

The prognostic value of lymph node ratio for local advanced gastric cancer patients with adjuvant chemoradiotherapy after D2 gastrectomy

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Abstract

This study aimed to find the prognostic factors of local advanced gastric cancer patients with adjuvant concurrent chemoradiotherapy after radical D2 gastrectomy, and explore the prognostic value of lymph node ratio (LNR).

We retrospectively analyzed 164 gastric cancer patients enrolled in West China Hospital from 2006 to 2013, who underwent D2 radical gastrectomy and adjuvant chemoradiotherapy. With univariate analysis and the Cox regression model, we evaluated the association of LNR and other clinical pathological characteristics with overall survival (OS) and relapse-free survival (RFS) of patients.

Of 164 gastric cancer patients, the median age at diagnosis was 60 (IQR 51–66), with 121 males (73.78%) and 43 females (26.22%). The median follow-up time was 41.5 months. One-year and 3-year OS rate of the whole cohort was 97.6% and 88.4%, with 1-year RFS rate of 90.2% and 3-year RFS rate of 76.8%, respectively. In the univariate analysis, we found that age >60years ($P=.025$), TNM stage III ($P=.014$), LNR >0.25 ($P=.006$) and radiation dose <45Gy ($P=.048$) predicted worse OS. Further multivariate analysis indicated that age >60y (HR 2.375, 95% CI 1.100–5.128; $P=.028$), TNM stage III (HR 7.692, 95% CI 1.009–58.824; $P=.049$) and LNR >0.25 (HR 2.439, 95% CI 1.075–5.525; $P=.033$) were independent prognostic factors for unfavorable OS. The COX analysis showed that related prognostic factors of worse RFS were TNM stage III (HR 3.802, 95% CI 1.506–9.615; $P=.049$) and LNR >0.25 (HR 2.326, 95% CI 1.332–4.065; $P=.003$).

LNR can be used as an important prognostic indicator for gastric cancer patients with D2 resection and adjuvant chemoradiotherapy, and LNR more than 0.25 indicates poor prognosis.

Abbreviations: LNR = lymph node ratio, FOLFOX = oxaliplatin, 5-fluorouracil and leucovorin, SOX = S-1 and oxaliplatin, ROC = receiver-operating curves, OS = overall survival, RFS = relapse-free survival, pN = pathological metastatic lymph node number, LNtotal = total number of retrieved nodes, 3D-CRT = three-dimensional conformal radiation, IMRT = intensity-modulated radiation therapy, AJCC = American Joint Committee on Cancer, NLR = neutrophil-to-lymphocyte ratio, PDW = platelet distribution width, LDH = lactate dehydrogenase.

Keywords: adjuvant chemoradiotherapy, D2 resection, gastric cancer, lymph node ratio, survival

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All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required. A waiver of informed consent was requested, and approval was obtained from the institutional review board of West China Hospital.

The authors have no conflicts of interest to disclose.

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1. Introduction

Gastric cancer remains one of the most important global cancer burdens, which is the fifth common cancer and the third leading cause of cancer-caused deaths worldwide.^[1] Many gastric cancer patients present with advanced resectable disease, which is mostly treated with radical resection with regional lymph node dissection, and the long-term survival of patients is poor. However, the extent of lymph node dissection and the choice of adjuvant regimens remain controversies all around the world, and D2 lymphadenectomy with systemic chemotherapy or chemoradiotherapy is commonly used in China. Among these, a large number of gastric cancer patients received D2 resection and adjuvant concurrent chemoradiotherapy. Although treated with the same therapeutic regimen, the local advanced gastric cancer patients present totally different prognoses. Therefore, it is rather valuable to find reliable prognostic predictors for clinical judgments.

The lymph node ratio (LNR) stands for the ratio between pathological metastatic lymph node number (pN) and total number of retrieved nodes (LNtotal), which ranged from 0 to 1. In recent years, many clinical researches indicated LNR could be a significant prognostic factor of gastric cancer patients after surgery, even considered of better prognostic value than TNM staging.^[2–5] However, the reported LNR cutoff values of

distinguishing prognosis vary from 0.2 to 0.65, which needs more retrospective studies to further certify and explore.

In this study, we conducted a retrospective study on 164 local advanced gastric cancer patients treated with radical gastrectomy and D2 lymphadenectomy and adjuvant concurrent chemoradiotherapy, to carry out the survival analysis and prognostic factors analysis. This study was aimed to explore valuable prognostic related factors and predictive index, especially demonstrate the prognostic value of LNR and optimal cutoff value.

2. Materials and methods

2.1. Patients characteristics

Patients with resectable gastric cancer who underwent R0 gastrectomy and D2 lymph node dissection surgery with postoperative concurrent chemoradiotherapy in our hospital from 2006 to 2013 were evaluated. We included patients with the following eligibility criteria: age between 18 and 75 years, histologically proven gastric or gastroesophageal adenocarcinoma, American Joint Committee on Cancer (AJCC) stage IB–III (8th edition), underwent R0 gastrectomy and D2 dissection, Eastern Cooperative Oncology Group (ECOG) status of 0 to 1, no distant metastasis, without preoperative treatment, and with postoperative adjuvant chemoradiotherapy. Patients unable to tolerate chemotherapy or radiotherapy because of other systemic illnesses, treated with neoadjuvant chemotherapy or radiotherapy and coexisting with other malignancies were excluded from this study.

2.2. Treatment delivery

The D2 lymphadenectomy was performed in accordance with the Japanese Gastric Cancer Association (JGCA) criteria with more than 15 lymph nodes removed, without extra splenectomy or pancreatic tail resection.^[6]

All enrolled patients were treated with adjuvant concurrent chemoradiotherapy after D2 dissection, including Oxaliplatin, fluorouracil and leucovorin agents (FOLFOX) or SOX chemotherapy (S-1 and oxaliplatin [SOX] agents) and 50.4Gy in 28 fractions or 45Gy in 25 fractions radiotherapy. The radiotherapy was delivered with 3-dimensional conformal radiation (3D-CRT) or intensity-modulated radiation therapy (IMRT) techniques. Besides, the specific standard initiation time, duration and dosage of chemotherapeutic agents and radiotherapy were based on our previous trials design.^[7–9]

2.3. Follow-up and data collection

After surgery, we followed up all enrolled patients by telephone counseling or patients visit. The end point of follow-up was March 2017 or the date of death or loss to follow-up. We used the overall survival (OS) and relapse-free survival (RFS) to evaluate prognosis of patients, as OS was defined as the time from surgery to the last follow-up or death or loss to follow-up, and RFS was defined as the time from surgery to tumor recurrence or death or loss to follow-up. Moreover, relapse was defined as pathological confirmed or imaging highly suspicious of relapse, including local-regional relapse, peritoneum implanting and distant metastasis.

We collected records and reviewed many clinical pathological characteristics of enrolled patients, including age, sex, tumor

location, tumor size, pathological differentiated degree, tumor invasion depth, number of metastatic lymph nodes, all retrieved nodes number, TNM stage, adjuvant chemotherapy regimen, adjuvant radiotherapy dose, and relapse and survival information. TNM stages of gastric tumors were classified on pathological specimens, according to the 8th edition AJCC staging system.^[10] Besides, we collected the clinical hematologic parameters from the patients within 1 week before surgery. Most laboratory parameters were directly measured, but the neutrophil-to-lymphocyte ratio (NLR) was indirectly calculated by absolute counts ratio of 2 parameters.

2.4. Statistical analysis

All statistical analyses were developed with IBM SPSS statistics version 21 software. Means \pm standard deviation or medians (interquartile range [IQR]) were used to present the descriptive analysis of continuous variables for clinical characteristics. The Kaplan–Meier method was used to analyze the cumulative OS and RFS, and primary confirmatory analysis of the differences in survival was performed using the log-rank test. The receiver-operating characteristic (ROC) curve analysis and area under the curve were used to identify the optimal cut-off values of some continuous variables such as age, LNR and most laboratory parameters for the log-rank test. The hazard ratios between multivariate clinical pathological factors with OS and RFS prognosis were calculated by Cox proportional-hazards model. Two-tailed *P* values of less than .05 were considered to be statistical significant in all tests.

3. Results

3.1. Clinical pathological characteristics

A total of 164 patients were included in this study. The median age of patients at diagnosis was 60 (IQR 51–66) with 121 males (73.78%) and 43 females (26.22%). All patients went through R0 gastrectomy and D2 lymph node dissection. Pathological tumor size of patients was 4.9 ± 2.3 cm. According to AJCC 8th edition, 1 patient (0.6%) were categorized as stage Ib, 14 patients (8.5%) as stage IIa, 22 patients (13.4%) as stage IIb, 34 patients (20.7%), as stage IIIa, 42 patients (25.6%) as stage IIIb and 51 patients (31.1%) as IIIc disease, respectively. As to the pathological differentiation degree of tumor, no patients had well-differentiated tumors, 31 patients (18.9%) had moderately-differentiated tumors and 133 patients (81.1%) had poorly-differentiated tumors. After surgery, 99 patients (60.4%) underwent FOLFOX adjuvant chemotherapy, 65 patients (39.6%) accepted SOX regimen chemotherapy, and only 12 patients (7.3%) received incomplete adjuvant radiotherapy less than 45Gy.

In addition, the median LNtotal number was 25 (range, 15–103) with median pN of 5 (range, 0–50). As the ratio between pN and LNtotal, the mean LNR was 0.268 ± 0.219 . Of note, the ROC analysis indicated that the optimal cut-off value of LNR related to RFS distinction was 0.25, with specificity and sensitivity were 56.9% and 41.7%, respectively (AUC=0.623, 95% CI: 0.532~0.713, *P*=.012). The optimal cutoff value of LNR for OS prognosis was 0.28, with specificity of 0.621 and sensitivity of 0.387 (AUC=0.616, 95% CI: 0.503~0.729, *P*=.050). However, 0.25 could also be an appropriate LNR cut-off value for OS, with specificity of 0.621 and sensitivity of 0.431. Therefore, we divided all patients into high LNR group

Table 1**The clinical pathological characteristics of gastric cancer patients in low and high LNR groups.**

Clinical features	n (%)	LNR>0.25, n (%)	LNR≤0.25, n (%)	P
Sample size	164	73	91	—
Sex				
male	121 (73.8%)	52 (71.2%)	69 (75.8%)	.509
female	43 (26.2%)	21 (28.8%)	22 (24.2%)	
Age (years)				
≤60	89 (54.3%)	42 (57.5%)	47 (51.6%)	.455
>60	75 (45.7%)	31 (42.5%)	44 (48.4%)	
Tumor size (cm)				
≤ 5	114 (69.5%)	47 (64.4%)	67 (73.6%)	.204
> 5	50 (30.5%)	26 (35.6%)	24 (26.4%)	
Differentiated degree				
well	0 (0%)	0 (0%)	0 (0%)	.006
moderately	31 (18.9%)	7 (9.6%)	24 (26.4%)	
poorly	133 (81.1%)	66 (90.4%)	67 (73.6%)	
Tumor location				
GEJ	50 (30.5%)	20 (27.4%)	29 (31.9%)	.537
non-GEJ	114 (69.5%)	53 (72.6%)	62 (68.1%)	
T stage				
T1-2	20 (12.2%)	3 (4.1%)	17 (18.7%)	.004
T3	34 (20.7%)	15 (20.5%)	19 (20.9%)	
T4	109 (66.5%)	54 (74.0%)	55 (60.4%)	
N stage				
N0	13 (7.9%)	0 (0%)	13 (14.3%)	.001
N1	34 (20.7%)	1 (1.4%)	33 (36.3%)	
N2	52 (31.7%)	15 (20.5%)	37 (40.7%)	
N3	65 (39.6%)	57 (78.1%)	8 (8.8%)	
TNM stage (8th edition)				
I & II stage	38 (23.2%)	3 (4.1%)	35 (38.5%)	<.001
III stage	126 (76.8%)	70 (95.9%)	56 (61.5%)	
Adjuvant chemotherapy				
FOLFOX	99 (60.4%)	47 (64.4%)	52 (57.1%)	.294
SOX	65 (39.6%)	26 (35.6%)	39 (42.9%)	
Adjuvant radiation dose				
<45Gy	12 (7.3%)	6 (8.2%)	6 (6.6%)	.836
≥45Gy, <50.4Gy	34 (20.7%)	13 (17.8%)	21 (23.1%)	
≥50.4Gy	118 (72%)	54 (74%)	64 (70.3%)	

LNR = lymph node ratio, GEJ = gastroesophageal junction, non-GEJ = non-gastroesophageal junction.

(LNR>0.25) and low LNR group (LNR≤0.25), included 73 patients (44.5%) and 91 patients (55.5%), respectively. As shown in Table 1, most clinical pathological parameters and tumor characteristics between high and low LNR group were comparable, including sex, age, tumor size, tumor location, adjuvant chemotherapy regimen, and radiotherapy dose. However, it presented significant differences in tumor differentiated degree ($P=.006$), T stage ($P=.004$), N stage ($P=.001$) and TNM stage ($P<.001$) between 2 groups.

3.2. Survival rate analysis

The median follow-up time of our study was 41.5 months. Figure 1 presented survival curves of OS and RFS of all included gastric cancer patients with postoperative chemoradiotherapy agents, with 3-year OS of 88.4% and 3-year RFS of 76.8%.

Furthermore, we carried out Kaplan-Meier survival analysis and Log-rank analysis for LNR>0.25 and LNR≤0.25 patients, which showed both OS and RFS in low LNR group were prominently better than high LNR group (log-rank $P=.004$ and $.002$, respectively), and the related survival curves of 2 groups were showed in Figure 2. The 3-year OS rate in patients with LNR ≤ 0.25 and LNR >0.25 was 89.5% and 78.8%,

respectively. The 3-year RFS rate in patients with LNR ≤ 0.25 and LNR >0.25 was 81.0% and 63.1%, respectively.

3.3. Prognostic factors analysis

As shown in Table 2, we included important clinical and pathological characteristics into the OS prognostic analysis by Cox proportional-hazards model. The results of univariate analysis showed that patients with age over 60 (HR 2.328, 95% CI 1.111–4.881; $P=.025$), TNM stage III (HR 12.195, 95% CI 1.653–90.909; $P=.014$), LNR over 0.25 (HR 2.890, 95% CI 1.359–6.135; $P=.006$) and adjuvant radiation dose less than 45 Gy (HR 2.918, 95% CI 1.010–8.432; $P=.048$) correlated with more unfavorable OS prognosis. Gender, tumor location, tumor size, tumor differentiated degree, and different adjuvant chemotherapy regimen were not significantly correlated with OS. In further, we included all identified univariate factors associated with OS prognosis into the multivariable analysis using stepwise Cox regression, which showed that age over 60 (HR 2.375, 95% CI 1.100–5.128; $P=.028$), TNM stage III (HR 7.692, 95% CI 1.009–58.824; $P=.049$) and LNR over 0.25 (HR 2.439, 95% CI 1.075–5.525; $P=.033$) were independent prognostic factors for worse OS of gastric cancer patients after D2 lymphadenectomy with adjuvant concurrent chemoradiotherapy.

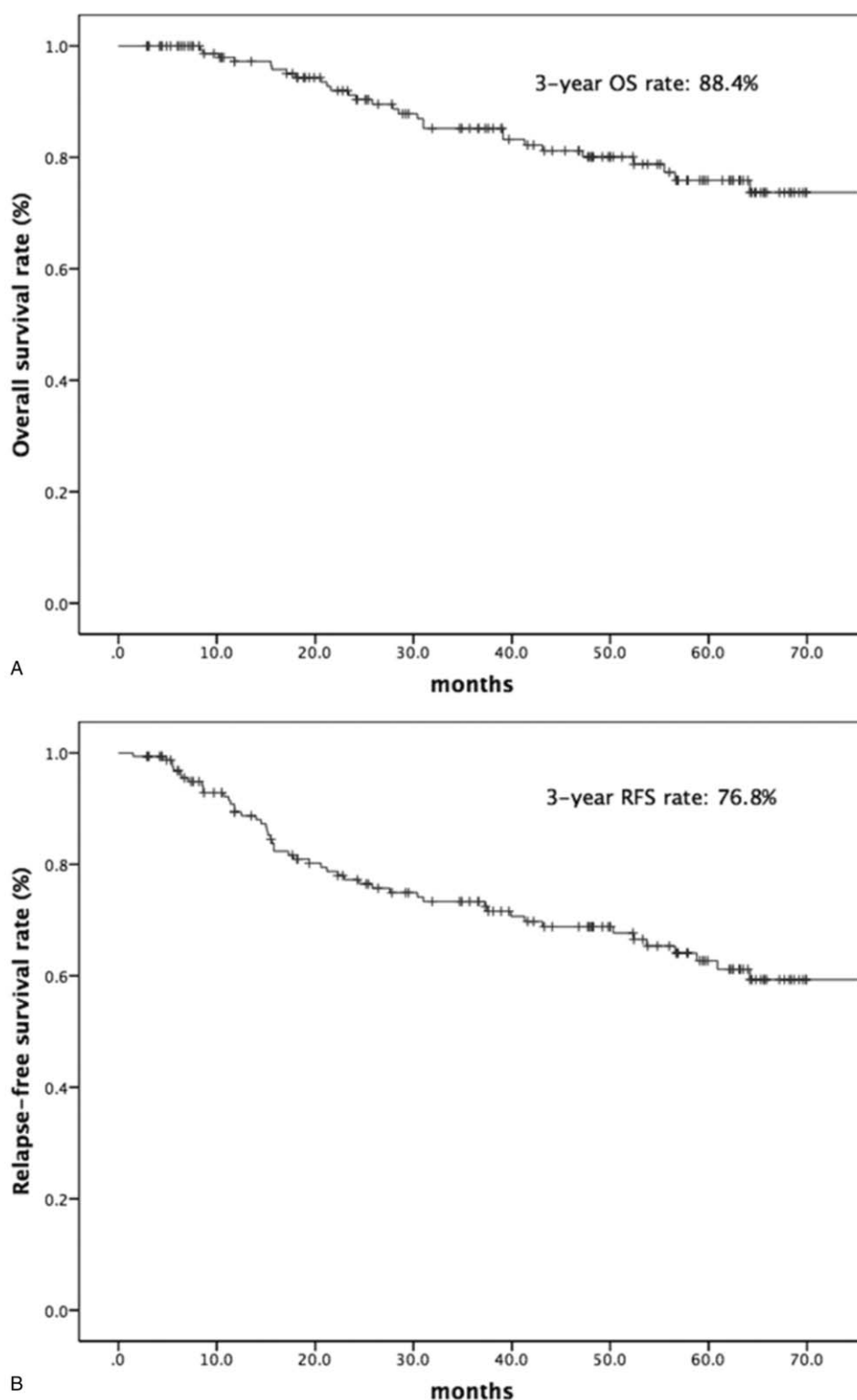


Figure 1. Kaplan-Meier curves for OS (A) and RFS (B). OS=overall survival, RFS=relapse-free survival.

In regard to the COX analysis of RFS, we found that only TNM stage III (HR 3.802, 95% CI 1.506–9.615; $P=.005$) and LNR over 0.25 (HR 2.326, 95% CI 1.332–4.065; $P=.003$) were significant prognostic factors for RFS, which indicated a more unfavorable RFS prognosis. Other different clinical and pathological characteristics showed no significant differences in

RFS outcome ($P>.05$), included age, gender, tumor location, tumor size, differentiated degree; different chemotherapy regimen and concurrent radiation dose (Table 3).

To further explore the role of many hematological variables which had been reported as prognostic biomarkers for gastric cancer patients in previous studies, we also evaluated several

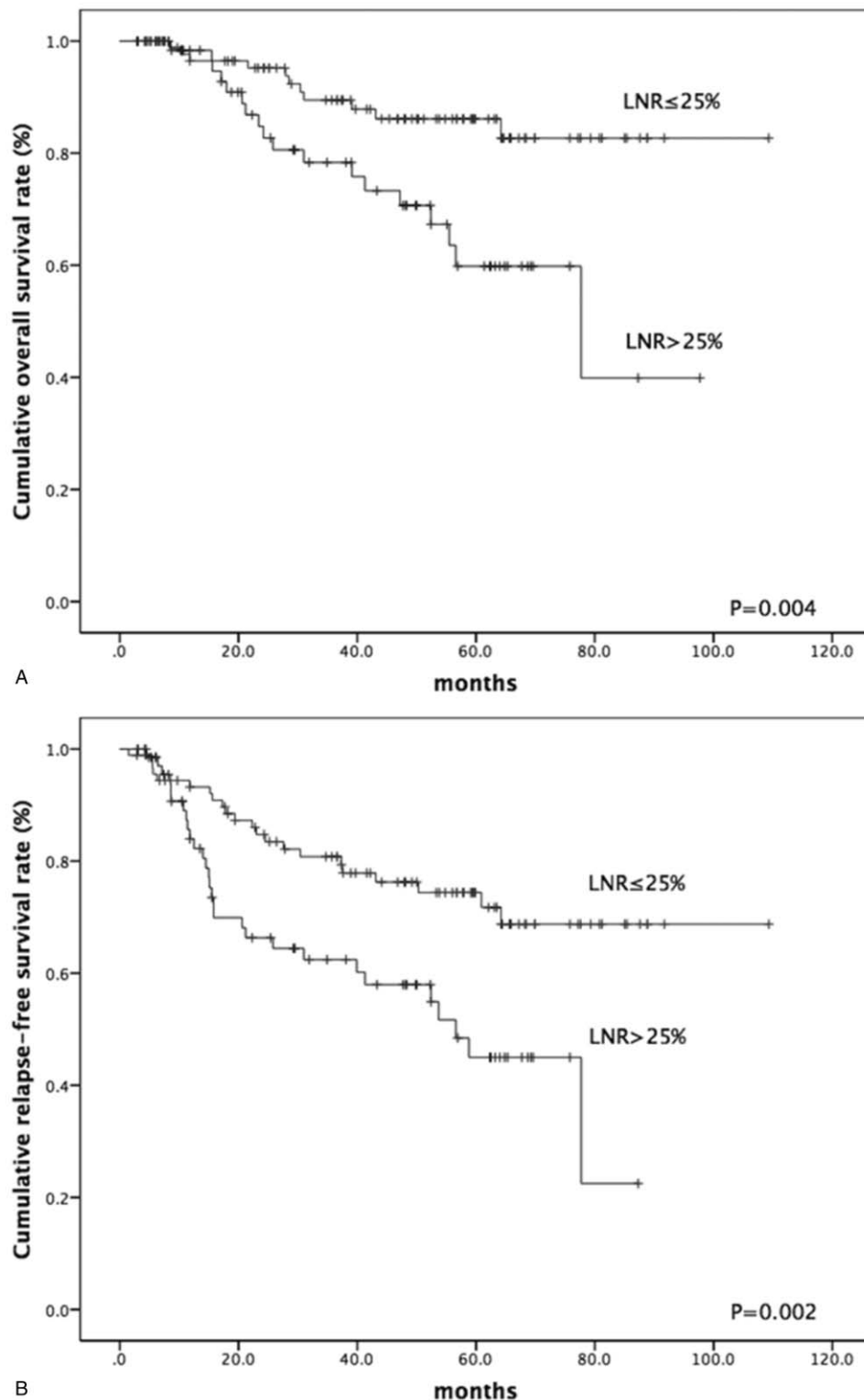


Figure 2. (A) Kaplan–Meier curves for overall survival of LNR >25% or ≤25% (B) Kaplan–Meier curves for relapse-free survival of LNR >25% or ≤25%. LNR = lymph node ratio.

hematological parameters collected from these 164 gastric adenocarcinoma patients within 1 week before surgery, including white blood cell (WBC), neutrophil proportion, lymphocyte proportion, NLR, mean platelet volume (MPV), platelet

distribution width (PDW), albumin and lactate dehydrogenase (LDH). All of these hematological parameters were continuous variables. According to the receiver-operating characteristics (ROC) curve analysis results, we found no significant cut-off

Table 2**The univariate and multivariate Cox analysis of prognostic factors for overall survival (OS).**

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age	2.328 (1.111–4.881)	.025*	2.375 (1.100–5.128)	.028*
≤ 60y vs >60y				
Gender				
Male vs Female	0.890 (0.405–1.956)	.772		
Tumor location				
GEJ vs non-GEJ	1.592 (0.734–3.452)	.239		
Tumor size				
≤ 5 cm vs >5 cm	1.114 (0.470–2.639)	.807		
Differentiated degree				
Medium-high vs low	1.274 (0.602–2.697)	.526		
TNM stage (8th edition)				
stage I-II vs III	12.195 (1.653–90.909)	.014*	7.692 (1.009–58.824)	.049*
LNR				
≤ 0.25 vs >0.25	2.890 (1.359–6.135)	.006*	2.439 (1.075–5.525)	.033*
Adjuvant chemotherapy				
FOLFOX vs SOX	1.344 (0.578–3.124)	.492		
Adjuvant radiation dose				
<45Gy vs ≥45Gy	2.918 (1.010–8.432)	.048*	2.782 (0.940–8.234)	.065
WBC (10 ⁹ /L)	1.092 (0.763–1.563)	.629		
Neutrophil ratio, %	0.993 (0.956–1.032)	.734		
lymphocyte ratio, %	1.003 (0.994–1.012)	.499		
NLR	0.854 (0.568–1.283)	.447		
MPV	1.096 (0.796–1.510)	.573		
PDW	0.899 (0.718–1.127)	.357		
serum albumin, g/L	1.005 (0.999–1.011)	.084		
LDH (U/L)	1.006 (0.993–1.018)	.356		

GEJ = gastroesophageal junction, non-GEJ = non-gastroesophageal junction, LNR = lymph node ratio, WBC = white blood cell, NLR = neutrophil-to-lymphocyte ratio, MPV = mean platelet volume, PDW = platelet distribution width, LDH = lactate dehydrogenase.

* P values < .05.

Table 3**The Cox analysis of prognostic factors for relapse-free survival (RFS).**

Variable	Cox univariate analysis	
	HR (95% CI)	P
Age	1.477 (0.856–2.551)	.161
≤ 60y vs >60y		
Gender		
Male vs Female	0.786 (0.440–1.402)	.414
Tumor location		
GEJ vs non-GEJ	1.148 (0.600–2.198)	.676
Tumor size		
≤5 cm vs >5 cm	1.056 (0.550–2.027)	.871
Differentiated degree		
Medium-high vs low	1.340 (0.604–2.976)	.471
TNM stage (8th edition)		
stage I-II vs III	3.802 (1.506–9.615)	.005*
LNR		
≤ 0.25 vs >0.25	2.326 (1.332–4.065)	.003*
Adjuvant chemotherapy		
FOLFOX vs SOX	1.348 (0.663–2.740)	.410
Adjuvant radiation dose		
< 45Gy vs ≥45Gy	1.296 (0.466–3.600)	.619
WBC (10 ⁹ /L)	0.838 (0.628–1.120)	.233
Neutrophil ratio, %	0.996 (0.965–1.028)	.801
lymphocyte ratio, %	1.001 (0.992–1.010)	.832
NLR	0.942 (0.758–1.170)	.588
MPV	1.148 (0.856–1.538)	.357
PDW	0.971 (0.815–1.158)	.746
serum albumin, g/L	1.003 (0.998–1.009)	.202
LDH (U/L)	1.003 (0.993–1.013)	.530

GEJ = gastroesophageal junction, non-GEJ = non-gastroesophageal junction, LNR = lymph node ratio, WBC = white blood cell, NLR = neutrophil-to-lymphocyte ratio, MPV = mean platelet volume, PDW = platelet distribution width, LDH = lactate dehydrogenase.

* P values < .05.

value of these preoperative hematological parameters, which could demarcate the different prognostic outcomes of gastric cancer patients in the present study (all $P > .05$). Besides, from the results of univariate COX analysis (Tables 2 and 3), we found that none of these preoperative hematological parameters was shown to be a significant predictive factor for OS and RFS prognoses (all $P > .05$).

4. Discussion

Radical gastrectomy and D2 lymphadenectomy have been widely performed in local advanced gastric cancer patients, and postoperative recurrence incidence remains high in spite of extended lymph nodes dissection. Many large worldwide clinical trial showed that combination of chemotherapy or chemoradiotherapy could improve survival outcomes of gastric cancer patients to some extent.^[11–13] The common and effective chemotherapy in gastric cancer were based on S-1, 5-fluorouracil and platinum, and combined radiotherapy at 45Gy-50.4Gy. However, there is no definitive recommended adjuvant treatment worldwide.

In this study, we retrospectively analyzed the database of gastric cancer patients with adjuvant chemoradiotherapy after D2 lymph node dissection in our hospital from 2006 to 2013. All patients applied FOLFOX or SOX chemotherapy regimen, combined with concurrent 3D-CRT or IMRT radiotherapy. The aim of this study was to explore probable prognostic factors in clinicopathologic factors, especially to study the prognostic value of LNR in the patients with gastric cancer after D2 resection and adjuvant chemoradiotherapy.

The 3-year OS and RFS rate of gastric cancer patients in this study was 88.4% and 76.8%, which was similar to the ARTIST trial outcomes of 3-year RFS rate of 78.2%,^[14] and prominently better than first reported survival outcomes of gastric cancer

patients with postoperative chemoradiotherapy in the INT0116 trial,^[15] which may attribute to the insufficient lymph nodes dissection with only 10% patients receiving D2 resection in INT0116, and large improvement of radiotherapy techniques from 2-dimensional radiotherapy to 3D-CRT and IMRT.

It remains large survival differences in advanced gastric cancer patients even treated with the same regimen, in accordance with complicated prognostic factors. It is valuable to find reliable prognosis predictive factors for clinical evaluation. Several studies have shown pN could be an important prognostic factor for patients with gastric cancer especially for less than 15, and the predictive value obviously decreased when it exceeds 15.^[3,16,17] In addition, LNR was first carried out by Nitti D, et al as a significant independent prognostic factor in gastric cancer.^[18] Except pN and LNR, LODDS as the log of the ratio between the number of positive and negative lymph nodes^[19] and Dukes-MAC-like pTN staging system^[20] were also shown as strong prognostic indicators in gastric cancer. However, many outcomes of latest researches have confirmed LNR's value and considered it could be better than other lymph node related parameters to predict prognosis because it is less affected by the extent of lymphadenectomy and the accuracy of positive lymph nodes number detected by pathologists.^[21-24] In the present study, we found both TNM stage and LNR were independent prognostic factors of OS and RFS in gastric cancer patients after D2 surgery, with no exact evidences shown a better predictive value in LNR.

Although the prognosis predictive value of LNR has been repeatedly certificated, the cutoff value of LNR distinguishing different prognoses remained uncertain, ranging from 0.2 to 0.65. Meanwhile, few previous studies analyzed the prognostic value of LNR in gastric cancer patients treated with chemoradiotherapy after a D2 resection surgery. According to this, we further analyzed the optimal cut-offs value of LNR with the survival prognosis by ROC curves analysis. Consequently, we found that 0.25 could be the most appropriate LNR cutoff value for predicting prognosis and LNR > 0.25 predicted a worse OS and RFS prognosis. In spite of different inclusion criteria, the LNR cutoff value and relative risk coefficient in our study were consistent with the outcomes of previous study by Yuhree Kim, et al including 719 gastric cancer patients from multi-institutional US Gastric Cancer Collaborative database.^[4] The similar findings indicated that LNR was a valuable, independent prognostic indicator of prognosis, while different adjuvant treatment regimens and surgical lymphadenectomy extent impacted little on prognosis evaluation of LNR.

We also recognized age as an independent prognostic factor correlated with OS of gastric cancer patients after D2 resection and adjuvant chemoradiotherapy, and patients with age >60 years showed a shorter OS time. We further analyzed clinical data of these older patients, and supposed worse OS could be attributed to poor conditions, poor surgical tolerance, higher incidence of incomplete postoperative adjuvant therapy and higher incidence of adverse reaction of older patients.

In addition, many researchers have explored the prognostic differences between different chemotherapy regimens in gastric cancer patients with adjuvant concurrent chemoradiotherapy, such as the American clinical trial CALGB 80101 compared epirubicin, cisplatin, and fluorouracil with fluorouracil and leucovorin within adjuvant chemoradiotherapy after curative resection of gastric cancer. The CALGB 80101 trial showed no significant prognostic differences between 2 different chemotherapies in patients with adjuvant chemoradiotherapy.^[25] The adjuvant chemoradiotherapy regimen of this study was

combination SOX or FOLFOX chemotherapy regimen with concurrent radiation. The efficacy and safety of SOX and FOLFOX chemotherapies treating gastric cancer had already been proved in our previous clinical trials^[7,8] or reported in other researches.^[26-30] Therefore, we further contrasted the prognosis of gastric cancer patients after D2 resection between SOX and FOLFOX chemotherapy regimens, which showed no significant differences ($P > .05$).

In the present study, we also explored probable preoperative predictive biomarkers in laboratory tests, but no hematological parameters or indexes were found with prognostic significance for gastric cancer patients after D2 lymphadenectomy with adjuvant chemoradiotherapy. Although some preoperative hematological parameters had been reported as valuable prognostic biomarkers in gastric cancer, such as blood albumin, lymphocytes, neutrophils, ALP, LDH, NLR, and PDW.^[31-34] It should be considered that these parameters may reflect some abnormal status of cancer patients at baseline, but not sensible enough to be predictive prognostic biomarkers. However, considering of small sample size of our study, there is also a possibility that some definitive predictive factors in preoperative blood tests may be insensible, thus larger scale clinical researches are needed to figure out probable predictive blood parameters in future.

In conclusion, we certified LNR could be a strong prognostic factor in gastric cancer patients with D2 dissection and adjuvant chemoradiotherapy in this study, and LNR over 0.25 predicted a worse OS and RFS prognosis. In addition to LNR > 0.25, age > 60 years, TNM stage III were also independent prognosis factors for more unfavorable OS in this retrospective study. Undeniably, our study had the limitations of retrospective study with small analyzed patients' number, which may lead to insufficient power. Therefore, a large-scale study is needed to further confirm the results of prognostic analysis, and further certify whether 0.25 could be the optimal cutoff value for distinguishing prognosis of gastric cancer.

Author contributions

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