

Impact of Harvested Lymph Node Count on Staging and Survival at Radical Resection for Non-small Cell Lung Cancer: A Minimum of 14 Lymph Nodes Should Be Sampled

Wenhua Liang, Hui Pan, Wenlong Shao, Gening Jiang, Qun Wang, Lunxu Liu, Deruo Liu, Zheng Wang, Zhihua Zhu, and **Jianxing He***

Disclosure slide

- All authors declare no conflicts of interest.

- **Lymph node (LN) involvement** is one of the most important **prognostic** factors in patients with resectable cancerous disease.
- The **significance** of LN harvested
 - A. clearance of the LN metastasis
 - B. precise stage (delivery of appropriate adjuvant therapies)may ultimately **reduce the recurrence/metastasis**

- The **association** between **lymph node harvest** and **improved patient survival** has been proved in many cancers
- **NCCN guidelines** have recommended the **minimal** number of LNs that should be removed or sampled for **adequate nodal staging** in gastric cancer, colorectal cancer, breast cancer, etc.

- However, the impact of total number of LNs being harvested during surgery on **staging** and **survival** (OS or DFS) **remains controversial** for **NSCLC**.
- In addition, **the minimal count** of harvested LNs that should be examined for **NSCLC patients** has not been recommended.

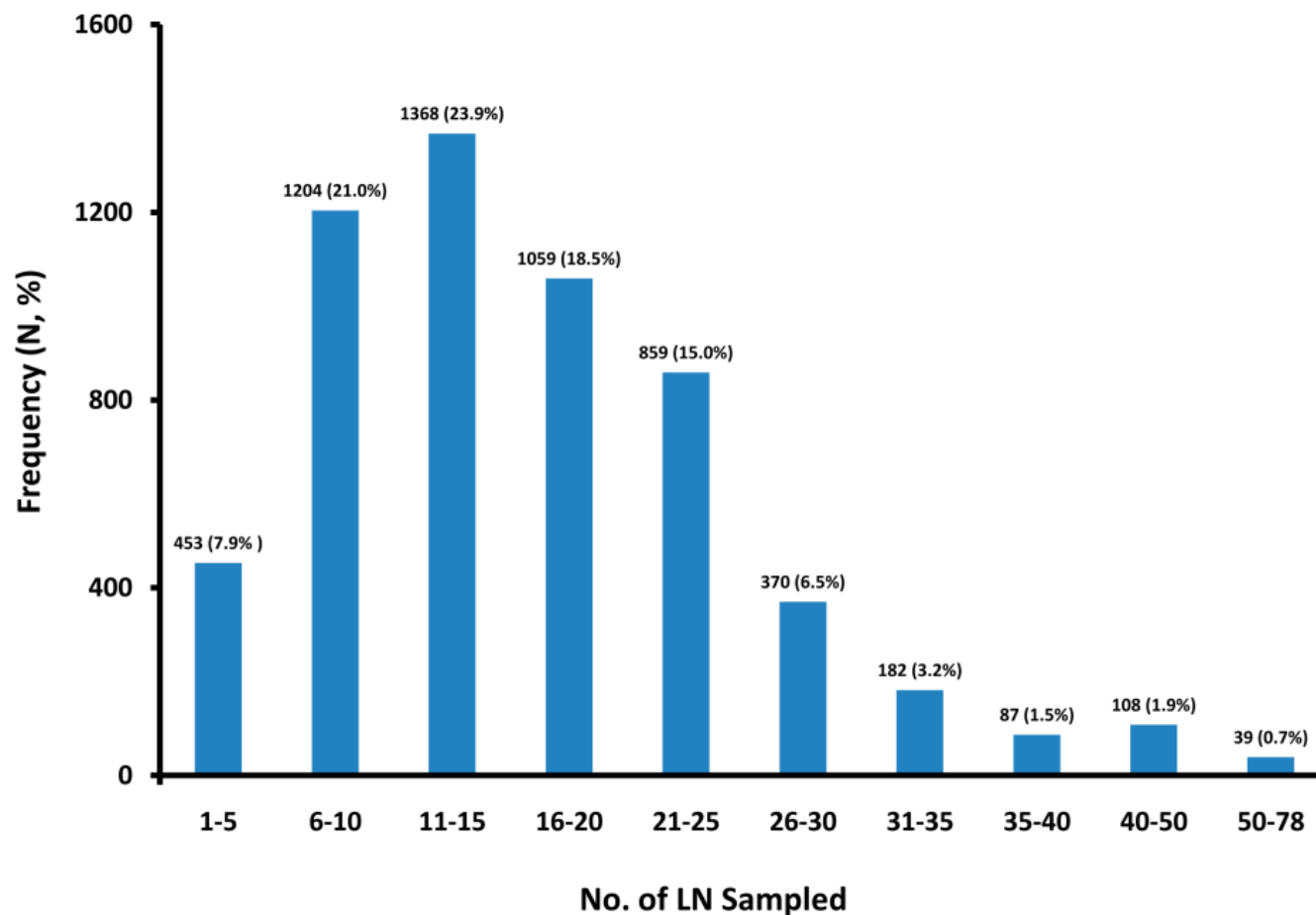
- A cohort of **5729 NSCLC patients** (2001-2008) from a **multi-institutional registry** (8 centers) in China.
- Survival analyses through K-M curve and Cox regression. **Optimal cut-point** was determined on the magnitude of the log-rank test χ^2 statistic. **Subgroup analyses** for patients with different characteristics were proposed.
- An independent cohort of **636 patients** from our center (2008-2010) on which **the systematic LN sampling was guaranteed**.

RESULTS

Patient Characteristics

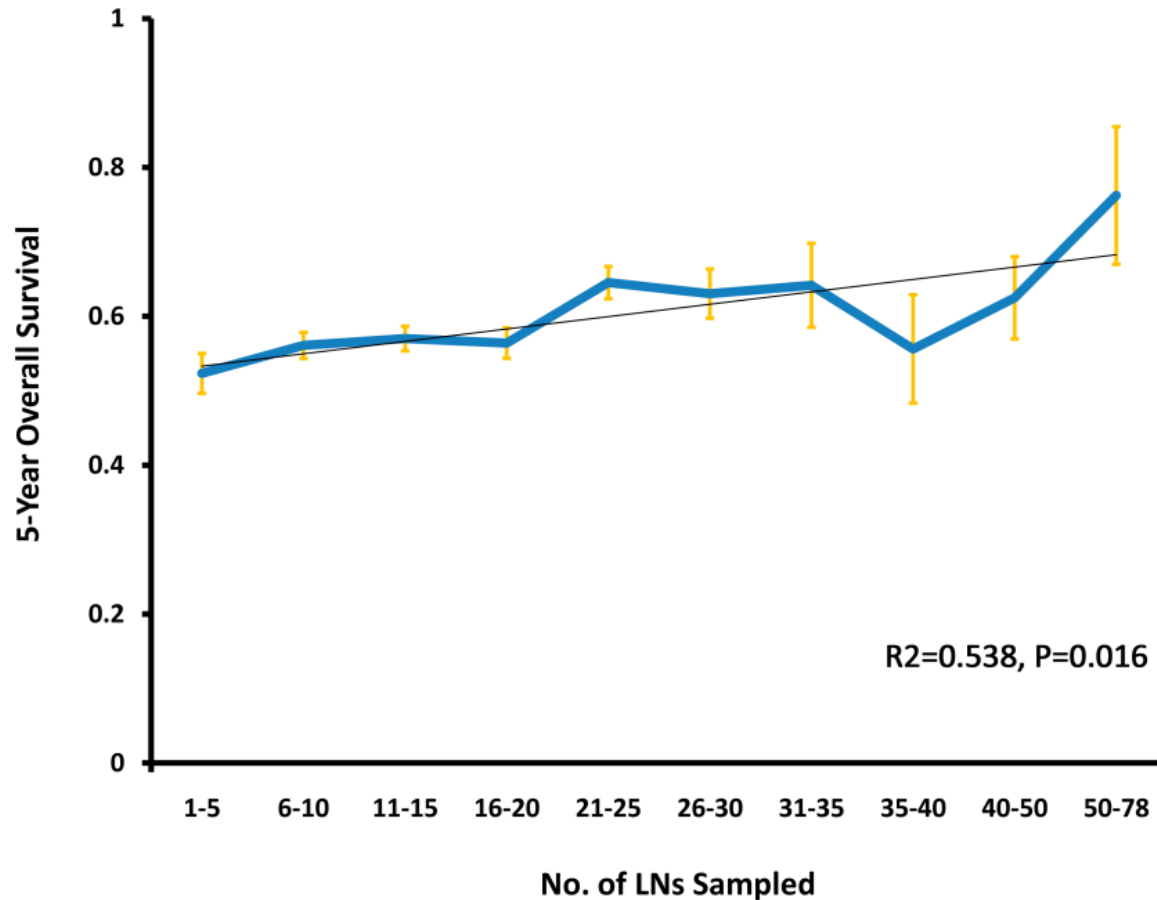
Characteristics	No. (N=5729)	%	Characteristics	No. (N=5729)	%
Sex			T stage		
Male	3985	69.6%	T1a	762	13.3%
Female	1744	30.4%	T1b	778	13.6%
Age			T2a	2709	47.3%
Above 65	3849	67.2%	T2b	687	12.0%
<65	1880	32.8%	T3	692	12.1%
Histology			T4	101	1.8%
BAC	278	4.9%	N stage		
Squamous	1790	31.2%	'N0'	3402	59.4%
Non-squamous	3661	63.9%	'N1'	965	16.8%
Harvested LNs			'N2'	1362	23.8%
<14	2552	44.5%			
≥14	3177	55.5%			

Distribution of LN count

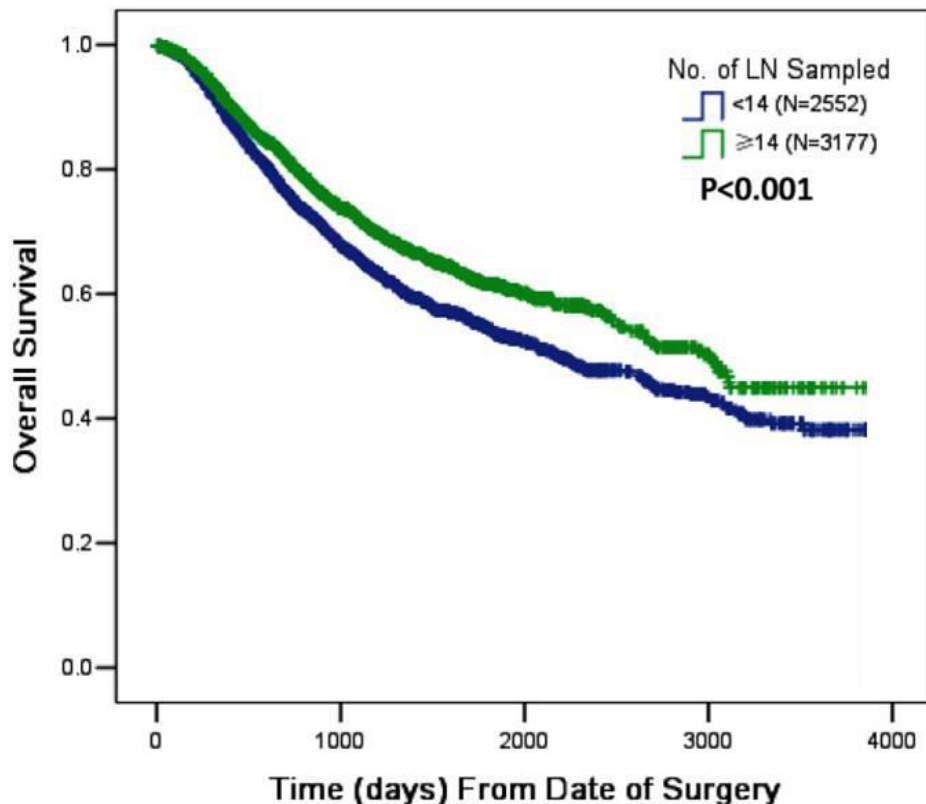


RESULTS

Correlation-LNs & OS



Cut-point and survival analysis



Cut-point analysis identified the **greatest survival difference** at **14 LNs examined** ($\chi^2=27.2$).

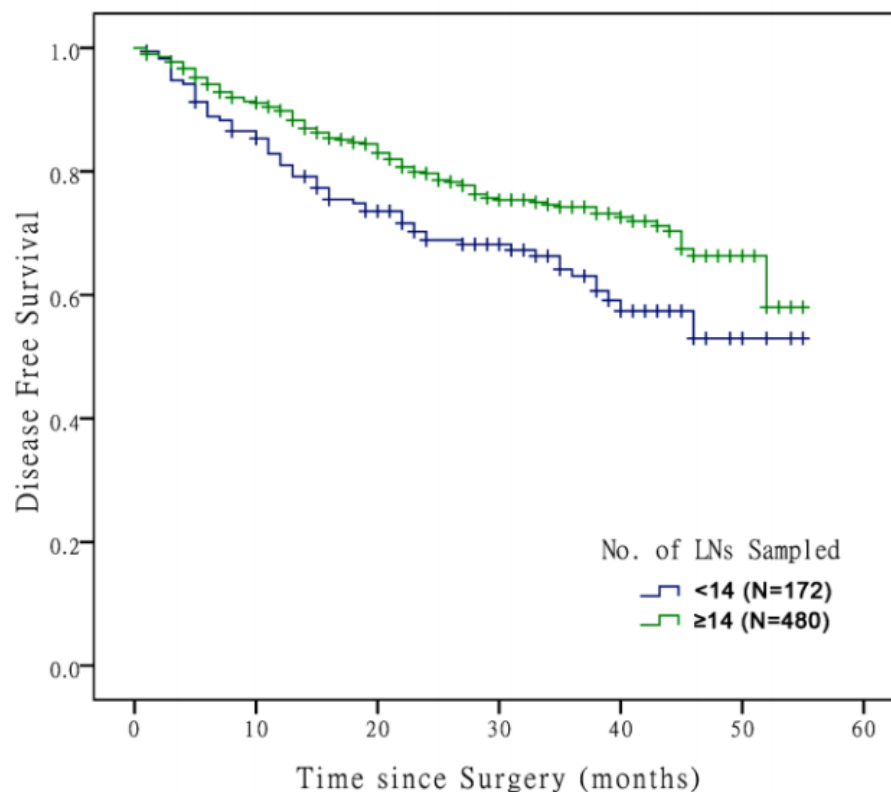
median OS
 ≥14 LNs 100 months vs.
 <14 LNs 73 months
 K-M log-rank, **P<0.001**

HR 0.73, 95% CI 0.66-0.81; **P<0.001**;
adjusting for histology, T stage, N stage, differentiation

Validation with 691 patients (2009 to 2011) in our center;
 the systematic LN sampling was guaranteed

The positive relationship
 between 5-year OS and LN
 count was confirmed

as well as the **favorable DFS**
 of patients in whom at least 14
 LNs were harvested (P=0.003).



RESULTS

Stage Migration

The linear regression results showed **a proportional increase in TNM(N) stage as the number of LNs examined increased** ($P < 0.001$).

LN _s sampled	N ₀	N ₁₋₂	N ₀₋₁	N ₂
<14	61%	39%	78%	22%
14 or more	57%	43%	73%	27%
		$P < 0.001$		$P < 0.001$

RESULTS

Subgroup analyses

Subgroup	N	HR	LL	UL	P value
Overall	5729	0.788	0.720	0.862	<0.001
Histology					
BAC	278	0.898	0.560	1.440	0.66
Squamous	1790	0.740	0.633	0.864	<0.001
Non-squamous	3661	0.783	0.699	0.876	<0.001
T stage					
T1	1540	0.852	0.692	1.050	0.13
T2	3396	0.784	0.699	0.880	<0.001
T3	692	0.671	0.545	0.827	<0.001
T4	101	0.551	0.313	0.969	0.04
N stage					
'N0'	3402	0.767	0.666	0.882	<0.001
'N1'	965	0.684	0.565	0.828	<0.001
'N2'	1362	0.756	0.652	0.876	<0.001
Differentiation					
Poor	919	0.792	0.644	0.973	0.03
Moderate	678	0.948	0.726	1.236	0.69
Well	175	0.642	0.364	1.134	0.13

The survival benefits of examining 14 or more LNs were shown

consistently in most subgroups

except for patients with

1. **BAC histology,**
2. **T1 diseases,**
3. **moderate/well differentiated tumors.**

RESULTS

Subgroup analyses

Subgroup	N	HR	LL	UL	P value
Overall	5729	0.788	0.720	0.862	<0.001
Histology					
BAC	278	0.898	0.560	1.440	0.66
Squamous	1790	0.740	0.633	0.864	<0.001
Non-squamous	3661	0.783	0.699	0.876	<0.001
T stage					
T1	1540	0.852	0.692	1.050	0.13
T2	3396	0.784	0.699	0.880	<0.001
T3	692	0.671	0.545	0.827	<0.001
T4	101	0.551	0.313	0.969	0.04
N stage					
'N0'	3402	0.767	0.666	0.882	<0.001
'N1'	965	0.684	0.565	0.828	<0.001
'N2'	1362	0.756	0.652	0.876	<0.001
Differentiation					
Poor	919	0.792	0.644	0.973	0.03
Moderate	678	0.948	0.726	1.236	0.69
Well	175	0.642	0.364	1.134	0.13

The survival benefits of examining 14 or more LNs were shown **consistently in most subgroups**

except for patients with

1. **BAC histology,**
2. **T1 diseases,**
3. **moderate/well differentiated tumors.**

RESULTS

Subgroup analyses

Subgroup	N	HR	LL	UL	P value
Overall	5729	0.788	0.720	0.862	<0.001
Histology					
BAC	278	0.898	0.560	1.440	0.66
Squamous	1790	0.740	0.633	0.864	<0.001
Non-squamous	3661	0.783	0.699	0.876	<0.001
T stage					
T1	1540	0.852	0.692	1.050	0.13
T2	3396	0.784	0.699	0.880	<0.001
T3	692	0.671	0.545	0.827	<0.001
T4	101	0.551	0.313	0.969	0.04
N stage					
'N0'	3402	0.767	0.666	0.882	<0.001
'N1'	965	0.684	0.565	0.828	<0.001
'N2'	1362	0.756	0.652	0.876	<0.001
Differentiation					
Poor	919	0.792	0.644	0.973	0.03
Moderate	678	0.948	0.726	1.236	0.69
Well	175	0.642	0.364	1.134	0.13

Both 'N0', 'N1', **'N2'** diseases benefit from more LNs sampled.

Significance

- Examine **more** LNs (both **Surgeons** and **Pathologists**)
- Definition of **Nx** (esp. Ib disease)
- Explain previous results of **systematic LN dissection vs. sampling**

More works on

- Impact of positive LNs ratio?
- Cut-point fits all situation?
- Minimal count for N2 or N1 (hilar or peripheral) respectively?
- Benefits from stage migration due to Ad-Chemo?
- Direct evidence supporting stage migration?

CONCLUSIONS

- **More LNs** being harvested **favours OS** and precise staging in patients underwent radical resection for NSCLC.
- We recommended **a minimum of 14 LNs** should be harvested to accurately stage the disease and to improve patient survival.
- However, the extension of LN examination should be **further discussed in some patients with low risk** for recurrence, such as BAC histology (major refer to the currently AIH and MIA histology), T1 diseases, and moderate/well differentiated tumors.

ACKNOWLEDGEMENT

Prof. He Jianxing and co-authors

Prof. Zhang li

Prof. Zhou Caicun

Thank you so much for the attention.

Median as cut-point

