Article

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Diagnostic Value of Serum Platelet-Derived Growth Factor and Correlation With Peripheral Oxygen Saturation in Patients With Obstructive Sleep Apnea-Hypopnea Syndrome and Concomitant Lung Cancer

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Background: Obstructive sleep apnea-hypopnea syndrome (OSAHS) can lead to intermittent hypoxia and systemic inflammatory response, which may influence the progression of lung cancer in patients. This study aims to evaluate the relationship between serum platelet-derived growth factor BB (PDGF-BB) and peripheral oxygen saturation (SpO_2), and to explore the diagnostic value of PDGF-BB in distinguishing mild-moderate and severe OSAHS in patients with lung cancer (LC).

Methods: This study is a retrospective study that included 76 patients diagnosed with OSAHS combined with LC from March 2021 to March 2023, as well as a control group comprising 72 healthy adults, 30 cases of OSAHS only, and 29 cases of LC only. All subjects underwent nighttime polysomnography to obtain Apnea Hypopnea Index (AHI), minimum/average SpO_2, and T90%. Serum PDGF-BB was measured by ELISA. Patients with OSAHS and concomitant LC were divided into two groups based on AHI: a mild-moderate group ($5 \leq AHI \leq 30$, n = 47) and a severe group (AHI >30, n = 29). Pearson correlation analysis was used to investigate the relationship between PDGF-BB and disease indicators. The efficacy of PDGF-BB in distinguishing the severity of the disease was evaluated by using receiver operating characteristic (ROC) curve.

Results: The OSAHS-with-concomitant-LC group showed significantly elevated PDGF-BB levels ($p < 0.05$) than the control group. PDGF-BB was significantly elevated in the severe group than in the mild-moderate group ($p < 0.001$). PDGF-BB was positively linked with AHI (r = 0.888, $p < 0.001$) and T90% (r = 0.750, $p < 0.001$), but was negatively linked with Min SpO_2 (r = –0.740, $p < 0.001$) and Mean SpO_2 (r = –0.534, $p < 0.001$). ROC curves demonstrated the AUC of PDGF-BB level for distinguishing the mild-moderate group from the severe group as 0.9912 (95% CI: 0.9770–1.0000, $p < 0.0001$), optimal cutoff value as 757.7 ng/L, sensitivity as 100.0%, and specificity as 95.74%.

Conclusion: Serum PDGF-BB is significantly elevated in patients with OSAHS and concomitant LC, and is highly correlated with the severity of hypoxia. It has high diagnostic value and can be used as a biomarker to assist in evaluating the severity of OSAHS.

Keywords: platelet-derived growth factor; lung cancer; obstructive sleep apnea-hypopnea syndrome; saturation of peripheral oxygen; diagnostic biomarker

Introduction

Obstructive sleep apnea-hypopnea syndrome (OSAHS) is a common sleep-related respiratory disease, in which repeated upper respiratory tract obstruction can cause intermittent hypoxia, sleep disruption, and sympathetic nervous system excitation. It is associated with various cardiovascular and cerebrovascular diseases, metabolic disorders, and systemic inflammatory responses [1,2]. The OSAHS-associated respiratory physiological responses include significant alterations in intrathoracic pressure, fragmented sleep, intermittent hypoxemia, and nocturnal awakenings [3]. Intermittent hypoxia not only damages systemic organ function, but may also participate in tumor occurrence and progression by promoting oxidative stress and chronic inflammation [4,5]. According to epidemiological statistics, the global prevalence of OSAHS is at approximately 936 million patients, and China was reported to bear

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the highest number of cases worldwide [6], indicating a disproportionately heavy disease burden within the country.

OSAHS is associated with an increase in incidence rate and mortality of various malignant tumors, among which colorectal cancer, prostate cancer, lung cancer (LC) and breast cancer have the highest incidence [7,8]. LC is the most common malignant tumor among OSAHS patients, usually demonstrating progression towards the moderate-to-severe stage by the time OSAHS is diagnosed and this significantly reduces the patient's quality of life and survival [9]. LC, as a malignant tumor with a high incidence rate and mortality worldwide, has about 2.2 million new cases and 1.79 million deaths every year. This makes it one of the main causes of cancer-related deaths [10]. OSAHS may promote the occurrence and progression of LC by exacerbating the inflammatory state caused by sleep disorders and intermittent hypoxia [11], suggesting that OSAHS is closely related and may serve as a risk factor for the occurrence and development of LC.

Currently, the diagnosis of OSAHS mainly relies on the Apnea hypopnea index (AHI) level obtained from nighttime polysomnography monitoring. However, polysomnography monitoring is complex, expensive, and may affect patients' sleep, limiting its clinical utility [12]. Peripheral oxygen saturation (SpO_2) is a commonly used indicator for the clinical evaluation of hypoxia, and is widely used in the auxiliary examination of patients with OSAHS [13]. However, reliance on individual physiological indicators is generally inadequate for accurate diagnosis. Therefore, novel biomarkers that are simple, economical, and indicative of OSAHS and its potential complications remain important. Advancements in OSAHS research have enabled the exploration of new biological indicators for simple and cost-effective diagnosis and assessment of disease severity.

Platelet-derived growth factor (PDGF) is an important factor that promotes the proliferation and migration of vascular smooth muscle cells. It has been shown to serve as an early warning of potential cardiovascular diseases [14,15]. The PDGF family members include PDGF-A, PDGF-B, PDGF-C, and PDGF-D [16]. PDGF-BB, among others, has been shown to promote tumor growth, lymphangiogenesis, and lymph node infiltration in non-small cell lung cancer (NSCLC), and is associated with poor prognosis [17]. Based on these findings, PDGF may play a bridging role in the pathological process of OSAHS with concomitant LC, but the clinical evidence base remains limited. To verify this potential role, this study aims to evaluate the changes of serum PDGF-BB in OSAHS patients with concomitant LC and its correlation with SpO_2, explore its value as a potential diagnostic indicator, and provide a basis for early disease identification and mechanistic research.

Methods

The Study Subjects

This is a retrospective study of 76 patients with comorbid OSAHS and LC diagnosed in Suqian Hospital of Nanjing Drum-Tower from March 2021 to March 2023, as well as 131 controls including: 72 healthy adults, 30 patients with OSAHS alone, and 29 patients with LC alone. The research subjects were all over 50 years old and had completed serum PDGF-BB testing at the time of diagnosis. Patients with OSAHS and concomitant LC were divided into the mild-moderate group (5 times/h $<$ AHI $\leq$ 30 times/h, n = 47) and the severe group (AHI $>$30 times/h, n = 29) based on the AHI [18].

The diagnostic criteria for OSAHS in this study referred to the revised 2018 edition of the "Guidelines for Primary Diagnosis and Treatment of Obstructive Sleep Apnea in Adults", with AHI as the primary criterion for assessing the severity of OSAHS. LC was diagnosed through surgery, percutaneous lung puncture, bronchoscopy, or thoracoscopy biopsy, and OSAHS was diagnosed simultaneously with LC. We excluded patients with tumors invading adjacent organs/tissues or metastatic tumors, patients with central sleep apnea, severe respiratory diseases (bronchial asthma, bronchiectasis, acute and chronic obstructive pulmonary disease, interstitial lung disease, tuberculosis, etc.), acute cardiovascular and cerebrovascular diseases, severe heart and kidney dysfunction, recent use of drugs that affect blood oxygen or platelet indicators, and those who were unable to complete overnight polysomnography monitoring.

The inclusion and exclusion criteria for the control group are as follows: the healthy adult group had no history of OSAHS or LC, and had normal physical examination and laboratory test results. Adults with recent infections, chronic diseases, pregnancy or lactation, and inability to provide a blood sample were excluded. The OSAHS group included patients without LC or other malignant tumors; those with central sleep apnea, severe respiratory diseases, acute cardiovascular and cerebrovascular events, and recent use of drugs that affect blood oxygen or platelet indicators were excluded. The LC group included patients with a pathological diagnosis of LC and without a history of OSAHS; those with other primary or metastatic tumors, central or obstructive sleep apnea, severe cardiac and renal dysfunction, and pregnancy or lactation were excluded.

This study was approved by Suqian Hospital of Nanjing Drum-Tower (No. 20220901). All research procedures followed the ethical principles of the Helsinki Declaration regarding human research. All patients or legal guardians signed informed consent forms and voluntarily participated in this study.

Table 1. Baseline data comparison among the four study groups.

	Healthy adult group (n = 72)	OSAHS-with-concomitant-LC group (n = 76)	Only OSAHS group (n = 30)	Only LC (n = 29)	K/χ^2	p value
Age (years)	68.00 (60.00, 71.00)	70.00 (62.50, 75.00)	71.50 (64.50, 76.00)	70.00 (61.50, 74.00)	6.791	0.079
Gender					3.191	0.363
Male	29 (40.28%)	30 (39.47%)	17 (56.67%)	14 (48.28%)		
Female	43 (56.72%)	46 (60.53%)	13 (43.33%)	15 (51.72%)		
BMI (kg/m^2)	23.37 (20.91, 25.63)	22.29 (21.14, 23.93)	29.38 (28.58, 31.72)^{ab}	25.06 (22.85, 27.14)^{bc}	74.412	<0.001
Neck circumference (cm)	39.00 (38.00, 40.00)	40.00 (39.00, 42.75)^{a}	40.00 (37.75, 43.00)	39.00 (38.00, 40.50)^{b}	17.055	0.001
Chest circumference (cm)	113.00 (110.00, 118.00)	119.00 (113.00, 124.00)^{a}	107.50 (102.50, 115.25)^{b}	112.00 (110.00, 118.00)^{b}	37.922	<0.001
Heart rate (time/min)	71.00 (67.00, 78.00)	81.00 (72.00, 91.75)^{a}	80.00 (78.00, 81.25)^{a}	70.00 (67.00, 80.00)^{b}	33.314	<0.001
Systolic pressure (mmHg)	142.00 (128.75, 154.00)	166.00 (150.75, 184.75)^{a}	173.50 (165.00, 178.00)^{a}	128.00 (121.50, 141.00)^{bc}	88.992	<0.001
Diastolic pressure (mmHg)	79.50 (72.25, 90.00)	98.00 (91.25, 107.00)^{a}	100.00 (95.50, 105.50)^{a}	74.00 (64.00, 78.00)^{bc}	90.018	<0.001
Triglycerides (mmol/L)	6.18 (4.93, 8.60)	8.43 (6.12, 10.29)^{a}	5.09 (3.76, 5.87)^{ab}	5.87 (4.77, 9.06)^{b}	33.460	<0.001
High-density lipoprotein cholesterol (mmol/L)	1.51 (1.08, 1.90)	1.62 (1.13, 1.94)	2.23 (0.38, 3.67)	1.14 (0.60, 1.93)	4.904	0.179
Low-density lipoprotein cholesterol (mmol/L)	3.50 (2.72, 3.94)	4.62 (3.58, 5.46)^{a}	3.55 (2.44, 4.61)^{b}	3.07 (1.66, 4.32)^{b}	31.941	<0.001
Total cholesterol (mmol/L)	5.93 (4.76, 8.44)	7.84 (5.88, 10.00)^{a}	5.90 (4.34, 6.78)^{b}	6.78 (5.21, 8.21)	20.991	<0.001
Serum glucose (mmol/L)	6.38 (4.33, 9.02)	7.25 (5.27, 10.15)	6.18 (4.31, 8.32)	5.33 (4.24, 6.98)^{b}	12.045	0.007
Serum creatinine (mmol/L)	68.55 (43.06, 89.51)	76.87 (49.07, 94.71)	82.70 (79.50, 93.20)^{a}	79.60 (52.65, 89.65)	10.273	0.016
Blood urea nitrogen (mmol/L)	4.85 (3.77, 7.75)	5.49 (4.27, 8.13)	5.90 (4.78, 7.09)	5.28 (3.95, 6.58)	2.971	0.396
Serum uric acid (mmol/L)	378.80 (318.90, 440.23)	446.15 (378.68, 491.88)^{a}	488.70 (401.65, 543.05)^{a}	437.40 (363.45, 512.65)	20.567	<0.001
PDGF-BB (pg/mL)	163.54 (135.92, 204.18)	729.85 (488.28, 967.81)^{a}	460.30 (373.48, 536.85)^{ab}	430.30 (368.90, 493.60)^{ab}	156.723	<0.001

Note: Non-normally distributed data are presented as median (P_{25}, P_{75}), inter-group comparisons were conducted using the Kruskal-Wallis test, and pairwise comparisons were adjusted for multiple testing using the Bonferroni correction.

a: vs healthy adult group, $p < 0.05$; b: vs OSAHS-with-concomitant-LC group, $p < 0.05$; c: vs only OSAHS group, $p < 0.05$.

BMI, Body Mass Index; PDGF-BB, Platelet derived growth factor BB; OSAHS, Obstructive sleep apnea-hypopnea syndrome; LC, lung cancer.

Clinical Indicator Collection

Data Collection and Processing

By reviewing outpatient and inpatient records, we collected the following clinical information from patients: age, gender, height, weight, neck circumference, chest circumference; history of present illness (including snoring, apnea, awakening from suffocation, daytime drowsiness, and morning headache); past medical history (including hypertension, coronary heart disease, other CVDs and surgical histories, as well as medication histories); personal history (including smoking, drinking), clinical symptoms and signs (including coughing, sputum production, breathing difficulty, chest pain, hemoptysis, weight loss, fatigue, pleural effusion); clinical features of LC (location of the lesion, histological type, clinical stage (staging), treatment method). We measured physiological indicators such as heart rate (HR), systolic pressure, and diastolic pressure, and calculated the body mass index (BMI) as mass/height (kg/m^2).

Collection and Analysis of Biochemical Indicators

We collected fasting peripheral venous blood from each of the study subjects. These samples were comprehensively assessed at the Hospital's Center for Clinical Testing for various biochemical indicators, including serum uric acid (UA), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), serum glucose (Glu), serum creatinine (Cr), blood urea nitrogen (BUN), total cholesterol (TC), and triglycerides (TG). Biological analyses were conducted using an automated biochemical analyzer, the AU5800 from Beckman Coulter, operated by a team of professional laboratory technicians.

Multi-Channel Sleep Apnea Monitoring

According to the Guidelines for Diagnosis and Treatment of Obstructive Sleep Apnea Hypopnea Syndrome (Basic Edition) [19], the core indicators of sleep monitoring are SpO_2 and AHI. We systematically collected and recorded these data. All study subjects underwent a 7-hour nocturnal sleep breathing monitoring, with the German WMN SOMNOlab2 polysomnography device employed. The data were analyzed using computer software before undergoing manual correction. During the two weeks leading up to the monitoring, participants were required to maintain regular sleep and diet. In the three days preceding the monitoring, stimulants such as tea, coffee, and alcohol were prohibited. The parameters recorded were: ① Minimum SpO_2; ② Mean SpO_2; ③ Percentage of time with SpO_2 below 90% (T90%) over the total monitoring period; ④ AHI.

PDGF-BB Detection in Serum

Serum PDGF-BB concentrations were measured using an enzyme-linked immunosorbent assay (ELISA) in patients from each group. The ELISA kits were procured from DaKeWe Biological Engineering Co., Ltd. in Shenzhen. Standard curves were generated in accordance with the standard operating procedure, and the concentrations of PDGF-BB were calculated accordingly in the samples. The test results were uniformly expressed in pg/mL (1 pg/mL = 1 ng/L).

Statistical Analysis

All statistical analyses were performed using SPSS 26.0 (IBM Corp., Armonk, NY, USA) and Graphpad Prism 8.0.2 (GraphPad Software, San Diego, CA, USA). The Shapiro-Wilk test was used to evaluate whether the distribution of continuous variables conformed to a normal distribution before analysis. Metric data that followed a normal distribution were expressed as mean $\pm$ standard deviation ($\bar{x} \pm s$), and the independent sample t-test was employed. Quantitative data that did not follow a normal distribution were represented by Median (P_{25}, P_{75}). Non-parametric tests (Mann-Whitney U test and Kruskal-Wallis test) were used for inter-group comparisons, and Bonferroni correction was applied to pairwise comparisons. The count data were described as a percentage [n (%)], and the chi-square test (χ^2)/continuity correction/Fisher's exact test were used for comparison between the two groups. Spearman's rank correlation analysis was used to investigate the correlation between serum PDGF and SpO_2 in OSAHS patients with concomitant LC. Receiver operating characteristic (ROC) curve analysis was used to test the discriminative ability of PDGF. The Area Under the Curve (AUC) was calculated to quantify diagnostic efficacy. The optimal cutoff value was determined based on the Jordan index. To further verify the reliability of AUC and estimate the 95% confidence interval, ROC analysis was performed using Bootstrap method (2000 self-sampling), and 10-fold cross-validation was used to evaluate the stability of the model. A $p < 0.05$ was considered statistically significant.

The G-Power software (version 3.1.9.7, Heinrich-Heine-University Düsseldorf, Düsseldorf, NW, Germany) was used for post-hoc power analysis. Based on the planned parameters, actual sample size (N), pre-specified significance level (α), and effect size, statistical power (1 - β) was evaluated for the primary analyses and exceeded 0.85, indicating that the study was adequately powered under these design assumptions.

Results

Patient Baseline Data Comparison

The baseline data of the four study groups are shown in Table 1. There was no statistically significant difference in age and gender composition among the four groups ($p > 0.05$). Compared with the healthy adult group, the neck circumference, chest circumference, heart rate, systolic pressure, diastolic pressure, TG, LDL-C, TC, and blood uric acid levels of the OSAHS group were higher (all $p < 0.05$). The BMI of the Only OSAHS group was higher

Table 2. Baseline data comparison of the mild-moderate group and the severe group of OSAHS-with-concomitant-LC patients.

	Mild-moderate group (n = 47)	Severe group (n = 29)	t/χ^2 value	p value
Age (years)	70.00 (62.00, 75.00)	69.50 (61.75, 75.75)		0.860
Gender			0.047	0.829
Male	19 (40.4%)	11 (37.9%)		
Female	28 (59.6%)	18 (62.1%)		
BMI (kg/m^2)	22.72 ± 2.24	22.24 ± 1.74	0.981	0.330
Neck circumference (cm)	40.00 (39.00, 42.00)	41.00 (39.00, 56.25)		0.115
Chest circumference (cm)	119.00 (113.00, 122.00)	125.00 (113.00, 136.25)		0.045
AHI (time/hour)	17.00 (9.40, 28.60)	49.60 (42.85, 68.43)		<0.001
Min SpO_2 (%)	86.00 (83.00, 89.00)	68.50 (56.00, 74.50)		<0.001
Mean SpO_2 (%)	92.00 (90.00, 93.00)	83.50 (80.00, 86.00)		<0.001
T90%	38.00 (16.00, 89.00)	91.00 (87.25, 93.00)		<0.001
Heart rate (time/min)	82.00 (76.00, 91.00)	79.00 (70.00, 94.50)		0.275
Systolic pressure (mmHg)	160.00 (145.00, 169.00)	186.00 (165.50, 193.00)		<0.001
Diastolic pressure (mmHg)	97.00 (87.00, 101.00)	101.00 (96.25, 110.00)		0.013
Triglycerides (mmol/L)	8.49 (6.13, 10.12)	7.40 (6.04, 10.77)		0.826
High-density lipoprotein cholesterol (mmol/L)	1.56 (1.14, 1.98)	1.72 (0.94, 1.94)		0.835
Low-density lipoprotein cholesterol (mmol/L)	4.61 (3.43, 4.89)	5.29 (3.89, 6.45)		0.024
Total cholesterol (mmol/L)	8.49 (5.87, 10.56)	7.10 (5.84, 9.41)		0.271
Serum glucose (mmol/L)	6.83 (5.19, 9.78)	8.74 (5.64, 14.50)		0.093
Serum creatinine (mmol/L)	59.19 (48.09, 89.12)	84.25 (76.40, 102.58)		0.002
Blood urea nitrogen (mmol/L)	5.20 (4.26, 6.45)	6.82 (4.38, 9.91)		0.052
Serum uric acid (mmol/L)	468.90 (379.50, 492.10)	424.00 (365.85, 496.95)		0.451
PDGF level (ng/L)	582.00 (387.20, 725.50)	978.64 (923.51, 996.39)		<0.001
Snoring			-	-
No	0	0		
Yes	47 (100.0%)	29 (100.0%)		
Sleep apnea			-	-
No	0	0		
Yes	47 (100.0%)	29 (100.0%)		
Awakening from Suffocation			-	-
No	0	0		
Yes	47 (100.0%)	29 (100.0%)		
Daytime drowsiness			1.060	0.152
No	1 (2.1%)	3 (10.3%)		
Yes	46 (97.9%)	26 (89.7%)		
Morning headache			10.802	0.001
No	22 (46.8%)	3 (10.3%)		
Yes	25 (53.2%)	26 (89.7%)		
Hypertension			9.701	0.002
No	25 (53.2%)	5 (17.2%)		
Yes	22 (46.8%)	24 (82.8%)		
Coronary heart disease			36.512	<0.001
No	45 (95.7%)	9 (31.0%)		
Yes	2 (4.3%)	20 (69.0%)		
Other CVDs			1.060	0.152
No	46 (97.9%)	26 (89.7%)		
Yes	1 (2.1%)	3 (10.3%)		
Surgical history			35.490	<0.001
No	47 (100.0%)	12 (41.4%)		
Yes	0	17 (58.6%)		
Medication history			27.640	<0.001
No	42 (89.4%)	9 (31.0%)		
Antihypertensive drugs	5 (10.6%)	20 (69.0%)		

Table 2. Continued.

	Mild-moderate group (n = 47)	Severe group (n = 29)	t/χ^2 value	*p* value
Smoking			5.020	0.025
No	2 (4.3%)	7 (24.1%)		
Yes	45 (95.7%)	22 (75.9%)		
Drinking			20.138	<0.001
No	4 (8.5%)	16 (55.2%)		
Yes	43 (91.5%)	13 (44.8%)		
Coughing			8.686	0.003
No	22 (46.8%)	4 (13.8%)		
Yes	25 (53.2%)	25 (86.2%)		
Sputum production			12.982	<0.001
No	24 (51.1%)	3 (10.3%)		
Yes	23 (48.9%)	26 (89.7%)		
Breathing difficulty			27.616	<0.001
No	43 (91.5%)	10 (34.5%)		
Yes	4 (8.5%)	19 (65.5%)		
Chest pain			2.279	0.131
No	44 (93.6%)	23 (79.3%)		
Yes	3 (6.4%)	6 (20.7%)		
Hemoptysis			2.574	0.109
No	29 (61.7%)	23 (79.3%)		
Yes	18 (38.3%)	6 (20.7%)		
Weight loss			0.575	0.448
No	25 (53.2%)	18 (62.1%)		
Yes	22 (46.8%)	11 (37.9%)		
Fatigue			3.165	0.075
No	19 (40.4%)	6 (20.7%)		
Yes	28 (59.6%)	23 (79.3%)		
Pleural effusion			6.064	0.014
No	24 (51.1%)	23 (79.3%)		
Yes	23 (48.9%)	6 (20.7%)		
Location of the LC lesion			9.978	0.007
Left lung	3 (6.4%)	6 (20.7%)		
Right lung	22 (46.8%)	19 (65.5%)		
Both	22 (46.8%)	4 (13.8%)		
Histological LC type			20.173	<0.001
Adenocarcinoma	22 (46.8%)	11 (37.9%)		
Squamous cell carcinoma	23 (48.9%)	5 (17.2%)		
Small-cell lung cancer	2 (4.3%)	13 (44.8%)		
Clinical stage			31.783	<0.001
I–II	1 (2.1%)	6 (20.7%)		
III–IV	44 (93.6%)	10 (34.5%)		
Extensive stage	2 (4.3%)	13 (44.8%)		

AHI, Apnea-hypopnea index; CVD, cardiovascular disease; LC, lung cancer; OSAHS, Obstructive sleep apnea-hypopnea syndrome; SpO_2, Peripheral oxygen saturation; T90%, Percentage of time with SpO_2 below 90%.

than OSAHS-with-concomitant-LC group, but chest circumference, TG, LDL-C, and TC were lowe (all $p < 0.05$). The BMI, systolic blood pressure, diastolic blood pressure, and blood glucose levels in the LC group were lower than those in the OSAHS-with-concomitant-LC group ($p < 0.05$). There were significant differences in PDGF-BB levels among the four groups, with the OSAHS-with-concomitant-LC group having the highest PDGF-BB levels, significantly higher than the other three groups ($p < 0.001$).

Comparison of Serum PDGF Levels in the OSAHS-With-Concomitant-LC, LC, OSAHS, and Healthy Adult Groups

The serum PDGF-BB levels of the four groups are shown in Fig. 1. The healthy adult group was 163.54 (135.92, 204.18) pg/mL, the OSAHS group was 460.30 (373.48, 536.85) pg/mL, the LC group was 83.70 (68.90, 93.95) pg/mL, and the OSAHS-with-concomitant-LC group was 729.85 (488.28, 967.81) pg/mL. There were significant differences ($p < 0.05$) in pairwise comparisons between the groups.

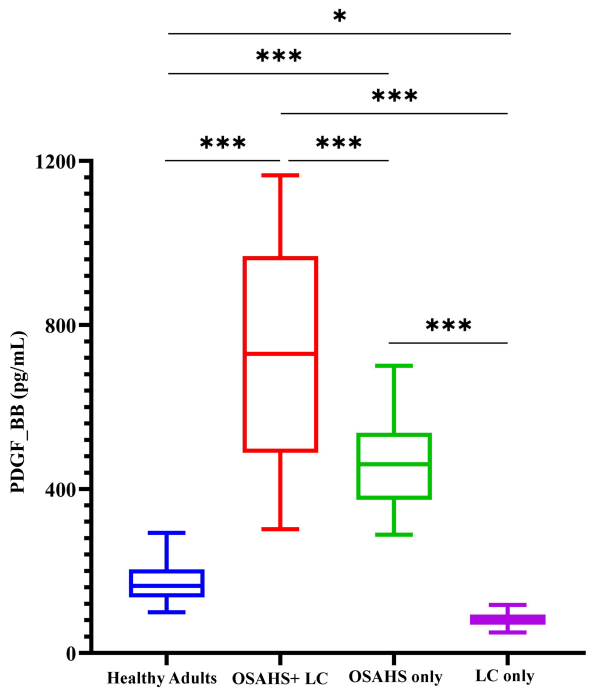

Fig. 1. Comparison of serum PDGF-BB levels in the OSAHS-with-concomitant-LC, LC, OSAHS, and healthy adult groups. *$p < 0.05$, ***$p < 0.001$. PDGF-BB, Platelet-derived growth factor BB; OSAHS, Obstructive sleep apnea-hypopnea syndrome; LC, lung cancer.

Serum PDGF Expression Levels and Their Association With Disease Severity

As shown in Table 2, 47 patients presented with mild-moderate symptoms, including 19 males (40.4%) and 28 females (59.6%), whereas 29 patients had severe symptoms, including 11 males (37.9%) and 18 females (62.1%). There was no statistically significant difference in basic characteristics such as gender, age, BMI, and neck circumference between the two groups ($p > 0.05$). The patients with severe symptoms had chest circumference that was slightly higher than in the mild-moderate group ($p = 0.045$). The severe group had more pronounced nocturnal hypoxia, with significantly lower levels of minimum SpO_2, average SpO_2, and T90% compared to the mild-moderate group ($p < 0.001$). Furthermore, the levels of systolic blood pressure, diastolic blood pressure, serum creatinine, low-density lipoprotein cholesterol, and PDGF-BB were significantly increased in the severe group ($p < 0.05$). In terms of clinical symptoms, the incidence of morning headaches, hypertension, coronary heart disease, surgical history, and medication history was higher in the severe group. At the same time, respiratory symptoms such as cough, sputum production, difficulty breathing, and pleural effusion were more common ($p < 0.05$). LC-related indicators showed that in the severe group, LC was mostly located in the right lung.

As shown in Fig. 2, the serum PDGF levels in the severe group of OSAHS-with-concomitant-LC patients were significantly higher than those in the mild-moderate group [978.49 (924.83, 994.01) vs. 582.00 (387.20, 725.50) pg/mL, $p < 0.001$].

In order to exclude the potential influence of the pathological classification and clinical staging of LC on serum PDGF-BB levels, we conducted grouping comparisons (Fig. 3). The levels of PDGF-BB were significantly higher in SCLC than in adenocarcinoma [978.49 (777.18, 988.55) pg/mL vs. 728.90 (471.70, 927.24) pg/mL, $p = 0.016$] and squamous cell carcinoma [978.49 (777.18, 988.55) pg/mL vs. 705.24 (461.61, 745.25) pg/mL, $p = 0.006$], but no significant difference was observed between adenocarcinoma and squamous cell carcinoma (Fig. 3A). In general, PDGF-BB levels were significantly higher in advanced stages (III–IV) [968.79 ng/L (927.45, 980.87) vs. 698.51 pg/mL (419.50, 731.95), $p < 0.001$]. There was no significant difference between stages I–II and III–IV (Fig. 3B).

We further explored the association between serum PDGF-BB expression levels in OSAHS patients with concomitant LC and the severity indicators of OSAHS. The serum PDGF-BB level was positively correlated with AHI and T90% (Fig. 4A,B) ($p < 0.001$), and negatively correlated with Min SpO_2 and Mean SpO_2 (Fig. 4C,D) ($p < 0.001$).

Discriminative Performance of Serum PDGF Levels for Differentiating the Severity Levels of OSASH Patients With Concomitant LC

ROC curve analysis (Fig. 5) showed that serum PDGF-BB levels in OSAHS had an AUC value of 0.9912 (Bootstrap 95% CI: 0.9736–1.0000, $p < 0.0001$). The optimal cutoff value was 757.7 pg/mL, corresponding to a sensitivity of 100.0% and a specificity of 95.7%. The average AUC across 10-fold cross-validation was 0.987 $\pm$ 0.042, indicating high and consistent discriminative ability.

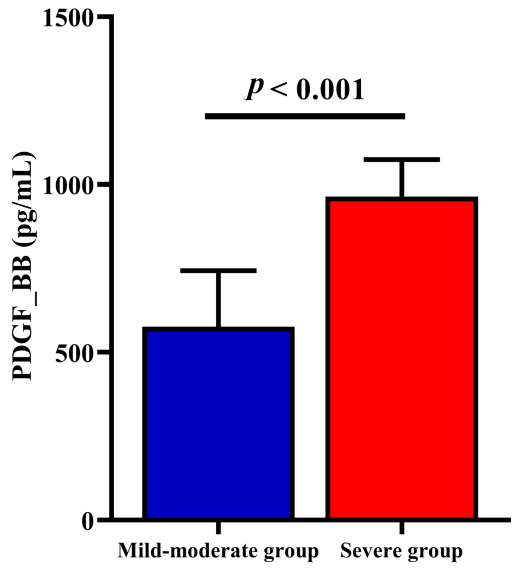

Fig. 2. Comparison of PDGF levels between the mild-moderate and severe groups. PDGF-BB, Platelet-derived growth factor BB.

Discussion

This study investigated the expression characteristics and potential clinical utility of serum PDGF-BB in OSAHS patients with concomitant LC. The results showed that the serum PDGF-BB levels in this population were significantly higher than in patients with OSAHS only, LC only, or healthy adults. PDGF-BB was also positively correlated with severity. In addition, ROC analysis suggested that PDGF-BB exhibited high sensitivity and specificity for distinguishing different stages of OSAHS and for identifying coexisting LC, providing preliminary evidence for the potential application of PDGF-BB as a biomarker in OSAHS patients with concomitant LC.

In this study, PDGF-BB was significantly elevated in OSAHS patients with concomitant LC, revealing its important role in the pathological process. As a key member of the platelet-derived growth factor family, PDGF-BB is widely involved in various physiological and pathological processes such as cell proliferation, migration, angiogenesis, and tissue repair [20,21]. Under intermittent hypoxia conditions, the expression level of PDGF-BB significantly increases, possibly due to the frequent hypoxic events experienced during sleep in OSAHS patients. Due to insufficient oxygen and nutrient supply, reduced coverage around cells can lead to vascular instability and remodeling [22], promoting deep cell necrosis in tumor clusters and further accelerating disease progression. The intermittent hypoxia experienced by OSAHS patients can also trigger various biological reactions, among which oxidative stress and chronic inflammatory response enhancement, immune dysfunction, and loss of homeostasis are the most important pathological features [23]. These factors work together to promote overexpression of PDGF-BB. Specifically, hypoxia promotes oxidative stress response, which generates free radicals, damages cell membranes and DNA, and activates intracellular signaling pathways [24]. Oxidative stress has been found to increase the expression of inflammatory factors such as IL-1β and TNF-α by regulating the NF-κB pathway, which can affect the expression of PDGF-BB [25,26]. In addition, chronic inflammatory response further enhances the role of PDGF-BB in the tumor microenvironment by stimulating the activation of inflammatory and immune cells, promoting tumor angiogenesis and cell migration, and playing a crucial role in the development and metastasis of tumors [27].

In the tumor microenvironment, PDGF-BB can also induce high expression levels of IL-33 in the surrounding cells and stromal cells, leading to the recruitment of a large number of tumor-associated macrophages to respond to the interactions at IL-33-ST2 receptors [28], further promoting disease progression. The elevation of PDGF-BB may also promote tumor growth, angiogenesis, and metastasis by acting on fibroblasts and endothelial cells in the tumor microenvironment, inducing their transformation into tumor-associated fibroblasts [29]. These mechanisms indicate that the elevation of PDGF-BB in OSAHS patients with concomitant LC is not only associated with oxidative stress and chronic inflammatory response, but it also enhances tumor invasiveness and metastasis by promoting changes in the tumor microenvironment, further promoting disease progression.

In this study, the abnormal gender distribution was noteworthy. Generally, OSAHS is considered a disease with a higher prevalence in males. A study reported 27% of women and 43% of men suffer from OSAHS in the 50–70 age group [30]. However, in our study, the proportion of female patients with OSAHS and concomitant LC was higher than that of male patients, in contrast to the existing literature. In recent years, the prevalence of OSA/OSAHS in women may have been underestimated [31]. Central obesity and hormonal status can affect the prevalence of sleep apnea in women, which may impact the diagnosis and severity of OSAHS in female patients [30]. Female OSA/OSAHS patients experience worsening symptoms around the age of 50, and their incidence rate significantly increases with age [32]. In this context, delayed or missed diagnosis is more common among women in clinical practice, which may lead to a higher proportion of female patients undergoing evaluation only when the disease is more advanced or severe. It should be emphasized that the sample size of this study is limited, and the uneven gender distribution may have a certain impact on the correlation analysis between PDGF-BB levels and disease severity, reducing the stability of statistical inference. However, overall, gender differences should be considered in the identification and management of OSAHS, especially in middle-

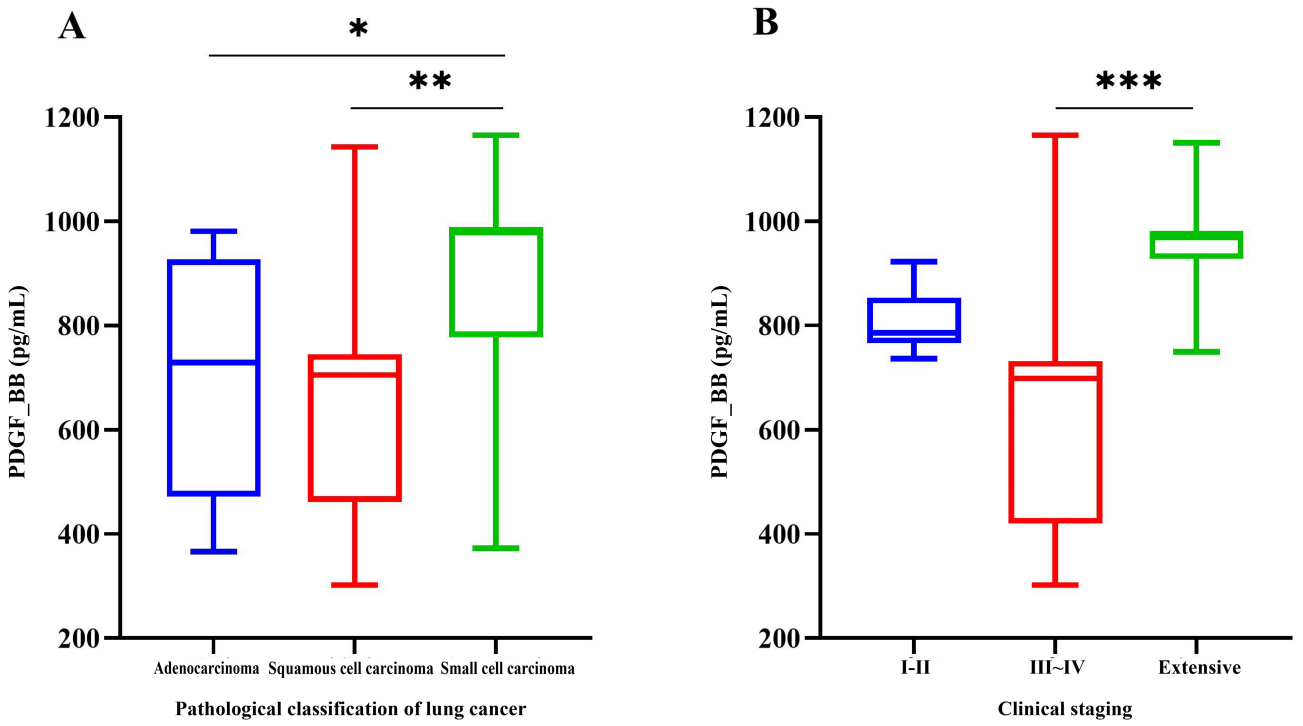

Fig. 3. PDGF levels in various histological subtypes of LC (A) and clinical stages (B). *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$. PDGF-BB, Platelet-derived growth factor BB.

aged and elderly women who may require more sensitive assessment strategies to reduce missed diagnoses and optimize clinical decision-making.

In addition, in this study, we observed that the serum PDGF-BB levels in patients with small cell lung cancer (SCLC) were significantly higher than those in patients with adenocarcinoma and squamous cell carcinoma. SCLC is known for its high invasiveness and strong metastatic ability [33]. It has been reported that patients with SCLC are in the advanced stage, involving metastasis to the contralateral chest cavity, distant organs (such as liver, brain, bone), and contralateral lymph nodes [34]. This finding suggests that high expression of PDGF-BB may be closely related to stronger angiogenesis and tumor progression in SCLC. It should be noted that the number of SCLC cases was only 15, so the relevant findings are still preliminary exploratory results and should be interpreted with caution. Nevertheless, this trend suggests the potential stratification value of PDGF-BB in different pathological types and stages of LC.

The increase in PDGF-BB levels is positively correlated with the severity of OSAHS, further confirming the diagnostic potential of PDGF-BB in clinical practice. ROC curve analysis shows that PDGF-BB has high sensitivity and specificity in distinguishing between different severity levels of OSAHS patients with concomitant LC. This indicates that PDGF-BB can be used as an effective biomarker for the diagnosis and staging of OSAHS. This discovery can help clinicians identify high-risk populations early and initiate continuous positive airway pressure ventilation or other comprehensive interventions in a timely manner to improve patients' oxygenation status and reduce inflammation levels [35]. In addition, accurate stratification of OSAHS severity may also guide other aspects of LC treatment. For example, severe OSAHS patients may have higher perioperative risks or poorer tolerance to treatment during surgical procedures or chemoradiotherapy. Therefore, using the PDGF-BB levels to assess the severity of OSAHS may provide important references for clinical decision-making and further optimize individualized treatment plans.

There are still several limitations to this study. Firstly, as a cross-sectional study, it only measured serum PDGF-BB levels at baseline, and this cannot reflect dynamic changes or determine causal relationships. Secondly, the small sample size of the SCLC subgroup limited the statistical power of subgroup comparisons and may reduce the robustness of the results. In addition, the correlation between PDGF-BB and the severity of OSAHS may have been influenced by factors such as the pathological type, clinical stage, and systemic inflammation of LC, making it difficult to completely rule out confounding factors. Meanwhile, the proportion of women in the OSAHS+LC group in this study was higher than in previous epidemiological data, and the imbalanced sample structure may have affected the extrapolation of the results. It should be emphasized that PDGF-BB, as a biological factor involved in multiple processes such as inflammation, angiogenesis, and tissue repair, is not a specific indicator for OSAHS or LC. The evaluation of its independent diagnostic value in a broader population

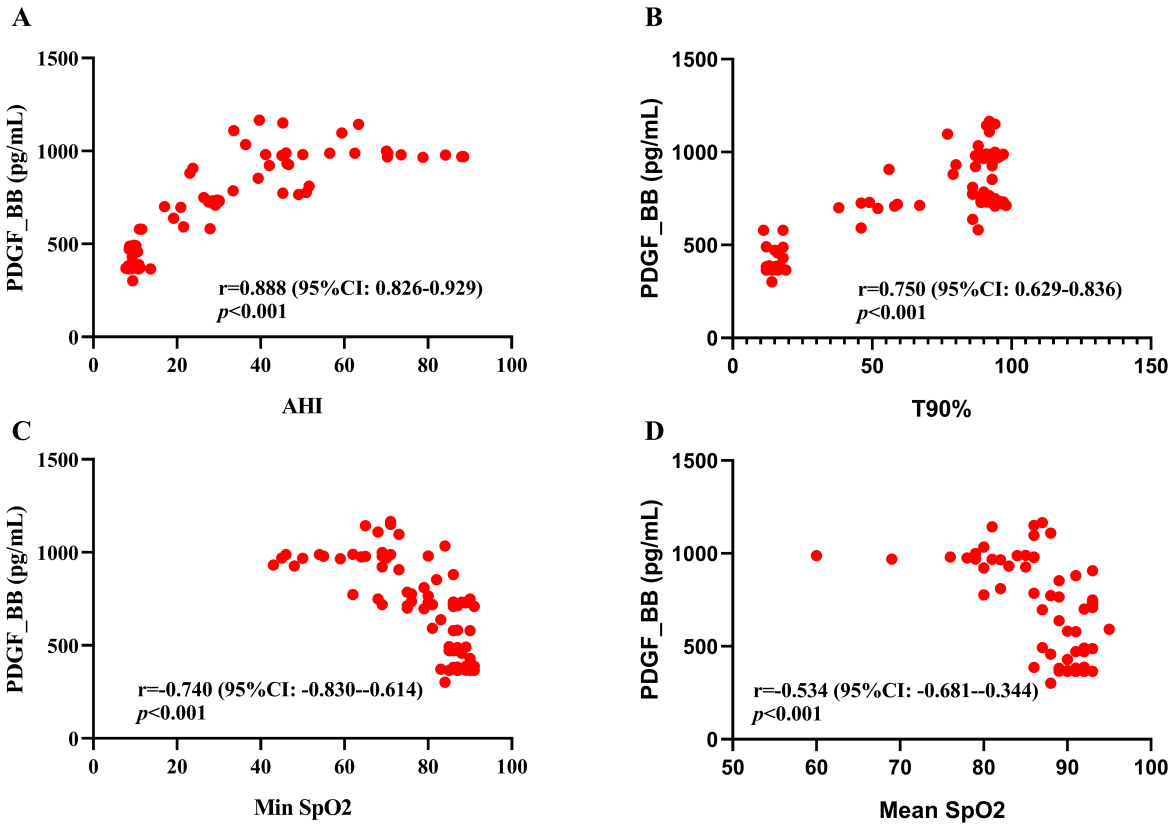

Fig. 4. The correlation between PDGF-BB levels and severity indicators in OSAHS patients with concomitant LC. (A) The correlation between PDGF-BB levels and AHI. (B) The correlation between PDGF-BB levels and T90%. (C) The correlation between PDGF-BB levels and Min SpO_2. (D) The correlation between PDGF-BB levels and Mean SpO_2. AHI, Apnea-hypopnea index; CVD, cardiovascular disease; LC, lung cancer; OSAHS, Obstructive sleep apnea-hypopnea syndrome; PDGF-BB, Platelet derived growth factor BB; SpO_2 Saturation of peripheral oxygen; T90%, Percentage of time with SpO_2 below 90%.

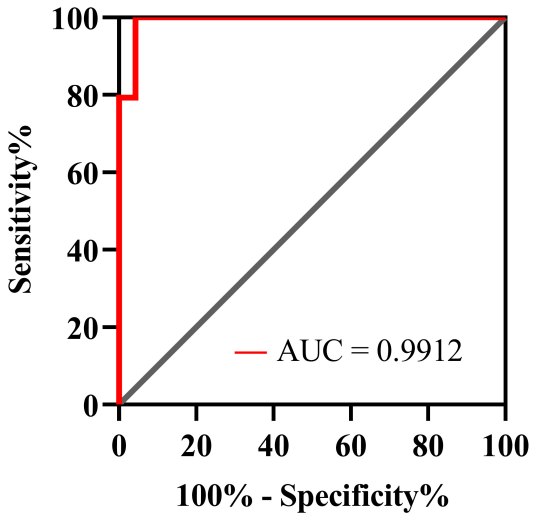

Fig. 5. ROC curve for distinguishing different severity categories of OSAHS patients with concomitant LC using serum PDGF levels. ROC, Receiver operating characteristic.

may be limited; therefore, further validation in conjunction with other clinical indicators or biomarkers is warranted. Finally, the potential mechanism proposed in this study is mainly based on inferences made from the existing literature and lacks experimental verification. In the future, longitudinal studies and mechanistic experiments are needed to further clarify the biological role and clinical application potential of PDGF-BB.

Conclusion

This study indicates that serum PDGF-BB levels are significantly elevated in OSAHS patients with concomitant LC, and can effectively distinguish between mild-moderate and severe patients, suggesting its potential diagnostic and stratification value. The level of PDGF-BB is significantly correlated with severity indicators of OSAHS, such as AHI, T90%, Min SpO_2, and Mean SpO_2, suggesting its possible involvement in disease progression mechanisms. Although this study is limited by a small sample size, cross-sectional design, and a single biomarker, the results still provide a

theoretical basis for applying serum PDGF-BB in OSAHS with concomitant LC, and serve as a reference for future mechanistic research and the development of combined-biomarker diagnostic models.

Availability of Data and Materials

Data are available from the corresponding author upon request.

Author Contributions

XYW, JYM, and WG designed the research study. XYW, JYM, and TW performed the research, collected and analyzed the data, and drafted the manuscript. All authors have been involved in revising it critically for important intellectual content. All authors gave final approval of the version to be published. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

This study was approved by Suqian Hospital of Nanjing Drum-Tower (No. 20220901). All the experiments of this study were conducted in accordance with the relevant guidelines and regulations or the Declaration of Helsinki. Written informed consent was obtained from all participants.

Acknowledgment

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

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