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Analysis of the morbidity characteristics and related factors of pulmonary nodules in patients with type 2 diabetes mellitus: a retrospective study

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Abstract

Objective To analyze the characteristics of pulmonary nodules (PNs) and related influencing factors in patients with type 2 diabetes mellitus (T2DM).

Methods Retrospectively analyzed the clinical and biochemical characteristics of 224 patients with PNs and 488 patients with non-PNs in patients with T2DM, and compared the clinical data of 72 patients with large nodules (≥ 5 mm) and 152 patients with small nodules (< 5 mm) in the pulmonary nodules (PNs) group.

Results Compared to the non-PNs group, the PNs Patients in the group had a longer duration of diabetes, higher age, serum creatinine (SCR), blood urea nitrogen (BUN) and the lower albumin (ALB) and body mass index (BMI); women, diabetic retinopathy (DR), diabetic peripheral neuropathy (DPN), and estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73m² were more represented in the PNs group; there were fewer patients with overweight in the PNs group. Age and eGFR < 60 ml/min/1.73m² were independent risk factors for PNs in patients with T2DM, and overweight was associated with a reduced risk of PNs. Compared with the small nodule group, patients in the large nodule group had higher fasting blood glucose (FBG) and lower fasting insulin (FINS); meanwhile, patients with decreased homeostasis model assessment- β (HOMA- β) and high smoking index (SI) were higher in the large nodule group; decreased HOMA- β and high SI were independent risk factors for large nodules.

Conclusions Age and eGFR < 60 ml/min/1.73m² were independent risk factors for pulmonary nodules in patients with T2DM, and overweight may be a protective factor. Moreover, decreased islet B-cell function and smoking may contribute to the presence of PNs with a diameter of over 5 mm.

Keywords Type 2 diabetes mellitus, Pulmonary nodules, Estimated glomerular filtration rate, Size of nodules, Overweight

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Introduction

Nowadays, pulmonary nodules (PNs) have become one of the most common clinical problems and their prevalence is increasing every year, with more than 1 million Americans being found to have PNs each year and one or more PNs being detected in approximately 30% of chest computed tomography (CT) scans [1–3]. Although most PNs are benign, there is still some risk of cancer [2]. In China, the detection rate of PNs in high-risk groups for lung cancer is about 22.9%, and the proportion of patients with PNs who have malignant nodules is 6.34% [4]. PNs are defined as focal, round-like, solid or subsolid lung shadows with an increased density ≤ 3 cm in diameter [5]. The high incidence of lung cancer has made screening for PNs increasingly common [6], yet most PNs are still found incidentally [3], and studies related to the morbidity of PNs are needed for more targeted detection and discovery. In addition, determining the nature of PNs is a common problem [7–9].

The global prevalence of diabetes mellitus (DM) exceeds 10% in 2021 [10] and the number of people with the disease may be expected to reach 700 million worldwide by 2045 [11]. Several reports have indicated [12–14] that diabetes may contribute to the increased risk of lung cancer and death due to lung cancer. And whether there is a correlation between the occurrence of PNs, which is one of the important hints for early screening of lung cancer, and diabetes also deserves our attention. With the prevalence of diabetes increasing year by year, there are no studies or investigations related to the incidence of combined PNs in patients with type 2 diabetes mellitus (T2DM) to guide clinical decision making. The purpose of this retrospective study was to investigate the incidence of pulmonary nodules in diabetes patients and the potential relationship between related indicators of diabetes and pulmonary nodules in order to identify high-risk groups of pulmonary nodules in diabetes patients before the start of clinical evaluation and play a useful role in the early prevention and screening of PNs and even lung cancer.

Materials and methods

General data Patients with T2DM who were hospitalized at Dongzhimen Hospital Affiliated to Beijing University of Chinese Medicine from December 2019 to December 2021 were selected for this study. There were 424 males and 288 females; age distribution ranged from 21 to 91 years old, with an average of 58.5 ± 13.1 years; disease duration ranged from 1 month to 46 years, with an average of 11.1 ± 8.0 years. Patients with acute complications, severe cardiac, hepatic and renal system diseases, previous history of tumor and autoimmune diseases were excluded from this study. The study was approved by the Medical Ethics Committee of Dongzhimen Hospital,

Beijing University of Traditional Chinese Medicine. Since this study was a retrospective study and data were collected from the inpatient electronic system, patients did not sign an informed consent form.

Methods and grouping (1) Diagnostic criteria: The diagnosis of type 2 diabetes was made with a reference to the 1999 World Health Organization diagnostic criteria [15]. For the diagnosis and size classification of pulmonary nodules refer to the guidelines for the management of pulmonary nodules published by the Fleischner Society [16]. $eGFR$ (calculated creatinine values by the CKD-EPI equation) = $141 \times \min(SCR/\kappa, 1)^\alpha \times \max(SCR/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018$ (if female) [$eGFR$ = estimated glomerular filtration rate, mL/min/1.73m²; SCR = serum creatinine, mg/dl; κ = 0.7 (female) / 0.9 (male); α = -0.329 (female) / -0.411 (male); Age = age]. (2) Grouping: Patients were classified according to the presence of PNs, and the patients in the PNs group were classified based on the size of the nodules (5 mm); body mass index (BMI) ≥ 24 kg/m² as supergroup, BMI < 24 kg/m² as non-supergroup; smoking > 400 cigarettes per year as high smoking index (SI) group, smoking ≤ 400 cigarettes per year as low SI group; Insulin secretion index was estimated by Homeostasis model assessment- β (HOMA- β), HOMA- $\beta \geq 50$ as normal islet B-cell function group, HOMA- $\beta < 50$ as the decreased islet B-cell function group [HOMA- $\beta = 20 \times \text{fasting insulin (FINS)} \div (\text{fasting blood glucose (FBG)} - 3.5)$]. (3) The clinical data of T2DM patients were reviewed, including general information such as age, sex, height and weight, medical history, such as current medical history, past medical history, history of smoking and alcohol, clinical test results such as blood biochemistry, fasting insulin (FINS), glycosylated hemoglobin (HbA1c), microalbuminuria (MAU) and lung CT examination reports, and the size, nature, boundary, location and whether the PNs were recorded. The size, nature, boundary, location, and whether they were solitary were recorded. The serum specimens were collected overnight in 8–10 h on an empty stomach and tested by the laboratory department of the hospital using an automatic biochemical analyzer (Beckman-DXC800, American).

Statistical methods SPSS software (Statistical Package for the Social Sciences, version 25.0, Chicago) was used for the study. We compared the clinical characteristics of subjects with and without pulmonary nodules, as well as subjects with pulmonary nodules of different diameters. The categorical data in the study was represented by frequency (percentage), and inter group comparisons were made using χ^2 test. The continuous data conformed to the non-normal distribution (determined by the Kolmogorov-Smirnov test with a significance level of $p < 0.1$ for each variable), so it was represented by the median (interquartile range), and the Mann Whitney U test was

used to compare the differences in clinical characteristics between groups. Spearman test was used to analyze factors associated with pulmonary nodules or the diameter of pulmonary nodules. Binary logistic regression models with multivariable adjustment for factors, including age, sex, overweight, disease duration, ALB, eGFR, DR and DPN were used to determine the factors that may affect the occurrence of pulmonary nodules. Additionally, binary logistic regression models with multivariable adjustment for factors, including sex, age, FINS, FBG, HOMA- β , SI, and DPN were used to determine the factors that may affect the diameter of pulmonary nodules. Statistical test level $\alpha=0.05$, $P<0.05$ was considered statistically different.

Result

The clinical characteristics of the subjects are presented in Table 1. A total of 712 cases of T2DM [224 cases in the combined pulmonary nodules (PNs) group and 448 cases in the non-pulmonary nodules (non-PNs) group] was included in this study. In our studied sample, the rate of PNs in patients with T2DM was 31.5%. Our findings showed a higher prevalence of PNs in women than in men (36.5% versus 28.1%, $P=0.018$), and that patients in the PNs group were older and had longer disease duration (64 (15) versus 58 (20), $P<0.001$; 11 (11) versus 10 (12), $P=0.001$), but had lower BMI and Albumin (ALB) (25.57 (5.02) versus 26.49 (4.94), $P=0.005$; 36.8 (5.7) versus 37.8 (5.2), $P=0.003$). Meanwhile, in comparison to the non-PNs group, there were fewer patients with overweight in the PNs group (67.0% versus 54.5%, $P=0.001$). In terms of diabetic complications, the PNs group had more patients with diabetic retinopathy (DR) or diabetic peripheral neuropathy (DPN) (46.9% vs. 38.3%, $P=0.031$; 87.1% vs. 76.8%, $P=0.002$). In addition, there were statistically significant differences in renal function between the PNs group and non-PNs group, with elevated SCR and Blood urea nitrogen (BUN) in the PNs group compared to the control group (68 (26) versus 63 (25), $P=0.031$; 5.4 (2.6) versus 5.0 (2.2), $P=0.007$), and with eGFR <60 ml/min/1.73m² was significantly higher in the proportion of patients (14.7% versus 7.4%, $P=0.002$). Smoking, alcohol consumption, lipids, blood glucose, HBA1C, MAU and related indices responding to insulin function were not significantly different between the two groups (Table 1).

Spearman correlation analysis showed that PNs were positively correlated with age, disease duration, SCR, BUN, eGFR <60 ml/min/1.73m², DR, and DPN (rs value: 0.192, $P<0.001$; rs value: 0.128, $P=0.010$; rs value: 0.081, $P=0.031$; rs value: 0.102, $P=0.007$; rs value: 0.115, $P=0.002$; rs value: 0.081, $P=0.031$; rs value: 0.119, $P=0.002$, respectively); PNs were negatively correlated with sex, BMI, and ALB (rs value: -0.089, $P=0.018$; rs

value: -0.106, $P=0.005$; rs value: -0.110, $P=0.003$, respectively) (Table 2).

Multivariate binary logistic regression analysis was performed with the occurrence of PNs as the dependent variable and age, sex, overweight, disease duration, ALB, eGFR <60 ml/min/1.73m², and concurrent DR or DPN as independent variables. The results showed that age, eGFR <60 ml/min/1.73m² was an independent risk factor for PNs in patients with T2DM ($\beta=0.030$, $P<0.001$, OR=1.031; $\beta=0.565$, $P=0.032$, OR=1.760), while overweight has the opposite effect on the onset of PNs in patients with T2DM ($\beta=-0.388$, $P=0.023$, OR=0.678) (Table 3).

We further divided the combined PNs group into small nodule groups and large nodule group (152 cases in the pulmonary nodules <5 mm group and 72 cases in the pulmonary nodules ≥ 5 mm group) for statistical analysis according to whether the PNs diameter was ≥ 5 mm. The results showed that compared with the small nodule group, patients in the large nodule group had higher FBG and lower FINS (9.10 (4.05) versus 8.25 (3.58), $P=0.016$; 10.40 (9.29) versus 12.90 (13.10), $P=0.020$), and patients with decreased HOMA- β and high SI accounted for a higher proportion in the large nodule group (66.7% versus 41.4%, $P<0.01$; 33.3% versus 19.1%, $P=0.019$) (Table 4).

Spearman correlation analysis showed that PNs diameter ≥ 5 mm was positively correlated with FBG, SI, HOMA- β , and DPN (rs value: 0.162, $P=0.016$; rs value: 0.157, $P=0.019$; rs value: 0.236, $P<0.001$; rs value: 0.152, $P=0.023$, respectively); and negatively correlated with FINS (rs value: -0.156, $P=0.019$) (Table 5).

Multivariate binary logistic regression analysis was performed with PNs diameter ≥ 5 mm as the dependent variable and sex, age, FINS, FBG, HOMA- β , SI, and DPN as independent variables. The results showed that decreased HOMA- β and high SI were independent risk factors for PNs diameter ≥ 5 mm in patients with T2DM combined with PNs ($\beta=0.995$, $P=0.001$, OR=2.706; $\beta=0.803$, $P=0.019$, OR=2.231) (Table 6).

Discussion

This investigation demonstrates that age and eGFR <60 ml/min/1.73m² were independent risk factors for pulmonary nodules in patients with T2DM, and overweight may be a protective factor. Besides decreased pancreatic B-cell function and smoking may contribute to the presence of larger volume pulmonary nodules. In recent years, along with the popularity of COVID-19, chest CT has been widely used in patients with diabetes and the detection rate of PNs has increased. Because of concerns about cancer, many of the patients diagnosed with PNs are stressed and anxious, and even about 20–25% of patients with incidental nodules experience

Table 1 Clinical and laboratory characteristics of study subjects

| Variables | Pulmonary nodules group (n = 224) | Non-pulmonary nodules group (n = 488) | z or χ^2 values | P values |
|---|-----------------------------------|---------------------------------------|----------------------|----------|
| Demographics | | | | |
| Sex | | | 5.602 | 0.018* |
| Male | 119 (53.1%) | 305 (62.5%) | | |
| Female | 105 (46.9%) | 183 (37.5%) | | |
| Age (years) | 64 (15) | 58 (20) | -5.133 | < 0.001* |
| BMI (kg/m²) | 25.57 (5.02) | 26.49 (4.94) | -2.821 | 0.005* |
| Overweight | | | 10.371 | 0.001* |
| Yes | 122 (54.5%) | 327 (67.0%) | | |
| No | 102 (45.5%) | 161 (33.0%) | | |
| SI | | | 0.072 | 0.788 |
| Low | 171 (76.3%) | 368 (75.4%) | | |
| High | 53 (23.7%) | 120 (24.6%) | | |
| Drinking | 52 (23.2%) | 125 (25.6%) | 0.474 | 0.491 |
| Laboratory measures | | | | |
| TG (mmol/L) | 1.59 (1.20) | 1.69 (1.34) | -1.595 | 0.111 |
| HDL (mmol/L) | 0.92 (0.37) | 0.89 (0.30) | -1.936 | 0.053 |
| LDL (mmol/L) | 2.48 (1.06) | 2.51 (1.14) | -0.668 | 0.504 |
| TC (mmol/L) | 4.20 (1.40) | 4.27 (1.45) | -0.876 | 0.381 |
| eGFR < 60 ml/min1.73m² | | | 9.490 | 0.002* |
| No | 191 (85.3%) | 452 (92.6%) | | |
| Yes | 33 (14.7%) | 36 (7.4%) | | |
| SCR (μmol/L) | 68 (26) | 63 (25) | -2.162 | 0.031* |
| BUN (mmol/L) | 5.4 (2.6) | 5.0 (2.2) | -2.712 | 0.007* |
| ALB (g/L) | 36.8 (5.7) | 37.8 (5.2) | -2.944 | 0.003* |
| Diabetes-related characteristics | | | | |
| Course of diabetes (years) | 11 (11) | 10 (12) | -3.423 | 0.001* |
| FBG (mmol/L) | 8.6 (3.6) | 8.3 (3.2) | -1.235 | 0.217 |
| HBA1C (%) | 9.10 (3.22) | 9.09 (3.24) | -0.180 | 0.858 |
| FINS (uIU/ml) | 11.92 (12.86) | 12.04 (10.14) | -0.135 | 0.892 |
| HOMA-β | | | 0.361 | 0.548 |
| Normal | 113 (50.4%) | 258 (52.9%) | | |
| Abnormal | 111 (49.6%) | 230 (47.1%) | | |
| HOMA-IR | 4.61 (4.98) | 4.42 (4.30) | -0.365 | 0.715 |
| Type 2 diabetes complications | | | | |
| DPN | | | 10.023 | 0.002* |
| No | 29 (12.9%) | 113 (23.2%) | | |
| Yes | 195 (87.1%) | 375 (76.8%) | | |
| DR | | | 4.645 | 0.031* |
| No | 119 (53.1%) | 301 (61.7%) | | |
| Yes | 105 (46.9%) | 187 (38.3%) | | |
| Microalbuminuria | | | 0.037 | 0.847 |
| Normal | 142 (63.4%) | 313 (64.1%) | | |
| Abnormal | 82 (36.6%) | 175 (35.9%) | | |

Note: Continuous variables were reported as median with interquartile range (IQR); categorical variables were reported as n (%)

clinically significant distress [17–18]. Whereas lung cancer remains the most prevalent tumor worldwide and has the highest associated mortality risk [19], the management of PNs has been the focus of research in recent years due to concern for lung cancer. However, the detection of PNs is mostly incidental [2–3], and their targeted screening is also generally aimed at high-risk groups for

lung cancer. While evidence of other risk factors is lacking [5], there has been a gap in studies related to DM and PNs, but the large patient population with DM and the association between DM and PN based on the association between diabetes and lung cancer cannot be ignored.

The prevalence of PNs among T2DM patients in this study (31.5%) was comparable to that reported in a study

Table 2 Correlation of pulmonary nodules (PNs) and factors

| Variable | rs values | P values |
|-------------------------------------|-----------|----------|
| Sex | -0.089 | 0.018* |
| Age (years) | 0.192 | < 0.001* |
| BMI (kg/m ²) | -0.106 | 0.005* |
| Overweight | -0.121 | 0.001* |
| SI | -0.010 | 0.789 |
| Course of diabetes (years) | 0.128 | 0.010* |
| FBG (mmol/L) | 0.046 | 0.217 |
| FINS (uIU/ml) | -0.005 | 0.829 |
| HOMA-β | 0.023 | 0.549 |
| SCR (μmol/L) | 0.081 | 0.031* |
| eGFR < 60 ml/min/1.73m ² | 0.115 | 0.002* |
| BUN (mmol/L) | 0.102 | 0.007* |
| DPN | 0.119 | 0.002* |
| DR | 0.081 | 0.031* |
| ALB (g/L) | -0.110 | 0.003* |

Table 3 Multivariate binary logistic regression analysis for factors of PNs

| | β values | 95% CI | OR | P values |
|-------------------------------------|----------|-------------|-------|----------|
| Age (years) | 0.030 | 1.017–1.045 | 1.031 | < 0.001* |
| Overweight | -0.388 | 0.486–0.947 | 0.678 | 0.023* |
| eGFR < 60 ml/min/1.73m ² | 0.565 | 1.051–2.949 | 1.760 | 0.032* |

in the United States [3], but significantly higher than the prevalence of PNs among the Chinese domestic population at high risk for lung cancer (22.9% [4]). Also, this study found a higher proportion of women with PNs among diabetic patients, about 36.5% compared to 28.1% of men; and the prevalence of PNs increased with age. Similar results were also found in a large retrospective epidemiological study of a community-based population in the United States [1].

Several studies have found a higher incidence of lung cancer in women [1, 19–22], and a study of an Asian population also found that women who never smoked appeared to have a higher risk of lung cancer compared to women living in Western countries [20]. The reason for this may be related to genetic differences, and a genome-wide association analysis of lung cancer in never-smoking Asian women in China, Korea, Japan, and Singapore identified three new susceptibility loci and confirmed associations with other loci [21]. This study also suggests that the high incidence of lung cancer in women may be related to genetic differences between the sexes. A meta-analysis also suggested that the incidence of lung cancer was also significantly higher in women with diabetes than in men with diabetes [22].

In addition, in recent years there has been a suggestion that obesity may reduce the risk of lung cancer and favorably affect its prognosis, which may seem to be different from what we have always thought, yet several studies have proven this idea [23–26]. The reasons for this may

be related to underlying biological mechanisms [26]. A Chinese cohort study of a male population found that overweight men had significantly lower levels of chromosomal damage and a lower risk of lung cancer [27]. A Japanese longitudinal study, on the other hand, found that weight loss was associated with increased oxidative DNA damage, a state that may be associated with an increased risk of cancer [28]. And it is extremely common for patients with T2DM to be obese in combination. Interestingly, our study came to similar conclusions, and it seems that obesity also plays a protective role among the factors influencing the development of PNs in T2DM patients, while the incidence of PNs is significantly lower in the obese population, for reasons that still need to be verified by further prospective studies and mechanistic explorations.

Our study also found that T2DM patients with combined PNs also had a longer duration of diabetes mellitus, and although there is a certain age factor involved, it may also be related to the presence of diabetic complications. The risk of developing diabetic peripheral neuropathy and diabetic chronic kidney disease increases with the duration of diabetes mellitus. In our study, a higher proportion of patients with combined diabetic peripheral neuropathy, diabetic retinopathy and reduced glomerular filtration rate (eGFR < 60 ml/min/1.73m²) were found in the pulmonary nodule group, and the results of multifactorial regression analysis also showed that the results of the multifactorial regression analysis also showed that eGFR < 60 ml/min/1.73m² was an independent risk factor for the development of pulmonary nodules in patients with T2DM. And many studies have found a correlation between chronic kidney disease (CKD) and lung cancer [29–33]. Huakang Tu et al. found in a large cohort study that patients with low glomerular filtration rate had a higher cancer risk of 11% compared to patients with glomerular filtration rate of 60–89 ml/min/1.73m² [29]. And a study from China on people ≥ 45 years of age also found a higher risk of lung cancer in patients with eGFR < 60 ml/min/1.73m². Germaine Wong also found that for every 10 ml/min decrease in glomerular filtration rate in middle-aged and older men with combined CKD, the risk of cancer increased by 29%, with a higher risk of lung cancer [30]. These studies also corroborate our findings to some extent, but most patients with pulmonary nodules still have predominantly benign nodules, and the effect of diabetic kidney disease on benign nodules may be related to chronic inflammatory response and granuloma formation [34], which still needs to be proved by further studies.

Nodule size remains one of the important determinants to assist in determining the nature of PNs [35], and several reports and studies have indicated that the cancer risk increases with increasing nodules size, while the

Table 4 Between-group variation comparison of PN's size

| | Pulmonary nodules < 5 mm group (n = 152) | Pulmonary nodules ≥ 5 mm group (n = 72) | z or χ^2 values | P values |
|---|---|---|----------------------|----------|
| Sex | | | -1.073 | 0.283 |
| Male | 77 (50.7%) | 30 (41.7%) | | |
| Female | 75 (49.3%) | 42 (58.3%) | | |
| Age (years) | 64.0 (17.0) | 64.5 (14.0) | -0.533 | 0.594 |
| BMI (kg/m²) | 25.71 (5.17) | 25.06 (4.61) | -1.598 | 0.110 |
| Overweight | | | -0.921 | 0.357 |
| Yes | 86 (56.6%) | 36 (50.0%) | | |
| No | 66 (43.4%) | 36 (50.0%) | | |
| SI | | | 5.496 | 0.019* |
| Low | 123 (80.9%) | 48 (66.7%) | | |
| High | 29 (19.1%) | 24 (33.3%) | | |
| Course of diabetes (years) | 10.00 (11.75) | 12.00 (12.75) | -1.108 | 0.268 |
| FINS (uIU/ml) | 12.90 (13.10) | 10.40 (9.29) | -2.412 | 0.020* |
| FBG (mmol/L) | 8.25 (3.58) | 9.10 (4.05) | -2.336 | 0.016* |
| HOMA-β | | | 12.431 | < 0.001* |
| Normal | 89 (58.6%) | 24 (33.3%) | | |
| Abnormal | 63 (41.4%) | 48 (66.7%) | | |
| DR | | | -0.358 | 0.721 |
| No | 82 (53.9%) | 37 (51.4%) | | |
| Yes | 70 (46.1%) | 35 (48.6%) | | |
| DPN | | | 5.143 | 0.023* |
| No | 25 (16.5%) | 4 (0.6%) | | |
| Yes | 127 (83.5%) | 68 (94.4%) | | |
| eGFR < 60 ml/min1.73m² | | | -0.647 | 0.517 |
| No | 128 (84.2%) | 63 (87.5%) | | |
| Yes | 24 (15.8%) | 9 (12.5%) | | |
| SCR (μmol/L) | 66 (26) | 71 (26) | -0.125 | 0.901 |
| BUN (mmol/L) | 5.4 (2.9) | 5.5 (2.1) | -0.788 | 0.431 |
| ALB (g/L) | 36.65 (5.50) | 37.15 (6.58) | -0.451 | 0.652 |

Note: Continuous variables were reported as median with interquartile range (IQR); categorical variables were reported as n (%)

Table 5 Correlation of PN's size and factors

| Variable | rs values | P values |
|---|-----------|----------|
| Sex | 0.072 | 0.284 |
| Age (years) | 0.036 | 0.595 |
| BMI (kg/m²) | -0.107 | 0.110 |
| Overweight | -0.062 | 0.358 |
| SI | 0.157 | 0.019* |
| Course of diabetes (years) | 0.121 | 0.070 |
| FBG (mmol/L) | 0.162 | 0.016* |
| FINS (uIU/ml) | -0.156 | 0.019* |
| HOMA-β | 0.236 | < 0.001* |
| SCR (μmol/L) | 0.053 | 0.432 |
| eGFR < 60 ml/min1.73m² | -0.043 | 0.519 |
| BUN (mmol/L) | 0.008 | 0.901 |
| DPN | 0.152 | 0.023* |
| DR | 0.024 | 0.722 |
| ALB (g/L) | 0.030 | 0.635 |

Table 6 Multivariate binary logistic regression analysis for factors of PN's size

| | β values | OR | 95% CI | P values |
|--------------------------------|----------------|-------|-------------|----------|
| HOMA-β | 0.995 | 2.706 | 1.473–4.969 | 0.001* |
| SI | 0.803 | 2.231 | 1.141–4.363 | 0.019* |

prevalence of malignancy in < 5 mm nodules is very low [35–36]. Smoking is one of the recognized risk factors for lung cancer [20, 37], and our study also found that SI was a significant influencing factor in the appearance of larger nodules (> 5 mm). Furthermore, although we did not find a direct association between islet function-related indices and the development of PN's in T2DM patients, but the comparison of differences in different nodules sizes (5 mm) nevertheless suggested that reduced insulin secretion index was significantly associated with the appearance of large nodules. In addition, the level of FBG in patients with the larger nodules was significantly higher. Impaired islet function is one of the main etiologies of T2DM [38], and reduced levels of B-cell function directly contribute to the development of hyperglycemia,

which may lead to enhanced WNT/ β -catenin protein signaling pathways that promote proliferation and senescence bypass in cancer cells [39], resulting in an elevated risk of lung cancer development.

This study is a single-center retrospective investigation, which has certain limitations. Owing to the restriction of sample size, the current study recognizes the potential influence on the stability and reliability of the results. Additionally, the type 2 diabetes patients we included were mainly inpatients, which may not be fully representative of all diabetic patient cohorts. Moreover, there is a lack of relevant data on pulmonary nodules in the non-diabetic population for comparison. However, this provides us with further research directions. It is suggested that future larger multicenter prospective studies and a control study of the non-diabetic populations can be carried out to enhance the robustness of the study results and further validate the uniqueness of characteristics such as eGFR, overweight, and islet B-cell function in pulmonary nodules of patients with type 2 diabetes, as well as the long-term predictive value and potential mechanisms for the occurrence and development of pulmonary nodules in patients with type 2 diabetes. Nevertheless, our findings still fill some gaps in the relevant fields, especially in terms of the association between pulmonary nodules and renal function and overweight in diabetic patients. These findings may have a beneficial role in the early prevention and screening of pulmonary nodules.

Conclusion

In conclusion, our study found that the prevalence of PNs among T2DM patients shouldn't be ignored. For T2DM patients, it seems that PNs are more common in female patients and that the prevalence of PNs increases with age. Moreover, it seems there is a correlation between eGFR < 60 ml/min/1.73m², overweight and the morbidity of PNs. In addition, reduced B-cell function and smoking may contribute to the appearance of PNs with a diameter of over 5 mm. Meanwhile, our findings clearly demonstrate some associations between diabetes and PNs, and the mechanisms underlying these associations need to be further investigated for more evidence.

Abbreviations

| | |
|---------------|---------------------------------------|
| ALB | Albumin |
| BMI | Body mass index |
| BUN | Blood urea nitrogen |
| CKD | Chronic kidney disease |
| DM | Diabetes mellitus |
| DPN | Diabetic peripheral neuropathy |
| DR | Diabetic retinopathy |
| eGFR | Estimated glomerular filtration rate |
| FBG | Fasting blood glucose |
| FINS | Fasting insulin |
| HbA1c | Glycosylated hemoglobin |
| HOMA- β | Homeostasis model assessment- β |

| | |
|------|--------------------------|
| MAU | Microalbuminuria |
| PN | Pulmonary nodule |
| SCR | Serum creatinine |
| SI | Smoking index |
| T2DM | Type 2 diabetes mellitus |

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12902-025-01857-9>.

Supplementary Material 1

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Not applicable.

Author contributions

J.Y. and W.W.S. designed the study. W.N.W., Y.Z.L. and C.Y.L. collected data. W.N.W. and W.W.S. analyzed and interpreted the data. J.Y. and W.N.W. drafted the manuscript. S.W.W. applied for ethical approval. All authors reviewed and approved the final manuscript.

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Data availability

The datasets generated and/or analyzed during the current study are not publicly available due to privacy and ethical considerations, but can be available from the corresponding author on reasonable request. The datasets that support the conclusions of this paper are included in the article.

Declarations

Ethics approval and consent to participate

The study was approved by the Medical Ethics Committee of Dongzhimen Hospital of Beijing University of Chinese Medicine (Project Approval No. 2022DZMEC-317-02). The basis of ethical review mainly includes the International Ethical Guidelines on Biomedical Research Involving Human Subjects (2002) issued by the Council for International Organizations of Medical Sciences, the Methodology for Ethical Review of Biomedical Research Involving Human Beings issued by the National Health Commission (No. 11, 2016), and the Declaration of Helsinki issued by the World Medical Association (2013), etc. This study was a retrospective study and data were collected from the inpatient electronic system, patients did not sign informed consent forms. The ethical review committee of Dongzhimen Hospital of Beijing University of Traditional Chinese Medicine also accepted our application for waiver of informed consent form in the process of ethical review.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Clinical trial number

Not applicable.

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