, no statistically significant difference between each subgroup was observed in the 5-year survival rate. They recommended that the MLR stage has a high power of capacity in judging the prognosis of patients with gastric cancer than pN stage, at least for patients with pN3 category. Coimbra FJ, et al. [33] got the similar results as well and suggested that combining the pN and MLR stage methods may be regarded as a new means to evaluate the prognosis value of metastasis lymph nodes in gastric cancer. They considered that the combination of these two methods has a better prognostic significance than any pure lymph node category. Our study arrived at a similar conclusion with previous reports.

In this research, we re-grouped the same MLR stage in different pN stages and we found that

in MLR1 stage, the different overall survival rate among the pN subgroups were statistical. Furthermore, we observed that the patients within pN3 stage were found to contain subgroups of patients with significantly heterogeneous overall survival rate when the same pN category was stratified into different subgroups by the MLR stage. The patients within pN3 stage had statistically different overall survival between subgroups within MLR have showed that if only based on pN criteria judgment the prognosis of patients within pN3 category may occur the phenomenon of stage migration and cannot truly reflect the survival of the patients. Compared with pN category, MLR was little influenced by the inspected number of lymph nodes in judging the prognosis of gastric cancer patients within pN3 stage. Therefore, we considered that MLR category is a more reliable prognostic indicator than pN stage, at least for patients with pN3 category. If MLR stage can be regarded as the supplement of pN stage or MLR combines with pN stage as a new means, these will have a better uniformity and applicability in judging the prognosis of patients with gastric cancer. Meanwhile, the study also found that the different overall survival rate in MLR1 stage was statistically as well. These were different from previous literature reports. No statistically significant difference of the

5-year survival rate between each pN subgroups were observed in MLR1 staging.

Wang J, et al. [34] analyzed the prognosis of 18043 cases of gastric cancer patients based on the SEER database, and reported that in the each MLR staging and different pN subgroups, only MLR2 stage had statistically difference in 5-year survival between subgroups. Meanwhile each pN stage with different MLR stages had significant difference of 5-year survival rate. The incidence of stage migration was only 12% by MLR staging, however, misclassified TNM staging systemis as high as 57%. The research confirmed that MLR stage can significantly decrease incidence of stage migration. To some scholars [35], the Subgroup analysis of MLR/pN redistribution of the Log-rank test was only discussed about the differences about survival rate between the MLR subgroups of the same pN category, not a further research of the differences about survival rate between the same MLR staging different pN subgroups was made. And they draw a conclusion that MLR staging system has more accurate and practical value in evaluating the prognosis of patients with gastric cancer it may reduce the phenomenon of stage migration. Therefore, we think the same MLR staging different survival rate if there is a significant difference between pN subgroups needs further research.

We considered the emergence of the above results as the following reasons: insufficient sample size, inclusion criteria and exclusion standard is inconsistent of different research units, unbalanced proportional in each group; inconsistencies number of Metastasis lymph node in body due to the biological characteristics of the tumor; the scope and depth and efficiency of lymph node dissection is different; pathologists inconsistent ability of detection and understanding of metastasis lymph nodes is different and disunion standard of the MLR stage caused by the internal inconsistencies of the composition of the case data in Each region of different medical institutions. Liu C, et al. [32] divided 224 cases of gastric cancer patients into four groups by MLR staging: 0%, < 40%, 40-80% and > 80% in evaluating the prognosis. Wang's [34] study defined the Cutoff points for MLR stage as 6%, 30% and 70%. This study defined staging criteria as four stages of MLR: 0, 0-0.3, 0.3-0.6, > 0.6, in reference to [26]. But various kinds of the MLR staging criteria can predict the prognosis of patients with gastric cancer worldwide, it is still lack of a concrete and effective uniform standard for MLR staging, which seriously restricted the popularization and application of the MLR. Future research should focus on larger number of sample, multicenter study to quantify the rationality of the MLR staging criteria to find a simple, practical and reliable optimum stage standard as soon as possible.

In this research, Univariate analysis has showed that MLR stage and pN category are all Prognostic risk factors of patients with gastric cancer. Yet, the multivariate analysis confirmed that MLR stage is an independent prognostic factor for patients with gastric cancer, but pN category is not. The result is similar to most of the literature that have been well documented at home and abroad in recent years [35-37]. Some researches have demonstrated that no matter how many the number of examined lymph nodes number is, MLR stage compared with pN category stage can better predict the survival prognosis of patients with gastric cancer and suggested that using MLR stage to replace the pN stage can assess lymph node metastasis status. Some researches [38] have demonstrated that Compared with JGAC staging system and the AJCC/UICC staging system, MLR staging system can preferably predict the prognosis of patients with gastric cancer. Furthermore, some reports [5]. have confirmed that MLR stage still can be used as an independent, significant prognostic parameters when the number of detected lymph nodes is no more than 15. Xu DZ, et al. [39] confirmed that whether the number of dissected lymph nodes can reach 15 or not, the MLR is the only independent prognostic Factor for patients underwent D2 radical resection for the first time, and it can avoid the phenomenon of stage migration. Others have suggested that the MLR stage should be considered as an important component of the lymph node category.

ROC curve and AUC can be used to judge the accuracy of the means of diagnosing has been widely used [40]. In this research, the ROC curves analysis demonstrated that Whether classified by MLR or not, its diagnosis value of judging the prognosis of patients with gastric cancer is equal to pN, but not superior to the latter. The results agree with the research at home and abroad in recent years. Xu DZ, et al.

[39] The 5-year survival rate after D2 resection in patients with gastric cancer were used as the gold standard to draw the ROC curve and they found that the corresponding AUC among MLR, pN and LODDS had no statistically significant difference Found the MLR, pN and LODDS there was no statistically significant difference of the AUC. Others [22, 23] reported that MLR stage can match the pN stage in accuracy of evaluating the prognosis of gastric cancer, however the applicability and uniformity are superior than those of pN stage.

Our study had several limitations. First of all, in consequence of the 7th edition of TNM staging criterion, if the examined number of lymph nodes are less than 15 that the lymph node staging will be defined as Nx. So Strictly according to the inclusion and exclusion criteria of this research criteria the patients of whom with a number of tested lymph nodes < 15 were excluded. It makes us unable to evaluate the prognostic value of MLR in patients with a detection of lymph nodes are less than 15. Second, the follow-up time frame may be too short to be able to calculate the median survival time. Third, MLR staging standard is not unified, this study does not further analyze and to explore the best boundary value, just simply in reference to the literature. Fourth, the small number of cases may affect the authenticity of results. The conclusion of this study must be weighed upon these points, which should be clarified in further studies.

In conclusion, the results of this study shows that, MLR stage is one of the independent prognostic factors in patients with gastric cancer, which is slightly affected by the number of examined nodes, and it can make up for the deficiencies of stage migration of the pN category in judging the prognosis of patients with gastric cancer on pN3 stage. Furthermore, Whether classified by MLR or not, its diagnosis value of judging the prognosis of patients with gastric cancer is equal to pN, but not superior to the latter. The findings in the research strongly suggest that the MLR stage has advantage over pN stage in judging the prognosis of gastric cancer on pN3 stage. These prompts us that if combines.

MLR as the supplement of pN stage to avoid the phenomenon of stage migration, it will make help to improve the lymph node staging system of gastric cancer, which is of fundamental importance in accurately judging prognosis and guiding treatment decisions, as well as evaluating curative effect of Patients with gastric cancer. However, whether the MLR stage can still be used to evaluate the prognosis of patients with gastric cancer when detected lymph nodes are less than 15 it still deserves further studies to demonstrate. At the same time, the uniform of the MLR staging standard seriously restricted its application, further studies should focus on more prospective study, Strengthen the multicenter cooperation, to quantify the rationality of the MLR staging criteria, in order to find a simple, practical and reliable optimum stage standard as soon as possible, to provide service for clinical work.

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Disclosure of conflict of interest

None.

Address correspondence to: Jianxin Ye, Department of Gastrointestinal Surgery 2 Section, The First Hospital Affiliated to Fujian Medical University, 20 Cha-Zhong Road, Fuzhou 350004, China. Tel: +8613809553280; Fax: +8659183318716; E-mail: yejianxinfuyi@126.com

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