Current Status, Challenges, and Coping Strategies for Populations with Impaired Lung Function and Normal FEV1/FVC Ratio: A Preprint

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Abstract

The population with preserved ratio impaired spirometry (PRISm) represents a high-risk group for developing chronic obstructive pulmonary disease (COPD). This population exhibits diverse clinical characteristics and developmental trajectories, and is closely associated with various systemic comorbidities and poor prognoses. Currently, research on PRISm both domestically and internationally remains in the exploratory stage. Due to insufficient understanding of PRISm—such as the lack of standardized clinical phenotyping, imaging assessment, precise diagnosis, and prevention and treatment strategies—it is easily overlooked or confused with other common respiratory and comorbid diseases, leading many patients to miss opportunities for early intervention. General practitioners should not only focus on whether a patient has PRISm but also pay full attention to its clinical heterogeneity, mechanistic relationships with comorbidities, early imaging features, and potential detection targets. Furthermore, greater emphasis should be placed on community screening and the management of comorbidities in the PRISm population. This article reviews the current status, challenges, and coping strategies regarding PRISm.

Full Text

Preamble

Research Progress on the Application of Machine Learning in the Diagnosis and Treatment of Diabetic Foot

Abstract

Diabetic foot (DF) is one of the most serious chronic complications of diabetes mellitus, characterized by high morbidity, high disability, and high mortality rates. Early diagnosis and precise treatment are essential for improving patient

prognosis. In recent years, the rapid development of machine learning (ML) has provided new technical support for the clinical management of DF. This article reviews the current application status of ML in the diagnosis and treatment of DF, specifically focusing on its roles in risk prediction, wound image recognition, classification and staging, and treatment outcome prediction. By analyzing the advantages and limitations of existing research, this review aims to provide a reference for the further integration of ML into the clinical management of diabetic foot.

1. Introduction

Diabetic foot (DF) refers to lower extremity infection, ulceration, and/or deep tissue destruction caused by neuropathy and peripheral vascular disease in patients with diabetes. According to global statistics, the lifetime risk of developing a foot ulcer in patients with diabetes is as high as 19% to 34%. If not treated effectively in the early stages, DF can lead to amputation or even death, imposing a heavy economic burden on families and society.

Traditional clinical diagnosis and treatment of DF rely heavily on the experience of clinicians and subjective assessments, which may lead to delayed diagnosis or inconsistent treatment plans. Machine learning (ML), as a core branch of artificial intelligence, possesses powerful data processing and pattern recognition capabilities. By learning from large-scale clinical data, ML can assist physicians in making more objective and accurate clinical decisions.

2. Application of Machine Learning in DF Risk Prediction

Early identification of high-risk patients is the key to preventing DF. ML models can integrate multi-dimensional data, such as demographic characteristics, laboratory indicators, and lifestyle habits, to construct risk prediction models.

Commonly used algorithms include Logistic Regression (LR), Support Vector Machines (SVM), Random Forests (RF), and Gradient Boosting Decision Trees (GBDT). Studies have shown that ML-based prediction models significantly outperform traditional risk scoring systems (such as the IWGDF risk stratification) in terms of sensitivity and specificity. For instance, by analyzing variables such as glycated hemoglobin (HbA_{1c}), duration of diabetes, and presence of peripheral neuropathy, ML models can accurately predict the probability of a patient developing a foot ulcer within the next 1-3 years.

3. Application in

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Preserved Ratio Impaired Spirometry (PRISm) represents a high-risk population for the development of Chronic Obstructive Pulmonary Disease (COPD). This group exhibits distinct clinical characteristics and developmental trajectories, and is closely associated with various systemic comorbidities and adverse prognoses. Currently, research on PRISm both domestically and internationally remains in the exploratory stage. Due to an insufficient understanding of PRISm—including the lack of standardized clinical phenotyping, radiographic assessment, precise diagnostic criteria, and prevention strategies—this condition is easily overlooked or confused with other common respiratory and comorbid diseases. Consequently, many patients miss the opportunity for early intervention. General practitioners must not only identify whether a patient has PRISm but also pay close attention to its clinical heterogeneity, mechanistic relationships with comorbidities, early radiographic features, and potential diagnostic biomarkers. Furthermore, emphasis should be placed on community screening and the management of comorbidities within the PRISm population. This article reviews the current status, challenges, and coping strategies regarding PRISm.

Keywords: Pulmonary Disease, Chronic Obstructive; Preserved Ratio Impaired Spirometry; Screening; Review

1 Introduction

Preserved Ratio Impaired Spirometry (PRISm) is defined by a normal forced expiratory volume in 1 second (FEV_1) to forced vital capacity (FVC) ratio ($FEV_1/FVC \geq 0.70$) but a reduced FEV_1 ($< 80\%$ of the predicted value). As a transitional state of lung function, PRISm is increasingly recognized as a critical precursor to Chronic Obstructive Pulmonary Disease (COPD). Despite its prevalence, the clinical significance of PRISm has historically been underestimated, often categorized simply as a "restrictive" pattern or dismissed as non-pathological.

Recent longitudinal studies have demonstrated that PRISm is not a stable state; individuals with PRISm exhibit high rates of progression to airflow obstruction, increased respiratory symptom burden, and higher all-cause mortality compared to those with normal spirometry. However, the clinical management of PRISm faces significant hurdles. The lack of unified diagnostic standards, the heterogeneity of its clinical presentation, and the complexity of its systemic comorbidities make early identification and intervention challenging in primary care settings.

2 Current Situation of PRISm

2.1 Epidemiology and Clinical Trajectories

The prevalence of PRISm varies across different populations, typically ranging from 7% to 20% in general population cohorts. Research indicates that the PRISm population is highly dynamic. While some individuals may return to normal lung function, a significant proportion transitions to COPD over time. This instability underscores the need for longitudinal monitoring rather than cross-sectional assessment.

2.2 Clinical Heterogeneity

PRISm is characterized by significant clinical heterogeneity. Patients often present with increased breathlessness, reduced exercise capacity, and a higher frequency of respiratory exacerbations. Unlike classic COPD, PRISm is frequently associated with metabolic syndrome, obesity, and cardiovascular diseases, suggesting that systemic inflammation and extrapulmonary factors play a substantial role in its pathogenesis.

3 Challenges in PRISm Management

3.1 Diagnostic Ambiguity and Misclassification

One of the primary challenges is the lack of a standardized definition. While the $FEV_1/FVC \geq 0.70$ and $FEV_1 < 80\%$ predicted criteria are widely used, variations in reference equations and the use of the Lower Limit of Normal (LLN) versus fixed ratios can lead to different classifications. Furthermore, PRISm is often confused with restrictive lung disease, although many PRISm patients do not exhibit true restriction when total lung capacity is measured.

3.2 Limitations in Radiographic and Biomarker Assessment

Early structural changes in PRISm are often subtle. Conventional imaging may fail to capture the early stages of small airway disease or vascular remodeling associated with this state. There is a critical need for more sensitive imaging techniques and validated biological markers to predict which PRISm individuals are at the highest risk for rapid lung function decline.

4 Coping Strategies and the Role of General Practitioners

4.1 Community-Based Screening

General practitioners (GPs) are at the forefront of early detection. Implementing targeted spirometry screening in community health centers for high-risk individuals—such as smokers, those with occupational exposures, and patients with metabolic comorbidities—is essential for identifying PRISm early.

4.2 Integrated Management of Comorbidities

Given the strong link between PRISm and systemic conditions, management should not be limited to the respiratory system. A holistic approach that includes weight management, cardiovascular risk reduction, and physical activity counseling is vital. GPs should focus on "multimorbidity management" rather than treating PRISm in isolation.

4.3 Longitudinal Follow-up and Early Intervention

Regular monitoring of lung function is necessary to track the developmental trajectory of PRISm patients. Early interventions, including smoking cessation, pulmonary rehabilitation, and potentially pharmacological therapies (though further clinical trials are needed), should be considered to slow the progression toward overt COPD.

5 Conclusion

PRISm is a complex and heterogeneous state that serves as a critical window for the prevention of chronic respiratory failure. Addressing the challenges of PRISm requires a shift from reactive treatment

Abstract

The preserved ratio impaired spirometry (PRISm) population is a high-risk group for chronic obstructive pulmonary disease (COPD), with different clinical characteristics and development trajectories, closely related to various systemic comorbidities and poor prognosis. Currently, researches on PRISm are still in the exploratory stage both domestically and internationally. Due to insufficient understanding of PRISm, such as the lack of standardized clinical classification, imaging evaluation, accurate diagnosis, and prevention and treatment strategies, it is easily overlooked or confused with other common respiratory and comorbidities, resulting in many patients missing the opportunity for early intervention. General practitioners should not only pay attention to the patients with PRISm, but also fully consider their clinical heterogeneity, mechanism relationship with comorbidities, early imaging features, and potential detection targets. They should also focus on community screening of PRISm population and management of comorbidities. This article provides an overview of the current status, challenges, and response strategies of PRISm.

Key words Pulmonary disease, chronic obstructive; Preserved ratio impaired spirometry; Mass Screening; Review ZHAO J Y, FAN J, YU D H. The current situation, challenges, and coping strategies of preserving ratio impaired spirometry[J]. Chinese General Practice, 2026.[Epub ahead of print] Editorial Office of Chinese General Practice.

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The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2023 report (hereafter referred to as GOLD 2023) formally introduced the concept of Preserved Ratio Impaired Spirometry (PRISm). This condition is defined by a post-bronchodilator ratio of forced expiratory volume in the first second to forced vital capacity (FEV_1/FVC) ≥ 0.7, yet accompanied by impaired ventilatory function, specifically an FEV_1 percentage of predicted value (FEV_1%pred) $< 80\%$. In its early stages, the PRISm population often presents with subtle, non-specific clinical symptoms. It is widely regarded as a transitional state toward chronic obstructive pulmonary disease (COPD), characterized by a proportional decline in both FEV_1 and FVC that maintains the FEV_1/FVC ratio within the reference range.

The GOLD 2024 report further emphasizes that PRISm is not a stable phenotype; its developmental trajectory is heterogeneous, with some individuals reverting to normal lung function while others progress to obstructive ventilatory dysfunction. GOLD identifies the PRISm population as a high-risk subgroup for the progression of COPD. Research indicates that a significant portion of individuals with PRISm will evolve into clinical COPD within 4 to 5 years [**?**]. Furthermore, this condition is significantly associated with increased morbidity from COPD-related complications and higher all-cause mortality rates. Consequently, early identification and intervention in the PRISm population are expected to reduce the risk of all-cause mortality and facilitate the "early prevention, diagnosis, and treatment" of these individuals [**?**].

In recent years, a growing body of evidence has demonstrated that PRISm is not only linked to respiratory diseases but is also closely associated with various systemic comorbidities. This article provides a comprehensive review of the current status, challenges, and management strategies regarding PRISm.

1 PRISm

Prevalence and Risk Factors of PRISm

The prevalence of Preserved Ratio Impaired Spirometry (PRISm) varies significantly across different regions. Research data from South America, the United States, and Denmark indicate prevalence rates of 5.0%, 17.3%, and 10.0%, respectively [**?**, **?**, **?**]. In Asian countries such as South Korea and Japan, reported PRISm prevalence rates are 8.9% and 20.1%, respectively. Currently, authoritative large-scale clinical studies, primarily the NHLBI study and the COPDGene study in the United States, show that the incidence of PRISm ranges from 8.5% to 12.5%. Data from the UK Biobank, covering 351,874 samples, reported a PRISm incidence of 11%, while the KNHANES study in South Korea suggested a prevalence of 6.74%. According to the China Pulmonary Health (CPH) study led by Academician Wang Chen, the prevalence of PRISm in China is 12.4%. At present, China still lacks large-sample, multicenter, long-term follow-up cohort

studies regarding the prevalence of PRISm.

The pathogenic mechanisms of PRISm remain elucidated. Current perspectives focus on small airway functional impairment and reduced total lung capacity resulting from inflammatory injury and tissue remodeling/repair. Some scholars also suggest that the upregulation or downregulation of key sites within the TGF-β pathway makes premature infants with bronchopulmonary dysplasia more susceptible to PRISm. Multiple studies in Europe and the United States have identified increased BMI, low body weight, female sex, current smoking status, history of asthma, body fat percentage, and serum expression levels of IL-6 and GDF-15 as risk factors for PRISm [**?**, **?**, **?**]. Research from Japan indicates that advanced age, increased BMI, and pre-existing lung diseases (such as interstitial pneumonia) are associated with the occurrence of PRISm, while renal insufficiency and cardiovascular disease significantly increase the mortality risk and all-cause mortality associated with PRISm. Investigations in South Korea show a higher prevalence among women, suggesting that gender is a risk factor contributing to prevalence differences. A meta-analysis of 33 studies found that PRISm prevalence is higher in low- and middle-income countries, and comorbid hyperglycemia is a significant risk factor associated with the condition. Currently, most research data come from prospective studies in Europe, the United States, Japan, and South Korea. Research identifying and targeting PRISm risk factors in China is relatively rare, particularly subgroup analyses concerning ethnicity, regional differences, clinical phenotyping, outcomes, and genomics. Further in-depth research in these areas is required.

Studies have found that all-cause mortality in the PRISm population shows a continuous upward trend, and the risk of death from related cardiovascular diseases is also significantly increased. Wan et al. and Kanetake et al. reported a significant correlation between the PRISm population and respiratory disease-related mortality. Furthermore, multiple studies have emphasized that the PRISm population exhibits higher all-cause mortality, respiratory mortality, and coronary heart disease mortality; PRISm is also associated with respiratory-related events and coronary heart disease events [**?**, **?**]. These findings highlight that the survival rate of the PRISm population is closely linked to their comorbidities. It is necessary to conduct deeper research into the underlying mechanisms between PRISm and its comorbidities to develop effective intervention strategies.

2 PRISm

Relationship Between PRISm and Comorbidities

In terms of clinical respiratory symptoms, individuals with Preserved Ratio Impaired Spirometry (PRISm) exhibit a higher probability of experiencing chronic bronchitis symptoms, such as cough, sputum production, and wheezing, as well as dyspnea. These individuals also report higher scores on the St. George' s Respiratory Questionnaire (SGRQ) and the modified Medical Research Council

(mMRC) dyspnea scale. Physiologically, their total lung capacity (TLC), vital capacity (VC), and inspiratory capacity (IC) are lower than those of individuals with normal lung function, while ventilatory function and small airway function show mild impairment. During exercise, the dyspnea/oxygen uptake ratio is higher, the increase in the tidal volume/inspiratory capacity ratio is more pronounced, and the 6-minute walk distance (6MWD) is significantly shorter [**?**]. These clinical manifestations are consistent with the characteristics of airway inflammation and Chronic Obstructive Pulmonary Disease (COPD).

In recent years, numerous studies have demonstrated that PRISm is not only associated with respiratory diseases but is also closely linked to various systemic comorbidities and adverse prognoses. Research indicates that compared to individuals with normal lung function, comorbidities are more common in the PRISm population, including aging, obesity, hypertension, diabetes, heart failure, coronary artery disease, stroke, and chronic kidney disease [**?**, **?**, **?**]. Further studies have confirmed a significantly higher incidence of comorbid diseases in the PRISm population; subjects with PRISm have an average of 2.45 comorbidities, which is higher than both the normal lung function group (2.1) and the COPD group (2.03). Among these, hypertension is the most common, followed by obesity, hypercholesterolemia, and diabetes. Furthermore, the exacerbation of these comorbidities is associated with an increased risk of mortality. For the PRISm population, it is necessary not only to focus on clinical respiratory features but also to strengthen the identification and treatment of comorbidities to manage multiple conditions more comprehensively and improve quality of life. Many studies have found a negative correlation between lung function and obesity or fat distribution, specifically regarding obesity-related indicators (weight, BMI) and fat distribution metrics (waist circumference, waist-to-height ratio, waist-to-hip ratio, body fat percentage, and skinfold measurements).

Research has found that the prevalence of PRISm increases significantly in patients with a higher BMI, which is consistent with the results of the COPDGene study [**?**, **?**]. This may be due to the direct impact of obesity on lung function through several pathways: (1) Fat accumulation in the chest or on the diaphragm restricts the descent of the diaphragm during deep inspiration, mechanically interfering with normal diaphragmatic movement. (2) Fat deposition between the muscles and ribs reduces chest wall compliance, thereby increasing the respiratory load in obese individuals. (3) Increased peripheral airway obstruction in obese patients leads to chronic hypoxia and activates the sympathetic nervous system, which increases pulmonary vascular resistance and results in reduced lung air volume. Notably, while obesity can physiologically explain PRISm, its relationship with PRISm prevalence appears contradictory in different regions. Studies in Europe and the United States show that PRISm prevalence is heavily influenced by obesity, whereas Japanese research found that a low BMI is a risk factor for PRISm progressing to COPD. This discrepancy in research results may be because patients in UK and European studies are typically more obese with less emphysema, while the emphysematous and lean phenotypes are more common in East Asian studies.

The COPDGene study indicated that elevated blood glucose is a risk factor for the occurrence of PRISm ($OR = 1.372$, $95\%CI = 1.111$–1.695), with the prevalence of diabetes in PRISm individuals being approximately twice that of those with normal lung function (21.6% vs. 11.6%, $P < 0.05$). Both epidemiological and clinical studies have shown that decreased lung function in adults with diabetes increases the likelihood of PRISm. Some scholars also suggest that abnormal lung function may precede the appearance of impaired glucose tolerance. In recent years, research has revealed significant genetic correlations between Type 2 diabetes and its related markers—including fasting insulin and glycated hemoglobin ($HbA1c$)—and lung function parameters such as FEV_1, FVC, and the FEV_1/FVC ratio [**?**, **?**]. Patients with a high genetic susceptibility to Type 2 diabetes often show a significant correlation with decreased FEV_1 and FVC and an increased FEV_1/FVC ratio, which is closely related to the increased incidence of PRISm. The mechanisms by which diabetes leads to PRISm may include: parenchymal damage and pulmonary fibrosis caused by oxidative stress [**?**]; changes in alveolar capillaries, pulmonary arterioles, and microvessels; chronic inflammation; autonomic nervous system dysfunction of the respiratory muscles; and reduced elastic recoil of lung tissue caused by pulmonary collagen glycosylation [**?**]. However, further research is still needed to clarify the specific roles of these factors in the development of PRISm.

PRISm and Cardiovascular/Cerebrovascular Diseases

Many previous studies have elucidated a clear link between lung function and cardiovascular disease [**?**]. Recent research shows that the risk of cardiovascular disease in the PRISm population is elevated compared to the normal population. A decline in lung function, particularly reductions in FVC and FEV_1, is associated with the occurrence of coronary artery disease and hypertension [**?**, **?**], with the relationship between Grade 3 hypertension and reduced FVC being most pronounced. Studies show that compared to the normal lung function population, the PRISm population has a higher proportion of comorbid hypertension (51.5% vs. 44.9%, $P < 0.05$). The mechanism by which long-term hypertension leads to decreased lung function and triggers PRISm may involve chronically elevated blood pressure causing left ventricular dysfunction, which increases left atrial pressure. This, in turn, leads to increased pulmonary artery pressure and pulmonary edema, affecting lung compliance and manifesting as increased functional residual capacity and decreased FEV_1 and FVC. Additionally, some patients take antihypertensive drugs such as β-blockers, which may induce bronchospasm and adversely affect lung function.

PRISm is also associated with the occurrence of cerebrovascular diseases. Studies have found a higher proportion of ischemic stroke among PRISm patients (3.5% vs. 1.6%, $P < 0.05$). It is considered that limited mobility in these patients may lead to restricted respiratory function and reduced levels of FEV_1 and FVC, resulting in PRISm. Furthermore, the Rotterdam Study pointed out that the PRISm population generally has poorer cognitive function and a

higher prevalence of lacunar infarction. However, other studies suggest that there may not necessarily be a direct causal relationship between obesity, diabetes, cardiovascular/cerebrovascular diseases, and PRISm [**?**, **?**]. Therefore, whether the association between PRISm and these comorbidities is mediated through shared metabolic pathways or other systemic processes needs to be further explored in future research. These studies will help clarify the mechanisms of PRISm progression. In clinical practice, in addition to monitoring lung function, there should be a focus on strengthening the monitoring and intervention of comorbid cerebrovascular diseases to reduce the overall disease burden.

3 PRISm

Lung Function Trajectories and Clinical Outcomes of PRISm: Investigating the lung function trajectories of Preserved Ratio Impaired Spirometry (PRISm) is essential for elucidating the progression and clinical outcomes of the disease. Existing research indicates that approximately 30% of the PRISm population eventually progresses to COPD [**?**, **?**]. A 42-year follow-up study identified three distinct lung function trajectories within the PRISm population: persistent PRISm, progression from normal lung function to PRISm, and recovery from PRISm to normal lung function. Compared to the recovery group, the first two groups exhibited significantly higher cumulative smoking exposure, BMI, high-sensitivity C-reactive protein, fibrinogen levels, and white blood cell counts. Furthermore, these groups showed a higher frequency of dyspnea, chronic bronchitis, and low physical activity, as well as an increased risk of cardiopulmonary-related and all-cause mortality [**?**, **?**]. Marott et al. also observed that lung function trajectories vary according to the severity of PRISm: individuals with mild PRISm (reduction in either FEV_1 or FVC) are more likely to recover to normal lung function, whereas those with severe PRISm (reduction in both FEV_1 and FVC) tend to remain persistent or progress to COPD GOLD grades 2–4. These studies suggest that the progression to COPD follows two distinct pathways:

Patients primarily presenting with emphysema tend to progress from COPD GOLD grade 1 to grades 2–4, while patients primarily presenting with airway obstruction often start at PRISm and subsequently progress to COPD grades 2–4.

Current research findings indicate that PRISm is associated with three distinct clinical outcomes: (1) progression to COPD within five years; (2) a high incidence of cardiovascular events and early mortality; and (3) persistent PRISm accompanied by physiological decline in lung function.

The clinical outcomes of PRISm vary across different lung function trajectories. The absolute and relative risks of all-cause mortality and coronary heart disease-related events (including hospitalization and mortality) are significantly higher in the PRISm population compared to both individuals with normal lung function and patients with COPD. Although the risk of respiratory-related events in PRISm is lower than that observed in the COPD group, it remains significantly

elevated compared to the population with normal lung function.

Ogata et al. further noted that clinical outcomes differ based on the severity of PRISm; severe PRISm is associated with a significantly increased risk of total mortality as well as respiratory and cardiovascular mortality, whereas the increase in these risks is limited in mild PRISm. Despite the variations in the development and clinical outcomes of PRISm and the associated increase in mortality risk, strengthening early identification, dynamic monitoring, and active intervention may help delay the progression of the PRISm population toward COPD.

4 PRISm

Challenges and Strategies in Clinical Diagnosis, Treatment, and Scientific Management

Although the global prevalence of Preserved Ratio Impaired Spirometry (PRISm) is approximately 10%, it is frequently overlooked in real-world clinical practice or confused with other common respiratory systems and comorbidities. This leads many patients to undergo pulmonary function testing only after symptoms become severe, thereby missing the window for early intervention. Currently, due to a lack of profound understanding of PRISm—manifested as the absence of standardized clinical phenotyping, imaging assessments, precision diagnosis, and prevention strategies—general practitioners in primary healthcare institutions face significant challenges in the timely identification, accurate diagnosis, and scientific management of PRISm during annual health screenings for community residents.

Lack of Unified Standards for Clinical Phenotyping

There is currently no unified standard for the clinical phenotyping of the PRISm population. Three main classification methods have been proposed: (1) Miura et al. [**?**] classified PRISm into restrictive and non-restrictive types based on the presence of restrictive ventilatory impairment. The latter is closer to obstructive airway disease in terms of imaging findings and lung function, with asthma history and smoking identified as independent risk factors; its mechanisms involve chronic airway inflammation, hyperreactivity, and emphysema. (2) Wan et al. [**?**] proposed an alternative classification: COPD subtype: characterized by decreased BMI and FEV_1/FVC, accompanied by significant emphysema and air trapping, showing changes similar to COPD; Restrictive subtype: characterized by elevated FEV_1/FVC and forced expiratory flow ($FEF_{25\%-75\%}$), reduced total lung capacity, and milder emphysema and air trapping; Hypermetabolic subtype:

characterized by increased BMI, decreased $FEV_1\%pred$ and $FEF_{25\%-75\%}$, thickened bronchial walls, and a higher proportion of comorbid diabetes and other conditions. (3) Based on UK population data, domestic scholars have classified

PRISm into mild (reduction in either FEV_1 or FVC) and severe (reduction in both FEV_1 and FVC). They found that compared to the mild PRISm group, the severe group was older, had lower education levels, lower marriage rates, higher current smoking rates, and significantly lower physical activity levels. Furthermore, the severe PRISm group exhibited more frequent and severe clinical symptoms such as cough, sputum production, wheezing, dyspnea, and emphysema, with a higher prevalence of multimorbidity (e.g., cardiovascular disease and malignancies) and lower mean FVC values [**?**]. Although various scholars have proposed different phenotyping methods, there is still a lack of clinical phenotyping standards based on large samples, particularly for the Chinese population. In-depth research is required to explore precision therapeutic intervention strategies.

Lack of Unified Standards for Radiographic Assessment

The COPDGene study suggested that the percentage of emphysema, gas trapping, and segmental airway wall area percentage on High-Resolution Computed Tomography (HRCT) can serve as radiological predictors for the PRISm phenotype. This underscores the significance of HRCT in diagnosing and defining PRISm phenotypes, particularly in identifying parenchymal and small airway changes, providing valuable insights for early screening and preventive intervention in community populations. A domestic study on the HRCT radiological characteristics of PRISm showed that compared to patients with mild or moderate COPD, the PRISm population exhibited significant differences in parameters related to lung parenchymal changes, while remaining largely consistent in airway and most vascular parameters. This suggests that the primary pathological changes in PRISm manifest in the small airways and small vessels. Further comparison among groups with normal lung function, PRISm, and mild-to-moderate COPD revealed that while total vascular volume showed no significant difference, most vascular parameters already exhibited differentiation, suggesting that small vessel lesions may be involved in the early stages. The radiological indicators for the PRISm phenotype are similar to those of mild-to-moderate COPD patients in most vascular indices but differ from normal populations. Therefore, some studies advocate for adopting COPD imaging strategies—combining visual scoring with quantitative indicators of lung parenchyma, airways, and vessels—to capture early imaging changes in PRISm. However, the current lack of consensus on chest imaging assessment for PRISm limits the accuracy of community screening and precision diagnosis.

Lack of Clear Markers for Precision Diagnosis

In recent years, research into the precision detection of the PRISm population has become a focal point. Studies have indicated that IL-6, hs-CRP, and GDF-15 can serve as risk predictors for PRISm [**?**]. Researchers in Taiwan found that levels of Activin A, a member of the TGF-β family, are significantly elevated in the PRISm population, which has been confirmed to be associated with air-

way inflammation [**?**]. Recently, Yoon et al. [**?**] suggested that Cathepsin L (CTSL) released by eosinophils (EOS) mediates the occurrence and progression of PRISm and drives the evolution of lung function deterioration toward COPD. Higbee et al. [**?**] and Choi et al. [**?**]

[52] conducted a Genome-Wide Association Study (GWAS) using the UK Biobank database and found a significant genetic correlation between PRISm and eosinophil-related genes ($rg = 0.06, P = 0.012$).

Through a meta-analysis of single nucleotide polymorphisms (SNPs) with genome-wide replication significance selected from 13 cohorts, they successfully identified 22 significant signals. Among these, four signals were associated with PRISm and identified as potential therapeutic targets: rs7652391 (MECOM), rs9431040 (HLX), rs62018863 (TMEM114), and rs185937162 (HLA-B). Additionally, 18 signals were related to diabetic traits and 7 to blood pressure traits.

This study confirms that genetic factors associated with PRISm may be closely linked to the risk of other pulmonary diseases and extrapulmonary comorbidities. This represents the first precision medicine study regarding PRISm-related comorbidities, and it is expected that further research will provide more precise diagnostic targets for the PRISm population and its associated comorbidities.

Lack of Unified Consensus on Prevention and Treatment Strategies

Although the PRISm population does not yet exhibit airflow obstruction, they face a higher incidence of complications and risk of all-cause mortality. Consequently, the latest guidelines suggest following the COPD management model, implementing systematic interventions for PRISm, and including it in chronic disease management. It is currently established that smoking cessation significantly improves the prognosis of the PRISm population [**?**, **?**]. Regular physical examinations and active physical exercise are also key measures to improve patients' quality of life.

However, evidence-based medical evidence such as expert consensus and guidelines for pharmacological prevention and treatment strategies remains scarce. Some studies suggest that bronchodilators can alleviate airway spasms by relaxing airway smooth muscle, thereby relieving symptoms and enhancing respiratory function. Glucocorticoids may help maintain or increase airway dilation due to their anti-inflammatory and anti-allergic effects, but the timing and indications for these drugs remain controversial. While biological agents have shown potential efficacy in treating PRISm, large-scale case-control studies are lacking. Whether these agents can reduce the risk of high-risk comorbidities and all-cause mortality in the PRISm population remains a potential new direction for future research.

Therefore, it is necessary to conduct in-depth research into the clinical characteristics, phenotyping standards, disease trajectories, imaging features, molec-

ular biology, and prevention strategies of the PRISm population. By utilizing big data and artificial intelligence technology to establish a disease database, risk models for the community PRISm population can be constructed to screen for risk factors. This will provide precise guidance for general practitioners regarding management strategies, community screening, and comorbidity management for the PRISm population. The goal is to reduce the risk of progression to COPD, the incidence of comorbidities, and all-cause mortality as early as possible. This also aligns with the policy requirements and practical needs of advancing the "Healthy China" strategy and incorporating COPD into national basic public health services.

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Abstract

Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable chronic airway inflammatory disease characterized by persistent respiratory symptoms and airflow limitation. It is associated with significant morbidity and mortality worldwide, posing a substantial burden on public health systems. Early diagnosis and accurate prognosis are essential for optimizing patient management and improving clinical outcomes. In recent years, machine learning and deep learning techniques have emerged as powerful tools in medical research, offering new possibilities for the analysis of complex clinical data. This review summarizes the current applications of machine learning and deep learning in the diagnosis, phenotyping, and prognosis of COPD. We discuss the integration of multi-modal data, including clinical characteristics, imaging, and biomarkers, to develop predictive models. Furthermore, we address the challenges and future directions of implementing these advanced computational methods in clinical practice to achieve personalized medicine for COPD patients.

Introduction

Chronic obstructive pulmonary disease (COPD) remains a major global health challenge, characterized by progressive airflow obstruction and significant systemic effects. According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), the diagnosis of COPD is based on clinical symptoms and confirmed by spirometry showing a post-bronchodilator $FEV_1/FVC < 0.70$. However, COPD is a highly heterogeneous disease with diverse clinical presentations, varying rates of progression, and different responses to therapy.

Traditional statistical methods often struggle to capture the complex, non-linear relationships inherent in the multi-dimensional data generated during COPD management. Machine learning (ML), a subset of artificial intelligence, provides a robust framework for identifying patterns within large datasets and making accurate predictions. Deep learning (DL), a more advanced form of ML utilizing neural networks with multiple layers, has shown exceptional performance in processing unstructured data such as medical imaging and physiological signals.

Applications in Diagnosis and Screening

The early detection of COPD is crucial for slowing disease progression. Machine learning algorithms have been applied to various data sources to improve screening efficiency.

1.1 Clinical and Electronic Health Record (EHR) Data

Researchers have utilized EHR data, including demographics, smoking history, and comorbidities, to train models such as Random Forests (RF) and Support Vector Machines (SVM). These models can identify high-risk individuals who may benefit from further diagnostic testing. For instance, predictive models incorporating patient-reported symptoms and history have demonstrated high sensitivity in primary care settings.

1.2 Imaging-Based Diagnosis

Computed Tomography (CT) is a vital tool for assessing

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Note: Figure translations are in progress. See original paper for figures.