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Prognostic Significance of Metastatic Lymph Node Ratio in Patients with pN3 Gastric Cancer Who Underwent Curative Gastrectomy

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Keywords

Gastric cancer · Metastatic lymph node ratio · N3 · Prognosis

Abstract

Background: Lymph node involvement is an important prognostic factor in patients with gastric cancer. The aim of this study was to determine the prognostic significance of metastatic lymph node ratio (MLNR) and compare it to the number of lymph node metastasis in pN3 gastric cancer. ***Methods:*** We retrospectively analyzed 207 patients with pN3 gastric cancer who had undergone radical gastrectomy. Prognostic factors and MLNR were evaluated by univariate and multivariate analysis. ***Results:*** An MLNR of 0.75 was found to be the best cut-off value to determine the prognosis of patients with pN3 gastric cancer ($p = 0.001$). The MLNR was significantly higher in patients with large-sized and undifferentiated tumors, vascular, lymphatic and perineural invasion, and total gastrectomy. In multivariate analysis, MLNR ($p = 0.041$), tumor differentiation ($p = 0.046$), and vascular invasion ($p = 0.012$) were found to be independent prognostic factors for disease-free survival, while both MLNR ($p < 0.001$) and pN stage ($p = 0.002$) were independent prognostic indicators, as was tumor size, for overall survival. There was significant difference with respect to the recurrence patterns between MLNR groups. Lymph node and peritoneal recurrences were significantly higher in patients with MLNR > 0.75 compared to the MLNR < 0.75 group ($p < 0.05$). However, recurrence patterns were similar between pN3a and pN3b. ***Conclusion:*** Our results showed that MLNR was a useful indicator to determine the prognosis and recurrence patterns of patients with radically resected gastric cancer. Moreover, MLNR is a beneficial and reliable technique for evaluating lymph node metastasis.

Introduction

Gastric cancer is one of the most common cancers and the third leading cause of cancer death worldwide [1, 2]. Although the worldwide incidence of gastric cancer has

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declined rapidly over the recent few decades, its long-term outcome has not improved much, and the cumulative 5-years survival rates of all patients have changed only slightly despite the recent advancements in medical treatment and surgical techniques [2, 3]. It is well documented that surgery is the only curative treatment, but it has a high rate of locoregional recurrence and distant metastasis. There is no effective treatment for recurrence, thus identifying prognostic and predictive markers may help to evaluate the precise status of disease and allow a more effective treatment of the patients [3, 4].

Accurate staging is important to predict the prognosis of patients with gastric cancer. Depth of tumor invasion (T stage) and nodal involvement (N stage) are the most important prognostic indicators in patients who are eligible for surgery [3–5]. In clinical practice, TNM, established collaboratively by the American Joint Committee on Cancer (AJCC) and the International Union for Cancer Control (UICC), is the most commonly used staging system. The 7th edition TNM staging classification requires a minimum of 15 lymph nodes to be removed during gastrectomy to determine the N stage [6]. However, the TNM system can potentially cause stage migration which appears to depend on the extent of the lymph node dissection [7–9]. Some studies have shown that the metastatic lymph node ratio (MLNR; quota between metastatic lymph nodes and retrieved lymph nodes) could be an alternative to the TNM staging classification to prevent stage migration. MLNR-based staging is also a feasible alternative for the prediction of prognosis in colorectal, gastric, breast, bladder, and pancreatic cancers [10, 11].

pN3 gastric cancer has been defined as a highly advanced disease with nodal metastasis according to the TNM staging classification. Recently, Komatsu et al. [12] reported that MLNR is useful to predict the prognosis and evaluate the extent of local tumor recurrence in patients with pN3 gastric cancer. In the current study, we also aimed to evaluate the prognostic significance of MLNR and compare it to the number of lymph node metastases in pN3 gastric cancer.

Patients and Methods

Between 2008 and 2013, a total of 207 patients with pathologically confirmed pN3 gastric cancer who had undergone curative gastrectomy were included in the study. The primary tumor was staged according to the AJCC 7th TNM staging classification for gastric cancer [6]. The clinicopathological findings were determined according to the Japanese Classification of Gastric Carcinoma (JCGC) [13]. All patients underwent D_2 or D_{2+} lymph node dissection.

Patient data were retrospectively obtained from patient charts with respect to age, sex, surgery type, histopathology, TNM stage, tumor size, tumor differentiation, lymph node involvement, pT stage, lymphatic invasion (LI), vascular invasion (VI) and perineural invasion (PI), adjuvant chemotherapy and/or radiation therapy, responses to treatment, and survival, after written informed consent had been obtained from patients or their relatives. The eligibility criteria consisted of a histologically confirmed R_0 gastric resection, which was defined as no macroscopic or microscopic residual tumor and a postoperative survival expectancy longer than 3 months. Patients with insufficient disease information and distant metastases at the time of diagnosis and those who received neoadjuvant chemotherapy were excluded from data analysis. The local ethics committee of our hospital approved the study.

All pathological specimens pertaining to the primary tumor and retrieved lymph nodes were re-evaluated according to the 7th TNM staging manual and 14th JCGC with respect to depth of invasion of primary tumor and retrieved lymph nodes by 2 pathologists with expertise in the area of gastric cancer [6, 13]. pN3 gastric cancer was classified into 2 subgroups; thus, pN3a refers to patients with 7–15 and pN3b to patients with more than 15 metastatic lymph nodes (TNM). MLNR was defined as the ratio of metastatic lymph nodes to the total number of dissected lymph nodes, and 0.75 was found to be the best cut-off value to determine the prognosis of patients with pN3 gastric cancer ($p = 0.001$) in terms of the log-rank statistics.

After surgery, patients were followed-up for recurrence with medical histories, physical examinations, complete blood counts, and biochemistry panels, as well as tumor markers, chest X-rays, and abdominal computed tomography scans. Gastroscopy was performed annually to control suspicious lesions in the gastric remnant.

A total of 157 (75.8%) patients received adjuvant chemoradiotherapy (CRT) within 4 weeks of surgery. Adjuvant CRT consisted of 5-fluorouracil 425 mg/m^2 per day, plus leucovorin 20 mg/m^2 per day for 5 days or capecitabine 1,650 mg/m^2 per day for 5 weeks, followed by 4,500 cGy of radiation at 180 cGy per day given 5 days per week for 5 weeks, with modified doses of fluorouracil and leucovorin on the first 4 and the last 3 days of radiotherapy or capecitabine 1,650 mg/m^2 per day for 5 weeks. 45 (21.7%) patients were treated with only capecitabine 2,000 mg/m^2 per day on days 1–14 or capecitabine and cisplatin 75 mg/m^2 on day 1, or capecitabine and oxaliplatin 130 mg/m^2 on day 1, repeated every 3 weeks without radiotherapy. Adjuvant treatment was not given to 5 (2.5%) patients because of comorbidities and poor performance status.

All recurrences were categorized as locoregional, peritoneal or hematogenous, or distant lymph node metastasis. Locoregional recurrences were defined as tumors within the gastric bed, regional gastric lymph nodes, and remnant stomach at the anastomosis or gastric stump. Peritoneal recurrences were classified as those cases with a positive cytology in the ascitic fluid, carcinomatosis, or ovarian metastasis. Hematogenous recurrences were described as visceral metastases. Distant lymph node metastases were also described as distant lymph nodes outside the regional basin.

Statistical Analysis

All data were analyzed with SPSS 16.0 (IBM Corp., Armonk, NY, USA) software. The clinicopathological factors of the MLNR groups were compared by means of the chi-squared test and Fisher's exact test. Survival analyses and curves were established with the Kaplan-Meier method and compared with the log-rank test. Disease-free survival (DFS) was defined as the time from curative surgery to disease progression or recurrence, or to the date of death or loss to follow-up. Overall survival (OS) was described as the time from diagnosis to the date of the patient's death or loss to follow-up. Univariate and multivariate analyses were performed with the Cox proportional hazards model to evaluate the importance of the MLNR and other clinicopathological features as prog-

Table 1. Correlation between metastatic lymph node ratio (MLNR) and clinicopathological factors

Factors	MLNR < 0.75, *n* (%)	MLNR ≥ 0.75, *n* (%)	*p*
Sex			0.09
Female	38 (37)	27 (26)	
Male	64 (63)	78 (74)	
Age, years			0.77
< 60	61 (60)	60 (57)	
≥ 60	41 (40)	45 (43)	
Surgery type			0.005
Subtotal gastrectomy	63 (62)	44 (42)	
Total gastrectomy	39 (38)	61 (58)	
Tumor diameter, cm			0.017
< 6	66 (64.7)	50 (47.6)	
≥ 6	36 (35.3)	55 (52.4)	
Tumor differentiation			< 0.001
Well	19 (18.6)	5 (4.8)	
Moderate	46 (45.1)	34 (32.2)	
Poor	37 (36.3)	66 (63.0)	
pN stage			< 0.001
N3a (7–15)	63 (62)	16 (15)	
N3b (> 16)	39 (38)	89 (85)	
pT stage			0.40
T1	8 (7.8)	10 (9.5)	
T2	11 (10.8)	12 (11.4)	
T3	50 (49.0)	60 (57.0)	
T4	33 (32.4)	23 (22.0)	
TNM stage			0.37
IIB	8 (7.8)	10 (9.5)	
IIIA	13 (12.7)	13 (12.4)	
IIIB	48 (47.1)	59 (56.2)	
IIIC	33 (32.4)	23 (21.9)	
Vascular invasion			0.016
Absent	28 (27.5)	15 (14.3)	
Present	74 (72.5)	90 (85.7)	
Lymphatic invasion			< 0.001
Absent	38 (37.3)	11 (10.5)	
Present	64 (62.7)	94 (89.5)	
Perineural invasion			0.03
Absent	39 (38.2)	19 (18.1)	
Present	63 (61.8)	86 (81.9)	

nostic factors. Multivariate p values were used to characterize the independence of these factors. The 95% confidence interval (CI) was used to quantify the relationship between survival time and each independent factor. All p values were 2-sided in tests, and p values of less than 0.05 were considered statistically significant.

Results

Overall, 65 (31.4%) patients were female and 142 (68.6%) were male, with a median age of 57 years (range 24–78 years). 121 (58.5%) patients were aged 60 years or younger. Postoperatively, of 207 patients, 18 (8.7%) were classified as having pT1 tumors, 23 (11.1%) as pT2, 110 (53.1%) as pT3, and 56 (27.1%) as pT4. In addition, 18 (8.7%) patients were staged as stage IIB, 26 (12.6%) as stage IIIA, 107 (51.7%) as stage IIIB, and 56 (27.1%) as stage IIIC. The median number of dissected and metastatic lymph nodes was 29 (range 17–67) and 17 (range 7–62), respectively. Based on the number of lymph node metastases, 79 (38.2%) patients were classified as pN3a and 128 (61.8%) as pN3b. Moreover, the median MLNR was 0.62 (range 0.16–1), and 102 (49.3%) patients were classified as MLNR < 0.75 and 105 (50.7%) as MLNR ≥ 0.75.

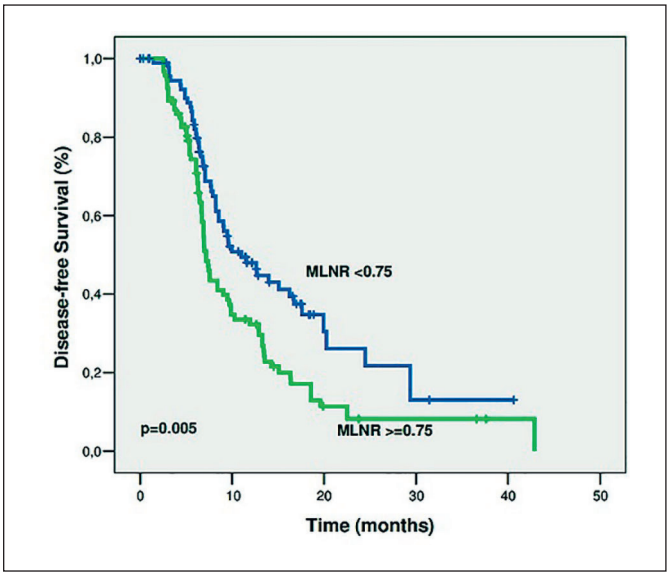

Fig. 1. Disease-free survival curves in metastatic lymph node ratio (MLNR) groups.

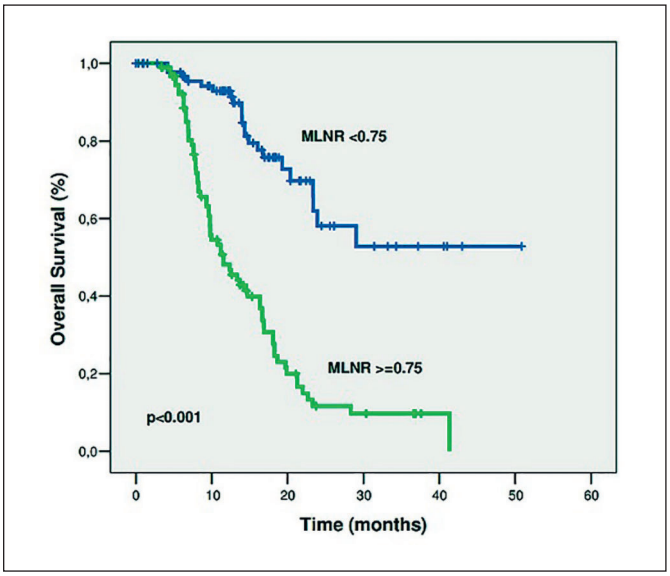

Fig. 2. Overall survival was significantly worse in patients with a metastatic lymph node ratio (MLNR) ≥ 0.75 than in those with an MLNR < 0.75.

Table 2. Univariate and multivariate analysis of disease-free survival (DFS) according to clinicopathological factors

Factors	Median DFS time, months	Univariate *p* values	Multivariate *p* values	HR (95% CI)
Sex		0.48		
Female	9.66			
Male	8.40			
Age, years		0.12		
≤ 60	9.46			
> 60	8.23			
Tumor size, cm		0.18		
< 6	9.40			
≥ 6	8.46			
Surgery type		0.86		
Subtotal	7.90			
Total	9.96			
Tumor differentiation		0.035	0.046	2.49 (1.01–6.11)
Well	19.9			
Moderate	9.4			
Poor	7.5			
pN stage		0.027	0.27	1.28 (0.82–2.0)
N3a (7–15)	11.5			
N3b (≥ 16)	7.4			
pT stage		0.24	0.64	0.70 (0.16–3.0)
T1	19.9			
T2	6.66			
T3	9.60			
T4	8.53			
TNM stage		0.44	0.61	1.43 (0.35–5.91)
IIB	19.9			
IIIA	6.9			
IIIB	9.6			
IIIC	8.5			
Vascular invasion		0.004	0.012	1.95 (1.16–3.29)
Absent	13.9			
Present	7.7			
Lymphatic invasion		0.38		
Absent	9.5			
Present	8.2			
Perineural invasion		0.18		
Absent	10.2			
Present	7.5			
MLNR		0.005	0.041	1.20 (0.79–1.14)
< 0.75	11.0			
≥ 0.75	7.1			

HR = Hazards ratio; CI = confidence interval, MLNR = metastatic lymph node ratio.

Significant differences were detected between MLNR groups with respect to surgery type, tumor size, tumor differentiation, VI, LI, and PI. The MLNR was significantly higher in tumors of large size ($p = 0.017$) and with an undifferentiated histology ($p < 0.001$). The prevalence of VI ($p = 0.016$), LI ($p < 0.001$), and PI ($p = 0.03$) was significantly higher for tumors with MLNR ≥ 0.75 than for those with MLNR < 0.75. Total gastrectomy was more frequently performed for tumors with MLNR ≥ 0.75, while subtotal gastrectomy was more frequently carried out for those with MLNR < 0.75 ($p = 0.005$). The relationship between subgroups of MLNR and clinicopathological factors is summarized in Table 1.

At a median follow-up of 27 months (range 7.5–55.8 months), the median DFS time of patients with MLNR < 0.75 tumors was better than that of patients with MLNR ≥ 0.75 tumors (11 vs. 7.1 months, $p = 0.005$) (Fig. 1). Furthermore, the median OS of patients with MLNR ≥ 0.75 tumors was significantly worse than that of patients with MLNR < 0.75 tumors (11.5 months vs. not reached,

Table 3. Univariate and multivariate analysis of overall survival (OS) according to clinicopathological factors

Factors	Median OS time, months	Univariate *p* values	Multivariate *p* values	HR (95% CI)
Sex		0.12		
Female	22.0			
Male	16.8			
Age, years		0.42		
≤ 60	16.6			
> 60	18.2			
Tumor size, cm		< 0.001	0.031	1.63 (1.04–2.54)
< 6	28.3			
≥ 6	16.3			
Surgery type		0.48		
Subtotal	19.3			
Total	18.1			
Tumor differentiation		0.30		
Well	23.9			
Moderate	19.3			
Poor	16.8			
pN stage		< 0.001	0.002	2.95 (1.49–5.86)
N3a (7–15)	41.3			
N3b (≥ 16)	18.8			
pT stage		0.76		
T1	23.9			
T2	18.2			
T3	18.1			
T4	19.7			
TNM stage		0.76		
IIB	23.9			
IIIA	16.3			
IIIB	18.1			
IIIC	19.7			
Vascular invasion		0.002	0.40	1.39 (0.63–3.08)
Absent	NR			
Present	16.6			
Lymphatic invasion		< 0.001	0.09	1.89 (0.89–3.99)
Absent	NR			
Present	16.7			
Perineural invasion		0.048	0.22	1.40 (0.80–2.44)
Absent	23.3			
Present	16.7			
MLNR		< 0.001	< 0.001	2.61 (1.55–4.41)
< 0.75	NR			
≥ 0.75	11.5			

HR = Hazards ratio; CI = confidence interval; NR = not reached; MLNR = metastatic lymph node ratio.

p < 0.001) (Fig. 2). According to the pN3 subclassification, the median DFS and OS times were better in patients with pN3a compared to those with pN3b (DFS: 11.5 vs. 7.4 months, p = 0.027; OS: 41.3 vs. 18.8 months, p < 0.001).

In the univariate analysis for DFS, tumor differentiation, pN stage, MLNR, and the presence of VI were found to be significant prognostic factors. However, when the univariate analysis was performed for OS, we detected that tumor size, pN stage, MLNR, VI, LI, and PI were important prognostic indicators. The results of univariate analysis for both DFS and OS are shown in Tables 2 and 3, respectively.

A multivariate analysis with the Cox proportional hazards model was performed in order to further evaluate all of the significant prognostic factors that were detected in the univariate analysis for patients with a pN3 gastric cancer. This showed that MLNR was an independent prognostic factor (hazard ratio 1.20, 95% CI 0.79–1.14; p = 0.042), as were tumor differentiation and the presence of VI for DFS (Table 2). Multivariate analysis for OS demonstrated that tumor size, pN stage, and MLNR were an independent prognostic indicators (Table 3).

Table 4. Recurrence pattern according to the metastatic lymph node ratio (MLNR) in patients with pN3 gastric cancer

Recurrence pattern	MLNR < 0.75, *n* (%)	MLNR ≥ 0.75, *n* (%)	*p*
All recurrences	58 (40.3)	86 (59.7)	0.003
Locoregional recurrence	4 (44.5)	5 (55.5)	0.691
Peritoneal recurrence	8 (16.0)	42 (84.0)	< 0.001
Hematogenous recurrence	37 (60.6)	24 (39.4)	0.032
Distant lymph node metastasis	5 (31.2)	11 (68.8)	0.022
Other	5 (55.5)	4 (44.5)	0.542

When patients were analyzed according to pT stages, pT3–4 stages were significantly correlated with large-sized (p = 0.005) and undifferentiated (p < 0.001) tumors. The prevalence of LI (p = 0.023) and PI (p < 0.001) was significantly higher in pT3–4 tumors compared with pT1–2 tumors. Moreover, pN3a was significantly associated with pT1–2 tumors, while N3b was associated with pT3–4 tumors (p < 0.001). However, there was no significant relationship with respect to MLNR, age, sex, VI, and surgery type between pT1–2 and pT3–4 groups (p > 0.05). On the other hand, median PFS and OS times for patient with pT1–2 tumors were similar compared to those with pT3–4 tumors (PFS: 6.6 vs. 9.0 months, p = 0.19; OS: 18.2 vs. 18.1 months, p = 0.72).

There was significant difference with respect to recurrence and recurrence patterns between MLNR groups. The rate of recurrence for patients with MLNR < 0.75 was significantly lower than that for patients with MLNR ≥ 0.75 (40.3 vs. 59.7%, p = 0.001). Peritoneal and lymph node recurrence rates were significantly higher in patients with MLNR ≥ 0.75 compared to the MLNR < 0.75 group (p < 0.001 and 0.022, respectively), while hematogenous recurrences were significantly lower in patients with MLNR ≥ 0.75 compared to the MLNR < 0.75 group (p < 0.032). However, total recurrence and recurrence patterns were similar between pN3a and pN3b (p = 0.088 and 0.268, respectively). Table 4 shows the rate of total recurrence and recurrence patterns according to the MLNR groups in patients with pN3 gastric cancer.

Discussion

In the present study, the prevalence of large-sized tumors, undifferentiated histology, LI, and PI was significantly higher in patients with MLNR ≥ 0.75 than in those with MLNR < 0.75. Moreover, total gastrectomy was more frequently carried out in patients with MLNR ≥ 0.75 compared to those with MLNR < 0.75. Using univariate analysis, we found that tumor differentiation, pN stage, MLNR, and the presence of VI were important prognostic factors for DFS, while tumor size, pN stage, MLNR, VI, LI, and PI were found to be significant prognostic indicators for OS. In addition, when data were evaluated by multivariate analysis in order to further elucidate independent prognostic indicators, MLNR was an independent prognostic factor, as were tumor differentiation and VI for DFS. For OS, MLNR, pN stage, and tumor size were independent prognostic indicators.

The determination of prognostic factors for patients with gastric cancer is essential for predicting the outcome and determining appropriate treatment strategies. It is generally accepted that depth of tumor invasion and lymph node metastasis are the most important prognostic indicators [5]. Although it remains unreliable whether the location or the number of metastatic lymph nodes is most important, some studies reported that the number of metastatic lymph nodes, but not their level, is an independent prognostic indicator [14, 15]. For correct pN stage, the number of resected lymph nodes is important, but this might be affected by certain surgical and pathological factors. In addition, stage migration occurs in 5–15% of cases with the AJCC TNM staging system [16]. To resolve these limitations, MLNR as a new prognostic factor has been previously presented by several studies [15–18]. It has proven to be a good option to prevent the 'stage migration' phenomenon and is also usable to determine an accurate prognosis, especially in patients with < 15 lymph nodes dissected or D_1 lymphadenectomy or non-curative resection, to aid decision-making for further treatment strategies [16–21]. In our study, MLNR was significantly greater in patients with large tumors and an undifferentiated histology, as well as LI, VI, and PI. Furthermore, MLNR was significantly correlated with total gastrectomy. Our results are compatible with the literature [19, 21].

pN3 gastric cancer has been defined as a highly advanced disease with nodal metastasis according to the TNM staging classification. Therefore, it has a very poor prognosis compared with pN1,N2 disease. Only 1 previous study, reported by Komatsu et al. [12], has investigated the clinical usefulness of the MLNR in patients with pN3 gastric cancer. In the current study, we also evaluated the prognostic significance of MLNR and compared it to pN stage in 207 patients with pN3 gastric cancer. Komatsu et al. [12] detected that an MLNR of 0.4 was the best cut-off value to stratify prognosis. However, in our study, an MLNR of 0.75 was found to be the best cut-off value to determine the prognosis of patients with pN3 gastric cancer in terms of the log-rank statistics. This difference, according to previous literature, may be related to the large sample size and patient heterogeneity in our study.

Komatsu et al. [12] showed that older age, tumor size, pT stage, LI, VI, pN stage, and MLNR were important prognostic indicators for OS in univariate analysis. On the other hand, multivariate analysis indicated that only older age, larger tumor size, and MLNR were independent prognostic indicators in pN3 gastric cancer. In our study, we detected tumor differentiation, pN stage, MLNR, and VI for DFS, and tumor size, pN stage, MLNR, VI, LI, and PI for OS as important factors in univariate analysis. In addition, when the multivariate analysis was performed, MLNR, tumor differentiation, and VI for DFS, and larger tumor size, pN stage, and MLNR for OS were found to be independent prognostic indicators. Our findings were thus compatible with the study by Komatsu et al. [12] in terms of tumor size and MLNR.

We found that the median DFS and OS times of patients with MLNR < 0.75 tumors were significantly better than those of patients with MLNR ≥ 0.75 tumors (PFS: 11 vs. 7.1 months; $p = 0.005$; OS: not reached vs. 11.5 months, $p < 0.001$). According to the pN3 subclassification, similarly, the median DFS and OS times were worse in patients with pN3b compared to those with pN3a (DFS: 7.4 vs. 11.5 months, $p = 0.027$; OS: 18.8 vs. 41.3 months, $p < 0.001$). The study by Komatsu et al. [12] showed that OS time was better for patients with both MLNR < 0.4 and pN3a compared to patients with both MLNR ≥ 0.4 and pN3b. DFS could not be analyzed in their study. Our OS results were thus similar to those of Komatsu et al.'s [12] study. These results showed that patients with both pN3b and MLNR ≥ 0.75 had a very poorer prognosis and needed further intensive systemic treatment after curative gastrectomy.

There was significant difference according to the recurrence patterns between MLNR groups. Firstly, the rate of recurrence for patients with MLNR ≥ 0.75 was significantly greater compared to patients with MLNR < 0.75. Moreover, peritoneal and lymph node recurrences were also significantly higher in the MLNR ≥ 0.75 group, similar to previous literature [12]. Although pN3 gastric cancer has been accepted as a highly advanced disease with highly nodal metastasis risk, MLNR may reflect the extent of local tumor clearance. However, hematogenous recurrences were higher in patients with MLNR< 0.75, and recurrence patterns were similar between pN3a and pN3b groups.

Because pN stage is sometimes affected by the number of retrieved lymph nodes, stage migration might occur in patients who underwent D_1 lymphadenectomy. To prevent this problem and for appropriate nodal staging, more than 25 lymph nodes are needed in both the 7th AJCC TNM and the 14th JCGC [6, 13]. Therefore, combining both nodal staging systems with the new MLNR system may be useful to achieve correct nodal staging. In addition, treatment decision making and allocation of intensive systemic therapy may be made more appropriate, especially in patients who underwent D_1 lymphadenectomy.

The retrospective nature of our study was an important limitation and might have influenced the findings. Another limitation was the short follow-up interval. Although our results should be confirmed by prospective studies and compared with all lymph node dissection types for gastric cancer in Westerns as well as Eastern countries, we believe that they contribute to the literature due to the large sample size and analysis of distinct prognostic factors as well as MLNR for both DFS and OS by multivariate analysis, which is different to the previous study evaluating pN3 gastric cancer [12].

In conclusion, our study indicates that the new MLNR and AJCC pN staging systems are independent prognostic indicators for both DFS and OS in patients with pN3 radically resected gastric cancer. Furthermore, high MLNR was significantly correlated with higher lymph node and peritoneal recurrence. Although superiority of MLNR over pN staging could not be proven, MLNR may be a useful and reliable technique to evaluate lymph node metastasis and to stratify prognosis in pN3 gastric cancer.

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Disclosure Statement

The authors declare that there are no conflicts of interest.

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