



# Diagnostic and Prognostic Value of Dynamic CT Time-Density Curve Parameters in Non-small Cell Lung Cancer: A Retrospective Cohort Study

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## Abstract

**Background:** Non-small cell lung cancer (NSCLC) is a commonly encountered type of lung cancer, accounting for over 85% of lung cancer cases.

**Objectives:** This retrospective cohort study aimed to evaluate the diagnostic differences in time-density curve (TDC) parameters between malignant and benign lung lesions and to explore the associations of these parameters with clinicopathological characteristics and survival outcomes among patients with NSCLC.

**Patients and Methods:** Consecutive patients diagnosed between July 2018 and June 2021 were included, comprising 90 pathology-confirmed, treatment-naïve NSCLC patients and 90 benign lung lesion controls. All patients underwent multi-slice computed tomography (MSCT) single-slice dynamic scanning, from which contrast enhancement ratio (CER), peak time (PT), and peak value (PV) were extracted. Diagnostic comparisons were performed between groups, and correlations with pathological features were analyzed. Prognostic performance of TDC parameters among NSCLC patients was assessed using receiver operating characteristic (ROC) analysis. Patients were followed for survival outcomes, with a median follow-up duration of 36 months. A P-value < 0.05 was considered statistically significant.

**Results:** A total of 90 NSCLC patients (mean age  $61.35 \pm 6.48$  years) were included, with 44 cases at tumor-node-metastasis (TNM) stage I-II and 46 at stage III-IV. Compared with benign lesions, malignant lesions exhibited a significantly delayed time-to-peak, higher peak enhancement, and greater overall enhancement. Within the NSCLC cohort, TDC parameters differed significantly across differentiation grades, TNM stages, and lymph node metastasis status ( $P < 0.001$ ). The areas under the ROC curves (95% confidence interval) of PT, PV, CER, and their combination for predicting survival outcomes in NSCLC patients were 0.769 (0.657 - 0.881), 0.776 (0.664 - 0.888), 0.837 (0.750 - 0.924), and 0.919 (0.860 - 0.977), respectively.

**Conclusion:** The MSCT-derived TDC parameters differed significantly between benign and malignant lung lesions and were correlated with pathological characteristics in NSCLC. Importantly, the prognostic associations observed in this study were restricted to the NSCLC cohort, where PT, PV, and CER showed exploratory associations with survival outcome. These findings provide preliminary, hypothesis-generating evidence supporting the potential role of TDC analysis in diagnostic assessment and risk stratification of NSCLC.

**Keywords:** Computed Tomography, Correlation, Lung Cancer, Prognosis, Scanning

## 1. Background

Non-small cell lung cancer (NSCLC) is a commonly encountered type of lung cancer, accounting for over 85% of lung cancer cases. Originating from bronchial mucosa, bronchial glands, and alveolar epithelial

tissues in most cases, NSCLC is characterized by abundant cytoplasm, heteromorphic nuclei, and large cells (1, 2). Seventy percent (70%) of NSCLC patients are already in the advanced stage at diagnosis and lose the optimal opportunity for surgery, since there are no

typical symptoms in the early stage of the disease and the tumors are highly aggressive. Helical multi-slice computed tomography (MSCT) has the advantages of multi-directional imaging and high resolution, in which contrast agents are utilized to enable dynamic scanning of lesions in the lungs. With MSCT, the blood supply characteristics at lesions can be comprehensively observed at different stages (arterial phase, venous phase, and equilibrium phase) (3, 4). In addition, MSCT enables quantitative assessment of the enhancement degree and process of tumor tissues by generating a time-density curve (TDC) through contrast-enhanced single-slice dynamic scanning. Single-slice dynamic scanning refers to the rapid and repeated acquisition of computed tomography (CT) images over time from a fixed axial slice through the lesion during contrast enhancement, enabling the construction of TDCs and the extraction of parameters such as contrast enhancement ratio (CER), peak time (PT), and peak value (PV) (5). Previous studies have shown that TDC-derived enhancement characteristics offer diagnostic and prognostic value in other solid tumors, reflecting factors such as invasiveness or microvessel density (6). However, research applying these TDC parameters specifically to lung cancer remains rare, and their associations with clinicopathological features and prognosis in lung cancer have not been fully elucidated.

## 2. Objectives

Given this, the TDC parameters were compared between NSCLC patients and patients with benign lung lesions in this study in order to evaluate their diagnostic value, and to investigate the associations of TDC parameters with pathological characteristics and prognosis of NSCLC patients, aiming to guide rational diagnosis and treatment in clinical practice.

## 3. Patients and Methods

### 3.1. Subjects

This was a retrospective cohort study including consecutively eligible patients. Ninety patients with lung cancer (a lung cancer group) and 90 patients with benign lung lesions (a benign group) hospitalized for treatment between July 2018 and June 2021 were enrolled. All imaging examinations were performed at baseline prior to any treatment and served as the cohort's starting point. The benign cohort was included

to provide a diagnostic comparison baseline. The lung cancer group was composed of 52 males and 38 females with an age of 41 - 75 years and a mean of  $(61.35 \pm 6.48)$  years. Pathologic type referred to the histological classification of NSCLC, including 54 cases of adenocarcinoma, 30 cases of squamous cell carcinoma, and 6 cases of adenosquamous cell carcinoma. Tumor type referred to the anatomical location of the lesion within the lung, with 55 cases of peripheral type and 35 cases of central type recorded. With respect to differentiation degree, there were 35, 27, and 28 cases of poorly, moderately, and highly differentiated tumors, respectively. As for tumor diameter, 30 cases of  $< 3$  cm and 60 cases of  $\geq 3$  cm were recorded. For tumor-node-metastasis (TNM) stage, there were 44 and 46 cases of stage I-II and III-IV, respectively. Lymph node metastasis was observed in 38 patients. The benign group consisted of 55 males and 35 females aged 43 - 72 years, with a mean of  $(62.03 \pm 6.87)$  years. As to disease type, 10 cases of pulmonary tuberculosis, 29 cases of pneumonia, and 51 cases of chronic obstructive pulmonary disease (COPD) were recorded. The age and gender were of no statistically significant differences between the lung cancer group and the benign group ( $P > 0.05$ ), which were comparable. This study was approved by the Ethics Committee of Gansu Provincial People's Hospital (approval date: March, 2018; approval number: GPPH-2018-032).

### 3.2. Inclusion and Exclusion Criteria

Patients were included if they met all of the following criteria: (1) Pathology-proven NSCLC prior to any treatment, (2) availability of preoperative MSCT single-slice dynamic scanning, (3) first-time diagnosis with no prior history of lung cancer, (4) no chemotherapy, radiotherapy, or targeted therapy before imaging examinations, (5) adequate renal function for contrast enhancement and no known iodinated contrast contraindications, (6) complete baseline clinical and imaging data, and (7) estimated survival time  $> 3$  months. The exclusion criteria were: (1) Patients complicated with autoimmune diseases or systemic acute or chronic infectious diseases, (2) coexisting malignant tumors, (3) coagulation disorders, (4) hepatic or renal failure, (5) poor CT image quality, or (6) incomplete follow-up or postoperative loss to follow-up.

### 3.3. Sample Size Justification

Sample size was additionally evaluated based on detecting correlations between TDC parameters and pathological characteristics. Assuming a moderate correlation ( $R = 0.30 - 0.35$ ) as suggested by preliminary observations, a minimum of 64 - 84 patients would be required to achieve 80% power at  $\alpha = 0.05$ . Therefore, the final sample size of 90 NSCLC patients was adequate for the planned correlation analyses.

#### 3.4. Multi-Slice Computed Tomography Single-Slice Dynamic Scanning

An IQon Elite Spectral CT scanner (Philips, USA) was employed for examination. In brief, after deprivation of food for 12 hours before examination, patients lay flat on the scanning bed and underwent plain scanning with the pitch, slice thickness, current, voltage, and matrix set to 1.25 mm, 1.25 mm, 200 - 250 mA, 120 kV, and  $512 \times 512$ , respectively. Afterwards, patients were injected with a nonionic contrast agent through the elbow vein with the help of a high-pressure syringe at an injection rate of 2.5 - 3 mL/s. Next, arterial phase scanning, venous phase scanning, and equilibrium phase scanning were accomplished at 25 - 35 seconds, 65 - 80 seconds, and 180 - 240 seconds after contrast agent injection, respectively. The images were saved and uploaded to the workstation, followed by automatic tracking enhancement quantitative analysis. Afterwards, the breath-holding period containing the arterial phase was chosen, and the sampling frame was placed in the region of interest (ROI), after which the TDC was automatically generated to acquire the TDC parameters. For lung cancer cases, the ROI was placed within the solid tumor component while avoiding visible necrosis, calcification, large vessels, and bronchi. For benign cases including COPD, the ROI was placed on the most representative area of parenchymal abnormality (such as regions showing inflammatory opacities or emphysematous changes). In COPD cases without a discrete opacity, the ROI was positioned on the area with the most typical COPD-related parenchymal alteration, while carefully avoiding major vessels, bronchi, and motion artifacts.

Malignant lesions typically demonstrated delayed time-to-peak, higher peak enhancement, and more sustained enhancement, whereas benign lesions showed earlier PT, lower enhancement, and faster wash-out on the TDC curves.

#### 3.5. Collection of Clinicopathological Characteristics

The age, gender, pathological type, tumor type, differentiation degree, tumor diameter, TNM stage, lymph node metastasis status, and other data of patients in the lung cancer group were recorded, and comparisons were conducted on the TDC parameters among lung cancer patients with different pathological characteristics.

#### 3.6. Prognostic Follow-up

Follow-up began at the date of baseline MSCT examination (preoperative scan) and continued for up to 3 years. The primary prognostic endpoint was all-cause mortality. Survival time was defined as the interval between the baseline CT examination and death or last follow-up. Survival status was assessed through hospital medical records and outpatient documentation, and further confirmed by telephone or WeChat contact with patients or their family members when necessary. Patients who were alive at the end of the follow-up period or lost to follow-up were censored at the date of last confirmed contact. No patients were lost to follow-up.

#### 3.7. Statistical Analysis

EpiData and SPSS 25.0 software were employed for data input and analysis, respectively. Normality of continuous variables was assessed, and measurement data were expressed as mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ) when approximately normally distributed and compared using the independent-samples *t*-test and one-way analysis of variance, as appropriate. Count data were represented as  $n$  (%) and compared via the  $\chi^2$  test. The candidate predictors for correlation and prognostic analyses were pre-specified as three continuous TDC parameters including PT, PV, and CER, which were based on prior studies and physiological considerations. Correlations between TDC parameters and clinicopathologic characteristics were assessed using Spearman rank correlation analysis for ordinal variables, including TNM stage and tumor differentiation. Given the fixed 3-year follow-up period, prognosis was analyzed as a binary outcome (survival vs death at 3 years). Given the limited number of death events, multivariable survival modeling was not performed to avoid model overfitting and unstable estimates. Receiver operating characteristic (ROC) curves were constructed within the lung cancer cohort to evaluate the prognostic performance of TDC

parameters (PT, PV, and CER). Optimal cutoff values for each parameter were determined using the maximum Youden Index, and their sensitivity and specificity were calculated. These cutoffs were derived entirely from the internal dataset, as external validation was not available. All analyses were conducted using complete-case data. No multiple imputation was performed because there were no missing values in the TDC measurements or survival outcomes.  $P < 0.05$  denoted a statistically significant difference.

## 4. Results

### 4.1. Time-Density Curve Parameters of Lung Cancer and Benign Groups

During the study period, a total of 260 patients with pulmonary lesions were initially assessed for eligibility. After exclusion of 80 patients who did not meet the predefined inclusion criteria (such as incomplete MSCT data, prior treatment before imaging, or lack of pathological confirmation), the final study population consisted of 90 patients with NSCLC and 90 patients with benign lung lesions. The lung cancer group showed significantly higher PT, PV, and CER values compared with the benign group ( $P < 0.001$ , [Table 1](#)). These comparisons were performed to evaluate the diagnostic efficacy of TDC parameters.

### 4.2. Time-Density Curve Parameters in Lung Cancer Patients with Different Pathological Characteristics

The PT, PV, and CER displayed no statistically significant differences among lung cancer patients with different genders, ages, pathological types, tumor types, and tumor diameters ( $P > 0.05$ ), whereas they were of statistically significant differences among lung cancer patients with different differentiation degrees, TNM stages, and lymph node metastasis statuses ( $P < 0.001$ , [Table 2](#)).

### 4.3. Correlations of Time-Density Curve Parameters with Pathological Characteristics of Lung Cancer Patients

Spearman rank correlation analysis showed that PT, PV, and CER were positively correlated with tumor differentiation degree, TNM stage, and lymph node metastasis status in lung cancer patients ( $\rho > 0$ , all  $P < 0.001$ , [Table 3](#)).

### 4.4. Time-Density Curve Parameters in Lung Cancer Patients with Different Prognoses

At the end of the 3-year follow-up, 26 patients had died and 64 patients were alive. The 3-year overall survival rate was 71.11%. The median follow-up time was 30 months (IQR: 22 - 36 months). The alive subgroup had lower PT, PV, and CER compared to the dead subgroup ( $P < 0.001$ , [Table 4](#)).

### 4.5. Values of Time-Density Curve Parameters for Predicting Prognosis of Lung Cancer Patients

Prognostic analyses were conducted exclusively within the lung cancer cohort. The ROC curves were plotted with the prognostic status of lung cancer patients as the state variable (alive/dead = 0/1) and TDC parameters (PT, PV, and CER) as the test variables ([Figure 1](#)). The areas under the curve (AUCs) with corresponding 95% confidence interval (95% CI) for predicting prognosis were 0.769 (0.657 - 0.881) for PT, 0.776 (0.664 - 0.888) for PV, and 0.837 (0.750 - 0.924) for CER. The combined model integrating PT, PV, and CER demonstrated the highest prognostic performance, with an AUC of 0.919 (0.860 - 0.977) ([Table 5](#)). To complement the binary prognostic assessment at the fixed 3-year endpoint, time-to-event survival analyses were further conducted using the Kaplan-Meier method, as presented below.

### 4.6. Kaplan-Meier Survival Analysis According to Time-Density Curve Parameters

Kaplan-Meier survival analyses were performed to further evaluate the prognostic value of TDC parameters in lung cancer patients using time-to-event data. Patients were stratified into high and low groups according to the optimal cut-off values of PT, PV, and CER determined by ROC curve analysis. The Kaplan-Meier curves demonstrated that patients with higher PT values had significantly poorer overall survival compared with those with lower PT values (log-rank test,  $P < 0.001$ ). Similarly, patients in the high PV group exhibited significantly reduced survival compared with those in the low PV group ( $P < 0.001$ ). In addition, elevated CER was associated with worse overall survival, with a clear separation of survival curves observed during follow-up ( $P < 0.001$ ) ([Figure 2](#)). These results indicate that PT, PV, and CER are significantly associated with overall survival in lung cancer patients at the univariate level.

**Table 1.** Comparison of Time-Density Curve Parameters Between Lung Cancer and Benign Groups ( $\bar{x} \pm s$ )<sup>a</sup>

| Groups      | N  | PT (s)       | PV (Hu)      | CER (%)      |
|-------------|----|--------------|--------------|--------------|
| Benign      | 90 | 22.65 ± 5.18 | 23.84 ± 6.32 | 11.03 ± 3.68 |
| Lung cancer | 90 | 37.49 ± 6.35 | 34.98 ± 5.58 | 14.87 ± 4.35 |
| t           | -  | 17.180       | 12.535       | 6.394        |
| P           | -  | < 0.001      | < 0.001      | < 0.001      |

Abbreviations: PV, peak value; PT, peak time; CER, contrast enhancement ratio; Hu, hounsfield unit.

<sup>a</sup> Values are expressed as mean ± SD.

**Table 2.** Comparison of Time-Density Curve Parameters Among Different Subgroups of Patients with Lung Cancer ( $\bar{x} \pm s$ )<sup>a</sup>

| Variables                            | PT (s)       | t/F    | P       | PV (Hu)      | t/F    | P       | CER (%)      | t/F   | P       |
|--------------------------------------|--------------|--------|---------|--------------|--------|---------|--------------|-------|---------|
| <b>Gender</b>                        |              | 0.649  | 0.518   |              | 0.072  | 0.943   |              | 0.320 | 0.750   |
| Male (n = 52)                        | 37.85 ± 5.98 |        |         | 35.02 ± 5.68 |        |         | 14.98 ± 4.48 |       |         |
| Female (n = 38)                      | 37.00 ± 6.35 |        |         | 34.93 ± 6.02 |        |         | 14.65 ± 5.28 |       |         |
| <b>Age (y)</b>                       |              | 0.038  | 0.970   |              | 0.614  | 0.871   |              | 0.831 | 0.408   |
| < 60 (n = 35)                        | 37.52 ± 5.85 |        |         | 34.86 ± 5.52 |        |         | 14.28 ± 4.85 |       |         |
| ≥ 60 (n = 55)                        | 37.47 ± 6.25 |        |         | 35.06 ± 5.74 |        |         | 15.20 ± 5.28 |       |         |
| <b>Pathological type</b>             |              | 0.059  | 0.943   |              | 0.133  | 0.876   |              | 0.091 | 0.913   |
| Adenocarcinoma (n = 54)              | 37.58 ± 5.48 |        |         | 35.02 ± 5.69 |        |         | 15.03 ± 4.65 |       |         |
| Squamous cell carcinoma (n = 30)     | 37.49 ± 6.98 |        |         | 34.71 ± 5.18 |        |         | 14.68 ± 4.49 |       |         |
| Adenosquamous cell carcinoma (n = 6) | 36.68 ± 6.52 |        |         | 35.97 ± 6.02 |        |         | 14.38 ± 5.18 |       |         |
| <b>Tumor type</b>                    |              | 0.073  | 0.942   |              | 0.720  | 0.788   |              | 0.256 | 0.798   |
| Periphery (n = 55)                   | 37.45 ± 6.38 |        |         | 35.11 ± 5.68 |        |         | 14.97 ± 4.87 |       |         |
| Central (n = 35)                     | 37.55 ± 6.21 |        |         | 34.78 ± 5.59 |        |         | 14.71 ± 4.39 |       |         |
| <b>Differentiation degree</b>        |              | 54.378 | < 0.001 |              | 61.332 | < 0.001 |              | 7.936 | < 0.001 |
| Poorly differentiated (n = 35)       | 39.26 ± 5.25 |        |         | 38.45 ± 5.65 |        |         | 15.85 ± 5.02 |       |         |
| Moderately differentiated (n = 27)   | 34.56 ± 4.69 |        |         | 32.12 ± 6.12 |        |         | 13.02 ± 4.98 |       |         |
| Highly differentiated (n = 28)       | 25.76 ± 5.39 |        |         | 21.93 ± 5.98 |        |         | 10.78 ± 5.18 |       |         |
| <b>Tumor diameter (cm)</b>           |              | 0.673  | 0.503   |              | 0.202  | 0.840   |              | 0.169 | 0.866   |
| < 3 (n = 30)                         | 36.98 ± 4.89 |        |         | 35.15 ± 5.84 |        |         | 14.97 ± 3.87 |       |         |
| ≥ 3 (n = 60)                         | 37.75 ± 5.22 |        |         | 34.90 ± 5.38 |        |         | 14.82 ± 4.02 |       |         |
| <b>TNM stage</b>                     |              | 2.902  | 0.005   |              | 6.998  | < 0.001 |              | 3.726 | < 0.001 |
| Stage I-II (n = 44)                  | 35.59 ± 6.32 |        |         | 31.25 ± 4.87 |        |         | 12.98 ± 4.25 |       |         |
| Stage III-IV (n = 46)                | 39.31 ± 5.84 |        |         | 38.55 ± 5.02 |        |         | 16.68 ± 5.11 |       |         |
| <b>Lymph node metastasis</b>         |              | 3.803  | < 0.001 |              | 6.859  | < 0.001 |              | 3.978 | < 0.001 |
| Yes (n = 38)                         | 40.26 ± 6.32 |        |         | 39.46 ± 5.84 |        |         | 17.02 ± 4.98 |       |         |
| No (n = 52)                          | 35.47 ± 5.58 |        |         | 31.71 ± 4.86 |        |         | 13.30 ± 3.89 |       |         |

Abbreviations: PT, peak time; PV, peak value; CER, contrast enhancement ratio; TNM, tumor-node-metastasis; Hu, hounsfield unit.

<sup>a</sup> Values are expressed as mean ± SD.

and support their potential prognostic relevance when time-to-event information is fully considered.

## 5. Discussion

The NSCLC often lacks specific symptoms in its early stage, and many patients present only when cough, chest pain, or hemoptysis develop. Consequently, a

substantial proportion of patients are diagnosed at advanced stages, when opportunities for curative treatment are limited and overall prognosis is poor (7, 8). Therefore, early diagnosis of NSCLC, identification of pathological characteristics, and adoption of timely targeted treatment are particularly crucial for enhancing the survival rate of patients.

**Table 3.** Spearman Correlations of Time-Density Curve Parameters with Clinicopathologic Characteristics of Lung Cancer Patients

| Parameters and Statistic | Differentiation Degree | TNM Stage | Lymph Node Metastasis |
|--------------------------|------------------------|-----------|-----------------------|
| <b>PT</b>                |                        |           |                       |
| $\rho$                   | 0.60                   | 0.37      | 0.41                  |
| P                        | < 0.001                | < 0.001   | < 0.001               |
| <b>PV</b>                |                        |           |                       |
| $\rho$                   | 0.66                   | 0.41      | 0.43                  |
| P                        | < 0.001                | < 0.001   | < 0.001               |
| <b>CER</b>               |                        |           |                       |
| $\rho$                   | 0.44                   | 0.39      | 0.42                  |
| P                        | < 0.001                | < 0.001   | < 0.001               |

Abbreviations: TNM, tumor-node-metastasis; PT, peak time; PV, peak value; CER, contrast enhancement ratio.

**Table 4.** Comparison of Time-Density Curve Parameters in Different Lung Cancer Patients Based on Survival ( $\bar{x} \pm s$ )<sup>a</sup>

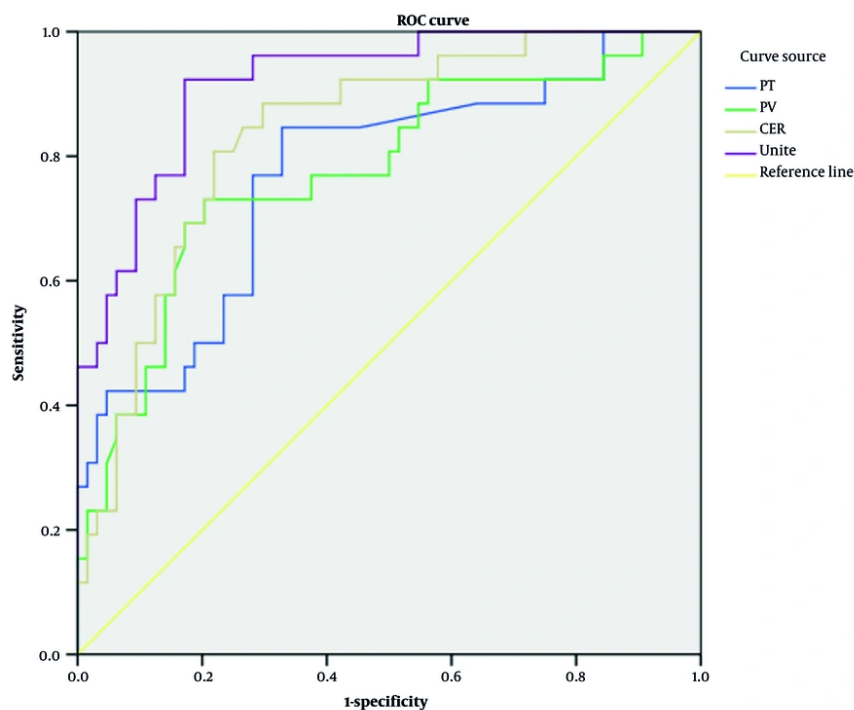
| Groups | N  | PT (s)     | PV (Hu)      | CER (%)      |
|--------|----|------------|--------------|--------------|
| Alive  | 64 | 35.68±5.58 | 33.25 ± 5.86 | 13.24 ± 4.02 |
| Dead   | 26 | 41.95±6.32 | 39.24 ± 6.02 | 18.88 ± 5.13 |
| t      | -  | 4.648      | 4.361        | 5.557        |
| P      | -  | < 0.001    | < 0.001      | < 0.001      |

Abbreviations: PT, peak time; PV, peak value; CER, contrast enhancement ratio; Hu, hounsfield unit.

<sup>a</sup> Values are expressed as mean ± SD.

The MSCT single-slice dynamic scanning, based on radio-indicator dilution principles, enables extraction of quantitative TDC parameters such as PT, PV, and CER, which can non-invasively reflect aspects of tumor microvascular characteristics (9, 10). Moon et al. (11) reported that the PV obtained by MSCT had a significant relation to the 5-year overall survival rate of patients with stage IA NSCLC (HR: 1.18, 95% CI: 1.01 - 1.38,  $P = 0.04$ ), which could serve as a potential factor for predicting the prognosis of patients with early-stage NSCLC. Hence, the TDC in MSCT single-slice dynamic scanning is of great significance in the diagnosis and differentiation of the nature of malignant tumors or thoracic nodules, but this technique in evaluating the pathological characteristics of patients with lung cancer has been rarely reported. In the present study, PT, PV, and CER were significantly higher in malignant lesions than in benign lesions, and these parameters were positively associated with differentiation degree, TNM stage, and lymph node metastasis. These results suggest that TDC parameters in MSCT single-slice dynamic scanning can help distinguish benign from malignant lung lesions and are associated with clinicopathological

characteristics of NSCLC. The possible reasons are as follows. The CER, PT, and PV in tumors depend upon both technical factors like contrast agent dosage, delay time, and injection speed, and internal factors such as tumor blood supply characteristics, namely: (1) The microvessels in the tumor stroma and parenchyma, including both the unformed precapillary structure and capillary structure, (2) the blood-supplying venules and arterioles near tumors and in the tumor stroma, and (3) the diffusion function of tumors, defined as the diffusion degree and speed of contrast agents through microvessels to the tumor parenchyma (12, 13). Tumor angiogenesis acts as the basis for the infiltration, proliferation, and growth of benign and malignant tumors, and its abnormalities will elevate capillary permeability, giving rise to abnormal cerebral blood perfusion and thus increased PT, PV, and CER (14, 15). As tumors progress, the depth of tumor infiltration and invasion increases, aggravating lesion tissue enhancement and accordingly leading to higher PT, PV, and CER in patients with poorly differentiated cancer, TNM stage III-IV cancer, and lymph node metastasis (16, 17). With respect to prognosis, the survival analyses were



**Figure 1.** Receiver operating characteristic (ROC) curves of time-density curve (TDC) parameters for prediction of death among patients with lung cancer (Unite represents combined model integrating PT, PV, and CER).

**Table 5.** Diagnostic Efficacy Findings of Time-Density Curve Parameters for Prediction of Death Among Patients with Lung Cancer

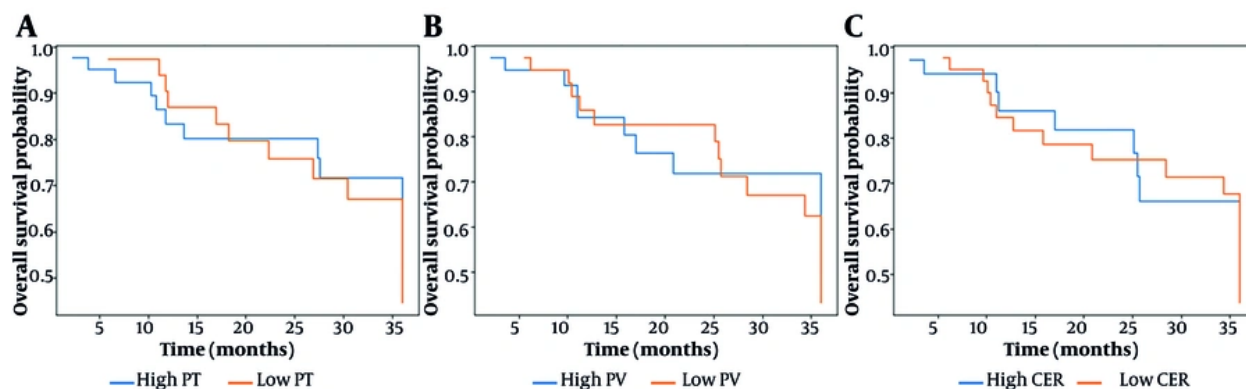
| Parameters         | AUC          | SE           | 95% CI               | Cut-off Value | P       | Sensitivity  | Specificity  |
|--------------------|--------------|--------------|----------------------|---------------|---------|--------------|--------------|
| PT                 | 0.769        | 0.057        | 0.657 - 0.881        | 38.152s       | < 0.001 | 0.788        | 0.820        |
| PV                 | 0.776        | 0.057        | 0.664 - 0.888        | 36.185Hu      | < 0.001 | 0.792        | 0.815        |
| CER                | 0.837        | 0.045        | 0.750 - 0.924        | 16.085%       | < 0.001 | 0.805        | 0.839        |
| <b>Combination</b> | <b>0.919</b> | <b>0.030</b> | <b>0.860 - 0.977</b> | -             | < 0.001 | <b>0.869</b> | <b>0.825</b> |

Abbreviations: AUC, area under the curve; PT, peak time; PV, peak value; CER, contrast enhancement ratio; CI, confidence interval; Hu, hounsfield unit; SE, standard error.

confined exclusively to patients with NSCLC. In this cancer cohort, higher PT, PV, and CER were observed in non-survivors, and ROC analyses demonstrated moderate discriminative ability for each parameter, with the combined model yielding the highest AUC (0.919). These results indicate an association between TDC parameters and overall survival and demonstrate their potential discriminative performance for prognostic stratification, rather than independent prognostic prediction. Given the lack of multivariable adjustment and the limited number of outcome events,

residual confounding cannot be excluded, and the prognostic findings should be interpreted as exploratory and hypothesis-generating rather than definitive. It is important to emphasize that our findings do not suggest that modifying PT, PV, or CER would alter patient outcomes; instead, these TDC features may function as imaging biomarkers reflecting underlying tumor biology.

This study has several limitations that should be acknowledged. First, the sample size was relatively small and derived from a single center, which may limit the



**Figure 2.** Kaplan-Meier survival curves of lung cancer patients stratified by (A) peak time (PT), (B) peak value (PV), and (C) contrast enhancement ratio (CER). Patients were divided into high and low groups according to the optimal cut-off values derived from receiver operating characteristic (ROC) curve analysis. Differences between groups were assessed using the log-rank test.

statistical power and generalizability of the findings. Second, the retrospective cohort design carries an inherent risk of selection bias, and the number of outcome events was limited, restricting the robustness of multivariable analyses. Importantly, although a sample size calculation was performed for the diagnostic correlation analyses, the study was not formally power-calculated for survival endpoints. Therefore, the prognostic analyses should be regarded as exploratory and hypothesis-generating. Third, all TDC parameters and prognostic cutoffs were developed and tested within the same dataset without external validation. Therefore, their reproducibility in independent populations remains uncertain. Fourth, although MSCT single-slice dynamic scanning provides quantitative enhancement information, variability in ROI placement and the absence of interobserver reproducibility assessment may affect measurement consistency. Finally, although multiple statistical tests were performed based on prespecified hypotheses, the possibility of type I error cannot be completely excluded. Future multicenter prospective studies with larger sample sizes and external validation cohorts are needed to confirm the diagnostic and prognostic utility of TDC parameters in NSCLC.

In conclusion, TDC parameters obtained from MSCT single-slice dynamic scanning differed significantly between malignant and benign lesions and were associated with several pathological characteristics in

patients with NSCLC. Among the NSCLC cohort, PT, PV, and CER also showed exploratory associations with overall survival, and their combined use demonstrated the strongest prognostic discrimination. These findings suggest a potential role for TDC parameters as imaging biomarkers for diagnostic assessment and risk stratification in NSCLC. However, the prognostic results should be interpreted as hypothesis-generating and require further validation in prospective, cancer-specific cohorts.

## Footnotes

**AI Use Disclosure:** The authors declare that no generative AI tools were used in the creation of this article.

**Authors' Contribution:** Conceptualization: H. F. J. and W. W. Sh.; Methodology: Y. Q. M. and M. Z. M.; Formal analysis and investigation: Y. Q. M. and Y. M.; Data curation: M. Z. M. and Y. M.; Writing-original draft preparation: H. F. J. and W. W. Sh.; Writing-review and editing: B. Y. Zh.; Supervision: B. Y. Zh.

**Conflict of Interests Statement:** The authors declare no conflict of interest.

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

**Ethical Approval:** The study was approved by the Ethics Committee of Gansu Provincial Hospital (No. GSH2018.33.045).

**Funding/Support:** Written informed consent was obtained from the participants.

**Informed Consent:** All patients in the study signed the informed consent form.

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