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# Predictive value of metabolic parameters and apparent diffusion coefficient derived from 18F-FDG PET/MR in patients with non-small cell lung cancer

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## Abstract

**Background** Multiple models intravoxel incoherent motion (IVIM) based $^{18}$F-fluorodeoxyglucose positron emission tomography-magnetic resonance($^{18}$F-FDG PET/MR) could reflect the microscopic information of the tumor from multiple perspectives. However, its value in the prognostic assessment of non-small cell lung cancer (NSCLC) still needs to be further explored.

**Objective** To compare the value of $^{18}$F-FDG PET/MR metabolic parameters and diffusion parameters in the prognostic assessment of patients with NSCLC.

**Meterial and methods** Chest PET and IVIM scans were performed on 61 NSCLC patients using PET/MR. The maximum standard uptake value ($SUV_{max}$), metabolic tumor volume (MTV), total lesion glycolysis (TLG), diffusion coefficient (*D*), perfusion fraction (*f*), pseudo diffusion coefficient (*D**) and apparent diffusion coefficient (ADC) were calculated. The impact of $SUV_{max}$, MTV, TLG, *D*, *f*, *D**and ADC on survival was measured in terms of the hazard ratio (HR) effect size. Overall survival time (OS) and progression-free survival time (PFS) were evaluated with the Kaplan–Meier and Cox proportional hazard models. Log-rank test was used to analyze the differences in parameters between groups.

**Results** 61 NSCLC patients had an overall median OS of 18 months (14.75, 22.85) and a median PFS of 17 months (12.00, 21.75). Univariate analysis showed that pathological subtype, TNM stage, surgery, $SUV_{max}$, MTV, TLG, *D*, *D** and ADC were both influential factors for OS and PFS in NSCLC patients. Multifactorial analysis showed that MTV, *D** and ADC were independent predicting factors for OS and PFS in NSCLC patients.

**Conclusion** MTV, *D** and ADC are independent predicting factors affecting OS and PFS in NSCLC patients. $^{18}$F-FDG PET/MR-derived metabolic parameters and diffusion parameters have clinical value for prognostic assessment of NSCLC patients.

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**Keywords** Non-small cell lung cancer, Metabolic parameters, Diffusion parameters, Positron emission computed tomography, Magnetic resonance imaging

## Introduction

Lung cancer is one of the most common cancers worldwide and the leading cause of cancer deaths in both developed and developing countries [1]. About 80% of the lung cancer patients are diagnosed with non-small cell lung cancer (NSCLC), and their 5-year survival rate is only 18% [1, 2]. Recent medical advances have stimulated a huge increase in overall cancer survival, but this improvement has not been ideal for lung cancer because most NSCLC has a relatively poor prognosis. Studies have shown that early assessment of prognostic factors in NSCLC patients is of great significance in determining and adjusting treatment plans, improving patient outcomes and enhancing patient quality of life [3].

Positron emission tomography-computed tomography(PET/CT) was often used to evaluate lung cancer because it was noninvasive and could provide both metabolic and morphological information about the lesion at the same time [4]. Maximum standard uptake value($SUV_{max}$) represents the highest metabolic value in the lesions, and some studies found that $SUV_{max}$ can predict the prognosis of NSCLC [5, 6]. This maybe because tumors with higher pathological grade and higher stage are more heterogeneity, and cell multiplication is usually more rapid and therefore their glucose uptake is higher. Metabolic tumor volume(MTV) and total lesion glycolysis(TLG) can integrate the volume of the lesion with the metabolism, which could reflect the overall metabolism of the tumor more sufficient.

With the introduction of the concept of molecular imaging, molecular imaging techniques represented by PET magnetic resonance (PET/MR) have shown their unique advantages in displaying characeristic lesions at the tissue, reflecting changes at the molecular level in the living organism in cellular and subcellular levels, and evaluating the features of the target area qualitatively and quantitatively. In contrast to CT, PET/MR has no radiation and it can provide multiple functional parameters along with morphological and metabolic information about the focus. Meanwhile application of quantitative and semi-quantitative indicators to predict early tumor response to therapy has received most attention [7–9]. Diffusion-weighted imaging (DWI) can reflect the microstructure of tissues by obtaining motion information of water molecules. The apparent diffusion coefficient (ADC) is a quantitative indicator of the degree of diffusion limitation in DWI response. ADC values inversely correlate with cellularity, it can reflect the diffusion of water molecules in biological tissues and is usually obvious lower in malignant tumors than normal tissues and benign lesions. Its value in distinguishing benign and malignant lesions in the lung and mediastinum is well documented, however, few articles have used it to evaluate the prognosis of lung cancer [10, 11].

The MRI technique known as Intravoxel incoherent motion (IVIM) was initially introduced by Le Bihan et al. [12]. They realized the separation of tissue water molecule diffusion from blood vessel water molecule diffusion, making up for the shortage of DWI. The most important advantage of IVIM is that, as a non-contrast perfusion imaging method, it can be used in some patients with contrast contraindications. The measurement parameters are as follows: (1) the diffusion coefficient (*D*), which reflects the diffusion of water molecules in interstitial tissues; (2) the perfusion fraction (*f*), which reflects the proportion of blood perfusion to total diffusion; and (3) the pseudo diffusion coefficient ($D^*$), is a false diffusion caused by blood microcirculation and belongs to rapid diffusion [13]. IVIM has already been applied to study a number of disease, including the breast cancer [14], cervical cancer [15], and prostatic cancer [16]. In this study, $^{18}$F-fluorodeoxyglucose ($^{18}$F-FDG) PET/MR was performed to assess the prognostic value of $SUV_{max}$, MTV, TLG and diffusion parameter *D, f,* $D^*$ and ADC in patients with NSCLC. As far as we know, these parameters are rarely used in the study of lung cancer prognosis, so our study is of great significance.

## Patients and methods

### Case selection and general information

This study was approved by the Ethics Committee of Henan Provincial People's hospital (2021 Lungren Trial No. 148) and each patient's written informed consent was obtained. From July 2020 to October 2021, a total of 135 patients with pulmonary lumps or nodules diagnosed by chest CT underwent chest PET/MRI. Two radiologists (N M and FF F with 10 and 15 years of experience in imaging diagnosis, respectively), blined to the clinical and pathological information of patients, interpreted MR and PET images. The inclusion criteria were as follows: 1. Diagnosis of NSCLC confirmed by cytology or histopathology; 2. The lesions were not treated with invasive treatment, radiotherapy or chemotherapy before PET/MRI examination; 3. Clinical data of patients were complete and follow-up information could be provided. The following patients were excluded: 1. Combination of severe heart,

liver, kidney and hematopoietic diseases, severe lung dysfunction and other malignancies ($n=18$); 2. Solid lesion component cross-sectional diameter < 10 mm ($n=14$); 3. No histopathological results ($n=22$); 4. Poor image quality or incomplete image sequences ($n=20$). Finally, a total of 61 patients (29 males and 32 females, age range 40–81 years) were included in this study. Analyses covered age, sex, smoking status, subtype, stage, lesion diameter, and related parameters.

### Imaging procotal

All patients underwent chest scanning with an integrated 3.0 T PET/MR (uPMR790, United Imaging Medical, Shanghai, China) and a 12-channel body coil. Fasting blood glucose level were < 8.0 mmol/L after at least 6 h of fasting before the examination (diabetic patients should take oral hypoglycemic drugs as prescribed to ensure fasting blood glucose < 8.0 mmol/L). $^{18}$F-FDG is produced by FracerLab FX-FDG (GE Minitrac) with a purity of over 95% and a pH value between 4.5 and 8.5. After intravenous injection of the tracer with a dose of 0.11 mCi/kg and resting for 1 h, the patient underwent a PET scan in a supine position, connected to a breathing belt to monitor breathing, with a scanning range from the apex of the lung to the angle of the diaphragm. The Dixon MRI sequence was used in PET scanning to attenuate gamma rays, and the ordered subset maximum expected (OSME) iterative method was used for image reconstruction. Upload the data to the workstation for post-processing. Simultaneously with PET scan (27 min), axial MR based magnetic resonance attenuation correction (MRAC), T2 weighted imaging (T2WI), T1 weighted imaging (T1WI), IVIM, and DWI were performed sequentially [17]. The summary of MRI acquisition parameters is shown in Table 1.

### Imaging processing

All PET/MR images were imported into a United Imaging Healthcare (UIH) workstation (uWS-MR: R005) for aftertreatment and measurement. Two radiologists (H J and ZQ L with more than 5 years of experience in imaging diagnosis),, blined to the clinical and pathological information of patients, manually delineated the regions of interest (ROIs) to allow measurement of DWI and IVIM parameters.When the patient had multiple lesions, we selected the primary lesion as the target lesion and measured its related parameters. When delineating the ROIs, the observers were required to avoid blood vessels, trachea, necrosis and bleeding to ensure selection of the solid region with uniform component [17]. The average value measured by two observers was used for statistical analysis. If necessary, solve discrepancies with the help of a third radiologist. Lesions were found on the IVIM pseudo-color map, and ROI was mapped to measure *D, f,* and $D^*$ values. $SUV_{max}$ and MTV were automatically calculated by the software, which automatically covers the whole lesion. $SUV_{max}$ is the highest SUV value of the lesion, and a 40% $SUV_{max}$ was applied as a threshold to quantitate the MTV. TLG is the product of MTV and mean standardized uptake value ($SUV_{mean}$) of the area of interest.

The parameter values of DWI and IVIM were calculated using the following equation, where b symbols the diffusion sensitivity, and ADC was computed using two b values (0,1000 s/mm$^2$) fitted to the model. *S(b)* is the signal strength for different b values, S0 is the signal strength at b = *0* s/mm$^2$, *f* is the perfusion fraction, *D* is the diffusion coefficient representing actually molecular diffusion, and $D^*$ is the pseudo-diffusion coefficient meaning separate microcirculation [18].

ADC calculation formula [19]:

**Table 1** Imaging protocol parameters

| Parameters | MRAC | T2WI | T1WI | DWI | IVIM |
|---|---|---|---|---|---|
| TR (msec) | 4.92 | 3315 | 4.24 | 1620 | 1620 |
| TE (msec) | 2.24 | 87.8 | 1.13 | 69.8 | 69.6 |
| FOV (mm$^2$) | 500×350 | 500×350 | 500×350 | 500×350 | 500×350 |
| Matrix | 192×192 | 320×70 | 320×70 | 128×100 | 128×100 |
| Slice thickness (mm) | 2 | 5 | 6 | 5 | 5 |
| Scanning time | 2min4s | 2min26s | 14 s | 40 s | 3min38s |
| b-values (s/mm$^2$) | / | / | / | 0, 1000 | 0, 25, 50, 100, 150, 200, 400, 600, 800 and 1000 |
| Breath control | Free | Navigation | Holding | Free | Free |
| Orientation | Axial | Axial | Axial | Axial | Axial |

*MRAC* MR-base attenuation correction, *T2WI* T2-weighted imaging, *T1WI* T1-weighted imaging, *DWI* Diffusion weighted imaging, *IVIM* Intravoxel incoherent motion, *TR/TE* Repetition time/echo time, *FOV* Field of view

$$exp(-bADC) = \frac{S(b)}{S0} \quad (1)$$

IVIM calculation formula:

$$S(b)/S0 = (1-f) \times exp(-bD) + f \times exp[-b \times (D*+D)] \quad (2)$$

### Treatment and follow-up

Of the 61 patients, 32 were treated surgically and 29 were treated non-surgically. Two radiologists (Y L and PY F with 3 years of experience in imaging diagnosis), blined to the clinical and imaging information of patients, collected the follow-up data. The starting time of follow-up was the day of pathological diagnosis (or the day of surgery), and patients were followed up by case retrieval or by telephone until September 30, 2022. All patients were not missed, and the follow-up rate was 100%. Overall survival (OS) was defined as the time from pathological diagnosis to death or the end of follow-up [20]. Progression-free survival (PFS) was defined as the time from pathological diagnosis to the first detection of tumor recurrence, progression, death, or the end of follow-up.

### Statistical analysis

Statistical analysis utilized SPSS 20.0, with SUVmax, MTV, TLG, D, f, D*, and ADC categorized as rank information data, while other count data were expressed as percentages. Interobserver reliability between two radiologists was assessed using the intragroup correlation coefficient (ICC), where ICC ≥ 0.75 indicated excellent reliability, 0.60 ≤ ICC < 0.75 indicated good reliability, ICC < 0.40 indicated poor reliability [21]. Survival curves were generated using the Kaplan–Meier method, and group differences were assessed using the Log-rank test. Cox regression analysis was employed for single-factor and multi-factor survival analysis. A significance level of $P < 0.05$ was applied to all statistical analyses.

## Results

### Consistency analysis

The parameters measured by the two researchers were in excellent agreement. The ICC values of *D, f, D**, ADC were 0.847, 0.956, 0.966, 0.900 respectively. The average value of the two reader parameters is used for subsequent analyses. The values include $SUV_{max}$, MTV and TLG were measured by workstation software automatically, and there was no need for a consistency check.

### Images and survival

Among the 61 patients, there were 29 males and 32 females with age (62.85 ± 9.63). Moreover, there are 38 patients with disease progression or death, and 23 without progression. Patients had an overall median OS of 18 months (14.75, 22.85) and a median PFS of 17 months (12.00, 21.75). The clinicopathological characteristics are shown in Table 2.

### Univariate and multifactorial analysis of prognostic impact

The results of univariate analysis showed that $SUV_{max}$, MTV, TLG, *D, D** and ADC were all influential factors for OS and PFS in NSCLC patients among PET/MR-derived metabolic and diffusion parameters ($P < 0.05$). Among clinical factors, pathological subtype, TNM stage (TNM classification, 8th edition, 2014) and surgery were influential factors for OS and PFS in NSCLC patients ($P < 0.05$). Factors that were statistically significant in the univariate analysis were introduced as variables in the Cox model for multifactor analysis, and the results showed that MTV, *D** and ADC were independent

**Table 2** Summary of characteristics

| Characteristics | Value |
|---|---|
| Age (years) | 62.85 ± 9.63 |
| Gender | |
| Male | 29(47.54%) |
| Female | 32(52.46%) |
| Pathological subtype | |
| Adenocarcinoma | 46(75.41%) |
| Squamous carcinoma | 15(24.59%) |
| Maximum diameter (mm) | 27.39 ± 16.78 |
| TNM staging | |
| I ~ II | 24(39.34%) |
| III ~ IV | 37(60.66%) |
| 0peration | |
| yes | 32(52.46%) |
| no | 29(47.54%) |
| EFGR mutation | |
| yes | 10(16.39%) |
| no | 51(83.61%) |
| PFS(month) | 17.00 (12.00, 21.75) |
| OS(month) | 18.00 (14.75, 22.85) |
| PET/MRI-derived Parameters | |
| $SUV_{max}$ | 5.90(4.38, 10.40) |
| MTV(mL) | 4.82(2.19, 7.91) |
| TLG(g) | 14.32(4.56, 37.61) |
| ADC($\times 10^{-3}$ $mm^2$ /s) | 1.42(1.27, 1.56) |
| *D* ($\times 10^{-3}mm^2$/second) | 1.20(1.02, 1.30) |
| *f* (%) | 34.62(24.49, 69.75) |
| *D** ($\times 10^{-5}mm^2$/second) | 49.68(16.59, 94.33) |

*PFS* Progression-free survival, *OS* Overall survival, $SUV_{max}$ Maximum standard uptake value, *MTV* Metabolic tumor volume, *TLG* Total lesion glycolysis, *D* Diffusion coefficient, *f* Perfusion fraction, *D** Pseudo diffusion coefficient, *ADC* Apparent diffusion coefficient, *EFGR* Epidermal Growth Factor Receptor

**Table 3** Prognostic analysis of OS

| Parameters | univariate analysis | | multifactor analysis | |
|---|---|---|---|---|
| | **HR (95% CI)** | ***P*-value** | **HR (95% CI)** | ***P*-value** |
| Gender | 0.399 (0.133—1.197) | 0.101 | / | / |
| Age | 1.037(0.975—1.102) | 0.249 | / | / |
| Diameter | 0.046 (0.000—2820.388) | 0.583 | / | / |
| Pathological subtype | 3.541 (1.239—10.118) | 0.018 | 5.407 (0.794—36.837) | 0.085 |
| TNM staging | 5.372 (1.178—24.491) | 0.030 | 5.189 (0.336—80.143) | 0.238 |
| Operation | 5.393 (1.483—19.610) | 0.011 | 0.420(0.090—1.947) | 0.267 |
| EFGR mutation | 0.846(0.189—3.785) | 0.827 | / | / |
| $SUV_{max}$ | 1.165 (1.026—1.324) | 0.018 | 1.124 (0.844—1.497) | 0.423 |
| MTV | 1.162 (1.082—1.248) | < 0.001 | 1.216 (1.020—1.450) | 0.029 |
| TLG | 1.036 (1.019—1.053) | < 0.001 | 0.995 (0.943—1.050) | 0.862 |
| ADC | 0.008 (0.000—0.123) | 0.001 | 0 (0.000—0.010) | 0.001 |
| D | 0.124(0.019—0.813) | 0.003 | 2.060(0.003—1546.416) | 0.831 |
| f | 1.001(0.999—1.004) | 0.315 | / | / |
| D* | 0.980(0.963—0.998) | 0.031 | 0.933(0.886—0.982) | 0.008 |

All factors with $P < 0.05$ in univariate analyses were included in multivariate regression analyses. The bold typeface in the table indicates the logistic regression analyses with statistical significance

*EFGR* Epidermal growth factor receptor, $SUV_{max}$ maximum standard uptake value, *MTV* Metabolic tumor volume, *TLG* Total lesion glycolysis, *D* Diffusion coefficient, *f* Perfusion fraction, *D** Pseudo diffusion coefficient, *ADC* Apparent diffusion coefficient, *HR* Hazard ratio, *CI* Confidence interval

**Table 4** Prognostic analysis of PFS

| Parameters | univariate analysis | | multifactor analysis | |
|---|---|---|---|---|
| | **HR (95% CI)** | ***P*-value** | **HR (95% CI)** | ***P*-value** |
| Gender | 0.453 (0.152—1.353) | 0.156 | / | / |
| Age | 1.034(0.974—1.099) | 0.269 | | |
| Diameter | 0.045 (0.000—958.904) | 0.543 | / | / |
| Pathological subtype | 3.286 (1.152—9.374) | 0.026 | 3.348 (0.576—19.447) | 0.178 |
| TNM staging | 4.600 (1.028—20.573) | 0.046 | 1.910 (0.145—25.072) | 0.622 |
| Operation | 5.105 (1.420—18.354) | 0.013 | 0.747 (0.155—3.605) | 0.717 |
| EFGR mutation | 0.908(0.203—4.059) | 0.899 | / | / |
| $SUV_{max}$ | 1.155 (1.019—1.309) | 0.024 | 1.138 (0.842—1.537) | 0.401 |
| MTV | 1.135 (1.063—1.213) | < 0.001 | 1.189 (1.005—1.407) | 0.043 |
| TLG | 1.033 (1.016—1.049) | < 0.001 | 0.987 (0.936—1.042) | 0.642 |
| ADC | 0.013 (0.001—0.179) | 0.001 | 0 (0.000—0.012) | 0.002 |
| D | 0.111(0.017—0.728) | 0.022 | 0.685(0.002—277.791) | 0.902 |
| f | 1.001(0.999—1.004) | 0.351 | / | / |
| D* | 0.978(0.961—0.996) | 0.018 | 0.931(0.887—0.978) | 0.004 |

All factors with $P < 0.05$ in univariate analyses were included in multivariate regression analyses. The bold typeface in the table indicates the logistic regression analyses with statistical significance

*EFGR* Epidermal growth factor receptor, $SUV_{max}$ Maximum standard uptake value, *MTV* Metabolic tumor volume, *TLG* Total lesion glycolysis, *D* Diffusion coefficient, *f* Perfusion fraction, *D** Pseudo diffusion coefficient, *ADC* Apparent diffusion coefficient, *HR* Hazard ratio, *CI* Confidence interval

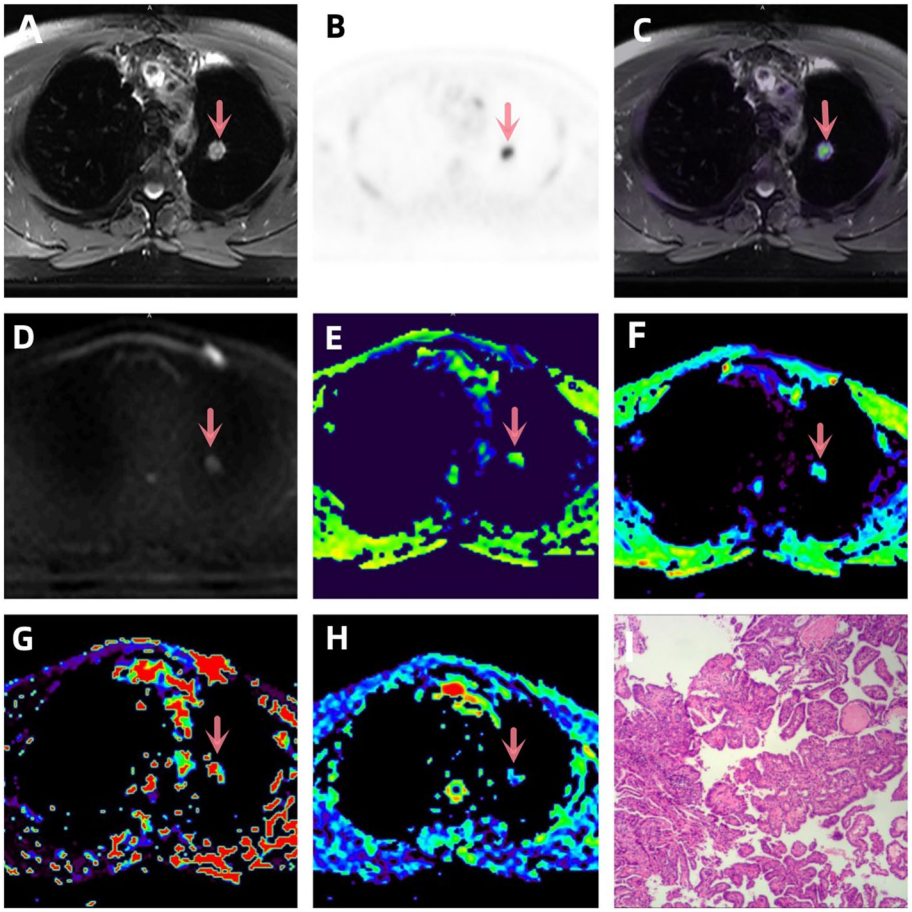


**Fig. 1** **A**-**I** a patient with lung adenocarcinoma (arrowheads, stage IVB). **A** T2WI, **B** PET original image, $SUV_{max}=7.72$, MTV = 1.207, TLG = 6.033, **C** PET and T2WI fusion map, **D** DWI original image (b = 1000 s/mm$^2$), **E** ADC pseudo-color map, ADC = $2.035\times10^{-3}$ mm$^2$ /s, **F** *D* pseudo-color map, $D=1.212\times10^{-3}$ mm$^2$ /s, **G** *D** pseudo-color map, $D^*=48.45\times10^{-5}$ mm$^2$ /s, **H** *f* pseudo-color map, $f=31.62\times10^{-3}$%, **I** hematoxylin and eosin (H&E) staining image

predicting factors for OS and PFS in NSCLC patients (Tables 3, 4; Figs. 1, 2).

## Discussion

Due to the high malignancy, aggressiveness and susceptibility to distant metastasiss of NSCLC, the fatality rate increases year by year [22]. Accurate assessment of the prognosis of NSCLC patients can help to develop better treatment plans and improve the 5-year survival rate. Compared with PET/CT, PET/MR can reduce radiation dose, improve soft tissue contrast, and provide functional information of the lesion, which shows higher value in early prediction of lung cancer treatment effect [23–26].

$SUV_{max}$ is the most commonly used semi-quantitative PET metabolic parameter in clinical practice. Some studies have explored its value in the prognostic assessment of NSCLC, but no unanimous conclusion has been reached. In the present study, OS and PFS were significantly lower in the $SUV_{max}>5.90$ group than in the $SUV_{max}\leq5.90$ group, and $SUV_{max}$ was an influential factor for OS and PFS in NSCLC patients. This is consistent with the findings of Liu et al. [27], however, Erdem et al. [28] and Nawara et al. [29] concluded that $SUV_{max}$ did not play a role in the survival of NSCLC patients. These inconsistent results may be due to the fact that $SUV_{max}$ is influenced by multiple factors, such as blood glucose, FDG injection scan time, device model, image reconstruction method, and partial volume effect. On the other hand, $SUV_{max}$ is a single pixel value, unlike MTV and TLG which can combine multiple factors to reflect more comprehensively the volumetric load and overall metabolic situation of the tumor. MTV and TLG have already been considered as prognostic indicators for a variety of malignancies, such as esophageal cancer [30], laryngeal cancer [31] and nasopharyngeal cancer [32]. This study used univariate Cox regression analysis to show that higher MTV and TLG were significantly associated with worse OS ($P<0.001$) and PFS ($P<0.001$) in patients with

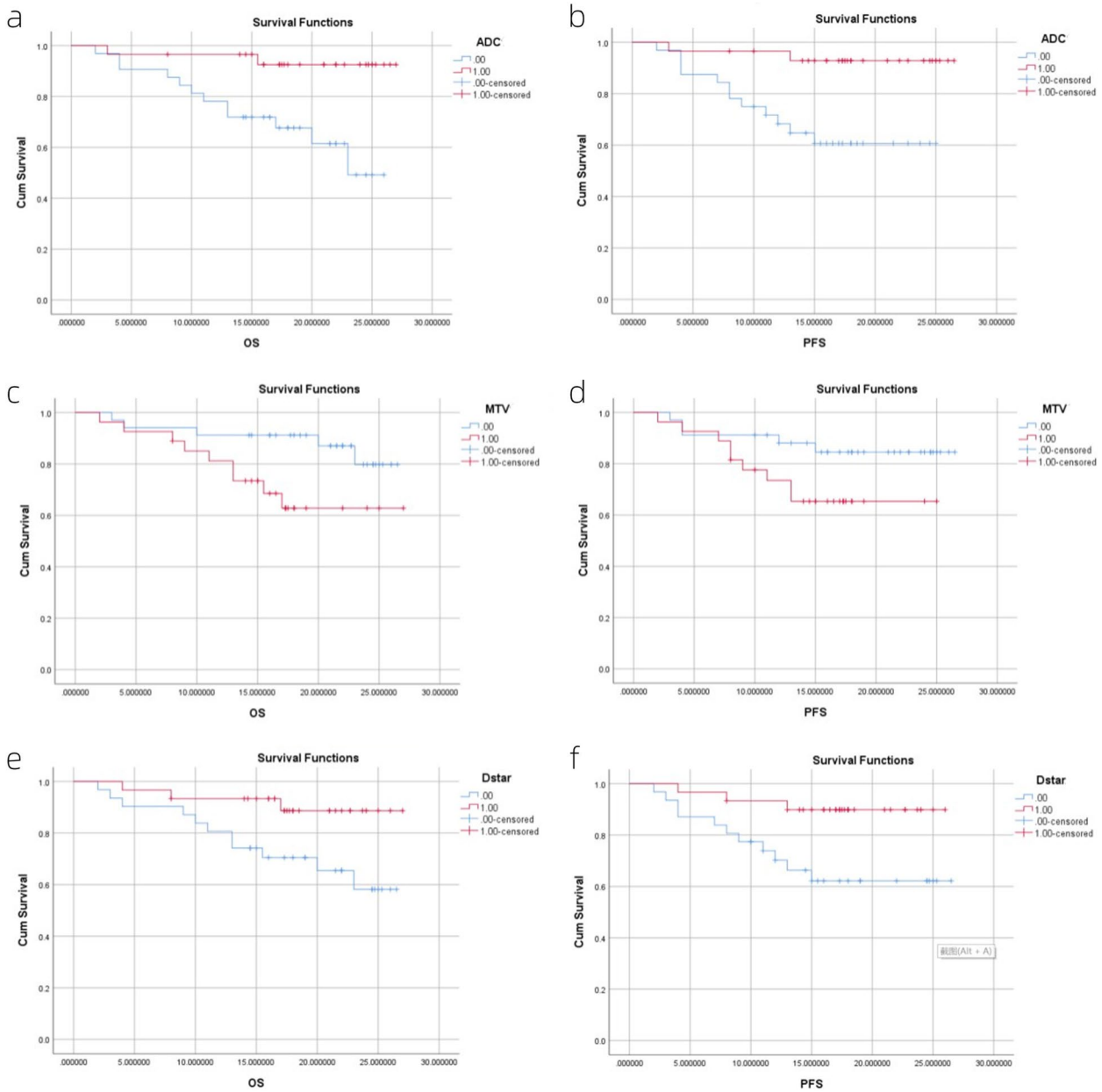


**Fig. 2** Kaplan–Meier survival curves of progression-free survival and overall survival stratified by prediction model. **a** The *P*-value of log-rank is 0.004; **b** the *P*-value of log-rank is 0.005; **c** the *P*-value of log-rank is 0.035; **d** the *P*-value of log-rank is 0.085; **e** the *P*-value of log-rank is 0.032; **f** the *P*-value of log-rank is 0.014. 1 means greater than the median, 0 means less than the median

treated NSCLC, and MTV was also an independent predicting factor for PFS and OS in NSCLC patients. Salavati et al. [33] showed that pretreatment tumor volume parameters, including MTV and TLG, had a strong prognostic effect and similar discriminatory power on OS in patients with locally advanced NSCLC by assessing the relationship between each parameter and the outcome of 196 NSCLC patients using Cox regression analysis. The results of Wen et al. [34] also validated that stage I/II NSCLC cases with increased MTV and TLG had a higher risk of side effects and that TLG was associated with an increased risk of death.

ADC is the representative parameter of DWI, which is usually influenced by cell density and can reflect the degree of restricted diffusion of water molecules in the tissue [35]. The parenchymal part of the tumor shows high signal on ADC, which can effectively highlight the lesion. Normally, the more obvious the diffusion

restriction of water molecules, the smaller the ADC value [36]. The multifactorial regression analysis in our study showed that ADC was an independent influence on OS and PFS in NSCLC patients. This is similar to the results of previous studies by Ohno et al. [19], in which ADC could be used as a functional indicator to assess the non-surgical outcome of NSCLC patients. This may be due to the fact that tumors with lower ADC values tend to have necrosis, hypoxia, acidification, and poor perfusion, resulting in lower therapeutic sensitivity to radiotherapy and chemotherapy, and therefore a poorer prognosis [37–39].

*D* is one of the IVIM parameters, which is influenced by cell density and the composition of extracellular matrix, and can reflect the diffusion of water molecules in tissue. This means that when the ratio of nuclei to the cytoplasm in tissues is high, or when the diffusion movement of water molecule is limited, resulting in a small extracellular space, the *D* value will be decreased [40]. In the IVIM sequence, both *D** and *f* are perfusion-related parameters, however, they represent different features of blood perfusion. *D** mainly reflects the average blood flow velocity, while *f* measures the fraction of blood volume in the capillary network, reflecting the microscopic translation movement related to blood microcirculation [41]. In this study, patients with high *D** value and *D* value group had higher OS than the low value group, and patients with high *D** value group had higher PFS than the low value group too. In addition, Cox regression analysis showed that *D** was also an independent influencing factor for OS and PFS. This is consistent with the study of Shi C [42] et al. This may be due to the rapid cell proliferation and microvascularity of tumor invasion resulting in decreased *D** values. In this study, there was no statistical difference between the high *f*-value group and the low *f*-value group. The reason for this result may be different treatment schemes will affect the *f*-value result. On the other hand, confounding factors, such as the properties of the tissue in the magnetic field, echo time, and relaxation time of the MRI scan, may also greatly affect the *f*-value [43]. Therefore, the potential of *f* in evaluating tumor microcirculation changes needs further study.

This study has several limitations. First, the relatively small number of NSCLC cases, due to the prospective nature of the study. It would lead to partial selection bias, and further studies with multiple centers and large samples are needed. Second, the ROIs of DWI and IVIM avoid necrosis, cystic degeneration and vascular areas, which may not be conducive to a comprehensive evaluation of tumor tissue structure. This is due to the large variation in these areas between lesions, which can interfere significantly with the parameter values. Third, the effect of cardiac and macrovascular pulsations on parameter measurements was not considered in this study.

## Conclusion

In summary, $SUV_{max}$, MTV, TLG, *D*, *D**, and ADC derived from $^{18}$F-FDG PET/MR imaging are all influential factors in the prognosis of NSCLC patients. Moreover, MTV, *D** and ADC are independent predicting factors for poor prognosis of NSCLC patients. These parameters can be jointly applied in clinical practice to predict treatment response and survival of NSCLC patients, and have important value in developing the personalized treatment and improving the survival for patients. In the future, the combination of PET/MR multi-models to predict NSCLC survival may be a new direction.

### Abbreviations

| | |
|---|---|
| PET/MR | Positron emission tomography-magnetic resonance |
| NSCLC | Non-Small cell lung cancer |
| $SUV_{max}$ | Maximum standard uptake value |
| MTV | Metabolic tumor volume |
| TLG | Total lesion glycolysis |
| *D* | Diffusion coefficient |
| *f* | Perfusion fraction |
| *D** | Pseudo diffusion coefficient |
| ADC | Apparent diffusion coefficient |
| DWI | Diffusion-weighted imaging |
| IVIM | Intravoxel incoherent motion |
| HR | Hazard ratio |
| OS | Overall survival time |
| PFS | Progression-free survival time |
| OSME | Ordered subset maximum expectation iteration method |
| MRAC | MR-based attenuation correction |
| $SUV_{mean}$ | Mean standardized uptake value |
| ICC | Intragroup correlation coefficient |

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### Authors' contributions

HJ: Data curation, Methodology, Formal analysis, Writing-Original draft preparation. ZL: Methodology, Writing-Reviewing and Editing. NM: Methodology, investigation. YL: Project administration, Investigation. PF: Project administration, Investigation. FF: Funding acquisition, investigation. YY: Project administration, Investigation. JY: Software, Writing-Reviewing and Editing. ZW: Software. All authors reviewed the manuscript. MW: Conceptualization, Funding acquisition, Methodology, Writing-Reviewing and Editing, Validation.

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### Data availability

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

## Declarations

### Ethics approval and consent to participate

This retrospective study was approved by the Ethics Committee of Henan Provincial People's Hospital (2021 Lungren Trial No.148), and the requirement for informed consent was obtained. All methods were carried out in accordance with relevant guidelines and regulations.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

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