Original Article

Prognostic value of thoracic tumor staging and volume parameters in non-small cell lung cancer patients with synchronous solitary bone metastasis

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Background: Non-small cell lung cancer (NSCLC) patients with synchronous solitary metastasis are a heterogeneous population. The analysis and evaluation of NSCLC patients with synchronous solitary bone metastases by cTN stage (thoracic tumor staging) and volume parameters have not yet been studied. The purpose of this study is to estimate the prognostic value of cTN stage and volume parameters obtained by fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) in NSCLC patients with synchronous solitary bone metastasis.

Methods: A total of 157 NSCLC patients with synchronous solitary bone metastasis were retrospectively analyzed. Patients' cTN stage, metabolic tumor volume (MTV) parameters, and clinical data were collected. Kaplan-Meier survival analysis and a Cox regression model were performed to determine the association between each factor and overall survival (OS). Finally, time-dependent receiver operating characteristic (TDROC) curve analysis was used to assess the predictive capacity of the independent prognostic factors.

Results: Kaplan-Meier survival analysis showed significant differences between subgroups in terms of cTN stage. The median OS of group I was 44 months, and the 5-year survival rate was 39.6%. In the multivariate Cox regression analysis, cTN stage, MTV of the whole body (MTVwb), and MTV of thorax (MTVtho) were significantly associated with patient OS, even after adjusting for other clinical factors. However, MTV of bone (MTVbon) was not found to be an independent prognostic factor. TDROC curve analysis showed that cTN stage, MTVwb, and MTVtho had good predictive capacity for NSCLC patients with synchronous solitary bone metastasis. Compared with cTN stage and MTVtho, MTVwb had obviously better predictive specificity and sensitivity for the 5-year survival rate [5-year area under the curve (AUC) of MTVwb =0.844 *vs.* cTN stage (P=0.035) *vs.* MTVtho (P=0.052)]. The best cutoff value of MTVwb was 33.05.

Conclusions: The results of this study confirmed that cTN stage, MTVwb, and MTVtho were independent prognostic factors of NSCLC patients with synchronous solitary bone metastases. These factors can be used for risk stratification of these patients. TDROC curve analysis indicated that cTN stage, MTVtho, and MTVwb had good performance for survival prediction.

Keywords: Fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT); metabolic tumor volume (MTV); non-small cell lung cancer (NSCLC); oligometastasis; TNM stage

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Introduction

The concept of oligometastasis was introduced into the M component of the eighth edition lung cancer stage classification, in which single distant (extrathoracic) metastasis was defined as M1b, and M1b was classified as stage IVA (1,2). The prognosis of patients with M1b disease was similar to that of patients with M1a disease, with a median survival of 11.4 months, and the 5-year survival rate of stage IVA patients, which includes the M1a and M1b categories, was 10% (1,2). However, in recent years, a large number of retrospective studies have found that the 5-year survival rate in some non-small cell lung cancer (NSCLC) patients with solitary metastasis could exceed 30%, even reaching 50% in some cases, which was close to the 5-year survival rate of NSCLC patients without metastatic disease (3-6). These data show that there is significant heterogeneity among NSCLC patients with solitary metastasis, but the stratification and treatment of such patients currently mainly depend on the subjective preferences of doctors, as no standardized regimen is available.

Fluorodeoxyglucose (FDG) is a glucose analog that can be absorbed by most tumor cells. Its usage has greatly improved the sensitivity of positron emission tomography (PET)/computed tomography (CT) in the detection of malignant tumors. It enables PET/CT to be successfully applied to the diagnosis, staging, treatment, efficacy evaluation, and follow-up of cancer patients (7). By quantitative analysis of whole-body FDG PET/CT scan images, in addition to the cTNM stage of patients, parameters of metabolic tumor volume (MTV) can be extracted, which represents the systemic tumor burden including the primary tumor, metastatic lymph nodes, and distant metastases. The current prognostic assessment of NSCLC without metastasis depends primarily on cTN stage (thoracic tumor staging) (2). Whether NSCLC patients with synchronous solitary bone metastasis can be analyzed and evaluated by cTN stage (thoracic tumor staging) and volume parameters has not yet been investigated. Volume parameters have been found to be strongly associated with overall survival (OS) in patients with different types of malignant tumors, including NSCLC (8-14). Therefore, we speculated that cTN stage and MTV parameters were independent prognostic factors of NSCLC patients with synchronous solitary bone metastasis and that they could be used to stratify these patients and identify the differences in prognosis and the risk of death among such patients. The purpose of this study was to test these hypotheses. We present the following article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-113/rc).

Methods

Patients

This retrospective study was approved by the institutional review board of Naval Medical Center of People's Liberation Army, Naval Medical University. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Individual consent for this retrospective analysis was waived. Patient information was obtained from the institutional tumor registry and clinical records. This research reviewed patients who underwent baseline FDG PET/CT at our institution (Naval Medical Center) from January 2008 to December 2015. The inclusion criteria were as follows: (I) pathologically confirmed as NSCLC; (II) underwent a baseline FDG PET/CT scan before initial treatment; (III) no current or previous diagnosis of any other primary tumor; (IV) no known brain metastasis; (V) in addition to intrathoracic primary tumor and intrathoracic metastatic lymph nodes, there were no other intrathoracic tumor lesions (lung/pleural/pericardial lesion), and solitary bone metastasis was a unique extrathoracic lesion.

FDG PET/CT data acquisition and analysis

According to the existing protocol, patients were required to fast for at least 6 hours before PET/CT scans. Before intravenous injection of FDG, the fasting blood glucose level was lower than 200 mg/dL. The whole body scan (from mid-thigh to mid-head) was performed 1 hour following intravenous injection. Images were acquired using a PET/CT scanner (Discovery ST, GE Healthcare, USA).

The volume-based parameters of FDG PET/CT were determined using a dedicated postprocessing workstation (Advantage Workstation 4.5, GE Healthcare, USA). First, based on a threshold of 25–30, Deposit Bookmark software

Table 1 Clinical characteristics of patients

Characteristics	All patients (n=157)
Gender, n (%)	
Male	98 (62.4)
Female	59 (37.6)
Age (year)	
Mean ± SD	64.66±10.15
BMI (kg/m^2)	
Mean ± SD	22.78±3.35
Histology, n (%)	
Adenocarcinoma	90 (57.3)
SCC	62 (39.5)
Other	5 (3.2)
cTN stage (NSCLC)*, n (%)	
I	38 (24.2)
II	38 (24.2)
III	81 (51.6)
PET volume parameters (mL), mean (range)	
MTVtho	52.56 (1.37–488.52)
MTVbon	18.29 (0.78–332.00)
MTVwb	70.85 (3.91–497.42)

*, according to the various T and N descriptors, patients were divided into three cTN stage groups on the basis of the 8th edition TNM stage grouping. BMI, body mass index; SCC, squamous cell carcinoma; NSCLC, non-small cell lung cancer; PET, positron emission tomography; MTVtho, metabolic tumor volume of thorax; MTVbon, metabolic tumor volume of bone; MTVwb, metabolic tumor volume of the whole body.

generated whole-body 3D regions of interest (ROIs). Next, regions corresponding to physiological uptake and/or uptake of benign lesions were excluded. Finally, 3D ROIs corresponding to thoracic tumors and solitary bone metastasis were obtained. MTV of thorax (MTVtho), MTV of bone (MTVbon), and MTV of the whole body (MTVwb) were measured and recorded.

T, N, and M descriptors were recorded for each patient. According to the various T and N descriptors, patients were divided into three cTN stage groups on the basis of the 8th edition TNM stage grouping: group I, like stage I, included T1–T2a N0 tumors; group II, like stage II, included T2b–T3 N0 and T1–2 N1 tumors; group III, like stage III, included T4 N0/T3–4 N1/all Tx N2/all Tx N3 tumors.

Statistical analysis

OS was defined as the interval from the date of FDG PET/CT scan to either the date of death or the date at the end of the study. The Kaplan-Meier method was used to estimate survival curves of OS. The log-rank test was used to compare the differences in OS between subgroups. A univariate Cox proportional hazards model was used to determine potential prognostic factors with P values less than 0.1. The problem of multicollinearity among potential prognostic factors was avoided by calculating Cramer's V and the correlation coefficient matrix. Potential prognostic factors were included in a series of multivariate models to identify independent prognostic factors. All tests were two-sided and P values <0.05 were considered statistically significant. SPSS software (version 21, Chicago, IL, USA) was used for the survival analysis.

Time-dependent receiver operating characteristic (TDROC) curves were used to evaluate independent prognostic factors by the R software package "timeROC" (15). The areas under the curves (AUCs) of each independent prognostic factor from the TDROC curves were calculated and compared. Statistical analyses were performed with R (version 4.0.3).

Results

Patient characteristics

A total of 157 patients were eligible and enrolled in the study. The study population consisted of 98 males and 59 females. The mean age at the time of scanning was 64.66 years. The mean body mass index (BMI) was 22.78 kg/m^2. Adenocarcinoma was the most common pathological subtype. The median survival time of the 157 patients was 24 months. The cTN stage and PET volume parameters of the study population are described in *Table 1*.

Kaplan-Meier analysis

In the cTN stage groups (P<0.001), the median OS was 44 [95% confidence interval (CI): 32.7–55.3], 28 (95% CI: 12.2–43.8), and 19 (95% CI: 15.2–22.8) months for group I, group II, and group III, respectively. The 5-year survival rates were 39.6% in group I, 21.3% in group II, and 12.8% in group III. The Kaplan-Meier survival curve of cTN stage

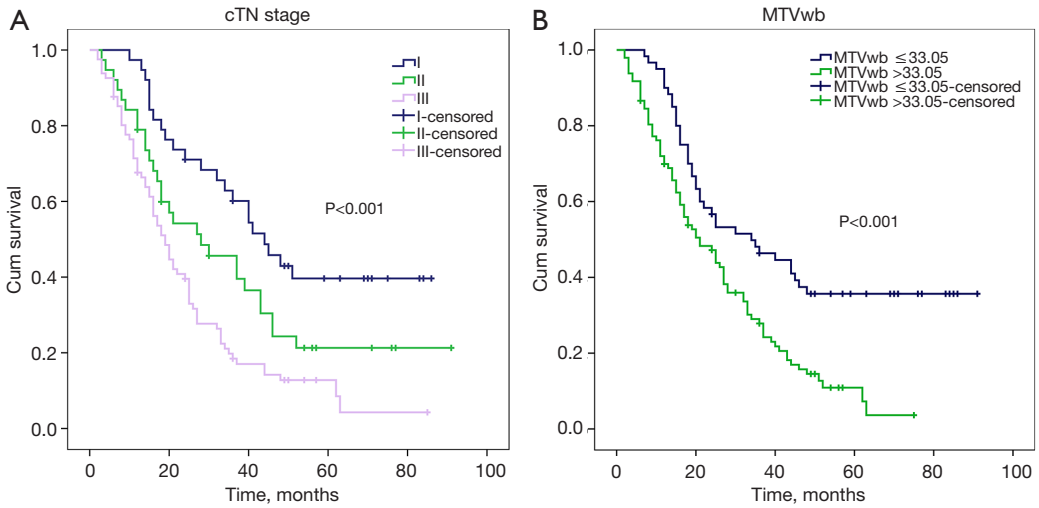

Figure 1 Kaplan-Meier analyses show significant differences in OS between (A) subgroups of cTN stage, (B) groups dichotomized by the optimal cutoff value for MTVwb. MTVwb, metabolic tumor volume of the whole body; OS, overall survival.

is shown in *Figure 1A*.

There was a statistically significant difference in OS between the groups when dichotomized by the cancer cachexia criteria of BMI (≤20 *vs.* >20, P=0.042) (16).

The optimal cutoff value for the MTVwb TDROC curve was determined to be 33.05 mL using the Youden index, which is commonly used in the assessment of the diagnostic accuracy of medical tests (17). Kaplan-Meier curves and log-rank tests showed that there was a statistically significant survival difference between patients with MTVwb ≤33.05 and those with MTVwb >33.05. The median OS of the MTVwb ≤33.05 group was 34 (95% CI: 17.19–50.81) months, and the median OS of the MTVwb >33.05 group was 21 (95% CI: 14.32–27.68) months. The 5-year OS rates of the MTVwb ≤33.05 group were 35.7% and the MTVwb >33.05 group were 10.9%, respectively (*Figure 1B*).

Univariate Cox regression analysis

The univariate Cox regression analysis results are shown in *Table 2*. Univariate Cox proportional hazards regression of cTN stage showed significantly worse OS for patients in group II than for those in group I [hazard ratio (HR) =1.763; 95% CI: 1.007–3.086; P=0.047]. Similar results were obtained for group III patients (HR =2.833; 95% CI: 1.741–4.610; P<0.001) compared to group I patients.

In the univariate analysis, OS was significantly associated with MTVwb (P<0.001) and MTVtho (P<0.001). MTVbon was not significantly associated with OS (P=0.058).

Multivariate Cox regression models

In the correlation coefficient matrix, MTVwb was highly correlated with MTVtho (r=0.895; P<0.001), MTVwb was moderately correlated with MTVbon (r=0.422; P<0.001), and MTVtho was not correlated with MTVbon (r=–0.027; P=0.371).

According to the correlation between MTV parameters, 2 multivariate Cox regression models were established, with one group including MTVwb and another group including MTVtho and MTVbon. Model 1 with MTVwb showed that MTVwb (P=0.018), histology (P=0.003), and cTN stage (P=0.010) were significantly associated with patient OS, and model 2 with MTVtho and MTVbon showed that MTVtho (P=0.023), histology (P=0.003), and cTN stage (P=0.013) were significantly associated with patient OS, while MTVbon (P=0.405) was not (*Table 3*). The adjusted survival curve of cTN stage in each model is shown in *Figure 2*.

TDROC curve analysis and the optimal cutoff value

To compare the predictive effect among independent prognostic factors related to cTN stage, MTVwb, and MTVtho, TDROC curve analysis was used to illustrate the prognostic capacity. The AUCs of 1-, 3-, and 5-year OS in cTN stage were 0.683, 0.715 and 0.758, that of 1-, 3-, and 5-year OS in MTVwb were 0.723, 0.714 and 0.844, and that of 1-, 3-, and 5-year OS in MTVtho were 0.728, 0.708

Table 2 Univariate Cox regression analysis of prognostic factors

Factor	HR	95% CI	P value
Age	1.011	0.993–1.030	0.219
Gender			
Male	Reference		
Female	0.713	0.490–1.036	0.076
BMI group (kg/m^2)[#]			
<20	Reference		
≥20	0.638	0.410–0.994	0.047
Histology			<0.001
SCC	Reference		
Adenocarcinoma	0.441	0.304–0.640	<0.001
Other	0.862	0.311–2.389	0.776
cTN stage (NSCLC)*			<0.001
I	Reference		
II	1.763	1.007–3.086	0.047
III	2.833	1.741–4.610	<0.001
MTVtho	1.004	1.002–1.006	<0.001
MTVbon	1.004	1.000–1.008	0.058
MTVwb	1.004	1.003–1.006	<0.001

[#], all patients were dichotomized by criterion of tumor cachexia; *, according to the various T and N descriptors, patients were divided into three cTN stage groups on the basis of the 8th edition TNM stage grouping. HR, hazard ratio; CI, confidence interval; BMI, body mass index; SCC, squamous cell carcinoma; NSCLC, non-small cell lung cancer; MTVtho, metabolic tumor volume of thorax; MTVbon, metabolic tumor volume of bone; MTVwb, metabolic tumor volume of the whole body.

and 0.786 respectively (*Figure 3*). The AUCs of cTN stage, MTVwb, and MTVtho for the 5-year OS were compared: cTN stage *vs.* MTVwb (P=0.035), MTVwb *vs.* MTVtho (P=0.052), and cTN stage *vs.* MTVtho (P=0.425).

Discussion

This study analyzed the prognostic value and evaluated the predictive role of cTN stage and volume parameters obtained by FDG PET/CT in NSCLC patients with synchronous solitary bone metastasis. This is the first study to compare and evaluate cTN stage (thoracic tumor staging) and volume parameters in an attempt to improve outcome prediction for NSCLC patients with synchronous solitary metastasis at the same site (bone). The results of this study showed that cTN stage and volume parameters (MTVwb, MTVtho) are independently associated with OS in NSCLC patients with synchronous solitary bone metastasis, even after adjusting for other clinical factors. The TDROC curve analysis suggested that the prognostic value of cTN stage and volume parameters (MTVwb, MTVtho) is robust and reliable for survival prediction in NSCLC patients with synchronous solitary bone metastasis.

In previous years, due to the low incidence of this particular NSCLC presentation, these patients would receive the same "one size fits all" systemic treatment as patients with multiple distant metastases (18). The 8th edition lung cancer stage classification categorizes a single distant metastatic lesion under the M1b classification, which is indicative of the rational definitions for an "oligometastatic disease subset" in NSCLC (1,19,20). A growing body of evidence has shown that NSCLC patients with solitary metastasis could achieve long-term survival, with some even approaching the 5-year survival rates achievable by patients with early-stage NSCLC without metastasis (3-6). In this study, patients in group

Table 3 Multivariate Cox regression analysis of the prognostic model

Model	Factor	HR	95% CI	P value
Model 1	MTVwb	1.003	1.000–1.005	0.018
	Gender	0.859	0.573–1.289	0.463
	BMI group[#]	0.788	0.492–1.260	0.319
	Histology	0.574	0.399–0.826	0.003
	cTN stage (NSCLC)*			0.010
	I	Reference		
	II	1.394	0.785–2.476	0.257
	III	2.154	1.282–3.621	0.004
Model 2	MTVtho	1.003	1.000–1.005	0.023
	MTVbon	1.002	0.997–1.006	0.405
	Gender	0.873	0.576–1.323	0.523
	BMI group[#]	0.776	0.483–1.247	0.294
	Histology	0.566	0.391–0.820	0.003
	cTN stage (NSCLC)*			0.013
	I	Reference		
	II	1.383	0.777–2.460	0.270
	III	2.123	1.255–3.589	0.005

[#], all patients were dichotomized by criterion of tumor cachexia; *, according to the various T and N descriptors, patients were divided into three cTN stage groups on the basis of the 8th edition TNM stage grouping. HR, hazard ratio; CI, confidence interval; MTVwb, metabolic tumor volume of the whole body; BMI, body mass index; NSCLC, non-small cell lung cancer; MTVtho, metabolic tumor volume of thorax; MTVbon, metabolic tumor volume of bone.

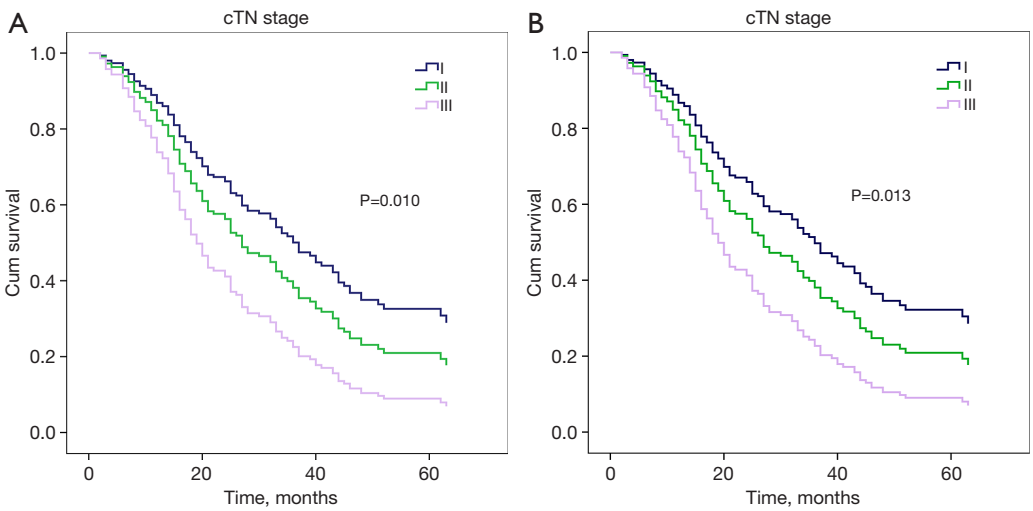

Figure 2 Adjusted survival curves estimated by multivariate cox proportional hazards models show significant differences in OS between (A) subgroups of cTN stage for model 1, (B) subgroups of cTN stage for model 2. OS, overall survival.

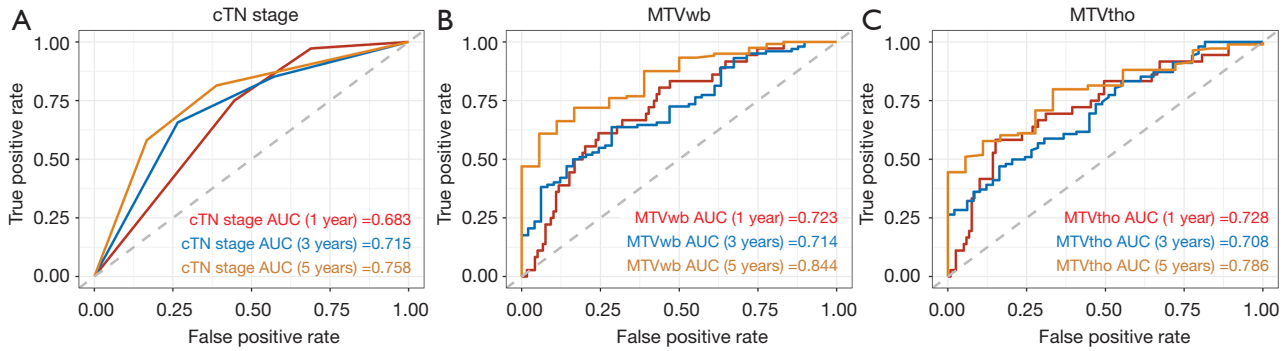

Figure 3 Time-dependent ROC curve analyses illustrate the prognostic capacity of (A) cTN stage, (B) MTVwb, (C) MTVtho. MTVwb, metabolic tumor volume of the whole body; MTVtho, metabolic tumor volume of thorax; AUC, area under the curve; ROC, receiver operating characteristic.

I in the cTN stage also had a favorable prognosis. The median OS was 44 months and the 5-year survival rate was 39.6%. This study showed that patients in group I who received aggressive treatment (primary tumor surgical resection and metastatic disease surgery and/or combined chemoradiotherapy) achieved long-term survival. This is consistent with many retrospective studies on stage IV lung cancer with oligometastasis (21-25). Although there was no statistically significant difference in OS between group I and group II in the multivariate analysis, there was a significant clinical difference (44 *vs.* 28 months; 39.6% *vs.* 21.3%). This could be the result of low statistical power due to the small sample size. Nonetheless, this study showed that cTN stage was an independent prognostic factor that could be used to stratify NSCLC patients with synchronous solitary bone metastasis.

Although cTN stage can solve the problem of stratification in NSCLC patients with synchronous solitary bone metastasis, it also has some limitations. For example, information on bone metastasis was not available. The "T" description provides only information about the primary tumor size, and the "N" description provides only information about whether lymph node metastasis is present, so it does not truly reflect the tumor burden on the whole body (26). The volume parameter MTV, obtained by FDG PET/CT, perfectly provided this information about tumor burden, which was recognized as important and found to be significantly associated with the prognosis of cancer patients (8-14). In the multivariate Cox analysis of model 1, MTVwb was shown to be an independent prognostic indicator in NSCLC patients with synchronous solitary bone metastasis, even after adjusting for other prognostic factors including cTN stage. Patients with lower MTVwb had a better prognosis. In the multivariate Cox analysis of model 2, MTVtho was an independent prognostic indicator but MTVbon was not. This finding showed that although the location and size of these solitary bone metastases may vary, due to their solitary characteristics, there is no significant difference in the tumor burden of bone metastasis between patients, and the difference in the OS of these patients is mainly caused by the difference in thoracic tumor burden. This indirectly confirmed the effectiveness of stratification by cTN stage (thoracic tumor staging).

TDROC curve analysis showed that cTN stage, MTVwb, and MTVtho had good predictive capacity for NSCLC patients with synchronous solitary bone metastasis. Compared with cTN stage and MTVtho, MTVwb had obviously better predictive specificity and sensitivity for 5-year survival. Finally, to facilitate the clinical stratification of patients by MTVwb, we calculated the best cutoff value of MTVwb, which was 33.05. Patients with MTVwb ≤33.05 had better prognoses.

After long-term investigation, the stratification and treatment of synchronous solitary metastatic NSCLC remains disputed. We believe that cTN stage and MTV parameters can provide valuable prognostic information that can be utilized in the clinic to develop appropriate stratification and treatment strategies. In the analysis and quantitative research of MTV, the cutoff values were different, and the methods of determining the optimal cutoff values were also different (27-31). It will therefore be necessary to standardize protocols and procedures for the analysis and quantification of MTV.

There are several limitations to our study. First, this was a single-center retrospective study with a limited sample

size. Thus, these results need to be verified further by other large sample size retrospective studies or prospective observational studies. However, because of the lower incidence rate, multicenter cooperation is required. Second, due to the small sample size, we did not analyze the OS and prognosis of the cTN stage subgroup. Finally, not all patients included in this study had EGFR and ALK gene status recorded in their medical records, even though this information is closely related to patient prognosis.

Conclusions

This study verified that cTN stage, MTVwb, and MTVtho were independent prognostic factors for NSCLC patients with synchronous solitary bone metastasis and that they can be used for risk stratification of these patients. TDROC curve analysis indicated that cTN stage, MTVtho, and MTVwb had good performance for survival prediction.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-113/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-113/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-113/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This retrospective study was approved by the institutional review board of Naval Medical Center of People's Liberation Army, Naval Medical University. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Individual consent for this retrospective analysis was waived.

References

1. Eberhardt WE, Mitchell A, Crowley J, et al. The IASLC Lung Cancer Staging Project: Proposals for the Revision of the M Descriptors in the Forthcoming Eighth Edition of the TNM Classification of Lung Cancer. J Thorac Oncol 2015;10:1515-22.
2. Detterbeck FC, Boffa DJ, Kim AW, et al. The Eighth Edition Lung Cancer Stage Classification. Chest 2017;151:193-203.
3. Jones GD, Lengel HB, Hsu M, et al. Management of Synchronous Extrathoracic Oligometastatic Non-Small Cell Lung Cancer. Cancers (Basel) 2021;13:1893.
4. Shi Y, Yang J, Yao N, et al. Factors Affecting the Survival of Patients with Oligometastatic Non-Small-Cell Lung Cancer: A Meta-Analysis. Can Respir J 2019;2019:2153170.
5. Kaba E, Yardımcı EH, Kakuturu J, et al. In Spite of Curative Radical Pulmonary Procedures, Lesser Pulmonary Resection Shows More Favorable Prognosis in Surgically Treated NSCLC With Synchronous Isolated Cranial Oligometastases. Front Surg 2021;8:645870.
6. Tönnies S, Tönnies M, Kollmeier J, et al. Impact of preoperative 18F-FDG PET/CT on survival of resected mono-metastatic non-small cell lung cancer. Lung Cancer 2016;93:28-34.
7. Krause BJ, Schwarzenböck S, Souvatzoglou M. FDG PET and PET/CT. Recent Results Cancer Res 2013;187:351-69.
8. Werner J, Strobel K, Lehnick D, et al. Overall Neutrophil-to-Lymphocyte Ratio and SUVmax of Nodal Metastases Predict Outcome in Head and Neck Cancer Before Chemoradiation. Front Oncol 2021;11:679287.
9. Rocha ALG, da Conceição MAM, da Cunha Sequeira Mano FXP, et al. Metabolic active tumour volume quantified on [18F]FDG PET/CT further stratifies TNM stage IV non-small cell lung cancer patients. J Cancer Res Clin Oncol 2021;147:3601-1.
10. Zhang F, Wu X, Zhu J, et al. 18F-FDG PET/CT and

circulating tumor cells in treatment-I patients with non-small-cell lung cancer. Eur J Nucl Med Mol Imaging 2021;48:3250-9.
11. Mallick A, Das J, Shaw MK, et al. Prognostic Value of Metabolic Tumor Parameters in Pretreatment 18F-Fluorodeoxyglucose Positron Emission Tomography-Computed Tomography Scan in Advanced Non-Small Cell Lung Cancer. Indian J Nucl Med 2021;36:107-13.
12. Tatewaki Y, Terao CM, Ariake K, et al. Defining the Optimal Method for Measuring Metabolic Tumor Volume on Preoperative 18F-Fluorodeoxyglucose-Positron Emission Tomography/Computed Tomography as a Prognostic Predictor in Patients With Pancreatic Ductal Adenocarcinoma. Front Oncol 2021;11:646141.
13. Choi BW, Kang S, Bae SU, et al. Prognostic value of metabolic parameters on 18F-fluorodeoxyglucose positron tomography/computed tomography in classical rectal adenocarcinoma. Sci Rep 2021;11:12947.
14. Naghavi-Behzad M, Petersen CB, Vogsen M, et al. Prognostic Value of Dual-Time-Point 18F-Fluorodeoxyglucose PET/CT in Metastatic Breast Cancer: An Exploratory Study of Quantitative Measures. Diagnostics (Basel) 2020;10:398.
15. Blanche P, Dartigues JF, Jacqmin-Gadda H. Estimating and comparing time-dependent areas under receiver operating characteristic curves for censored event times with competing risks. Stat Med 2013;32:5381-97.
16. Fearon K, Strasser F, Anker SD, et al. Definition and classification of cancer cachexia: an international consensus. Lancet Oncol 2011;12:489-95.
17. Fluss R, Faraggi D, Reiser B. Estimation of the Youden Index and its associated cutoff point. Biom J 2005;47:458-72.
18. Tibdewal A, Agarwal JP, Srinivasan S, et al. Standard maintenance therapy versus local consolidative radiation therapy and standard maintenance therapy in 1-5 sites of oligometastatic non-small cell lung cancer: a study protocol of phase III andomized controlled trial. BMJ Open 2021;11:e043628.
19. Blumenthaler AN, Antonoff MB. Classifying Oligometastatic Non-Small Cell Lung Cancer. Cancers (Basel) 2021;13:4822.
20. Gauvin C, Krishnan V, Kaci I, et al. Survival Impact of Aggressive Treatment and PD-L1 Expression in Oligometastatic NSCLC. Curr Oncol 2021;28:593-605.
21. Zhu J, Wang W, Xu S, et al. Evaluation of the Effect of Lymph Node Status on the Survival of Non-Small Cell Lung Cancer Patients With Brain Metastases: Applications of a Novel Grade Prognostic Assessment Score Model Involving N Stage. Front Oncol 2020;10:563700.
22. Sakai K, Takeda M, Hayashi H, et al. Clinical outcome of node-negative oligometastatic non-small cell lung cancer. Thorac Cancer 2016;7:670-5.
23. Zhao T, Gao Z, Wu W, et al. Effect of synchronous solitary bone metastasectomy and lung cancer resection on non-small cell lung cancer patients. Oncol Lett 2016;11:2266-70.
24. Takahashi Y, Adachi H, Mizukami Y, et al. Patient outcomes post-pulmonary resection for synchronous bone-metastatic non-small cell lung cancer. J Thorac Dis 2019;11:3836-45.
25. Ni Y, Ye X, Yang X, et al. Microwave ablation for non-small cell lung cancer with synchronous solitary extracranial metastasis. J Cancer Res Clin Oncol 2020;146:1361-7.
26. Ball DL, Fisher R, Burmeister B, et al. Stage is not a reliable indicator of tumor volume in non-small cell lung cancer: a preliminary analysis of the Trans-Tasman Radiation Oncology Group 99-05 database. J Thorac Oncol 2006;1:667-72.
27. Hyun SH, Ahn HK, Ahn MJ, et al. Volume-Based Assessment With 18F-FDG PET/CT Improves Outcome Prediction for Patients With Stage IIIA-N2 Non-Small Cell Lung Cancer. AJR Am J Roentgenol 2015;205:623-8.
28. Im HJ, Pak K, Cheon GJ, et al. Prognostic value of volumetric parameters of (18)F-FDG PET in non-small-cell lung cancer: a meta-analysis. Eur J Nucl Med Mol Imaging 2015;42:241-51.
29. Finkle JH, Jo SY, Ferguson MK, et al. Risk-stratifying capacity of PET/CT metabolic tumor volume in stage IIIA non-small cell lung cancer. Eur J Nucl Med Mol Imaging 2017;44:1275-84.
30. Lapa P, Oliveiros B, Marques M, et al. Metabolic tumor burden quantified on [18F]FDG PET/CT improves TNM staging of lung cancer patients. Eur J Nucl Med Mol Imaging 2017;44:2169-78.
31. Pu Y, Zhang JX, Liu H, et al. Developing and validating a novel metabolic tumor volume risk stratification system for supplementing non-small cell lung cancer staging. Eur J Nucl Med Mol Imaging 2018;45:2079-92.

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