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Mediastinal staging lymph node probability map in non-small cell lung cancer

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Abstract

Background Mediastinal lymph node (LN) staging is routinely performed using PET/CT and EBUS-TBNA. Promising predictive algorithms for lymph nodes have been reported for each technique, both individually and in combination. This study aims to develop a predictive algorithm that combines EBUS, PET/CT and clinical data to provide a probability of malignancy.

Methods A retrospective study was conducted on consecutive patients with non-small cell lung carcinoma staged using PET/CT and EBUS-TBNA. Lymph nodes were identified by level (N1, N2, and N3) and anatomical region (AR) (subcarinal, paratracheal, and hilar). A Standardized Uptake Value (SUV) was determined for each sampled LN. The ultrasound features collected included diameter in the short axis (DSA), morphology, border, echogenicity and the presence of the vascular hilum. A robust logistic regression model was used to construct an algorithm to estimate the probability of malignancy of the lymph node.

Results A total of 116 patients with a mean age of 66, 93% of whom were men, were included. 358 lymph nodes were evaluated, 51% of which exhibited adenocarcinoma and 35% were squamous, while 14% were classified as non-small-cell lung carcinoma. The model estimated the probability of malignancy for each lymph node using age, DSA, SUVmax, and AR. The Area Under the ROC curve, was 0.89. A user-friendly application was also developed (https://ubidi.shinyapps.io/lymma/.)

Conclusions The integration of patient clinical characteristics, EBUS features, and PET/CT findings may generate a pre-sampling malignancy probability map for each lymph node. The model requires prospective and external validation.

Summary at a glance

A predictive algorithm for lymph metastasis in NSCLC combining the patient clinical characteristics, EBUS features, and PET/CT findings could facilitate the estimation of the specific probability of malignancy of a single lymph node in the lymph node probability map.

Keywords Lung cancer, Mediastinal staging, Lymph node, EBUS, PET/CT

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Background

Staging is the main prognostic factor in lung cancer [1], and fast, precise and safe staging therefore determines the available treatment, as well as impacting survival [1]. The mediastinal staging of non-small cell lung cancer (NSCLC) is initially clinical Tumor-Node-Metastasis (cTNM)-basis staging [2, 3], which may be confirmed with surgical staging when required [3]. Clinical staging is based on 2-deoxy-2-[18 F] fluoro-D-glucose positron emission tomography-computed tomography (PET/CT), and its histological confirmation is recommended by Endobronchial Ultrasound-Guided Fine Needle Aspiration (EBUS-TBNA) due to its high clinical efficacy, with a high sensitivity and positive predictive value, safety and cost-effectiveness [3, 4].

Various predictive factors have been proposed to increase the sensitivity and positive predictive value of PET/CT and EBUS. Mediastinal lymph nodes ≥ 1 cm in diameter in the short axis as measured in CT and with a maximum Standard Uptake Value (SUVmax) ≥ 2.5 are usually considered to be suspicious for malignancy [3]. However, because of their limited accuracy and higher rate of false positives, other SUVmax cut-offs, SUV measurements and SUV ratios have been proposed [5–9]. In addition, SUV depends on glucose metabolism, which is influenced by a distinct tumor histology and a patient's systemic inflammation or infection [10–13]. Therefore, in order to homogenize those factors, the ratio of SUV lymph node to lung primary mass, mediastinal blood pool and liver pool were proposed [10–13].

At the same time, various ultrasonographic EBUS characteristics were also proposed as a predictive factor for benignity / malignancy. In initial studies, ultrasonographic features, namely shape, echogenicity, margin, central necrosis/coagulation, short axis diameter and central hilar structure, were described as suspicious for malignancy or benignity with an accuracy between 56.5 and 79.1 [14–17]. Later studies proposed the combination of these characteristics to increase their predictive power [18–21].

However, there are to date no studies that explore the diagnostic capacity of combining EBUS, PET/CT, and patient data. Furthermore, no studies have focused on assessing the probability of malignancy as a continuous probability map.

Methods

This study aims to devise a clinical prediction model based on anatomical and PET/CT factors that could help predict the probability of malignancy before sampling mediastinal lymph nodes.

Patients

We included all subjects with anatomopathologically confirmed NSCLC, and for whom mediastinal staging was based on PET/CT and EBUS-TBNA, from January 2012 to January 2018 at a single tertiary hospital. Age, gender, diabetes, autoimmune diseases, tobacco status (smoker, former smoker or never smoker), cumulative tobacco dose, lung disease (chronic obstructive lung disease [COPD], asthma and interstitial lung disease) and pulmonary function test were collected from our prospective registry cases based on our medical records. Final primary lung cancer histological confirmation was required to include the patient. The International Association for the Study of Lung Cancer (IASLC) lymph node map [2] was used to determine TNM.

PET/CT

PET/CT was performed as part of the standard diagnostic workup for lung cancer [22] using Discovery ST PET/CT (GE Healthcare, Milwaukee, Wis) or Discovery IQ PET/CT (GE Healthcare, Milwaukee, Wis). Protocol-optimized images and compliance with the European Association of Nuclear Medicine (EANM) and Society of Nuclear Medicine (SNM) guidelines [23] regarding patient preparation, data acquisition, reconstruction parameters and definition of volume of interest in the tumors were followed strictly in our study in order to minimize SUV bias. Our PET/CT systems were harmonized in both the preparation of the patient in the PET unit and the acquisition and reconstruction parameters in order to minimize variability in semi-quantitative measurements when SUV is used as a diagnostic tool in studies with different PET/CT systems [23]. For the retrospective study, two nuclear medicine experts reviewed the integrated PET/CT scans blindly to determine SUVmax, SUVmean, and SUVpeak for every single sampled lymph node, as well as for the pulmonary mass, liver, and mediastinal blood pool. Lymph node/pulmonary mass ratio, lymph node/liver ratio, and lymph node/blood pool ratio were calculated. Lymph node diameter in the short axis (DSA) measured by EBUS-TBNA was used for the development of the predictive model. Additionally, the short-axis diameters of 33 lymph nodes were also measured by PET/CT to explore the PET/CT - EBUS measuring correlation.

EBUS-TBNA

The Olympus BF-UC180F (Tokyo, Japan) and Fujifilm EB-530 US (Tokyo, Japan) were used for mediastinal staging under general anesthesia through a laryngeal mask (iGel, Intersurgical, Berkshire, UK). All lymph nodes with a DSA greater than 5 mm were sampled, as were shorter nodes in the presence of suspected PET/CT or EBUS. Lymph nodes were sampled using endobronchial

Table 1 Demographic characteristics

Lymph nodes sampled, *N*		**358**
Patient studied, N		116
Age, mean (SD)		66.2 (10.3)
Sex, N (%)	Male	96 (83%)
Tobacco, N (%)	Smoker	50 (43%)
	Former smoker	61 (53%)
Tobacco cumulative dose, median (Q1; Q3)		43.5 (3;18)
Lung disease, N (%)	COPD	42 (37%)
	ASTHMA	2 (2%)
	Interstitial Lung Disease	2 (2%)
Diabetes, N (%)	present	24 (21%)
Lung function test, median (Q1; Q3)	FVC % predicted	90.5 (76.7;107)
	FEV1% predicted	76.6 (61.7;90.1)
	FEV1/FVC	67.1 (57.1;73.0)

Table 2 Lung cancer characteristics

Localization, *N* (%)	**Right Upper Lobe**	**53 (46%)**
	Median lobe	5 (4%)
	Right Lower Lobe	10 (9%)
	Left Upper Lobe	32 (28%)
	Left Lower Lobe	16 (14%)
Histology, N (%)	Adenocarcinoma	184 (51%)
	Squamous cell carcinoma	125 (35%)
	Non-small-cell lung carcinoma not otherwise specified	49 (14%)
Lymph node level, N (%)	N1	41 (12%)
	N2	151 (42%)
	N3	133 (46%)
Anatomical region, N (%)	Paratracheal	151 (42%)
	Hilar	130 (36%)
	Subcarinal	77 (22%)
Diameter short axis, mm (SD)		9,01 (3,57)
Shape, N (%)	Oval	137 (39%)
	Round	138 (39%)
	Elongate	50 (14%)
	Triangular	20 (6%)
	Irregular	10 (3%)
Margin, N (%)	Distinct	318 (90%)
Echogenicity, N (%)	Heterogeneous	151 (42%)
Vascular hilum, N (%)	Presence	103 (29%)
SUVmax, median (Q1; Q3)		2,6 (2,0 ; 3,8)
SUVpeak, mean (SD)		2,63 (1,9)
SUVmean, mean (SD)		2,17 (1,49)

ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) with 22-gauge needles. A minimum of three aspirations were performed per lymph node, with suction applied during the final pass. Sampling was deemed successful only if the EBUS-TBNA operator considered the sample valid, and a representative sample of the lymph node was confirmed by a pathologist through rapid on-site evaluation (ROSE). The lymph node staging level (N1, N2, and N3), anatomical region (AR) (subcarinal, paratracheal, and hilar), ultrasound characteristics, including the diameter on the short axis (DSA) (millimeter), shape (round, oval, triangular, irregular), margins (distinct or indistinct), echogenicity (heterogenous or homogenous) and central hilar structure (absent or present), were recorded for every lymph node. Lymph nodes with suspected non-representative samples or those not meeting the confidence threshold of the biopsy performer or pathologist were excluded.

Statistical analysis

The baseline characteristics of participants were described using mean and standard deviation for continuous variables and frequencies for categorical variables. The association between the lymph node clinical profile and PET/CT performance and pathology result (negative/positive) was quantified by an odds ratio from a univariate mixed logistic regression model adjusting for patient clustering.

A multivariate mixed logistic regression model was estimated to predict lymph node pathology results (negative/positive). Those with lymph node clinical profile characteristics and a PET/CT performance that showed a statistically significant association were considered for inclusion in the predictive model. All variables collected and calculated ratios were tested in the model. No variable selection strategy was defined due to the limited number of factors available. Different estimated models were compared using the best fit according to Akaike's information criteria. Model performance was assessed in terms of calibration and discrimination. Interval validation was performed by bootstrapping. External validation was not possible due to lack of data. Confidence intervals set at 95% were reported for estimates. Statistical significance was fixed at 0.05 probability. All statistical analyses were conducted using R version 3.4.5 for Windows.

Results

Patients' characteristics are shown in Table 1. One hundred and sixteen patients with mediastinal staging of 358 lymph nodes anatomopathologically positive for NSCLC based on PET/CT and EBUS-TBNA were performed between 2010 and 2018. Ninety-six of these patients were men, 66 years old on average, and COPD was the main comorbidity.

Lung cancer characteristics are depicted in Table 2. Adenocarcinoma was the most prevalent histology. A total of 358 lymph nodes were sampled, mainly

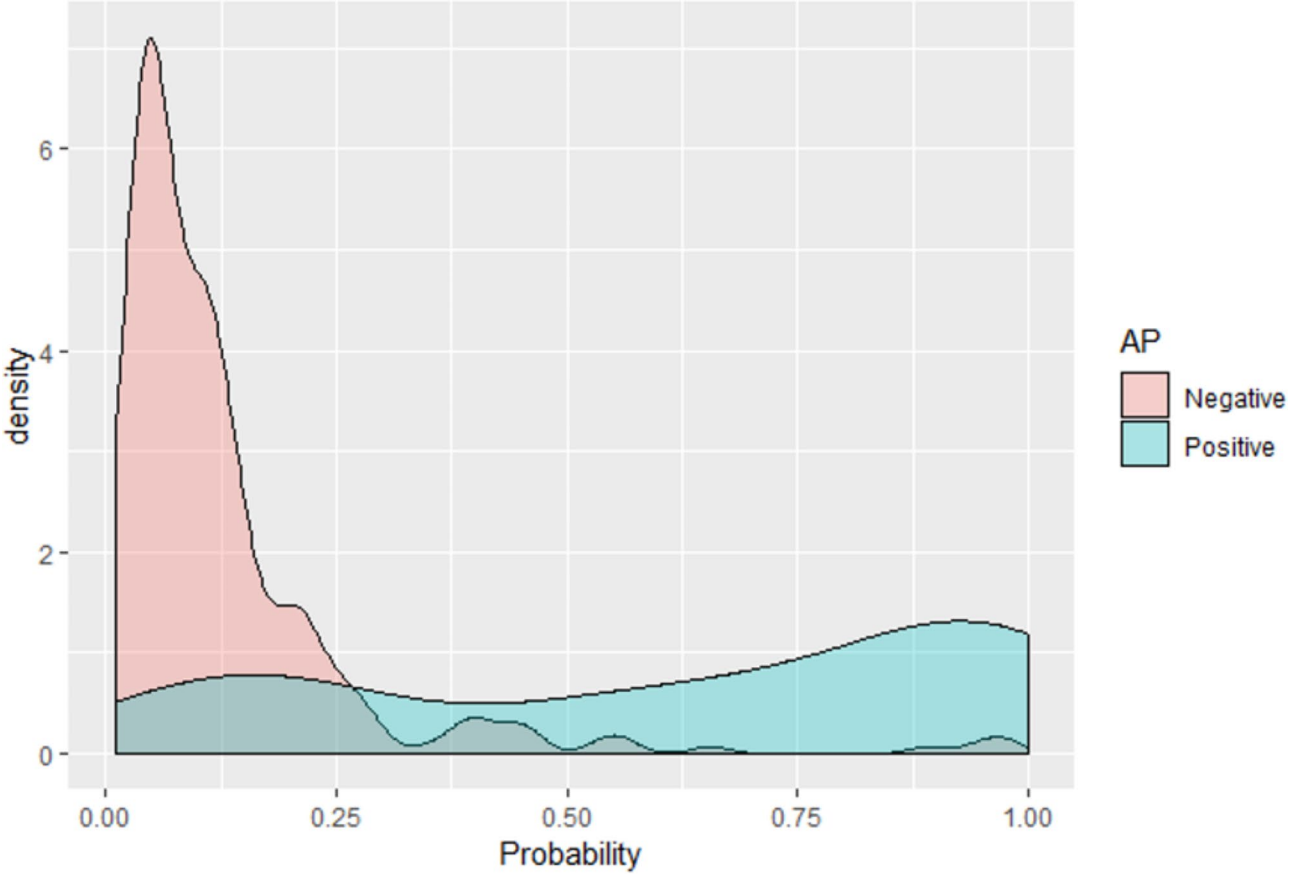
mediastinal, hilar and subcarinal. Graphic 1 shows the distribution density for the probability of positive and negative lymph nodes.

Significance in the univariant analysis is shown in Table 3, with lymph node staging, histology, morphological EBUS characteristics, and metabolic parameters on PET/CT all being significant. On the other hand, no significant differences were found in the univariate analysis when it was adjusted by age, gender, lung cancer localization, smoke status, cumulative tobacco doses, lung diseases, diabetes or lung function at diagnosis.

After comparing different models, the best model in terms of fit was the one with age, DSA, SUV maximum and anatomical area as predictors, as shown in Table 4. No other combination or addition of variables improved the model. The discriminative ability of the model as measured by the Area Under the Roc curve was = 0.89 (95% confidence interval from 0.84 to 0.94). Calibration showed a good observed/expected ratio. A web application (https://ubidi.shinyapps.io/lymma) was developed to make the estimation of the probability of a malignant tumour easily available and practical. Giving these promising results, and taking into account the fact that DSA was the only variable measured by EBUS which was required in the probability model, DSA was measured by PET/CT in an aleatory subgroup of 33 lymph nodes. A correlation of 0.91 was found between both measurements (EBUS – PET/CT), as shown in Table 5.

Discussion

Mediastinal staging for NSCLC is based on PET/CT image study and confirmed by EBUS-TBNA, because of limited PET/CT accuracy [3]. In current practice, DSA is used to guide lymph node puncture. A diameter of 5 mm has been chosen as the optimal size for balancing sensitivity and specificity for malignancy. This is supported by necropsy studies in non-neoplastic patients, where the average short diameter was less than 5 mm, although the range varied considerably from 1.0 mm to nearly 15 mm [24]. Nevertheless, in recent years researchers have proposed different scoring systems and algorithms to personalize the approach, utilizing PET/CT scans [21, 24–26] and EBUS findings [16–20]. The latest proposals combine the predictive power of both techniques with promising results [21, 25]. However, to the best of our knowledge, a combination of PET/CT, EBUS and clinical data has not yet been explored.



Graphic 1 Distribution density of probability of positive and negative lymph nodes

Table 3 Univariant analysis

		Negative	Positive	OR	*p.* value
		N **= 283**	***N*** **= 75**		
Lung cancer characteristics					
Lymph node staging, N (%):	N1	24 (8.48%)	17 (22.7%)	Ref.	Ref.
	N2	106 (37.5%)	45 (60.0%)	0.60 [0.29;1.24]	0.167
	N3	153 (54.1%)	13 (17.3%)	0.12 [0.05;0.28]	< 0.001
Anatomical Area, N (%):	Mediastinal	112 (39.6%)	39 (52.0%)	Ref.	Ref.
	Hilar	107 (37.8%)	23 (30.7%)	0.62 [0.34;1.10]	0.103
	Subcarinal	64 (22.6%)	13 (17.3%)	0.59 [0.28;1.16]	0.129
Histology, N (%):	Adenocarcinoma	138 (48.8%)	46 (61.3%)	Ref.	Ref.
	Squamous cell carcinoma	110 (38.9%)	15 (20.0%)	0.41 [0.21;0.76]	0.004
	Non-small-cell lung carcinoma not otherwise specified	35 (12.4%)	14 (18.7%)	1.20 [0.58;2.41]	0.609
EBUS characteristics					
Diameter short axis, mm (SD)		8.33 (2.89)	11.6 (4.60)	1.26 [1.17;1.36]	< 0.001
Shape, N (%):	Oval	115 (40.9%)	22 (29.7%)	Ref.	Ref.
	Round	96 (34.2%)	42 (56.8%)	2.27 [1.28;4.14]	0.005
	Elongated	45 (16.0%)	5 (6.76%)	0.59 [0.19;1.57]	0.309
	Triangular	19 (6.76%)	1 (1.35%)	0.31 [0.01;1.64]	0.201
	Irregular	6 (2.14%)	4 (5.41%)	3.48 [0.80;13.6]	0.093
Margin, N (%):	Indistinct	33 (11.8%)	2 (2.70%)	Ref.	Ref.
	Distinct	246 (88.2%)	72 (97.3%)	4.50 [1.32;30.5]	0.013
Heterogenicity, N (%):	No	172 (61.0%)	33 (44.6%)	Ref.	Ref.
	Yes	110 (39.0%)	41 (55.4%)	1.94 [1.16;3.27]	0.012
Central hilar structure, N (%):	Absent	186 (66.7%)	65 (86.7%)	Ref.	Ref.
	Present	93 (33.3%)	10 (13.3%)	0.31 [0.14;0.61]	< 0.001
PET/CT characteristics					
Time between PET-EBUS, Mean (standard deviation)		28.1 (14.7)	24.1 (15.1)	0.98 [0.96;1.00]	0.036
SUVmax, Mean (standard deviation [SD])		12.9 (7.48)	10.1 (5.17)	0.94 [0.90;0.98]	0.003
SUVpeak, Mean (SD)		10.3 (6.29)	7.82 (4.48)	0.93 [0.88;0.97]	0.002
SUVmean, Mean (SD)		7.78 (4.72)	6.19 (3.65)	0.92 [0.86;0.98]	0.008
MTV, Mean (SD)		232 (441)	125 (253)	1.00 [1.00;1.00]	0.061
SUVmax vascular, Mean (SD)		640 (5103)	15.5 (22.8)	0.99 [0.98;1.00]	0.035
SUVmax liver, Median [Q1; Q3]		2.20 [1.89;2.50]	2.30 [1.95;2.60]	1.71 [1.00;2.93]	0.052
SUVmax, Median [Q1; Q3]		2.30 [1.90;3.10]	5.50 [3.35;8.75]	2.06 [1.71;2.47]	< 0.001
SUVpeak, Median [Q1; Q3]		1.90 [1.50;2.31]	4.10 [2.30;7.10]	2.81 [2.13;3.72]	< 0.001
SUVmean, Median [Q1; Q3]		1.58 [1.30;1.90]	3.30 [2.10;5.10]	3.44 [2.47;4.79]	< 0.001
SUVmax lymph node/primary lung mass index, Median [Q1; Q3]		0.20 [0.13;0.32]	0.57 [0.32;0.99]	1.85 [1.39;2.46]	< 0.001
SUVmax lymph node/vascular index, Median [Q1; Q3]		1.07 [0.89;1.47]	2.55 [1.56;4.14]	3.20 [2.37;4.32]	< 0.001
SUVmax lymph node/liver index, Median [Q1; Q3]		0.80 [0.63;1.14]	1.83 [1.14;3.10]	5.09 [3.30;7.86]	< 0.001
SUVpeak lymph node/primary lung mass index, Median [Q1; Q3]		0.20 [0.13;0.33]	0.65 [0.31;1.18]	2.05 [1.50;2.82]	< 0.001
SUVmean lymph node/primary lung mass index, Mean (SD)		0.45 (0.73)	0.97 (1.03)	1.84 [1.37;2.45]	< 0.001

Table 4 Model of the probability of lymph node malignancy. Robust logistic model

Predictors	Odds Ratio	95% CI	*p*
Age	0.93	0.9–0.97	0.0025
SUVmax	1.99	1.4–2.84	0.0001
Diameter short axis	1.23	1.1–1.39	0.0001
Hilar lymph node	0.39	0.19–0.82	0.0121
Subcarinal lymph node	0.16	0.06–0.46	0.0006

Table 5 Diameter in short axis correlation EBUS vs. PET/CT

Diameter in short axis for both methods	All (*n* = 33)
EBUS, Mean (SD)	8.78 (3.10)
EBUS, Median [Q1; Q3]	8.10 [6.60;10.0]
PET/CT, Mean (standard deviation)	9.50 (2.85)
PET/CT, Median [Q1; Q3]	8.80 [7.40;10.6]

The results of our univariate analysis were mostly consistent with previous PET/CT and EBUS studies. Regarding NSCLC mediastinal staging by PET/CT, lymph node SUVmax was used firstly with a threshold level for malignancy of ≥ 2.5 [26], but latterly the optimal SUVmax cutoffs proposed range from 2.5 to 6.2 [6, 27–29]. Among the different individual SUV-based metrics are suboptimal parameter due to noise-induced bias [30] reporting a variability of up to 15% in SUVmax reconstruction between centers [31, 32]. Thus, the ratios between the SUVmax of the lymph node and the primary tumor, vascular mediastinal pool and liver pool were estimated. The primary tumor ratio aims to homogenize the variability of the glucose metabolic activity of each histologic tumor [10–13], whereas ratios to the vascular mediastinal pool and liver pool seek to avoid false positives due to other hypermetabolic situations such as systemic inflammatory diseases or systemic infections [6, 11]. Concordantly, our univariate analysis found that mediastinal lymph node SUVmax, mean, peak, and median were useful to predict the lymph's probability of malignancy. On the other hand, since Fujiwara et al. [16] proposed a round shape, distinct margin, heterogeneous echogenicity and the presence of coagulation necrosis signs as EBUS features independently predictive of metastasis, other studies have incorporated short axis diameter, the presence of a central hilar structure, and elastography features [14, 17, 18, 33]. Similarly, we found a round shape, distinct margin, heterogenicity and the presence of vascular hilum to be significant EBUS predictive metastasis factors.

The proposed model requires the patient's age and the lymph's node short axis diameter, SUVmax, and anatomical area, which combines EBUS, PET/CT, and clinical data. Despite the large number of variables significantly suggestive of malignancy, no other combination or additional variables successfully improved diagnostic accuracy. Other characteristics, such as cancer histology, PET/CT ratios and mediastinal lymph node staging (N1, N2, and N3), were also identified as predictive factors for metastasis. However, and surprisingly, they did not improve the predictive model and were therefore excluded. This finding should be validated through external validation in prospective multicenter studies. Distinct, Martinez-Zayas et al. [34] proposed and recently prospective externally validated [35] a model combining PET/CT and clinical data (Help with Oncologic Mediastinal Evaluation for Radiation [HOMER]) which uses patient age, tumor location, cancer histology and mediastinal staging to predict CT N0-N2 and PET N0-N3. A lymph node was considered positive by CT when it was ≥ 1 cm in the short axis, and by PET based on radiologist's interpretation or SUV ≥ 2.5 when available. With similar PET/CT criteria and including an EBUS study, Hylton et al. [25] reported 5.6% of false negatives for those lymph nodes in which PET/CT was not hypermetabolic and which presented less than two points in the ultrasonographic Canada Lymph Node Score. In contrast, Evison et al. [21] proposed an approach based on a risk stratification model for mediastinal lymph nodes which scores EBUS echogenicity, the SUV of the lymph node and the SUV lymph node/primary tumor ratio. However, a lymph nodes size larger than 1 cm in the short axis of central mediastinal stations (4 and 7) has been reported as normal in postmortem studies (chest malignancy or infection excluded as cause of death) [24, 36]. Therefore, the size of each lymph node station must be considered individually. This, added to the lack of consensus on the SUV cutoff point or ratios such as lymph node – primary tumor [6, 13, 27–29], may indicate that each lymph node station has a different normal size and glucose uptake, as well as being influenced by tumor histology, lymph node staging and clinical data such as the patient's age, the presence of diabetes, tobacco exposure, and inflammatory or infection systemic disease [6, 11, 13]. In light of these considerations, we developed a continuous probability map of malignancy for each mediastinal lymph station that includes influential factors to provide a specific probability of malignancy for each lymph node. In order to illustrate this functionality, a suitable application in English is available for free at the following web page https://ubidi.shinyapps.io/lymma/.

Our proposal is that, short of the surgical removal of all bilateral lymph nodes, absolute certainty regarding the absence of malignancy in any given lymph node cannot be achieved. We propose considering the probability of malignancy as a continuum, enabling personalized cut-offs based on: first, the patient's individual risk for the procedure, including factors such as frailty, comorbidities, and available therapeutic options; second, the specific diagnostic and therapeutic resources available at each center, such as the presence of a thoracic surgery team experienced in advanced mediastinoscopy techniques like VATS mediastinal lymphadenectomy (VMLA); and finally, the specific requirements and judgment of each Tumor Board. This approach must be clinically validated in a prospective trial.

The way to optimize mediastinal staging is currently under debate. Hylton et al. [25] calculated an approximate difference of 18 min vs. four minutes per patient between mediastinal systematic sampling and a directed sampling in their approach. In addition, 3.21% of complications were reported for transbronchial lung biopsy in NSCLC mediastinal staging [37]. Meanwhile, estimating the probability of N0-3 based on the HOMER model without histological confirmation [34, 35] has been proposed for patients with NSCLC potentially treatable with stereotactic ablative radiotherapy.

This study has several limitations. First, this is a retrospective single-center study with a small number of patients and samples. Second, the absence of mediastinoscopy or surgical sampling of the negative lymph nodes implies that, despite the validation requirements of both the EBUS-TBNA operator and the pathologist, it cannot be assured that there are no false negatives. Third, there is a lack of data for the performance of an external validation. This implies that the prediction model could be overfitted to the data of the analyzed cohort, leading to a lack of external validity and potentially underestimating variables such as histology or mediastinal staging, which in other studies have improved predictive models. Therefore, this model must be prospectively and externally validated and probably re-calibrated with larger prospective data, as was required with other models [34, 35]. Fourth, our proposal of a continuous malignancy probability, as opposed to other dichotomous predictive models (benign or malignant), may reduce the practicality of decision-making. However, in our view, this proposal, without a fixed cutoff point, could be a strength as it allows for individualized decision-making with a comprehensive view of the patient.

The study also has other several strengths, such as the fact that all the primary pulmonary mass was identified, all lymph nodes were individually evaluated by EBUS and PET/CT with an estimation of different SUV (max, mean, and peak) and lymph node ratios (primary pulmonary mass, vascular mediastinal pool, and liver pool) by two nuclear medicine experts.

Conclusion

The integration of patient clinical characteristics, EBUS features, and PET/CT findings may generate a pre-sampling malignancy probability map for each lymph node. This could facilitate the individualization of the decision regarding which lymph node to sample, based on a personalized assessment of the patient's clinical context, comorbidities, and available therapeutic options. Further studies and external validation are required. A prospective multicenter study is currently being conducted.

Abbreviations

AR	Anatomical region
cTNM	Clinical tumor-node-metastasis
DSA	Diameter on the short axis
EANM	European association of nuclear medicine
EBUS-TBNA	Endobronchial ultrasound-guided fine needle aspiration
HOMER	Help with oncologic mediastinal evaluation for radiation
IASLC	International association for the study of lung cancer
NSCLC	Non-Small cell lung cancer
PET/CT	Positron emission tomography-computed tomography
ROSE	Apid on-site evaluation
SNM	Society of nuclear medicine
SUVmax	Standard uptake value

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12931-025-03121-z.

Supplementary Material 1

Author contributions

Bordas-Martínez J: Conceptualization; Data curation; Investigation; Methodology; Writing - original draft. Vercher-Conejero JL: Conceptualization; Data curation; Investigation; Methodology; Resources; Writing - review & editing. Rodriguez-González G: Data curation; Investigation. Notta PC: Data curation; Investigation. Martin Cabeza C: Data curation; Investigation. Cubero N: Data curation; Investigation. Lopez-Lisbona RM: Data curation; Investigation. Diez –Ferrer M: Data curation; Investigation. Tebé C: Formal analysis. Santos S: Resources; Writing - review & editing. Cortes-Romera M: Resources; Writing - review & editing. Rosell A: Conceptualization; Investigation; Methodology; Resources; Funding acquisition; Writing - review & editing.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Bellvitge University Hospital (PR043/22).

Consent to participate

Due to the retrospective nature of the study, conducted more than five years after the last patient was studied, and its exploratory design, the institution's ethics committee determined that obtaining individual consent from each participant was not mandatory. This decision was based on the fact that no individual patient data are disclosed, nor can any participant be identified.

Consent to Publish

Not applicable.

Conference presentation

This work was presented in part at the XXXVII Diada Pneumològica April 4–6, 2019; 5th European Congress for Bronchology and Interventional Pulmonology (ECBIP), May 8–11, 2019; XXV Congreso AAER, May 24–25, 2019; 52º Congreso SEPAR, June 13–16, 2019; World Conference on Lung Cancer, September 7–10, 2019; ERS International Congress, September 28 – October 02, 2019 and Radiological Society of North America (RSNA) 105th Scientific Assembly and Annual Meeting December 1–6, 2019.

Conflict of interest

The authors have no commercial or financial interests to disclose related to this study.

Competing interests

The authors declare no competing interests.

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