The prognostic value of lymph node ratio and log odds of positive lymph nodes in patients with lung adenocarcinoma

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ABSTRACT

Objective: To investigate whether lymph node ratio and log odds ratio can be used for predicting the prognosis of patients with lung adenocarcinoma.

Methods: A total of 1097 patients with lung adenocarcinoma who underwent complete surgical resection and systematic lymph node dissection between 2008 and 2013 were studied retrospectively. Lymph node ratio was calculated as: $\frac{\text{positive lymph nodes}}{\text{total lymph nodes}}$. Log odds ratio was calculated as: $\log \frac{\text{positive lymph nodes} + 0.5}{\text{total lymph nodes} - \text{positive lymph nodes} + 0.5}$. Patients were grouped respectively into 4 groups by the use of recursive partitioning according to their lymph node ratio and log odds ratio. Linear trend χ^2 test was used for measuring monotonicity and discriminatory power.

Results: The 3-year survival rate was 91.0% (89.9%-92.1%) for group 0, 75.2% (71.4%-79.0%) for group 1, 56.5% (51.5%-61.5%) for group 2, and 41.4% (36.4%-46.4%) for group 3 of lymph node ratio, respectively. In addition, the 3-year survival rate was 89.9% (88.7%-91.1%) for group 1, 78.4% (74.4%-82.4%) for group 2, 56.0% (50.9%-61.1%) for group 3, and 41.0% (36.1%-45.9%) for group 4 of log odds ratio, respectively. Univariable and multivariable Cox models identified that both lymph node ratio and log odds ratio were significant prognostic factors for patients' survival. Log-rank test of trend χ^2 statistics of both lymph node ratio ($P < .001$) and log odds ratio ($P < .001$) showed significant differences.

Conclusions: Both lymph node ratio and log odds ratio can be used as prognostic factors for clinicians to predict patients' prognosis. (J Thorac Cardiovasc Surg 2017;153:702-9)

Overall survival grouped by the log odds ratio system.

Central Message

Both lymph node ratio and log odds ratio of positive lymph nodes are of prognostic value for patients' prognosis. They are worth considering when making therapeutic strategies.

Perspective

Our study reveals that although the number of metastatic lymph nodes plays no role in determining patients' N stage in lung cancer, it still has the prognostic value. Both lymph node ratio and log odds ratio of positive lymph nodes are good prognostic indices for lung cancer.

See Editorial Commentary page 710.

The prognosis for patients with non-small cell lung cancer currently is estimated based on the tumor, node, metastasis (TNM) system, which assigns nodal metastasis based on the involved lymph node station. The determination of the N stage of non-small cell lung cancer was based

mainly on the lymphatic region involved, according to the seventh and the upcoming eighth TNM staging system.^{1,2} This current approach does not take into consideration the number of involved lymph nodes, however, which may be limiting the precision of the prognostic estimates.

Although the number of metastatic lymph nodes plays no role in determining the N stage of a primary lung cancer, several studies have found that patients with a high lymph node ratio (LNR) tend to have a poor prognosis compared with those with a low LNR.³⁻⁹ Moreover, log odds ratio (LODDS), defined as the log of the ratio between the number of positive lymph nodes (PLNs) and the number of negative lymph nodes, has been proved effective in

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Abbreviations and Acronyms

AIC	= Akaike information criterion
IQR	= interquartile range
LNR	= lymph node ratio
LODDS	= log odds ratio
LR	= likelihood ratio
OS	= overall survival
PLN	= positive lymph node
pN	= pathologic N stage
RFS	= recurrence-free survival
TNM	= tumor, node, metastasis

predicting the prognosis of patients with head and neck, breast, gallbladder, gastric, and colorectal cancers.¹⁰⁻¹⁴ Whether LODDS can be used as a prognostic index of non–small cell lung cancer, however, is still unclear.

Our study aims to determine the discriminatory accuracy of LODDS for prognosis after surgical resection in patients with resectable non–small cell lung cancer. Our secondary aim was to compare the prognostic stratification of LNR and LODDS with the current N-staging system.

PATIENTS AND METHODS

Patients

A total of 1097 patients with clinically resectable lung adenocarcinoma who did not have invasive mediastinal staging between May 2008 and May 2013 in Fudan University Shanghai Cancer Center were included in this study (Figure 1). All patients received a surgical R0 resection and systematic lymph node dissection. The modality of skeletal systematic lymph node dissection was performed according to the tumor location. Lymph node stations 7, 8, 10, and 11 were dissected routinely regardless of the tumor location. In addition, for a tumor located in the left upper lobe, lymph node stations 4, 5, and 6 were dissected routinely. For a tumor located in the left lower lobe, lymph node stations 4, 5, 6, and 9 were dissected routinely. For a tumor located in the right upper lobe, lymph node stations 2 and 4 were dissected routinely, and station 3 was dissected optionally. For a tumor located in the right middle lobe, lymph node stations 2 and 4 were dissected routinely, and station 3 was dissected optionally. For a tumor located in the right lower lobe, lymph node stations 2, 4, and 9 were dissected routinely, and station 3 was dissected optionally (Video 1). Patients with stage II or III diseases received a 4-cycle, platinum-based doublet chemotherapy 3 to 4 weeks after surgery. No patients underwent neoadjuvant therapy. None of the included patients received invasive mediastinal staging before surgery. Resected tumors and lymph nodes were labeled in the operation room and reviewed by pathologists to determine their pathologic stage, according to the current seventh TNM staging system for lung cancer.¹ All lymph nodes resected were identified and reported by pathologists. This study was approved by the Committee for Ethical Review of Research (Fudan University Shanghai Cancer Center IRB# 090977-1). Patients' informed consents were waived because this was a retrospective study.

Follow-up Protocol

The start point of a patient's follow-up data is considered the day he/she received surgery. Patients came to hospital to take a routine

FIGURE 1. Inclusion and exclusion criteria.

examination including chest computed tomography, brain magnetic resonance imaging, and abdominal ultrasonography every 3 months for the first 2 years after surgery, every 6 months for the next 2 years after surgery, and once a year from then on. Recurrence was defined as local if it was at the site of the excised lobe (including infiltrations along the stapler line and stumps of bronchi and vessels), regional if it involved mediastinal or hilar lymph nodes, or an ipsilateral lobe, distal if it occurred at other organs or as a pleural diffuse. A telephone follow-up would be made if the patient didn't come to the clinic. The follow-up work started in May 2008 and ended in October 2016. Overall survival (OS) was considered as the time between the day of surgery and the day of death from any cause. Recurrence-free survival (RFS) was considered as the time between the day of surgery and the day of disease recurrence. Patients who died before disease recurrence were censored on the date of their last day alive and patients with no events were censored at the date of their last follow-up.

VIDEO 1. Left upper lobe–lingual segmentectomy plus systematic lymph node dissection. Video available at: [http://www.jtcvsonline.org/article/S0022-5223\(16\)31672-5/addons](http://www.jtcvsonline.org/article/S0022-5223(16)31672-5/addons).

Definition of LNR and LODDS

LNR was defined as the ratio between the number of PLNs and the number of total lymph nodes retrieved. LNR was divided into 4 groups by the use of recursive partitioning: LNR0 ($\text{LNR} = 0$), LNR1 ($0 < \text{LNR} \leq 0.14$), LNR2 ($0.14 < \text{LNR} \leq 0.38$), and LNR3 ($0.38 < \text{LNR} \leq 1$). LODDS was defined as the log ratio between the number of PLNs and the number of negative lymph nodes, it was calculated as: $\log \frac{\text{PLN} + 0.5}{\text{TLN} - \text{PLN} + 0.5}$, where 0.5 was added into both the numerator and the denominator to avoid singularity.¹⁵ Based on the LODDS calculated, LODDS was divided into 4 groups using recursive partitioning: LODDS1 ($-2.10 \leq \text{LODDS} \leq -1.01$), LODDS2 ($-1.01 < \text{LODDS} \leq -0.70$), LODDS3 ($-0.70 < \text{LODDS} \leq -0.20$), and LODDS4 ($-0.20 < \text{LODDS} \leq 1.74$).

Statistical Analyses

Clinical and pathologic characteristics, including patient sex, age, smoking status, pathologic T stage, pathologic N stage, pathologic TNM stage, lymphovascular invasion status, number of lymph nodes resected, number of positive nodes, Charlson comorbidity index, surgery type, tumor location, LNR, and LODDS were recorded. Log-rank test was performed to analyze the correlation between patients' clinicopathologic characteristics and 3-year OS. Number of lymph nodes resected was dichotomized with the receiver operating characteristic curves, where 14.50 was chosen as the cut-point where the predictive performance was the highest. Number of positive nodes was grouped by the use of recursive partitioning. Kaplan-Meier survival curves were used to compare the RFS and OS between different groups of patients. Log-rank test of trend χ^2 statistics were used to assess discriminatory ability and monotonicity. In addition, we performed a 2-step univariable and multivariable Cox proportional hazards regression model to identify independent prognostic factors for patients with lung adenocarcinoma. First, univariable analysis was performed to identify which among those confounding factors, including sex, age, smoking status, surgery type, Charlson comorbidity index, percent of forced expiratory volume in 1 second predicted, adjuvant chemotherapy, pathologic T stage, pathologic N stage, TNM stage, tumor location, number of lymph nodes resected, number of PLNs, LNR, and LODDS, were prognostic factors. Second, we separately included N, LNR, and LODDS in 3 multivariable Cox regression models, along with those factors with a P value $< .1$ in the first step to identify independent prognostic factor(s). The Spearman rank correlation was used to assess the correlation between LNR and LODDS. Model fit was examined with the Akaike Information Criterion (AIC), and the Harrell C-statistic was used to assess discriminatory accuracy of each model. All statistical analyses were performed with SPSS (version 22.0; IBM Corp, Armonk, NY) and R (version 3.3.0; R Foundation for Statistical Computing, Vienna, Austria). Survival curves were depicted using GraphPad Prism (version 6.01; GraphPad Software Inc, La Jolla, Calif).

RESULTS

For all the 1097 patients, the median number of lymph node stations dissected was 6, and the median number of lymph nodes dissected was 16. The median follow-up time was 40.0 (interquartile range [IQR], 22.2-51.6) months. Of them, 729 were in the LNR0 group, 157 were in the LNR1 group, 101 were in the LNR2 group, and 110 were in the LNR3 group. For the LODDS system, 762 were in the LODDS1 group, 118 were in the LODDS2 group, 106 were in the LODDS3 group, and 111 were in the LODDS4 group (Table 1). The median follow-up time was 41.5 (IQR, 27.4-53.3), 40.8 (IQR, 23.1-52.8), 32.0 (IQR,

13.4-45.0), and 23.4 (IQR, 11.7-42.3) months for patients in the LNR0, LNR1, LNR2, and LNR3 groups. The median follow-up time was 41.5 (IQR, 27.3-54.2), 40.0 (IQR, 23.2-50.1), 31.6 (IQR, 13.2-44.9), and 23.2 (IQR, 11.8-42.2) months for patients in the LODDS1, LODDS2, LODDS3, and LODDS4 groups. The relationship between clinicopathologic characteristics and 3-year OS was shown in Table 1. Patients who were male, former/current smokers, with lymphovascular invasion, with more lymph nodes dissected, with more positive nodes examined, with a greater Charlson comorbidity index, who received more invasive surgery, and received adjuvant chemotherapy tended to have a lower 3-year survival rate. In addition, T stage, N stage, TNM stage, LNR group, and LODDS group had a significant influence on patients' 3-year OS. Basically, the greater the stage, the poorer the prognosis. Each variable in Table 1 also was stratified by the LODDS strata, and the distribution of pathologic N stage (pN) in the LNR strata is shown in Table E1.

RFS and OS for pN, LNR, and LODDS were analyzed by the use of Kaplan-Meier survival curves, which are shown in Figure 2 and Figure 3. All 3 systems were associated strongly with patients' RFS (Figure 2) and OS (Figure 3). Log-rank test of trend χ^2 statistics showed pN ($P < .001$), LNR ($P < .001$), and LODDS ($P < .001$) showed good discriminatory ability and monotonicity. Among 426 patients with recurrent diseases, local recurrence was seen in 22 patients, regional recurrence was seen in 90 patients, distal recurrence was seen in 221 patients, and data of recurrent site for 93 patients were unavailable. A comparison between single or multiple lymph node stations involved in patients with N1 and N2 diseases is shown in Table E2. As shown in Figures 2 and 3, there were significant differences in patients' RFS and OS in all 3 systems. Moreover, we used Cox proportional hazards regression model to assess whether this result could be influenced by other clinical and pathologic factors. In the univariable Cox model, the results showed that sex, smoking status, surgery type, percent of forced expiratory volume in 1 second predicted, adjuvant chemotherapy, pathologic T stage, pathologic N stage, pathologic TNM stage, tumor location, total number of lymph nodes resected, number of PLNs, and LNR and LODDS were all prognostic factors (Table 2). Then, in the multivariable analysis 1, when put all the clinical and pathologic risk factors together, both LNR ($P = .073$) and LODDS ($P = .046$) were shown to be independent prognostic factors, whereas pN stage failed to show a significant difference ($P = .284$, Table 2).

With the previous results strongly supporting the point that LNR and LODDS were able to predict patients' prognoses, we next performed likelihood ratio (LR) test, calculated the Harrell Concordance index and AIC of pN, LNR, and LODDS systems. The results are shown in

TABLE 1. Clinicopathologic characteristics of patients with lung adenocarcinoma (n = 1097)

	No.	LODDS1	LODDS2	LODDS3	LODDS4	3-y OS%	P value
	cases	(−2.10 < LODDS ≤ −1.01)	(−1.01 < LODDS ≤ −0.70)	(−0.70 < LODDS ≤ −0.20)	(−0.20 < LODDS ≤ 1.74)	(95% CI)	(log-rank test)
Sex							
Male	609	439	67	51	52	76.3 (74.2-78.4)	.004
Female	488	323	51	55	59	83.1 (81.5-84.7)	
Age group, y							
≤60 (mean age)	541	355	61	59	66	81.7 (79.9-83.5)	.326
>60	556	407	57	47	45	78.5 (76.6-80.4)	
Smoking status							
Former/current	353	227	37	50	39	71.6 (69.0-74.2)	<.001
Never	744	535	81	56	72	84.1 (82.7-85.5)	
T stage							
1	638	493	60	46	39	89.1 (87.8-90.4)	<.001
2	384	231	55	47	51	72.7 (70.3-75.1)	
3	56	31	3	9	13	42.3 (35.1-49.5)	
4	19	7	0	4	8	49.9 (38.0-69.8)	
N stage							
0	729	702	22	5	0	91.0 (89.9-92.1)	<.001
1	108	30	49	17	12	83.5 (79.7-87.3)	
2	260	30	47	84	99	50.8 (47.6-54.0)	
TNM stage							
I	663	635	23	5	0	94.1 (93.1-95.1)	<.001
II	142	80	37	15	10	75.5 (41.5-79.5)	
III	292	47	58	86	101	53.1 (50.1-56.1)	
Lymphovascular invasion							
Yes	178	46	27	43	62	56.2 (52.1-60.3)	<.001
No	919	716	91	63	49	84.6 (83.3-85.9)	
Number of lymph nodes dissected							
<15	443	314	48	39	42	85.8 (84.0-87.6)	<.001
≥15	654	448	70	67	69	76.1 (74.3-77.9)	
Number of positive nodes							<.001
0	729	702	22	5	0	91.0 (89.9-92.1)	
1-2	157	58	78	16	5	76.3 (72.7-79.9)	
3-6	101	2	18	58	23	54.8 (49.6-60.0)	
>6	110	0	0	27	63	39.5 (34.5-44.5)	
Charlson comorbidity index							<.001
0	782	540	89	75	78	79.5 (77.9-81.1)	
1	262	184	24	25	29	81.1 (78.5-83.7)	
2	47	34	4	6	3	85.0 (79.3-90.7)	
3	6	4	1	0	1	66.7 (47.5-85.9)	
Surgery type							<.001
Wedge/seg	131	89	13	15	14	90.8 (88.0-93.6)	
Lob/bilobectomy	946	667	102	86	91	79.7 (78.3-81.1)	
Pneumonectomy	20	6	3	5	6	39.7 (28.0-51.4)	
Adjuvant chemotherapy							<.001
Yes	445	186	84	83	92	68.4 (66.0-70.8)	
No	652	576	34	23	19	88.3 (87.0-89.6)	
Tumor location							
LUL	291	186	38	30	37	78.6 (76.0-81.2)	.483
LLL	185	122	17	27	19	75.5 (72.2-78.8)	.047
RUL	352	263	37	28	24	84.2 (82.1-86.3)	.094
RML	82	55	9	8	10	79.7 (72.6-85.0)	.391
RLL	207	147	17	17	26	76.2 (72.9-79.5)	.394

(Continued)

TABLE 1. Continued

	No.	LODDS1	LODDS2	LODDS3	LODDS4	3-y OS%	P value
	cases	(−2.10 < LODDS ≤ −1.01)	(−1.01 < LODDS ≤ −0.70)	(−0.70 < LODDS ≤ −0.20)	(−0.20 < LODDS ≤ 1.74)	(95% CI)	(log-rank test)
LNR							
0 (LNR = 0)	729	702	22	5	0	91.0 (89.9-92.1)	<.001
1 (0 < LNR ≤ 0.14)	157	60	90	0	0	75.2 (71.4-79.0)	
2 (0.14 < LNR ≤ 0.38)	101	0	6	100	2	56.5 (51.5-61.5)	
3 (0.38 < LNR ≤ 1)	110	0	0	1	109	41.4 (36.4-46.4)	
LODDS							
1 (−2.10 < LODDS ≤ −1.01)	762	762	0	0	0	89.9 (88.7-91.1)	<.001
2 (−1.01 < LODDS ≤ −0.70)	118	0	118	0	0	78.4 (74.4-82.4)	
3 (−0.70 < LODDS ≤ −0.20)	106	0	0	106	0	56.0 (50.9-61.1)	
4 (−0.20 < LODDS ≤ 1.74)	111	0	0	0	111	41.0 (36.1-45.9)	

LODDS, Log odds ratio; OS, overall survival; CI, confidence interval; TNM, Tumor, Node, Metastasis; seg, segmentectomy; Lob, lobectomy; LUL, left upper lobe; LLL, left lower lobe; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LNR, lymph node ratio.

Table 3. Among these 3 systems, the LODDS system showed greater LR, c-index, and lower AIC. According to our data, the LODDS system has the greatest ability to allow accurate prognostic stratification (by the linear trend test and by c-index) and homogeneity (by the LR test), along with greatest model fit (by the AIC). Based on the previous results, the next step is to see whether there is a good agreement between LNR and LODDS. As for the correlation between LNR and LODDS, the Spearman rank correlation coefficient was calculated to be 0.805 ($P < .001$).

DISCUSSION

Despite the definition of the N stage, several studies have reported that LNR, the ratio between PLNs and total lymph nodes retrieved, is of prognostic value for lung cancer.³⁻⁵ In addition, LODDS, although not having been discussed in lung cancer, has been found of good prognostic value for gallbladder,¹⁰ head and neck,¹¹ breast,¹² colorectal,^{13,15,16} and gastric cancers.¹⁴ In clinical practice, the retrieved lymph nodes sometimes are not of sufficient quality for analyzing. Thus, compared with the number of metastatic lymph nodes, LNR and LODDS are thought to be more

FIGURE 2. RFS for pN, LNR, and LODDS. A, RFS for patients in different pN groups. B, RFS for patients in different LNR groups. C, RFS for patients in different LODDS groups. LNR, Lymph node ratio; LODDS, log odds ratio.

FIGURE 3. OS for pN, LNR, and LODDS. A, OS for patients in different pN groups. B, OS for patients in different LNR groups. C, OS for patients in different LODDS groups. *LNR*, Lymph node ratio; *LODDS*, log odds ratio.

reliable. In this study, we included both LNR and LODDS and compared them with pN stage to find out whether LNR and LODDS are of prognostic value and furthermore, whether they have equal performance as the current pN staging system.

On the basis of our data, Table 1 shows that with the 3-year OS is associated significantly with pN stage ($P < .001$), LNR ($P < .001$), and LODDS ($P < .001$). Patients in the lowest stage in each grouping systems had similar 3-year OS (91.0% for the N0 and LNR0 group and 89.9% for the LODDS1 group). However, the difference becomes increasingly greater when stages go greater (50.8% for N2 group, 41.4% for LNR3 group, and 41.0% for LODDS4 group). This suggests the potential ability of the LNR and LODDS grouping system to distinguish patients' prognoses when they are in greater stages.

LODDS also can be used for considering the problem of false negativity. According to our results, the Spearman correlation test showed strong correlation between LNR and LODDS. Although LNR and LODDS appear to be different transformations of the same thing, LODDS can give us more information when LNR is equal. This raises an interesting question by Wang and colleagues¹⁵: does patient A with 4 PLNs of 4 lymph nodes retrieved have the same prognosis as patient B with 20 PLNs of 20? Here, we may ask another question: does patient C with

0 PLNs of 4 have the same prognosis as patient D with 0 PLNs of 20? Intuitively, patient A should have a better prognosis than patient B, and patient C should have a worse prognosis than patient D. Patient A and B have the same LNR, and so do patient C and D, but LODDS remains different (LODDS = 0.95 for patient A, 1.61 for patient B, -0.95 for patient C, and -1.61 for patient D, respectively). According to our grouping strategy, patient A and patient B should be in the LODDS4 group, patient C should be in the LODDS2 group, and patient D should be in the LODDS1 group. In this situation, patients with the same LNR (especially 0) can have different LODDSs; thus, they are in different groups and have different prognoses. Furthermore, LNR0 has the same meaning as N0, this means that N0 patients can have different LODDSs, thus different prognoses. It is of great value when making treatment strategies since the LODDS system has the ability to separate N0 patients into different groups to predict their prognoses because of the different number of lymph nodes retrieved. For example, when a patient has N0 disease but a high LODDS, a false-negative nodal status should be reasonably suspected, and a close follow-up is required. This also leads to another question that still hasn't reached a consensus: To resect how many lymph nodes would it be enough and how many would it be excess for surgical resectable non-small cell lung adenocarcinoma? Many

TABLE 2. Univariable and multivariable Cox model of prognostic factors for overall survival

	Univariable analysis			Multivariable analysis 1			Multivariable analysis 2			Multivariable analysis 3		
	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
Sex	1.477	1.129-1.932	.004	0.825	0.505-1.346	.441	0.795	0.490-1.290	.353	0.810	0.501-1.310	.391
Age	1.007	0.994-1.021	.298									
Smoking status	1.934	1.477-2.534	<.001	1.702	1.043-2.779	.033	1.755	1.082-2.847	.023	1.739	1.072-2.820	.025
Surgery type			<.001			<.001			<.001			<.001
Wedge/seg	-			-			-			-		
Lob/bilob	2.331	1.234-4.406	.009	2.697	1.290-5.636	.008	2.907	1.381-6.118	.005	3.035	1.442-6.386	.003
Pneumo	10.398	4.489-24.08	<.001	7.220	2.681-19.44	<.001	7.838	2.860-21.48	<.001	7.824	2.852-21.46	<.001
Charlson comorbidity index			.677				0.359		.338			.371
0	-			-			-			-		
1	0.978	0.714-1.340	.978									
2	0.691	0.324-1.474	.338									
3	1.706	0.423-6.886	.453									
FEV1%	0.992	0.984-1.001	.096	0.997	0.987-1.006	.492	0.996	0.986-1.006	.382	0.996	0.986-1.006	.397
Adjuvant chemotherapy	3.187	2.394-4.243	<.001	0.633	0.419-0.955	.029	0.609	0.402-0.923	.019	0.585	0.388-0.883	.011
pT stage			<.001			.003			.003			.001
1	-			-			-			-		
2	2.557	1.886-3.467	<.001	1.289	0.902-1.843	.164	1.235	0.862-1.770	.251	1.274	0.892-1.821	.183
3	6.732	4.383-10.34	<.001	2.605	1.473-4.608	.001	2.557	1.454-4.497	.001	2.806	1.629-4.833	<.001
4	6.937	3.673-13.10	<.001	2.768	1.296-5.912	.009	2.620	1.226-5.600	.013	2.791	1.313-5.934	.008
pN stage			<.001			.284						
0	-			-			-			-		
1	2.454	1.479-4.071	.001	0.689	0.334-1.420	.312						
2	7.484	5.516-10.16	<.001	1.175	0.529-2.609	.691						
pTNM stage			<.001			<.001			<.001			<.001
1	-			-			-			-		
2	4.621	2.875-7.427	<.001	4.377	2.165-8.850	<.001	4.185	2.085-8.403	<.001	3.396	1.790-6.440	<.001
3	10.24	7.160-14.64	<.001	7.356	3.155-17.15	<.001	8.999	4.136-19.58	<.001	6.405	3.401-12.06	<.001
Lymphovascular invasion	3.465	2.616-4.589	<.001	1.413	0.992-2.014	.056	1.345	0.946-1.914	.099	1.365	0.962-1.937	.081
Tumor location			.010			.500			.378			.315
RUL	-			-			-			-		
RML	0.668	0.319-1.399	.285	0.439	0.185-1.038	.061	0.439	0.185-1.039	.070	0.446	0.189-1.053	.066
RLL	1.242	0.826-1.867	.298	0.931	0.593-1.464	.758	0.890	0.567-1.399	.614	0.909	0.579-1.429	.680
LUL	1.227	0.852-1.765	.272	0.916	0.613-1.369	.669	0.866	0.577-1.299	.486	0.874	0.583-1.310	.514
LLL	1.467	0.991-2.174	.056	0.959	0.599-1.535	.861	0.861	0.539-1.376	.531	0.872	0.546-1.392	.565
Number of LN resected	1.705	1.272-2.285	<.001	1.054	0.742-1.499	.768	1.286	0.888-1.864	.184	1.326	0.909-1.934	.143
Number of positive LN	1.117	1.101-1.134	<.001	1.031	1.002-1.061	.035	1.000	0.960-1.041	.994	0.992	0.952-1.034	.706
LNR			<.001						.073			
0	-						-					
1	3.177	2.116-4.770	<.001				0.733	0.367-1.462	.378			
2	6.554	4.482-9.583	<.001				1.118	0.536-2.334	.767			
3	10.16	7.165-14.41	<.001				1.703	0.720-4.027	.225			
LODDS			<.001									.046
1	-									-		
2	2.529	1.624-3.940	<.001							1.165	0.668-2.032	.590
3	5.872	4.060-8.494	<.001							1.682	0.944-2.996	.078
4	9.081	6.504-12.68	<.001							2.658	1.296-5.449	.008

LNR was categorized into 4 groups: LNR0 (LNR = 0), LNR1 (0 < LNR ≤ 0.14), LNR2 (0.14 < LNR ≤ 0.38) and LNR3 (0.38 < LNR ≤ 1). LODDS was categorized into 4 groups: LODDS1 (-2.10 < LODDS ≤ -1.01), LODDS2 (-1.01 < LODDS ≤ -0.70), LODDS3 (-0.70 < LODDS ≤ -0.20), and LODDS4 (-0.20 < LODDS ≤ 1.74). HR, Hazard ratio; CI, confidence interval; seg, segmentectomy; Lob, lobectomy; Bilob, bilobectomy; Pneumo, pneumonectomy; FEV1%, percent of forced expiratory volume in 1 second predicted; pT, pathologic T stage; pN, pathologic N stage; pTNM, pathologic TNM stage; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; LN, lymph node; LNR, lymph node ratio; LODDS, log odds ratio.

TABLE 3. Measurement of homogeneity, discriminatory ability, and monotonicity of pN, LNR, and LODDS systems

	Linear trend test (χ^2)	Likelihood ratio test (χ^2)	HC index	AIC
pN	222.5	255	0.8016	619.1
LNR	255.8	257	0.8019	619.2
LODDS	249.9	259	0.8025	617.1

pN, Pathologic N stage; LNR, lymph node ratio; LODDS, log odds ratio; HC index, Harrell C index; AIC, Akaike information criterion.

studies have contributed to this topic and it still needs further proving.¹⁷⁻²⁰

In conclusion, LNR and LODDS are of good prognostic value in predicting patients' prognoses. They can be taken into consideration for clinicians when predicting patients' prognosis and making personalized therapeutic strategies. Particularly, LODDS can be taken into consideration the problem of false-negativity when none of the resected lymph nodes is positive. And of course, we can use all the 3 systems together to have more information. With few studies discussing the value of LODDS in lung cancer, we hope our study contributes to the literature and more data come out in the future to gain a better understanding of this topic.

Conflicts of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: prognostic value, lymph node ratio, log odds ratio, lung adenocarcinoma

TABLE E1. Distribution between pN and LNR

	LNR0	LNR1	LNR2	LNR3
N0	729	0	0	0
N1	0	77	20	11
N2	0	73	88	99

pN, Pathologic N stage; *LNR*, lymph node ratio.

TABLE E2. A comparison between single or multiple lymph node stations involved in patients with N1 and N2 diseases

	Single station involved	Multiple stations involved	<i>P</i> value
N1 (n = 63)	75 (69.4%)	33 (30.6%)	<.001
N2 (n = 165)	53 (20.4%)	207 (79.6%)	

P value was calculated with Pearson χ^2 test.