Crimson Publishers
Wings to the Research

Research Article

The Incidence of N1 And N2 Metastases in Relation to the Presence/Absence of the Peritumoral Lymphovascular Invasion

Pilav I[1], Mušanović S[1]*, Karavdić K[2], Alihodžić-Pašalić A[1], Dapčević M[1], and Čustović O[1]

[1]Department of Thoracic Surgery, Bosnia and Herzegovina

[2]Department of Pediatric Surgery, Bosnia and Herzegovina

ISSN: 2578-0204

***Corresponding author:** Mušanović S, Department of Thoracic Surgery, Bosnia and Herzegovina

Submission: June 23, 2020

Published: January 27, 2021

Volume 3 - Issue 3

How to cite this article: Pilav I, Mušanović S, Karavdić K, Alihodžić-Pašalić A, Dapčević M, Čustović O. The Incidence of N1 And N2 Metastases in Relation to the Presence/Absence of the Peritumoral Lymphovascular Invasion. Open J Cardiol Heart Dis. 3(3). OJCHD.000565. 2021. DOI: 10.31031/OJCHD.2021.03.000565

Abstract

Introduction: The incidence of N1 and N2 metastases in relation to the presence of peritumoral lymphovascular infiltration and tumor grade in bronchial carcinoma still remain insufficiently researched areas that could provide valuable guidance. Several studies have shown a statistically significant difference in the occurrence of N1 and N2 metastases in relation to the type and size of the bronchial carcinoma. The relationship between the occurrence of N1 and N2 metastases and the degree of immaturity of the tumor in the bronchial carcinoma remains insufficiently documented.

Patients and methods: This study included 331 patients of all ages, both men and women, diagnosed with bronchial carcinoma using various diagnostic procedures. In these patients, surgical treatment was indicated and the anatomical resection was performed.

Result: A total of 331 patients were included in the study and N1 metastases were present in 39.88% of cases, while N2 metastases were present in 4.53% of cases with bronchial carcinoma. Peritumoral lymphovascular invasion was present in 37.55% of cases (86 out of 229 patients) with N0 disease, in 55.89% of cases (128 out of 229 patients) with N1 disease, and in 6.55% of cases (15 out of 229 patients) with confirmed N2 disease.

Conclusion: The presence of the peritumoral lymphovascular invasion is more often accompanied by metastases in corresponding regional lymph nodes. By calculating the total relative risk, there is almost a 30-fold higher risk of developing metastases in N1 and N2 lymph nodes in the presence of peritumoral lymphovascular invasion.

Keywords: Bronchial carcinoma; Lymph node metastases; Lymphovascular invasion

Introduction

The incidence of N1 and N2 metastases in relation to the presence of peritumoral lymphovascular infiltration and tumor grade in bronchial carcinoma still remain insufficiently researched areas that can provide valuable guidance on cancer aggressiveness, disease spread, prognosis and treatment.

Being that each lung lobe has its own lymphatic drainage, metastatic spread of lung cancer by lymphatic route depends on its location. Consequently, understanding the metastatic spread of cancer to regional lymph nodes requires good knowledge of the anatomy of the lymphatic system of each lobe [1-6].

The influence of numerous factors, i.e., the most common types of lung cancer, tumor size as well as the degree of differentiation and stage of the malignant disease on the occurrence of N1 and N2 metastases has been thoroughly investigated. Several studies have shown a statistically significant difference in the occurrence of N1 and N2 metastases in relation to the type and size of the bronchial carcinoma. The relationship between the occurrence of N1 and N2 metastases and the degree of immaturity of the tumor in the bronchial carcinoma remains insufficiently documented [1-6].

A literature review of available medical databases and research articles over the past 10 years was conducted, but the strong association between the presence of N1 and N2

metastases and pathohistological confirmation of peritumoral lymphovascular invasion (a reliable indicator that correlates with the tumor aggressiveness in bronchial carcinoma) was not observed in other studies.

Patients and Methods

We analyzed data from patients diagnosed with bronchial carcinoma who underwent surgical resection during their hospital stay at the Clinic of Thoracic Surgery, Clinical Center University of Sarajevo from 01.01.2013 to 01.01.2018. In total, this study included 331 patients of all ages, both men and women, diagnosed with bronchial carcinoma using various diagnostic procedures. In these patients, surgical treatment was indicated, and the anatomical resection was performed.

Results

A total of 331 patients diagnosed with bronchial carcinoma underwent surgical resection during their hospital stay at the Clinic of Thoracic Surgery from 01.01.2013 to 01.01.2018. The mean age of the patients was 62.69 ± 7.46.

Histopathological findings in relation to the type of bronchial carcinoma are shown in Table 1.

Table 1: Definitive histopathological diagnoses in relation to the type of bronchial carcinoma.

Squamous cell carcinoma	54.98%	(182/331)
Adenocarcinoma	42.30%	(140/331)
Large cell carcinoma	2.72%	(9/331)
TOTAL:	100.00%	(331/331)

In our study, the squamous cell carcinoma was the most common type of bronchial carcinoma, found in 54.98% of cases (182 out of 331 patients), followed by adenocarcinoma, which was found in 42.30% of cases (140 out of 331 patients). The least common type of bronchial carcinoma was large cell carcinoma, found in 2.72% of cases (nine out of 331 patents).

The relation between the most common histopathological diagnoses and surgical resections is shown in Figure 1.

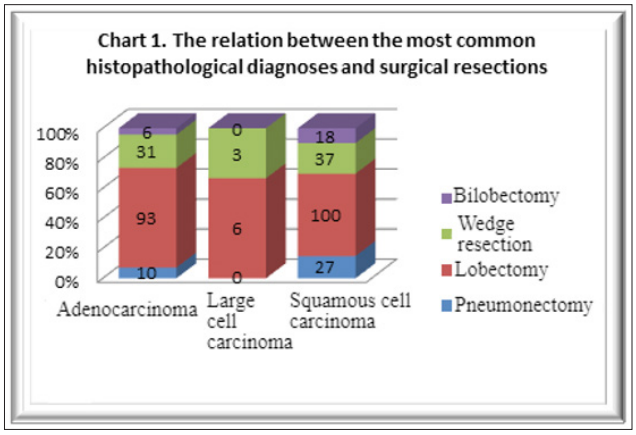

Figure 1: The relation between the most common histopathological diagnoses and surgical resections.

Standard lobectomy was the most common surgical resection of both squamous cell carcinoma, i.e., in 54.94% of cases (100 out of 182 patients) and adenocarcinoma, i.e., 66.42% of cases (93 out of 140 patients).

The prevalence of lymph node (N0, N1 and N2) involvement in bronchial carcinoma is shown in Table 2.

Table 2: The prevalence of lymph node involvement in patients diagnosed with bronchial carcinoma.

	%	n
N0	55.59%	(184/331)
N1	39.88%	(132/331)
N2	4.53%	(15/331)
TOTAL:	100.00%	(331/331)

The most common were cases without the presence of malignant cells in the lymph nodes (N0), i.e., 55.59% of cases (184 out of 331 patients), N1 metastases were present in 39.88% of cases (132 out of 331 patients), and N2 metastases were observed in 4.53% of cases (15 out of 331 patients).

The relation between N0, N1 and N2 metastases and the most common histopathological diagnoses is shown in Table 3.

Table 3: The prevalence of N0, N1 and N2 metastases and their relation to the most common histopathological diagnoses.

	Large Cell Carcinoma		Squamous Cell Carcinoma		Adenocarcinoma	
	%	N	%	n	%	n
N0	66.67%	(6/9)	52.75%	(96/182)	58.57%	(82/140)
N1	33.33%	(3/9)	43.96%	(80/182)	35.00%	(49/140)
N2	0.00%	(0/9)	3.30%	(6/182)	6.43%	(9/140)
TOTAL:	100.00%	(9/9)	100.00%	(182/182)	100.00%	(140/140)

More than half of the patients with both squamous cell carcinoma, i.e., 52.75% of cases (96 out of 182 patients) and adenocarcinoma, i.e., 58.57% of cases (82 out of 140 patients) had no lymph node metastases (N0). N1 lymph node involvement (positive ipsilateral hilar lymph nodes) was present in 43.96% of cases with squamous cell carcinoma and in 35.00% of cases with adenocarcinoma. N2 lymph node involvement was present in 3.30% of cases with squamous cell carcinoma and in 6.43% of cases with adenocarcinoma.

The prevalence of the peritumoral lymphovascular invasion and its relation to the lymph node status is shown in Table 4.

Table 4: The prevalence of the peritumoral lymphovascular invasion and its relation to the lymph node status.

*PLVI	N0	N1	N2	Total
No	96% (98/102)	3.92% (4/102)	0.98% (1/102)	100% (102/102)
Yes	37.55% (86/229)	55.89% (128/229)	6.55% (15/229)	100% (229/229)
Total	55.58% (184/331)	39.87% (132/331)	4.53% (15/331)	100% (331/331)

*PLVI - peritumoral lymphovascular invasion.

Peritumoral lymphovascular invasion was present in 37.55% of cases (86 out of 229 patients) with N0 disease and in 55.89% of cases (128 out of 229 patients) with N1 disease as well as in 6.55% of cases (15 out of 229 patients) with confirmed N2 disease.

Peritumoral lymphovascular invasion was not present in 96% of cases (98 out of 102 patients) with NO disease, 3.92% of cases (4 out of 102 patients) with N1 disease as well as 0.98% of cases (1 out of 102 patients) with confirmed N2 disease.

Table 5: The frequency of lymph node metastases in relation to the presence of peritumoral lymphovascular invasion.

		Lymph Node Metastases		
		Yes	No	Total:
Peritumoral lymphovascular invasion	Yes	a=143	b=86	a+b=229
	No	c=4	d=98	c+d=102
Total:		a+c=147	b+d=184	N=331

The frequency of lymph node metastases in relation to the presence of peritumoral lymphovascular invasion is shown in Table 5.

It is possible to calculate the sensitivity, specificity, positive and negative predictive values of the peritumoral lymphovascular infiltration in relation to the presence of lymph node metastases. Their values were obtained as follows: sensitivity (97.27%), specificity (53.26%), positive predictive value (62.447%) and negative predictive value (96.07%). The overall accuracy was 72.8%.

Table 6: The prevalence of N1 lymph node metastases in relation to the presence of peritumoral lymphovascular infiltration.

	Peritumoral Lymphovascular Invasion			
		Yes	No	Total
Lymph node involvement	Yes	a=128	b=4	a+b=132
	No	c=86	d=98	c+d=184
Total:		a+c=214	b+d=102	N=316

Data for calculating the relative risk of N1 lymph node metastases in relation to the presence of peritumoral lymphovascular infiltration is shown in Table 6.

The risk of lymph node metastases in patients with peritumoral lymphovascular invasion was calculated as follows:

The risk among patients with PLVI = (a/b) = 128/4 = 31.00.

The risk of lymph node metastases in patients without peritumoral lymphovascular invasion was calculated as follows:

The risk among patients without PLVI = (c/d) = 86/98 = 0.87

We investigated the association between the peritumoral lymphovascular invasion and regional lymph node metastases using Spearman's rank correlation coefficient. There was a statistically significant correlation between the variables, i.e., $\rho = 0.544$, $n = 331$, $p < 0.0001$. The presence of peritumoral lymphovascular invasion was more often accompanied by the presence of metastases in the corresponding regional lymph nodes.

Discussion

The presence of N1 disease significantly affects the five-year survival rate, and it has been observed that the same corresponds to the number of involved N1 lymph nodes. The presence of N2 disease is still the subject of much debate, which leads to the fact that most surgeons and oncologists at present opt for a combined approach to N2 NSCLC. It has been shown that patients who have been preoperatively diagnosed with N2 lymphadenopathy do not benefit much from surgical treatment [7-10]. In contrast, patients whose N2 disease is not clearly clinically classified, but diagnosed *via* surgical treatment or using the histopathological examination, have a better postoperative outcome [11,12].

Lymph nodes in patients diagnosed with bronchial carcinoma who were treated in this study were not proportionally affected by metastatic spread of the disease as seen from the obtained results. The most common were patients without the presence of malignant cells in the lymph nodes (N0), i.e., 55.59% of cases, N1 metastases were present in 39.88% of cases, and N2 metastases in 4.53% of cases of bronchial carcinoma.

Almost similar results have been published in several other literature reports [1-9]. Given the fact that the majority, i.e., 95.47%, of patients who have undergone surgical treatment had N0 and N1 lymph node status, it can be assumed and concluded that there was a relatively good diagnostic assessment of patients as well as clinical determination of the disease stage and selection of patients for surgical treatment.

In more than half of the patients, both in the squamous cell population group, i.e., 52.75% of cases (96 out of 182 patients) as well as in the adenocarcinoma population group, i.e., 58.57% of cases (82 out of 140 patients), no lymph node metastases were present.

In relation to the presence or absence of peritumoral lymphovascular invasion in patients diagnosed with bronchial carcinoma, the following results were obtained:

Peritumoral lymphovascular invasion was present in 72.46% of cases (229 out of 316 patients) with the presence of lymph node metastases in 62.44% of cases [N1 metastases in 89.51% of cases (128 out of 143 patients) and N2 in 10.49% of cases (15 out of 143 patients)].

Based on the available data, sensitivity (97.27%), specificity (53.26%), positive predictive value (62.447%) as well as the negative predictive value (96.07%) were calculated. The overall accuracy was 72.8%.

The total relative risk of lymph node metastases in relation to the presence of peritumoral lymphovascular invasion is 35.63, which means that there is a 35.63 times higher chance of developing disease with the lymph node metastasis in the presence of peritumoral lymphovascular invasion compared to when it is not present.

The study unequivocally confirmed that the presence of peritumoral lymphovascular invasion was more often accompanied by the presence of metastases in the corresponding regional lymph nodes. An association between the presence of peritumoral lymphovascular invasion and the frequency of N1 and N2 metastases was observed.

The presence of peritumoral lymphovascular invasion can serve as a good predictor in relation to the assessment of the lymph node status, and indirectly have both prognostic and therapeutic significance for these patients.

However, there are reports in the available literature on other types of malignancies, primarily breast cancer and cervical cancer, in which similar studies (the presence of peritumoral lymphovascular invasion and the lymph node status) have been conducted and have shown an association between the peritumoral lymphovascular invasion and more frequent occurrence of lymph node metastases [7-13].

Conclusion

a) Peritumoral lymphovascular invasion was present in 70.52% of cases (229 out of 331 patients) diagnosed with bronchial carcinoma.

b) Lymph nodes were involved in 70.52% of cases (229 out of 331 patients) with present lymphovascular invasion and in only 3.30% of cases (4 out of 331 patients) in which the lymphovascular invasion was not present.

c) Lymph nodes were not involved in 84% of cases (86 out of 229 patients) with present lymphovascular invasion and in 53.00% of cases (98 out of 102 patients) in which the lymphovascular invasion was not present.

d) In those cases, without lymph node involvement (N0) peritumoral lymphovascular invasion was present in 46.13% of cases (86 out of 244 patients).

e) Peritumoral lymphovascular invasion was present in 53.26% of cases (143 out of 244 patients) with confirmed N1 disease.

f) Peritumoral lymphovascular invasion was present in 100% of cases (all 15 patients) with confirmed N2 disease.

g) Regardless of the fact that the presence of the peritumoral lymphovascular invasion was not accompanied by the occurence of N1 and N2 metastases in all patients diagnosed with bronchial carcinoma, it was found that there was a statistically significant difference in metastatic lymph node involvement in relation to the presence of the peritumoral lymphovascular invasion.

h) By calculating the total relative risk, there is almost a 30-fold higher risk of developing metastases in N1 and N2 lymph nodes in the presence of the peritumoral lymphovascular invasion.

The presence or absence of the peritumoral lymphovascular invasion can be used both in predicting and excluding the presence or absence of the lymph node involvement.

References

1. (2009) Cancer facts and figures. American Cancer Society.
2. Shields TW (2005) Pathology of carcinoma of the lung. In: General Thoracic Surgery. (6th edn), Lippincott Williams and Wilkins, USA, pp. 1455-1480.
3. Mostertz W, Stevenson M, Acharya C, Chan I, Walters K, et al. (2010) Age- and sex-specific genomic profiles in non-small cell lung cancer. JAMA 303(6): 535-543.
4. Porta RR, Crowley JJ, Goldstraw P (2009) The revised TNM staging system for lung cancer. Ann Thorac Cardiovasc Surg 15(1): 4-9.
5. De la Guerra A (2010) New TNM classification for lung cancer - Part I: The changes.
6. Padilla J, Calvo V, Penalver JC, Sales G, Morcillo A (1997) Surgical results and prognostic factors in early non-small cell lung cancer. Ann Thorac Surg 63(2): 324-326.
7. Lantuejoul S, Brambilla E (2006) Prognostic biomarkers in non-small cell lung carcinoma. Curr Diagn Pathol 2: 418-428.
8. Sakao Y, Nakazono T, Sakuragi T, Natsuaki M, Itoh T (2004) Predictive factors for survival in surgically resected clinical IA perpiheral adenocarcinoma of the lung. Ann Thorac Surg 77(4): 1157-1162.
9. (2009) National Comprehensive Cancer Network. NSCLC Practice Guidelines.
10. Marra A, Hillejan L, Zaboura G, Fujimoto T, Greschuchna D, et al. (2003) Pathologic N1 non-small cell lung cancer: Correlation between pattern of lymphatic spread and prognosis. J Thorac Cardiovasc Surg 125(3): 543-553.
11. Heerma van Voss MR, vander Groep P, Bart J, vander Wall E, van Diest (2010) Lymphovascular invasion in BRCA related breast cancer compared to sporadic controls. BMC Cancer 10: 145.
12. Parsons A, Daley A, Begh R, Aveyard P (2010) Influence of smoking cessation after diagnosis of early-stage lung cancer on prognosis: Systematic review of observational studies with meta-analysis. BMJ 340: b5569.
13. Yoshino I, Baba H, Fukuyama S, Kameyama T, Shikada Y, et al. (2002) A time trend of profile and surgical results in 1123 patients with non-small lung cancer. Surgery 131: S242-S428.