

## Characteristics and Risk Factors of Preserved Ratio Impaired Spirometry in Health Check-up Populations (Postprint)

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### Abstract

**Background:** Preserved Ratio Impaired Spirometry (PRISm) refers to a non-obstructive pulmonary function abnormality where the forced expiratory volume in one second to forced vital capacity ratio (FEV1/FVC) is normal but the forced expiratory volume in one second (FEV1) is reduced. The PRISm population may represent one of the pre-chronic obstructive pulmonary disease (COPD) groups. However, the prevalence, characteristics, and risk factors of PRISm in health examination populations in China remain unclear.

**Objective:** To analyze the characteristics and influencing factors of PRISm in health examination populations.

**Methods:** A total of 970 individuals undergoing health examinations at the Third Medical Center of Chinese PLA General Hospital from January 2017 to December 2019 were selected. General information and physical examination results were collected, and pulmonary function was measured: vital capacity (VC), forced vital capacity (FVC), FEV1, forced expiratory volume in six seconds (FEV6), FEV1/FVC, peak expiratory flow (PEF), forced expiratory flow at 25% of vital capacity (FEF25), forced expiratory flow at 50% of vital capacity (FEF50), forced expiratory flow at 75% of vital capacity (FEF75), with “%pre” indicating the percentage of predicted values for relevant indices. Participants were grouped according to FEV1/FVC and FEV1%pre: FEV1/FVC < 0.7 as the airflow obstruction group (n = 61); FEV1/FVC ≥ 0.7 and FEV1%pre < 0.8 as the PRISm group (n = 111); and FEV1/FVC ≥ 0.7 and FEV1%pre ≥ 0.8 as the normal pulmonary function group (n = 798). The prevalence of PRISm in the health examination population was calculated, basic characteristics and pulmonary function indices were compared among different pulmonary function groups, and ordinal Logistic regression analysis was used to explore influencing factors of pulmonary function impairment.

Results: The prevalence of PRISm was 11.4% (111/970) and airflow obstruction was 6.3% (61/970) in the 970 health examination participants. The proportion of individuals aged > 60 years in both the PRISm and airflow obstruction groups was greater than that in the normal pulmonary function group, while the proportion of individuals aged 41–60 years was smaller than that in the normal pulmonary function group ( $P = 0.019$ ). The proportion of smokers in the PRISm group was greater than that in the normal pulmonary function group ( $P < 0.001$ ). The proportion of individuals with hypertension in the PRISm group was greater than that in the normal pulmonary function group ( $P = 0.03$ ). The normal pulmonary function group had higher VC%pre, FVC%pre, FEV1%pre, FEV6%pre, PEF%pre, FEF25%pre, FEF50%pre, and FEF75%pre than the PRISm and airflow obstruction groups ( $P < 0.001$ ); the PRISm group had higher VC%pre, FVC%pre, FEV6%pre, PEF%pre, FEF25%pre, FEF50%pre, and FEF75%pre than the airflow obstruction group ( $P < 0.05$ ). The normal pulmonary function and PRISm groups had higher FEV1/FVC than the airflow obstruction group ( $P < 0.001$ ). Using different pulmonary function groups as the dependent variable, ordinal Logistic regression analysis revealed that age > 60 years [OR = 0.951, 95%CI (0.602–1.504),  $P = 0.002$ ], smoking history [OR = 2.201, 95%CI (1.519–3.187),  $P < 0.001$ ], and hypertension history [OR = 1.673, 95%CI (1.106–3.187),  $P = 0.015$ ] were risk factors for pulmonary function impairment in health examination populations.

Conclusion: PRISm is prevalent in health examination populations. Individuals aged > 60 years, with a smoking history, and with hypertension should receive focused attention on pulmonary function changes, and early intervention may slow the progression of COPD.

## Full Text

### Characteristics and Risk Factors of Preserved Ratio Impaired Spirometry in Health Check-up Population

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## Abstract

**Background:** Preserved Ratio Impaired Spirometry (PRISm) refers to non-obstructive pulmonary function abnormalities characterized by reduced forced

expiratory volume in one second ( $FEV_1$ ) while the  $FEV_1$ /forced vital capacity (FVC) ratio remains normal. The PRISm population may represent a pre-chronic obstructive pulmonary disease (COPD) cohort. However, the prevalence, characteristics, and risk factors of PRISm among health check-up populations in China remain unclear.

**Objective:** To analyze the characteristics and influencing factors of PRISm in a health check-up population.

**Methods:** A total of 970 individuals who underwent physical examination at the Third Medical Center of Chinese PLA General Hospital between January 2017 and December 2019 were selected. Baseline data and physical examination results were collected. Pulmonary function parameters were measured, including vital capacity (VC), forced vital capacity (FVC),  $FEV_1$ , forced expiratory volume in six seconds ( $FEV_6$ ),  $FEV_1$ /FVC, peak expiratory flow (PEF), forced expiratory flow at 25% of FVC ( $FEF_{25}$ ), forced expiratory flow at 50% of FVC ( $FEF_{50}$ ), and forced expiratory flow at 75% of FVC ( $FEF_{75}$ ). All parameters were expressed as percentages of predicted values (%pre). Participants were divided into three groups based on  $FEV_1$ /FVC and  $FEV_1$ %pre: airflow obstruction group ( $FEV_1$ /FVC < 0.7, n = 61), PRISm group ( $FEV_1$ /FVC  $\geq$  0.7 and  $FEV_1$ %pre < 0.8, n = 111), and normal lung function group ( $FEV_1$ /FVC  $\geq$  0.7 and  $FEV_1$ %pre  $\geq$  0.8, n = 798). The prevalence of PRISm was calculated, baseline characteristics and lung function indices were compared among groups, and ordinal logistic regression analysis was used to identify influencing factors of lung function impairment.

**Results:** The prevalence of PRISm was 11.4% (111/970), and the prevalence of airflow obstruction was 6.3% (61/970). The proportion of individuals aged >60 years was higher in both the PRISm and airflow obstruction groups compared with the normal lung function group, while the proportion aged 41-60 years was lower (P = 0.019). The smoking rate was significantly higher in the PRISm group than in the normal lung function group (P < 0.001). The prevalence of hypertension was also higher in the PRISm group (P = 0.03). All lung function indices (VC%pre, FVC%pre,  $FEV_1$ %pre,  $FEV_6$ %pre, PEF%pre,  $FEF_{25}$ %pre,  $FEF_{50}$ %pre,  $FEF_{75}$ %pre) were higher in the normal lung function group than in the PRISm and airflow obstruction groups (P < 0.001). The PRISm group showed higher values for VC%pre, FVC%pre,  $FEV_6$ %pre, PEF%pre,  $FEF_{25}$ %pre,  $FEF_{50}$ %pre, and  $FEF_{75}$ %pre compared with the airflow obstruction group (P < 0.05).  $FEV_1$ /FVC was higher in both the normal lung function and PRISm groups than in the airflow obstruction group (P < 0.001). Ordinal logistic regression analysis, with lung function group as the dependent variable, revealed that age >60 years [OR = 0.951, 95%CI (0.602-1.504), P = 0.002], smoking history [OR = 2.201, 95%CI (1.519-3.187), P < 0.001], and hypertension history [OR = 1.673, 95%CI (1.106-3.187), P = 0.015] were risk factors for lung function impairment in the health check-up population.

**Conclusion:** PRISm is common among health check-up populations. Special attention should be paid to lung function changes in individuals aged >60 years,

those with smoking history, and those with hypertension. Early intervention may slow the progression of COPD.

**Keywords:** PRISm; Lung function; Health check-up population; Physical examination; Influencing factor analysis

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## 1. Subjects and Methods

Chronic obstructive pulmonary disease (COPD) is a common chronic disease and the third leading cause of death worldwide after ischemic heart disease and stroke [1]. The prevalence of COPD among individuals over 40 years old in China is as high as 13.7% [2]. Underdiagnosis of COPD may result from limited public awareness, low utilization of pulmonary function testing, and missed diagnoses [3]. Pulmonary function testing is a recognized and valuable tool for early identification of individuals with airflow obstruction and increased risk of COPD [4].

Preserved Ratio Impaired Spirometry (PRISm) is a common but clinically overlooked state of lung function impairment, defined as non-obstructive pulmonary function abnormality with normal  $FEV_1/FVC$  ratio ( $\geq 0.7$ ) but reduced  $FEV_1$  ( $< 80\%$  predicted) [5]. Although it does not meet the diagnostic criteria for COPD, PRISm is associated with increased risks of chronic respiratory symptoms and all-cause mortality, suggesting that PRISm may represent a pre-COPD population [6-7]. The prevalence and characteristics of PRISm among health check-up populations in China remain unclear. Therefore, this retrospective study analyzed the prevalence, characteristics, and risk factors of PRISm in a health check-up population to enable early identification of individuals with impaired lung function and provide evidence for prevention and treatment of pre-COPD populations.

### 1.1 Study Subjects

A total of 970 individuals who underwent physical examination at the Third Medical Center of Chinese PLA General Hospital between January 2017 and December 2019 were selected. Inclusion criteria: complete clinical data; pulmonary function test quality grade B or above. Exclusion criteria: neuromuscular disease, cardiac insufficiency, chronic pulmonary heart disease, pulmonary or abdominal surgery; incomplete clinical data; duplicate annual examinations. This study was approved by the Ethics Committee of the Third Medical Center of Chinese PLA General Hospital [Ethics Review No. (2022-033)], and all participants provided informed consent.

Participants were divided into three groups based on  $FEV_1/FVC$  and  $FEV_1\%pre$ : airflow obstruction group ( $FEV_1/FVC < 0.7$ ,  $n = 61$ ), PRISm group ( $FEV_1/FVC \geq 0.7$  and  $FEV_1\%pre < 0.8$ ,  $n = 111$ ), and normal lung function group ( $FEV_1/FVC \geq 0.7$  and  $FEV_1\%pre \geq 0.8$ ,  $n = 798$ ).

According to the “Guidelines for Prevention and Control of Overweight and Obesity in Chinese Adults (Excerpt)” [8], body mass index (BMI) was categorized as normal ( $18.5 < \text{BMI} < 24 \text{ kg/m}^2$ ), overweight ( $24 < \text{BMI} < 28 \text{ kg/m}^2$ ), and obese ( $\text{BMI} \geq 28 \text{ kg/m}^2$ ).

## 1.2 Methods

Baseline survey included: (1) General data: gender, age, medical history (hypertension, coronary heart disease, diabetes, stroke, etc.), and smoking history [9] defined as regular smoking for at least ten years before the examination with a cumulative total of  $\geq 100$  cigarettes. (2) Physical examination: height, weight, and BMI calculation. (3) Pulmonary function measurement: vital capacity (VC), forced vital capacity (FVC),  $FEV_1$ , forced expiratory volume in six seconds ( $FEV_6$ ),  $F_{25-75}$  were used to evaluate small airway function.

## 1.3 Quality Control of Lung Function Measurement

All pulmonary function tests were performed by a fixed operator who thoroughly reviewed medical histories and excluded contraindications. According to the Pulmonary Function Testing Guidelines [11], test results were graded as quality level B when the difference between the best two  $FEV_1$  and FVC values among three acceptable tests was within 0.200 L. Only tests with quality grade B or above were included.

## 1.4 Statistical Methods

SPSS 22.0 software was used for statistical analysis. Normally distributed continuous data were expressed as mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ) and compared among groups using analysis of variance, with pairwise comparisons performed using LSD-t tests. Categorical data were expressed as relative frequencies and compared using  $\chi^2$  tests. Ordinal logistic regression analysis was used to identify factors influencing lung function impairment.  $P < 0.05$  was considered statistically significant.

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## 2. Results

### 2.1 Basic Characteristics

The 970 participants ranged in age from 18 to 80 years, including 752 males and 218 females. The prevalence of PRISM was 11.4% (111/970), and the prevalence of airflow obstruction was 6.3% (61/970).

### 2.2 Comparison of General Data Among Groups

Significant differences were observed among the three groups in age distribution, smoking history, and hypertension prevalence ( $P < 0.05$ ). The airflow obstruction

tion group had a lower proportion of individuals aged <40 years compared with the normal lung function and PRISm groups. The PRISm group had a lower proportion of individuals aged 41-60 years compared with the normal lung function group, while both the PRISm and airflow obstruction groups had higher proportions of individuals aged >60 years compared with the normal lung function group ( $P < 0.05$ ). The smoking rate was higher in both the PRISm and airflow obstruction groups compared with the normal lung function group ( $P < 0.05$ ). The prevalence of hypertension was also higher in the PRISm and airflow obstruction groups compared with the normal lung function group ( $P < 0.05$ ). No significant differences were found in gender distribution, coronary heart disease prevalence, diabetes prevalence, stroke prevalence, or BMI among the three groups ( $P > 0.05$ ). See Table 1 .

### 2.3 Comparison of Lung Function Indices Among Groups

Significant differences were observed among the three groups in VC%pre, FVC%pre, FEV<sub>1</sub>%pre, FEV<sub>6</sub>%pre, PEF%pre, FEF<sub>25</sub>%pre, FEF<sub>50</sub>%pre, and FEF<sub>75</sub>%pre ( $P < 0.001$ ). The normal lung function group showed higher VC%pre than both the PRISm and airflow obstruction groups ( $P < 0.001$ ), while the PRISm group had higher VC%pre than the airflow obstruction group ( $P < 0.05$ ). The normal lung function group also demonstrated higher FVC%pre than the PRISm and airflow obstruction groups ( $P = 0.005$ ), with the PRISm group showing higher FVC%pre than the airflow obstruction group ( $P < 0.001$ ). FEV<sub>1</sub>%pre was higher in the normal lung function group compared with the PRISm and airflow obstruction groups ( $P < 0.001$ ). FEV<sub>1</sub>/FVC was higher in both the normal lung function and PRISm groups compared with the airflow obstruction group ( $P < 0.001$ ). The normal lung function group exhibited higher FEV<sub>6</sub>%pre than the PRISm and airflow obstruction groups ( $P = 0.001$ ), while the PRISm group showed higher FEV<sub>6</sub>%pre than the airflow obstruction group ( $P < 0.001$ ). Additionally, the normal lung function group had higher PEF%pre, FEF<sub>25</sub>%pre, FEF<sub>50</sub>%pre, and FEF<sub>75</sub>%pre than the PRISm and airflow obstruction groups ( $P < 0.001$ ), and the PRISm group showed higher values for these parameters than the airflow obstruction group ( $P < 0.001$ ). See Table 2 .

### 2.4 Ordinal Logistic Regression Analysis of Risk Factors for Lung Function Impairment

Using lung function group as the dependent variable (airflow obstruction group = 1, PRISm group = 2, normal lung function group = 3) and gender (male = 1, female = 2), age (>60 years = 1, 41-60 years = 2, ≤40 years = 3), hypertension (yes = 1, no = 2), coronary heart disease (yes = 1, no = 2), diabetes (yes = 1, no = 2), stroke (yes = 1, no = 2), smoking history (yes = 1, no = 2), and BMI (obese = 1, overweight = 2, normal = 3) as independent variables, ordinal logistic regression analysis revealed that age >60 years [OR = 0.951, 95%CI (0.602-1.504),  $P = 0.002$ ], smoking history [OR = 2.201, 95%CI (1.519-3.187),

$P < 0.001$ ], and hypertension history [OR = 1.673, 95%CI (1.106–3.187),  $P = 0.015$ ] were risk factors for lung function impairment in the health check-up population. See Table 3 .

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## Discussion

PRISm is prevalent in the general population, and its prevention and control depend on the identification of high-risk factors. This study found that lung function impairment is common among health check-up populations, with 11.4% exhibiting PRISm and 6.3% showing airflow obstruction. Although research on PRISm remains limited in China, international studies have reported varying prevalence rates: 16.7% among Japanese aged  $\geq 40$  years in the OCEAN study [12], 7.1% among Europeans aged  $>45$  years in the ROTTERDAM study [13], and 11% among UK Biobank participants aged 40–69 years [14]. Despite differences in geography, age, and ethnicity, PRISm is consistently prevalent across populations. WIJNANT et al. [13] reported that the mortality rate in the PRISm group was 18.7%, only slightly lower than the 20.8% in the COPD group and significantly higher than the 10.3% in the normal airflow group, suggesting that PRISm may represent an important stage in COPD development.

This study demonstrated that the proportion of individuals aged  $>60$  years was significantly higher in the PRISm group than in the normal lung function group, and age  $>60$  years was identified as a risk factor for lung function impairment. Research indicates that FEV<sub>1</sub> and FVC decline with age in healthy adults, with FEV<sub>1</sub> showing a more pronounced decrease [15], attributable to age-related changes in thoracic shape, respiratory muscle strength, and lung elastic recoil [16]. Consequently, both PRISm and airflow obstruction may be more likely to occur in older populations.

The smoking rate was higher in the PRISm group compared with the normal lung function group, and ordinal logistic analysis identified smoking as a factor exacerbating lung function injury. The Korea National Health and Nutrition Examination Survey found a higher smoking rate in the PRISm group compared with controls, suggesting smoking as a risk factor for PRISm [17], consistent with our findings. Smoking can cause airway inflammation, bronchial hyperresponsiveness, and alveolar structural damage leading to emphysema and COPD. Studies have shown that smoking not only accelerates lung function decline in healthy adults but also accelerates disease progression in COPD patients [18].

This study also found that the prevalence of hypertension was higher in both the PRISm and airflow obstruction groups compared with the normal lung function group, with hypertension identified as a risk factor for lung function injury. Research has demonstrated an inverse correlation between FEV<sub>1</sub> and blood pressure, with each 10% decrease in FEV<sub>1</sub> associated with a 1.8% increased risk of hypertension [19]. Inflammation, endothelial dysfunction, and hypoxia

may contribute to both lung function decline and hypertension, representing potential mechanisms for their interplay [20].

Our results showed no significant correlation between BMI and lung function impairment. However, other studies have identified low BMI, overweight, or obesity as risk factors for PRISm [6, 12], possibly through metabolic and inflammatory effects of adipose tissue (high BMI) or impaired lung growth and development (low BMI). A prospective study of Chinese community populations found no statistical difference in BMI between PRISm and control groups [21], possibly due to differences in study populations, ethnicity, and sample sizes. In our study, the majority of participants had BMI  $>18.5$  kg/m<sup>2</sup>.

Regarding flow parameters, no significant difference in FEV<sub>1</sub>/FVC was observed between the PRISm and normal lung function groups, but FEV<sub>1</sub>%pre and FVC%pre differed significantly, possibly because FEV<sub>1</sub> and FVC decline proportionally in PRISm, making the impairment less apparent. Between the PRISm and airflow obstruction groups, FEV<sub>1</sub>%pre showed similar changes, while FVC%pre and FEV<sub>1</sub>/FVC differed, suggesting PRISm may represent a distinct stage in COPD development. The COPDGene study found that 22.2% of subjects diagnosed with PRISm transitioned to GOLD stage 0, while 25% progressed to GOLD stages 1-4 after 5-year follow-up [22]. Additionally, our results showed that while FEV<sub>1</sub>%pre did not differ between PRISm and airflow obstruction groups, FEV<sub>6</sub>%pre showed significant differences, suggesting FEV<sub>6</sub>%pre may be more sensitive than FEV<sub>1</sub>%pre. Some studies have highlighted the importance of FEV<sub>6</sub> in COPD diagnosis or early screening [23-24].

Our results also demonstrated differences in small airway indices (PEF%pre, FEF<sub>25</sub>%pre, FEF<sub>50</sub>%pre, FEF<sub>75</sub>%pre) among the three groups. Moreover, three of these indices were  $<80\%$  in the PRISm group, while all four were  $<60\%$  in the airflow obstruction group, indicating that both groups already exhibited small airway dysfunction. Recent SPIROMICS cohort studies have shown that low FEF<sub>25</sub>%pre-FEF<sub>75</sub>%pre correlates with COPD severity [25], suggesting that small airway function represents an earlier and more sensitive indicator of airway disease, though it is often overlooked clinically due to the absence of obvious symptoms.

In conclusion, PRISm is prevalent among health check-up populations but is often clinically overlooked. Special attention should be paid to lung function in older individuals, smokers, and those with hypertension. Early intervention may slow COPD progression.

This study has several limitations. As a retrospective analysis based on existing clinical data, the study population's age, gender, BMI, and comorbidities may differ from the general population. Future multicenter, large-sample, prospective studies are needed to validate our findings.

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**Author Contributions:** SHANG Jimmeng contributed to study conception, data analysis and interpretation, statistical processing, and manuscript writing. DENG Xiaowei contributed to data collection, manuscript revision, and quality control.

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