

Factors Associated With Lymph Node Yield and Effects of Lymph Node Density on Survival of Patients With Pulmonary Sarcomatoid Carcinoma

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Objective: The objective of this study was to identify factors associated with lymph node yield (LNY) during surgeries for pulmonary sarcomatoid carcinoma (PSC) and to determine effects of lymph node density (LND) on the overall survival (OS) of patients with PSC.

Materials and Methods: The SEER Research Plus database was searched for data on patients with PSC from 1988 to 2018. Poisson regression was used of all patients with PSC to identify relevant factors associated with LNY. Univariate and multivariate Cox regression analyses were adopted for lymph node (LN)-positive patients to evaluate the impact of LND on OS. The 5-year OS rates of patients with PSC were compared based on their LN status and LND.

Results: There were 545 eligible patients in the study sample, 175 of which were LN-positive. These patients had significantly lower 5-year OS than those with no positive LNs ($P < 0.001$). Poisson regression analysis indicated relevant factors increasing LNY included higher diagnosis age, non-Hispanic American Indian or Alaska Native races, larger tumor, pleomorphic carcinoma histology, and more advanced disease stages. The Cox regression analysis indicated higher LND ($P = 0.022$) was probably associated with a worse prognosis for LN-positive patients. The group with $LND \geq 0.12$ had a higher risk of death than the group with $LND < 0.12$ ($P < 0.001$) among LN-positive patients with PSC.

Conclusions: Patients with PSC with high LND experienced worse outcomes than those with low LND. Further risk stratification of

patients with PSC may help to improve survival benefits based on prognostic indicators of LND.

Key Words: pulmonary sarcomatoid carcinoma, lymph node density, SEER research plus database, risk stratification

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Pulmonary sarcomatoid carcinoma (PSC), which constitutes <1% of lung cancers, is an uncommon type of non-small cell lung cancer (NSCLC), and is rare, highly invasion, and poorly differentiated.^{1,2} PSC often has a poor prognosis due to its high malignancy in sarcomatoid change.³ According to the 2021 World Health Organization (WHO) classification of thoracic tumors in the lung cancer chapter, PSC has 3 independent categories: pleomorphic carcinoma, pulmonary blastoma, and carcinoma.⁴ The 2021 WHO classification differs from the 2015 version as it considers spindle cell, giant cell, and pleomorphic carcinomas as subtypes of pleomorphic carcinoma rather than as a separate category under the term PSC.

Surgery is accepted as the primary treatment for most patients with NSCLC who are clinically suitable for surgery based on clinical practice guidelines.⁵ Lymph node (LN) dissection is the main part of surgical treatment. Various types of LN dissection are widely applied in clinical practice, such as specific LN dissection, systematic LN dissection, extended LN dissection, and LN sampling.⁶

Lymph node density (LND), which is the proportion of positive LNs to total LNs sampled, has been reported to be associated with worse outcomes among patients with LN-positive NSCLC.⁷ However, multiple studies have indicated that PSC is more aggressive than other types of NSCLC, accompanied by a worse prognosis and higher rate of resistance to conventional chemotherapy regimens.^{8–10} Due to inadequate investigations of LND among patients with PSC, the effect of LND among these patients also remains unclear.

This study had 2 purposes. The first was to identify relevant factors associated with lymph node yield (LNY) in PSC surgery by analyzing the SEER Research Plus database.¹¹ The second purpose was to determine the potential effects of LND on overall survival (OS) among patients with PSC. Those whose LND exceeded an estimated cutoff point were expected to have worse OS and cancer-specific survival (CSS). The current study was presented in accordance with the STROBE reporting checklist.

MATERIALS AND METHODS

Data Source

Data from 1988 to 2018 were collected from the following 3 data sets in the SEER Research Plus database by using

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This study was granted exemption from requiring ethics approval by the ethics committee of the First Affiliated Hospital of Jinan University. Central cancer registries are authorized by the state to collect or receive information for the purposes of public health surveillance and are exempt from HIPAA. The SEER data that NCI receives from the cancer registries and releases as a research file is deidentified. Deidentified health information is also exempt from HIPAA and can be used for research purposes without an Informed Consent and Consent for Publication and Health Information Use and Disclosure Authorization.

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SEER*Stat software (version 8.3.9.2): SEER Plus 9 registries (1975-2017), Plus 13 registries (1992-2017), and Plus 18 registries (2000-2018). The first 2 data sets were published in April 2020 from the November 2019 submission and the third was published in April 2021 from the November 2020 submission. These data sets were merged into a single data set to expand the sample size of patients with PSC thanks to the larger number of rare disease cases in the SEER Research Plus database^{12,13}; duplicate cases were removed and the most recent record of each patient was used. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Study Population and Inclusion Criteria

The study collected patients diagnosed with PSC from 1988 to 2018 as defined by the 2021 WHO classification of thoracic tumors and the International Classification of Disease for Oncology, Third Edition. Patients with PSC were identified using primary site codes (C34.0-C34.9) and morphology codes including pleomorphic carcinoma (8022/3), giant cell carcinoma (8031/3), spindle cell carcinoma (8032/3), pulmonary blastoma (8972/3), and carcinosarcoma (8980/3). Among these patients, the inclusion criteria were narrowed to only include those with a single primary tumor and who had undergone surgery, had been confirmed by positive histology, and whose source document was not only from an autopsy or death certificate. Exclusion criteria included having stage IV cancer, distant metastasis, preoperative radiation, unknown clinical stage at diagnosis, unknown tumor size, incomplete follow-up, and survival-time data, no or unknown number of examined LNs, or an unknown number of positive LNs. The steps in this study to select PSC cases under these criteria are illustrated in Figure 1. For patients with positive LNs, each case had an LND calculated and separate survival analysis was carried out to further explore the potential effects of LND.

Covariates

The covariates in this study included age at diagnosis, sex, race, tumor size, chemotherapy status, histology, disease stage, LNY, and LND. Disease stages were based on the American Joint Committee on Cancer staging guidelines from the corresponding year of diagnosis.

Statistical Analysis

The primary outcome was to identify factors that may influence LNY. Poisson regression was used to identify these factors and analyze their impact on LNY among patients with PSC. Kaplan-Meier survival curves were drawn for the patients with PSC according to their LN status, with log-rank tests conducted and the 5-year OS calculated for comparison.

The secondary outcome focused on LN-positive patients to determine the impact of LND on OS. Univariate and multivariate Cox regression analyses were conducted on LN-positive patients to evaluate the impact of LND. Meanwhile, the study divided these patients into groups with LND ≥ 0.12 and <0.12 to compare 5-year OS and CSS rates. The LND cutoff point of 0.12 was calculated by a log-rank test statistic¹⁴ that was initially introduced by Contal and O’Quigley.¹⁵ Likewise, LN-positive patients with low LNYs (below the median) and with high LNYs (above the median) were separated into 2 groups under the optimal LND cutoff point to compare 5-year OS rates. Multivariate Cox regression was then conducted to analyze the impact of LND on the OS of patients with low and high LNYs.

Stata software (Stata SE, version 17.0) was used for all statistical analyses. The proportional-hazards assumption was based on Schoenfeld residuals and all tests were 2-tailed when P value <0.05 was considered to demonstrate statistical significance.

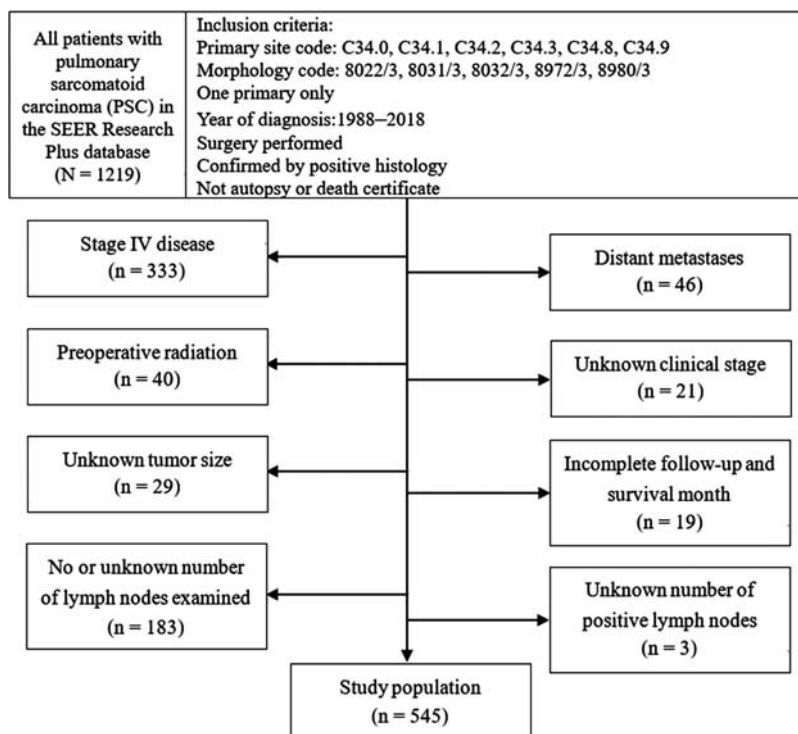


FIGURE 1. The flowchart of patient selection.

RESULTS

Patient Characteristics

The characteristics of overall and LN-positive patients with PSC are listed in Table 1. For PSC cases diagnosed during 1988-2018, 545 were identified, and 175 patients had positive LNs. Most patients with PSC were male (56.33%), non-Hispanic White (73.21%), did not receive chemotherapy (68.07%), had a pleomorphic carcinoma (44.22%), were in stage I (47.89%), had > 12 examined LNs (29.36%) and had no positive LNs (67.89%). Most of the LN-positive patients with PSC were in stage II or III. The median number of LNs examined was 11 (interquartile range = 7 to 16) for LN-positive patients and 8 (interquartile range = 4 to 14) for all patients. LN-positive patients had a 5-year OS of 27.11% (95% CI = 20.27-34.40), which was worse than that of 43.71% for patients with no positive LNs (95% CI = 38.24-49.04) ($P < 0.001$) (Fig. 2).

TABLE 1. Characteristics of Overall and LN-positive Patients With Pulmonary Sarcomatoid Carcinoma

Variables	n (%)	
	All Patients	LN-positive Patients
Total number	545	175
Age, median (IQR) (y)	66 (58-73)	65 (58-73)
Sex		
Female	238 (43.67)	79 (45.14)
Male	307 (56.33)	96 (54.86)
Race		
Non-Hispanic White	399 (73.21)	135 (77.14)
Non-Hispanic Black	82 (15.05)	26 (14.86)
Hispanic (all races)	28 (5.14)	6 (3.43)
Non-Hispanic Asian or Pacific Islander	31 (5.69)	5 (2.86)
Non-Hispanic American Indian/Alaska Native	5 (0.92)	3 (1.71)
Tumor size, median (IQR)	4.5 (3-7)	4.5 (3-7)
Chemotherapy	174 (31.93)	75 (42.86)
Histology		
Pleomorphic carcinoma	241 (44.22)	85 (48.57)
Giant cell carcinoma	114 (20.92)	44 (25.14)
Spindle cell carcinoma, NOS	108 (19.82)	27 (15.43)
Pulmonary blastoma	17 (3.12)	2 (1.14)
Carcinosarcoma, NOS	65 (11.93)	17 (9.71)
LNs examined, median (IQR)	8 (4-14)	11 (7-16)
1-3	109 (20.00)	19 (10.86)
4-6	99 (18.17)	22 (12.57)
7-9	100 (18.35)	31 (17.71)
10-12	77 (14.13)	39 (22.29)
> 12	160 (29.36)	64 (36.57)
LNs positive, median (IQR)	0 (0-1)	2 (1-4)
0	370 (67.89)	
1	72 (13.21)	72 (41.14)
≥ 2	103 (18.90)	103 (58.86)
Disease stage		
I	261 (47.89)	1 (0.57)
II	121 (22.20)	75 (42.86)
III	163 (29.91)	99 (56.57)
LND, median (IQR)	—	0.20 (0.13-0.42)
Estimated 5-y OS (95% CI)	38.35 (33.97-42.70)	27.11 (20.27-34.40)

IQR indicates interquartile range; LN, lymph node; LND, lymph node density; NOS, not otherwise specified; OS, overall survival.

Factors Affecting LNY

Table 2 lists the results of the Poisson regression analysis, which indicated that the relevant factors increasing LNY included higher diagnosis age (adjusted rate ratio [aRR] = 1.03, 95% CI = 1.02-1.04, $P < 0.001$), non-Hispanic American Indian or Alaska Native races (vs. non-Hispanic White: aRR = 2.44, 95% CI = 1.76-3.38, $P < 0.001$), larger tumor (aRR = 1.16, 95% CI = 1.11-1.22, $P < 0.001$), pleomorphic carcinoma histology (pulmonary blastoma vs. pleomorphic carcinoma: aRR = 0.31, 95% CI = 0.13-0.72, $P = 0.007$), and a more advanced disease stage (I vs. III: aRR = 0.49, 95% CI = 0.36-0.68, $P < 0.001$). Among these patients, the estimated 5-year OS was 38.35% (95% CI = 33.97-42.70) (Table 1).

Prognostic Impact of LND

Univariate and multivariate Cox regression analyses within LN-positive patients are listed in Table 3. Higher LND (hazard ratio [HR] = 2.51, 95% CI = 1.15-5.48, $P = 0.022$) was indicated to be significantly linked with a worse prognosis for LN-positive patients. Higher diagnosis age (HR = 1.02, 95% CI = 1.00-1.04, $P = 0.020$) and larger tumors (HR = 1.24, 95% CI = 1.17-1.32, $P < 0.001$) were also associated with worse prognoses, while patients who received chemotherapy (HR = 0.54, 95% CI = 0.35-0.83, $P = 0.005$) had better prognoses than those who did not. Moreover, patients with histology of giant cell carcinoma (HR = 2.33, 95% CI = 1.42-3.82, $P = 0.001$), spindle cell carcinoma (HR = 2.34, 95% CI = 1.46-3.78, $P < 0.001$), and carcinosarcoma (HR = 2.65, 95% CI = 1.53-4.58, $P < 0.001$) have a significantly worse OS than those with pleomorphic carcinoma.

Subgroup Analyses

Subgroup analyses were performed to further analyze the impact of LND on LN-positive patients. After dividing these patients into groups with LND ≥ 0.12 and < 0.12 , those with LND ≥ 0.12 had a higher risk of death, which was reflected in their significantly worse 5-year OS rate than those with LND < 0.12 (19.40% vs. 54.36%, respectively, $P < 0.001$) (Fig. 3). Similarly, patients with LND ≥ 0.12 had significantly worse 5-year CSS than those with LND < 0.12 (25.00% vs. 54.36%, respectively, $P < 0.001$) (Supplemental Figure 1, Supplemental Digital Content 1, <http://links.lww.com/AJCO/A430>). Among LN-positive patients, both the low (LNY ≤ 11) and high (LNY > 11) LNY groups were separated into 2 groups under the optimal LND cutoff point of 0.12. Within the low-LNY group, those with LND < 0.12 had a better 5-year OS rate than those with LND ≥ 0.12 (60.58% vs. 18.11%, respectively, $P = 0.010$) (Supplemental Figure 2A, Supplemental Digital Content 1, <http://links.lww.com/AJCO/A430>). Likewise, within the high-LNY group, patients with LND ≥ 0.12 also had worse prognoses with a significantly worse 5-year OS than those with LND < 0.12 (21.46% vs. 51.50%, respectively, $P = 0.006$) (Supplemental Figure 2B, Supplemental Digital Content 1, <http://links.lww.com/AJCO/A430>). Subsequent multivariate Cox regression analyses for the low- and high-LNY groups among LN-positive patients were used to determine the actual effects of LND on OS. For the low-LNY group, LND was a significant independent prognostic factor for OS ($P < 0.001$), while it did not show the significance for the high-LNY group ($P = 0.840$) (Supplemental Table 1, Supplemental Digital Content 2, <http://links.lww.com/AJCO/A431>).

DISCUSSION

PSC is a unique, poorly differentiated type of NSCLC that is highly aggressive and has worse OS rates than other types of

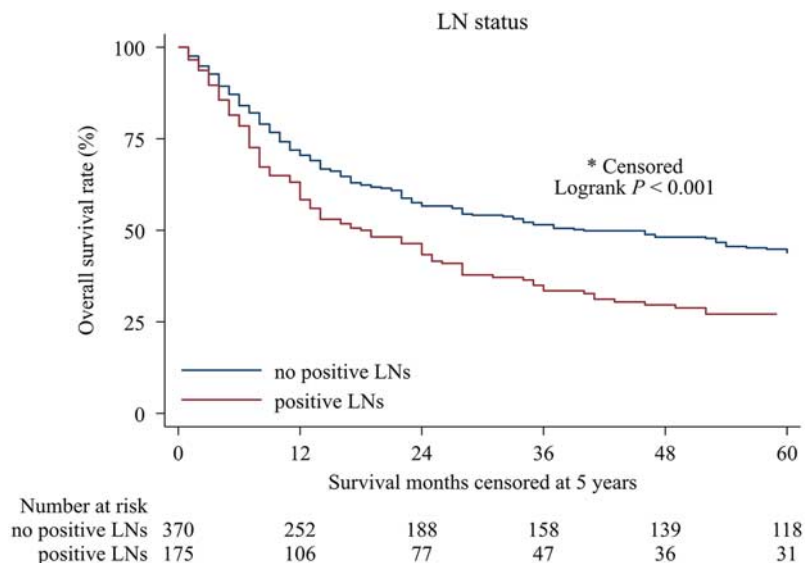


FIGURE 2. Five-year overall survival curves of pulmonary sarcomatoid carcinoma patients with LN sampling by LN status: no positive LNs (blue) versus positive LNs (red). LN indicates lymph node. [full color online](#)

NSCLC.¹⁶ Current PSC treatments mostly include surgery, radiotherapy, chemotherapy, targeted therapy, antiangiogenic therapy, immunotherapy, and combination therapy.¹⁷ However, there is no consensus on the standard treatment for PSC.¹⁸ Fortunately, there is abundant evidence of the survival benefits for patients with early-stage PSC undergoing surgery.^{8,19,20} Surgical resection is the preferred treatment for early-stage PSC

and is also the basis of comprehensive treatment according to the 2021 National Comprehensive Cancer Network guidelines.⁵ The current study, therefore, focused on patients with PSC in stages I to III who received surgery with the aim of identifying characteristics that may affect LNY at the time of surgery and determining the impact of LND on OS among patients with LN-positive PSC.

TABLE 2. Poisson Regression Analysis for Prediction of LNY (N = 545)

Variables	aRR	95% CI		P
		Lower	Upper	
Age (continuous)	1.030	1.019	1.041	< 0.001
Sex				
Male	1.000			
Female	1.056	0.799	1.395	0.702
Race				
Non-Hispanic White	1.000			
Non-Hispanic Black	1.423	0.994	2.037	0.054
Hispanic (all races)	1.624	0.806	3.272	0.175
Non-Hispanic Asian or Pacific Islander	1.430	0.884	2.316	0.145
Non-Hispanic American Indian/Alaska Native	2.439	1.761	3.379	< 0.001
Tumor size (continuous)	1.162	1.110	1.217	< 0.001
Chemotherapy				
No/unknown	1.000			
Yes	1.241	0.915	1.683	0.165
Histology				
Pleomorphic carcinoma	1.000			
Giant cell carcinoma	0.791	0.584	1.072	0.130
Spindle cell carcinoma, NOS	0.843	0.543	1.308	0.446
Pulmonary blastoma	0.307	0.131	0.720	0.007
Carcinosarcoma, NOS	0.957	0.655	1.399	0.822
Disease stage				
I	0.492	0.355	0.681	< 0.001
II	0.976	0.689	1.383	0.892
III	1.000			

aRR indicates adjusted rate ratio; LNY, lymph node yield; NOS, not otherwise specified.

To avoid radiotherapy affecting the accuracy of LN, patients who received preoperative radiation were excluded. This ensured that the actual impact of LND was identified where patients with PSC actually benefited from LN sampling in PSC surgery.

Multiple studies have confirmed the prognostic value of LND toward survival for various types of cancer such as penile,²¹ papillary thyroid,²² laryngeal,²³ bladder,²⁴ and gastric²⁵ cancers. Previous studies have also identified the significance of its association with OS among patients with NSCLC.²⁶⁻²⁸ As an unconventional type of NSCLC, PSC is usually treated with the NSCLC standard treatment, which introduces the need of establishing a more specific and formal guideline for patients with PSC, especially for LN sampling in PSC surgery. The current study made great efforts to determine the importance of reducing LND through adequate LN sampling in PSC surgery among LN-positive patients, which may further help the risk stratification of these patients by using LND as a prognostic indicator.

While there was already evidence in the literature that LND is a significant prognostic factor for patients with NSCLC, this current study is the first that we are aware of that has separated specific PSC from other common types of NSCLC to further analyze the factors that may influence LN sampling patterns during PSC surgery and to investigate the potential effects of LND on OS among LN-positive patients with PSC.

In the current study, the Poisson regression model indicated that elderly, non-Hispanic American Indians or Alaska Natives diagnosed with pleomorphic carcinoma with large tumors in advanced stages were more likely to have more LNs sampled at the time of PSC surgery (Table 2). Previous studies on NSCLCs have produced similar findings, in that patients with NSCLC had significantly more LNs removed with large tumors or in more advanced stages,²⁹ while the current study

TABLE 3. Univariate and Multivariate Cox Regression Analyses Within LN-positive Patients (N=175)

Variables	Univariate Analysis				Multivariate Analysis			
	HR	95% CI Lower	95% CI Upper	P	HR	95% CI Lower	95% CI Upper	P
Age (continuous)	1.029	1.011	1.047	0.001	1.024	1.004	1.044	0.020
Sex								
Male	1.000				1.000			
Female	0.869	0.617	1.225	0.423	1.107	0.737	1.663	0.623
Race								
Non-Hispanic White	1.000				1.000			
Non-Hispanic Black	0.932	0.508	1.709	0.820	1.450	0.837	2.510	0.185
Hispanic (all races)	2.848	1.355	5.989	0.006	1.556	0.672	3.599	0.302
Non-Hispanic Asian or Pacific Islander	0.798	0.281	2.263	0.671	0.588	0.231	1.495	0.265
Non-Hispanic American Indian/Alaska Native	0.947	0.644	1.392	0.783	2.680	0.840	8.551	0.096
Tumor size (continuous)	1.154	1.092	1.219	<0.001	1.241	1.169	1.318	<0.001
Chemotherapy								
No/unknown	1.000				1.000			
Yes	0.558	0.394	0.791	0.001	0.535	0.347	0.825	0.005
Histology								
Pleomorphic carcinoma	1.000				1.000			
Giant cell carcinoma	2.613	1.720	3.969	<0.001	2.325	1.417	3.818	0.001
Spindle cell carcinoma, NOS	2.585	1.485	4.499	0.001	2.343	1.455	3.773	<0.001
Pulmonary blastoma	0.532	0.080	3.558	0.515	0.342	0.147	0.800	0.013
Carcinosarcoma, NOS	3.345	2.110	5.303	<0.001	2.647	1.530	4.579	<0.001
LNY								
≤ 11 LNs	1.000				1.000			
> 11 LNs	0.734	0.519	1.037	0.080	0.921	0.620	1.370	0.685
LND (continuous)	2.276	1.286	4.029	0.005	2.505	1.145	5.483	0.022
Disease stage								
I	1.600	1.224	2.092	0.001	0.925	0.454	1.885	0.829
II	0.934	0.661	1.320	0.698	0.954	0.645	1.411	0.813
III	1.000				1.000			

HR indicates hazard ratio; LN, lymph node; LND, lymph node density; LNY, lymph node yield; NOS, not otherwise specified.

additionally included the impacts of non-Hispanic American Indian or Alaska Native races and histology type on LNY. Whether and how the factors of race as a patient characteristic and histology as a tumor characteristic contributed to the

differences in LNY among patients with PSC remains unclear and needs to be further explored.

The Cox regression analysis also indicated that elderly patients with LN-positive PSC with larger tumors and higher

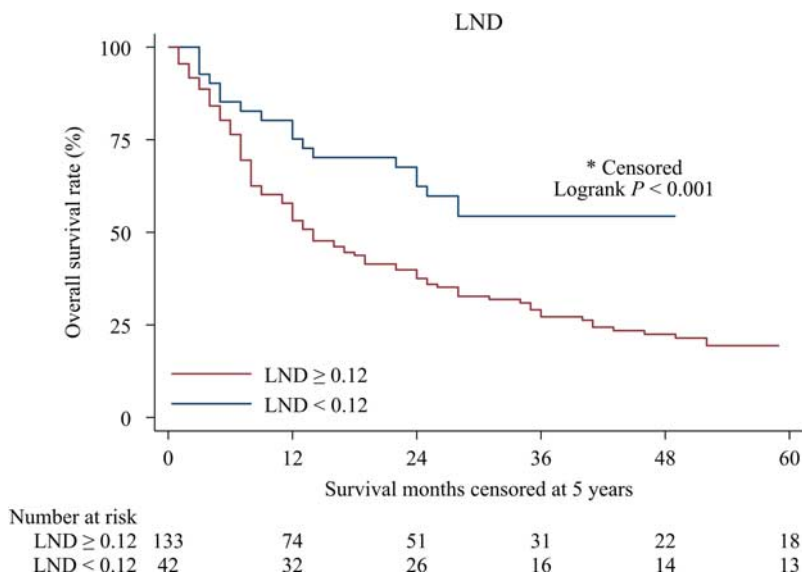


FIGURE 3. Five-year overall survival curves of pulmonary sarcomatoid carcinoma patients with positive LNs by LND: LND ≥ 0.12 (red) versus LND < 0.12 (blue). LN indicates lymph node; LND, lymph node density.

LNDs had worse prognoses, whereas LN-positive patients who received chemotherapy or were diagnosed with pulmonary blastoma had a comparatively prolonged OS (Table 3). Our study particularly supported that patients with PSC with LND above the optimal cutoff point of 0.12 were likely to have worse OS and CSS than those below the cutoff point. One possible explanation of the association between higher LND and worse survival is that these patients have a higher risk of local recurrence.³⁰ LND is a metric describing both the disease process reflected as a numerator and the extent of LNY reflected as a denominator, which may account for how LND influences OS and CSS.³¹ It is feasible to influence that denominator by increasing LNY in PSC surgery, while it is difficult to influence the numerator by controlling the nodal spread process.³¹ Efforts to reduce LND by adequate LN sampling in PSC surgery may therefore have positive impacts on OS and CSS among LN-positive patients. Taking LND into account as a prognostic indicator, further risk stratification of these patients may help to improve the survival benefits. To achieve this, adequate attention to the value of LND assessments and continuous education on the surgery are needed.

There were several limitations in the current study. First, information on patient characteristics such as the smoking history, family medical history, and occupation was not available. Second, information on the surgical factors of LN sampling patterns was lacking, including the extent, location, and surgeon preference. Third, PSC is a rare disease, which resulted in a small sample of those who met the inclusion criteria (n = 545). More evidence from larger samples needs to be obtained to confirm our results. Notwithstanding these limitations, the current study supports the vital role of LND in predicting the survival of patients with PSC. Future work involving further risk stratification among patients with LN-positive PSC based on different LND intervals may be a new treatment option that would provide better outcomes.

CONCLUSIONS

In conclusion, characteristics that may increase LNY during PSC surgery included high diagnosis age, non-Hispanic American Indian or Alaska Native races, large tumor, pleomorphic carcinoma histology, and advanced disease stages. Higher LND was significantly associated with worse prognoses among patients with LN-positive PSC. Further risk stratification of patients with PSC may help to improve survival benefits based on LND as a prognostic indicator.

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REFERENCES

- Xiao C, Yang X, Hao J, et al. Clinicopathological features and prognostic analysis of metastatic pulmonary sarcomatoid carcinoma: a SEER analysis. *J Thorac Dis*. 2021;13:893–905.
- Jiao Y, Liu M, Luo N, et al. Successful treatment of advanced pulmonary sarcomatoid carcinoma with the PD-1 inhibitor toripalimab: a case report. *Oral Oncol*. 2021;112:104992.
- Boland JM, Mansfield AS, Roden AC. Pulmonary sarcomatoid carcinoma—a new hope. *Ann Oncol*. 2017;28:1417–1418.
- Nicholson AG, Tsao MS, Beasley MB, et al. The 2021 WHO Classification of Lung Tumors: impact of advances since 2015. *J Thorac Oncol*. 2022;17:362–387.
- National Comprehensive Cancer Network (NCCN). National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer. Version 6. 2021. Available at: <https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1450>. Accessed December 27, 2021.
- Korasidis S, Menna C, Andreotti C, et al. Lymph node dissection after pulmonary resection for lung cancer: a mini review. *Ann Transl Med*. 2016;4:368.
- Deng W, Xu T, Wang Y, et al. Log odds of positive lymph nodes may predict survival benefit in patients with node-positive non-small cell lung cancer. *Lung Cancer*. 2018;122:60–66.
- Rahouma M, Kamel M, Narula N, et al. Pulmonary sarcomatoid carcinoma: an analysis of a rare cancer from the Surveillance, Epidemiology, and End Results database. *Eur J Cardiothorac Surg*. 2018;53:828–834.
- Yendamuri S, Caty L, Pine M, et al. Outcomes of sarcomatoid carcinoma of the lung: a Surveillance, Epidemiology, and End Results Database analysis. *Surgery*. 2012;152:397–402.
- Maneenil K, Xue Z, Liu M, et al. Sarcomatoid carcinoma of the lung: The Mayo Clinic experience in 127 patients. *Clin Lung Cancer*. 2018;19:e323–e333.
- National Cancer Institute. Surveillance, Epidemiology, and End Results Program (SEER). SEER Research Plus Data, 9 Registries (1975–2017), 13 Registries (1992–2017) released April 2020, and 18 Registries (2000–2018) released April 2021. Available at: <https://seer.cancer.gov/data/>. Accessed December 23, 2021.
- Wu WT, Li YJ, Feng AZ, et al. Data mining in clinical big data: the frequently used databases, steps, and methodological models. *Mil Med Res*. 2021;8:44.
- Yang J, Li Y, Liu Q, et al. Brief introduction of medical database and data mining technology in big data era. *J Evid Based Med*. 2020;13:57–69.
- Walker JP, Johnson JS, Eguchi MM, et al. Factors affecting lymph node sampling patterns and the impact on survival of lymph node density in patients with Wilms tumor: a Surveillance, Epidemiology, and End Result (SEER) database review. *J Pediatr Urol*. 2020;16:81–88.
- Contal C, O'Quigley J. An application of changepoint methods in studying the effect of age on survival in breast cancer. *Comput Stat Data Anal*. 1999;30:253–270.
- Shum E, Stuart M, Borczuk A, et al. Recent advances in the management of pulmonary sarcomatoid carcinoma. *Expert Rev Respir Med*. 2016;10:407–416.
- Li X, Wu D, Liu H, et al. Pulmonary sarcomatoid carcinoma: progress, treatment and expectations. *Ther Adv Med Oncol*. 2020;12:1758835920950207.
- Chen M, Yang Q, Xu Z, et al. Survival analysis and prediction model for pulmonary sarcomatoid carcinoma based on SEER Database. *Front Oncol*. 2021;11:630885.
- Zeng Q, Li J, Sun N, et al. Preoperative systemic immune-inflammation index predicts survival and recurrence in patients with resected primary pulmonary sarcomatoid carcinoma. *Transl Lung Cancer Res*. 2021;10:18–31.
- Lin Y, Yang H, Cai Q, et al. Characteristics and prognostic analysis of 69 patients with pulmonary sarcomatoid carcinoma. *Am J Clin Oncol*. 2016;39:215–222.
- Gao P, Zhu T, Gao J, et al. Impact of examined lymph node count and lymph node density on overall survival of penile cancer. *Front Oncol*. 2021;11:706531.
- Amit M, Tam S, Boonsripitayanon M, et al. Association of lymph node density with survival of patients with papillary thyroid cancer. *JAMA Otolaryngol Head Neck Surg*. 2018;144:108–114.
- Petrarolha S, Dedivitis R, Matos L, et al. Lymph node density as a predictive factor for worse outcomes in laryngeal cancer. *Eur Arch Otorhinolaryngol*. 2020;277:833–840.
- May M, Herrmann E, Bolenz C, et al. Lymph node density affects cancer-specific survival in patients with lymph node-positive urothelial bladder cancer following radical cystectomy. *Eur Urol*. 2011;59:712–718.
- Ema A, Waraya M, Yamashita K, et al. Identification of EGFR expression status association with metastatic lymph node density (ND) by expression microarray analysis of advanced gastric cancer. *Cancer Med*. 2015;4:90–100.

26. Zhou X, Wu C, Cheng Q. Negative lymph node count predicts survival of resected non-small cell lung cancer. *Lung*. 2020;198:839–846.
27. Nwogu CE, Groman A, Fahey D, et al. Number of lymph nodes and metastatic lymph node ratio are associated with survival in lung cancer. *Ann Thorac Surg*. 2012;93:1614–1619; discussion 1619–1620.
28. Chiappetta M, Leuzzi G, Sperduti I, et al. Lymph-node ratio predicts survival among the different stages of non-small-cell lung cancer: a multicentre analysis. *Eur J Cardiothorac Surg*. 2019;55:405–412.
29. David EA, Cooke DT, Chen Y, et al. Does lymph node count influence survival in surgically resected non-small cell lung cancer? *Ann Thorac Surg*. 2017;103:226–235.
30. Zhou J, Lin Z, Lyu M, et al. Prognostic value of lymph node ratio in non-small-cell lung cancer: a meta-analysis. *Jpn J Clin Oncol*. 2020;50:44–57.
31. Saltzman AF, Carrasco A Jr, Amini A, et al. Patterns of lymph node sampling and the impact of lymph node density in favorable histology Wilms tumor: an analysis of the national cancer database. *J Pediatr Urol*. 2018;14:161.e1–161.e8.