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REVIEW

Preserved Ratio Impaired Spirometry (PRISm): A Global Epidemiological Overview, Radiographic Characteristics, Comorbid Associations, and Differentiation from Chronic Obstructive Pulmonary Disease

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Abstract: Preserved Ratio Impaired Spirometry (PRISm) manifests notable epidemiological disparities across the globe, with its prevalence and influential factors showcasing pronounced diversities among various geographical territories and demographics. The prevalence of PRISm fluctuates considerably among regions such as Latin America, the United States, and Asian nations, potentially correlating with a myriad of determinants, including socioeconomic status, environmental factors, and lifestyle modalities. Concurrently, the link between PRISm and health risks and other disorders, especially its distinction and interrelation with chronic obstructive pulmonary disease (COPD), has become a pivotal subject of scientific enquiry. Radiographic anomalies, such as perturbations in the pulmonary parenchyma and structural alterations, are posited as salient characteristics of PRISm. Furthermore, PRISm unveils intricate associations with multiple comorbidities, inclusive of hypertension and type 2 diabetes, thereby amplifying the intricacy in comprehending and managing this condition. In this review, we aim to holistically elucidate the epidemiological peculiarities of PRISm, its potential aetiological contributors, its nexus with COPD, and its association with radiographic aberrations and other comorbidities. An integrative understanding of these dimensions will provide pivotal insights for the formulation of more precise and personalised preventative and therapeutic strategies.

Keywords: PRISm, pulmonary function, epidemiology, comorbid associations

Introduction

Chronic obstructive pulmonary disease (COPD), which is particularly prevalent among older adults, is a significant contributor to global mortality. A recent proposal suggests that impaired lung growth can lead to COPD, even in the absence of a rapid decline in lung function, and preserved ratio impaired spirometry (PRISm) has been proposed as a concept of low lung growth or early COPD.[1,2] PRISm is a condition characterised by a decline in the one-second ratio with normal pulmonary function. PRISm represents a prevalent yet under-researched state of diminished lung functionality, defined by a forced expiratory volume in one second (FEV1) that is less than 80% of the predicted value, whilst maintaining a FEV1/forced vital capacity (FVC) ratio ≥0.7.[3] This pathological state, although common, has been sparsely researched. Previous investigations have linked it to respiratory symptoms.[4,5] Recently, PRISm has been identified as a subtype that is more susceptible to developing COPD or experiencing acute exacerbations. Observational studies have

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reported that 32.6% of individuals with PRISm progressed to COPD within 4–5 years.[6,7] However, it remains unknown how PRISm influences the development of COPD.

In recent years, an increasing number of studies have been conducted on PRISm, especially in areas such as epidemiology, disease progression, and subtyping. Several studies have indicated associations between PRISm and diminished lung function, airway diseases, and emphysema.[8,9] These findings hold significant implications for understanding the heterogeneity of COPD and the natural history of PRISm. PRISm has also been correlated with various disorders, including obesity, diabetes, and hypertension.[5,10,11] The focal point of current research pivots on discerning individual characteristics of PRISm, and subtyping patients with PRISm, all of which will be important to elucidate its pathophysiological mechanism, optimise diagnosis, and deliver personalised treatment.

This review comprehensively encapsulates research pertaining to PRISm, spanning its epidemiology, aetiological factors, relationships with comorbidities, radiographic presentations, disease progression, and prognosis. The objective of this review is to equip clinicians and researchers with a holistic and up-to-date understanding of PRISm to foster improved diagnosis and therapeutic approaches.

Epidemiology of PRISm

Prevalence of PRISm

Globally, the global prevalence of PRISm, estimated at between 7%–13%, remains a focal point of interest.[6,11–15] Nevertheless, this figure does not wholly represent the real situation of PRISm. Significant disparities in the prevalence of PRISm emerge when contrasting regions and populations, such as certain Western countries and Asian nations. For instance, reported studies from regions such as Latin America, the United States, Denmark, and Malawi indicate PRISm prevalence of 5%,[16] 17.3%,[17] and 20.1%[8] respectively, whereas in Asia, the prevalence of PRISm reported in Korea and Japan is 8.9%[13] and 10%,[5] respectively. Notably, there has yet to be a report on the prevalence of PRISm in China.

The epidemiological characteristics of PRISm display marked variations across different regions, predominantly influenced by an array of determinants, including the natural environment, economic conditions, racial disparities, and lifestyle choices. To elucidate, Japan, compared to Western nations, has a lower obesity rate but a higher smoking prevalence, both of which are pivotal influencers of PRISm prevalence.[5,18–22] Moreover, rural areas, often exposed to biomass combustion and pesticide exposure,[23–25] contrast with urban areas, which face heightened threats from indoor air pollution and vehicular emissions.[26,27] Research also indicates lung function variations among different ethnicities, potentially attributed to environmental factors and lifestyle habits.[28,29] Additionally, the design and scope of different studies can lead to disparities in reported PRISm rates. For instance, studies conducted in the US primarily involved patients with myocardial infarction,[17] where multiple complications, such as congestive heart failure, leading to fluid accumulation in the lungs, or pulmonary embolism, resulting from thrombus detachment, can contribute to reduced lung function, potentially inflating the prevalence of PRISm.[30] Furthermore, the Danish research was conducted relatively earlier,[8] and the pulmonary function tests of that period may not align with contemporary standards, possibly leading to an overestimation of PRISm. Consequently, a simplistic, uniform assessment and management approach for PRISm is infeasible. It is imperative that regions and nations delve into comprehensive PRISm research, taking into account their unique environmental and cultural milieu, to secure more accurate data, which would, in turn, pave the way for devising more precise and efficacious prevention and treatment strategies tailored for their respective populations.

Mortality Rates Associated with PRISm

PRISm exhibits considerable heterogeneity and its mortality rates are influenced by both region and sex. Given that risk factors for PRISm, such as obesity and smoking, are closely associated with lifestyle, the mortality rates may show notable differences between different territories and races, such as between Asia and the West.[5,18–22,28,29] Several studies have demonstrated that PRISm is intricately linked with the overall health status and survival rate of patients. Specifically, there has been a continuous rising trend in the all-cause mortality rates of patients with PRISm, and the risk of death from associated cardiovascular diseases has also markedly increased.[8,9,31] The COPDGene study showed that the airway-predominant and emphysema-predominant subtypes of PRISm have different patterns of mortality risk.

As disease characteristics worsen, the risk of death increases for patients with both subtypes, but this is more pronounced in the airway-predominant subtype.[32,33]

In certain instances, the association of PRISm with specific mortality rates has been validated. Indeed, a previous study found a significant correlation between PRISm and mortality rates related to respiratory systems.[34] Moreover, some data have highlighted that PRISm is associated with higher all-cause mortality rates, respiratory system mortality rates, and coronary heart disease mortality rate, as well as being linked to respiratory-related events and coronary heart disease-related events (eg, hospitalizations and deaths).[6–8,35] Compared to individuals with normal lung function, those with PRISm face an elevated risk of all-cause mortality, cardiovascular death, and atrial flutter (AFL).[5,17] Additionally, a study focusing on the American population discerned that, in comparison to those diagnosed with obstructive pulmonary diseases, patients with PRISm manifest significantly higher all-cause mortality rates, coronary heart disease-related death rates, and both absolute and relative risks associated with coronary heart disease events.[34] To be more precise, the risk of all-cause death for patients with PRISm nearly doubled, while the risk of death from cardiovascular diseases increased by almost two-fold. These research findings underline the significance of PRISm in relation to mortality rates and other health outcomes, highlighting the need to delve deeper into the underlying mechanisms and formulate potential intervention strategies.

Etiological Factors of PRISm

The factors leading to PRISm are multifaceted. Firstly, studies by Marott et al, Shiraishi et al, and Miura et al have indicated that smoking is a crucial etiological factor.[8,12,36] Oxidative stress, inflammation, imbalance between protease and antiprotease, and small airway diseases caused by smoking not only damage lung function directly,[37,38] increasing the risk of PRISm, but may also lead to centrilobular emphysema (CLE) and peribronchial emphysema (PSE). CLE and PSE can result in a decline in lung function, particularly in the FEV1, thereby causing PRISm.[39,40] Research suggests a higher proportion of patients with PRISm have a history of smoking or are current smokers.[13] In the COPDGene cohort study, PRISm was found to have a higher percentage of current smokers and a higher average pack-year.[3] In conclusion, the prevalence of PRISm is higher among smokers, and smoking is an important etiological factor for PRISm.

An abnormal body mass index (BMI) is another significant factor triggering PRISm.[11,13,41] A high BMI can lead to mechanical compression and systemic inflammation, and is associated with asthma.[42,43] It is also worth noting that a low BMI, which results in diminished respiratory muscle function, impaired lung development, and an increased risk of infections, similarly elevates the risk of PRISm.[44]

Moreover, air pollutants, especially particulate matter, ozone, nitrogen oxides, and sulphur oxides have increased substantially with the progression of industrialisation and urbanisation.[45] Long-term exposure to these pollutants can induce oxidative stress, inflammatory responses, and chronic damage effects, such as injury to the alveoli and airway epithelial cells, leading to airway remodelling and functional impairment.[46–49] Animal models have further confirmed the correlation between pollution and PRISm, clarifying the relationship between inflammatory reactions from inhalation exposure and compromised FVC.[48]

Lastly, factors such as age, female sex, history of asthma, and educational level are also impactful determinants that should not be overlooked.[11,16,50]

Additionally, the GWAS conducted in the COPDGene study did not identify direct genetic variants associated with PRISm. However, the increased prevalence of PRISm in patients with Klinefelter syndrome hints at the potential influence of genetic factors on its development. Furthermore, SNPs within the PLEKHA5 and CACNB2 genes offer clues for exploring the genetic mechanisms behind PRISm.[3]

PRISm and COPD

COPD stands as one of the primary causes of mortality worldwide. Complications and acute exacerbations resulting from COPD have emerged as significant health concerns.[51,52] Factors contributing to COPD extend beyond just smoking, with poor lung development, respiratory infections, occupational exposures, and air pollution all known to be potential causative agents.[53,54] According to the GOLD guidelines, COPD is typically diagnosed based on restricted airflow indicated by an FEV1/FVC ratio < 0.7.[55] However, PRISm represents a distinct pulmonary function state characterised

by a proportional decline in both FEV1 and FVC, maintaining the FEV1/FVC ratio within the normal range.[3] This condition is also referred to as "GOLD unclassified" or "restrictive lung function". Even though PRISm does not initially exhibit airflow obstruction, smokers with PRISm face a heightened risk of progressing to COPD compared to smokers with normal lung volumes. A cohort study initiated in 1989 discovered that 32.6% of patients with PRISm developed COPD within 4 to 5 years, and also exhibited a higher mortality rate.[7,8]

PRISm is perceived as a transitional state to COPD and is also considered as a subtype that is prone to developing COPD or experiencing its acute exacerbations. A study conducted in Japan reported evidence of PRISm as an independent risk factor for progression to COPD. The research identified an optimal FEV1 cut-off point of 86% to predict the progression of PRISm to COPD; below this threshold, the progression rate to COPD increases by 23.6%, even if the FEV1/FVC ratio remains normal.[31] In other words, an FEV1 < 86% is associated with a higher risk of developing COPD, even if the FEV1/FVC ratio is within the normal range. PRISm subtypes reveal distinct COPD progression paths: airway-predominant types may evolve from GOLD 0 through PRISm to GOLD 2–4, while emphysema-predominant types can transition directly from GOLD 0 to GOLD 1 and beyond, highlighting the importance of early identification of PRISm in COPD management.[32,33] Additionally, PRISm is more common among males and smokers, both of whom are high-risk groups for COPD.[7,16] Smoking not only accelerates the decline in FEV1 and FVC but also increases the risk of PRISm developing into COPD. The results of longitudinal studies have indicated that approximately one-third of patients with PRISm eventually receive a COPD diagnosis.[6,7] Different subtypes of PRISm show varying disease trajectories, in that patients with mild PRISm are more likely to revert to normal lung function, while those with severe PRISm tend to progress to more advanced stages of COPD.[56]

Even if patients with PRISm do not exhibit obvious respiratory symptoms, their quality of life often suffers due to the underlying constraints in lung function. As PRISm does not completely fit the pulmonary function standards for COPD, these patients are frequently excluded from treatment plans, unquestionably disregarding their potential role in COPD progression.[4] Incorporating PRISm within an expanded COPD definition has been proposed to identify individuals with a high risk of rapid COPD progression during routine check-ups.[57] However, some PRISm cases are misclassified as COPD. Indeed, a previous study verified that 7% of patients with PRISm received a presumptive COPD diagnosis. This misclassification is common among the elderly and smokers, resulting in 82% of such patients enduring inappropriate treatment with inhaled steroids.[58]

Even though PRISm is not encompassed within the current COPD diagnostic pulmonary function criteria, it parallels COPD in terms of FEV1 decline. Similarly, PRISm is associated with the onset of respiratory symptoms, systemic inflammation, and an increased incidence and mortality rate from cardiovascular diseases.[3,6,59]

In conclusion, PRISm holds significant relevance in the progression of COPD, accentuating the need for more longitudinal research, including frequent pulmonary function tests and extended follow-ups, to comprehensively grasp the clinical and pathological implications of this unique pulmonary function status.

Relationship Between PRISm and Radiological Abnormalities

Computed tomography (CT), as the primary imaging screening and research tool, provides a series of vital radiological parameters. These parameters, including the emphysema index, air trapping percentage, average lung density, 10th percentile of airway perimeter (Pi10), airway wall thickness, airway wall area percentage, total lung capacity measured by computed tomography (TLCCT), and parameters related to lung vasculature, are of great significance in diagnosing and assessing the progression of pulmonary diseases. These radiological parameters can be analysed in correlation with spirometry parameters or can be used directly as predictive tools to assess the progression of associated lung diseases.

In the diagnosis of early-stage COPD, CT seems to be more sensitive than traditional pulmonary function tests (PFTs).[60,61] Current PFTs are suboptimal in identifying early lung function impairments and no longer meet the clinical demands for interventions in early-stage diseases. Therefore, we believe that it is crucial to delve into and summarise the radiological characteristics of PRISm on CT scans.

Radiological Features of PRISm on High-Resolution Computed Tomography (HRCT)

In a typological study addressing the distinct characteristics of PRISm via HRCT, researchers scrutinised parameters pertaining to the lung parenchyma, airways, and pulmonary vasculature. The outcomes revealed that, in contrast to patients with mild-to-moderate COPD, those with PRISm demonstrated notable disparities in parameters related to parenchymal destruction but remained largely congruent in terms of the airway and the majority of vascular parameters.[60] This finding underscores the notion that individuals with PRISm exhibit parenchymal attenuation closer to that of the healthy population, with the principal pathological changes manifesting within the small airways and small vessels. An investigation into the mean lung density (MLD) revealed pronounced variations among the three cohorts (early-stage COPD, PRISm, and normal group). The MLD of the early-stage COPD cluster was significantly reduced in comparison to the other two, while the PRISm cohort exceeded the controls.[60–62] The MLD exhibited marked deviations throughout the spectrum from normal pulmonary function to mild and moderate COPD. The study also accentuated that pulmonary function test maps (PRM) could effectively distinguish between the normal, PRISm, and mild-to-moderate COPD groups, with the PRM pertinent to pulmonary emphysema emerging as an independent predictor for mild-to-moderate COPD.[60] The percentage of airway wall area was also pinpointed as an independent prognostic marker for PRISm status. Intriguingly, this metric bore an inverse correlation with the predicted FEV1 percentage, thereby offering an indirect reflection of pulmonary function status.[3,63]

Research from the Genetic Epidemiology of COPD (COPDGene) initiative proposed that certain radiological parameters gauged via CT, including the percentage of pulmonary emphysema, gas trapping, and segmental wall area percentage, could serve as radiographic predictors for the PRISm phenotype.[3] Another in-depth exploration by COPDGene delineated the radiological traits of PRISm sub-groups, observing that in comparison to other pulmonary functional categories and sub-groups, patients with PRISm were more predisposed to progress into the GOLD1-4 cohort, with elevated TLC%, pulmonary emphysema percentage, and gas trapping percentage.[7] In summary, these studies highlight the paramount significance of HRCT in diagnosing and stratifying PRISm, particularly with regard to parenchymal and small airway alterations, providing valuable insights for subsequent clinical investigations and therapeutic interventions.

Radiological Features of PRISm in Specific Populations

In patients with PRISm with chronic bronchitis, imaging studies have shown that the emphysema index, airway wall area percentage, and lung volumes are similar to those of patients with chronic bronchitis but normal lung function, but significantly different from those of patients with early-stage COPD.[62] These findings emphasise the differences in radiological features between PRISm and early-stage COPD.

Another study focusing on PRISm in smokers found that, compared to smoking controls, patients with PRISm (or GOLD-Unclassified) exhibited increased airway wall thickness, but to a lesser extent than that observed in patients with COPD. More importantly, both the total lung capacity (TLC) and degree of emphysema were reduced in patients with PRISm compared to both groups.[63]

Emphysematous Features of PRISm

Certain research narratives emphasise that[64] patients with PRISm exhibit a higher prevalence of PSE compared to individuals with normal lung function, while the prevalence of CLE remains similar to that of healthy smokers. However, a multicentre inquiry[12] found no significant difference in the prevalence of PSE and CLE between PRISm smokers and those with preserved lung functionality. When compared to non-smoking individuals with PRISm, smokers within the PRISm category showed a higher frequency of both PSE and CLE. Several reports have indicated that diminished ratios of FVC/TLCct and FEV1/TLCct imply gas trapping.[65] Consequently, these ratios may serve as prognostic indicators for the exacerbation and progression of symptoms in smokers with PRISm, even heralding the transition to COPD. Additionally, a multicentre analysis that examined the relationship between PRISm and emphysema subtypes observed prevalent CLE and PSE in smokers with PRISm. Intriguingly, a unique correlation emerged between CLE and FVC/TLCct, suggesting that in smokers with PRISm, CLE rather than PSE correlates with gas trapping.[12] As a result, visual

CT has been endorsed as a potent predictive tool for identifying high-risk CLE individuals within the smoking PRISm cohort.[12] By employing visual scores on baseline CT scans, one can foresee the longitudinal evolution of PRISm, enabling a more tailored management approach for these smokers.[7]

Such scholarly revelations not only unveil the unique radiological attributes of PRISm across diverse cohorts (eg, individuals with chronic bronchitis and smokers) but also enrich our comprehension of PRISm across varying COPD stages. These radiological parameters serve a dual purpose: they refine the precision in diagnosing, evaluating, and forecasting the trajectory of PRISm and COPD, and also offer compelling evidence for the value of imaging metrics as prognostic tools for PRISm, furnishing pivotal insights for future clinical diagnoses and therapeutic endeavours.

Relationship Between PRISm and Concomitant Comorbidities

PRISm manifests significant associations with a myriad of health concerns, encompassing advanced age, obesity, hypertension, diabetes, heart failure, coronary artery disease, stroke, and an estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m².[8,9,34] A study from South Korea further substantiated that, when compared to other cohorts, individuals with PRISm exhibit a markedly heightened frequency of these comorbidities.[13] The exacerbation of these concurrent conditions often correlates with an augmented mortality risk for the affected individuals. For instance, heart failure is related to an increase in respiratory system-related mortality, whereas coronary artery disease corresponds to an increased risk associated with the cardiac ailment itself.[66–69] Further research has indicated a rising trend in the number of patients with PRISm being hospitalised due to cardiac complications.[13]

Relationship Between PRISm and Obesity

Several studies have examined the link between respiratory function and obesity or fat distribution, discovering a negative correlation between them. These associations mainly depend on various obesity metrics such as weight, BMI, and indicators related to fat distribution, such as waist circumference, the ratio of waist circumference to body surface area or height, body fat percentage, and skinfold measurements.[18,70–72] Some research has highlighted that in males, pulmonary function is negatively correlated with the waist-hip ratio, although this relationship is less evident in females.[73] Whether the relationship between waist-hip ratio and respiratory function can be elucidated solely by BMI requires further investigation.

Studies have reported that the prevalence of PRISm significantly escalates among patients with a higher BMI, which resonates with the findings of the COPD gene cohort study.[6,7] Obesity can exert a direct impact on respiratory function via multiple pathways. The accumulation of fat can mechanically interfere with the normal movement of the diaphragm, either due to fat build-up on the chest or diaphragm or because the descent of the diaphragm during deep inhalation is restricted.[42,73,74] Additionally, fat deposits between muscles and ribs can decrease chest wall compliance even at rest, increasing the respiratory workload for obese individuals.[75,76] Concurrently, individuals with chronic obesity have been found to exhibit peripheral airway obstruction unrelated to smoking.[77,78] The resulting chronic hypoxia could activate the sympathetic nervous system, escalating pulmonary vascular resistance and leading to a reduction in lung air capacity.[79,80]

While obesity can physiologically explain PRISm, its relationship with PRISm onset seems contradictory. In Western countries, the prevalence of PRISm is influenced by obesity, yet a Japanese study identified low BMI as a risk factor for PRISm developing into COPD,[31] in contrast to the former findings. This discrepancy between the findings may be due to the fact that patients in British and European studies are often more obese and lack pulmonary emphysema, whereas in East Asian countries, emphysematous and lean phenotypes are more prevalent. Furthermore, studies from both Venezuela and the BOLD cohort found associations between PRISm and a lower BMI, as well as poverty.[81,82]

Relationship Between PRISm and Diabetes

Epidemiological and clinical studies consistently indicate that lung function is diminished in adults with diabetes compared to those without, potentially elevating the risk for PRISm.[83]

In recent years, studies have unveiled a correlation between type 2 diabetes (T2D) and various lung function parameters, including FEV1, FVC, and the FEV1/FVC ratio.[84–87] These studies have shown significant genetic correlations between these lung function measures and T2D and its associated markers, including fasting insulin, fasting

glucose, and haemoglobin A1c levels.[88] Some studies have highlighted a notable correlation between higher genetically predicted FEV1 and FVC values and a lower risk of T2D. Moreover, individuals with a higher genetic susceptibility to T2D often show a close association with a decline in FEV1 and a heightened incidence of PRISm.[88] Furthermore, previous research has suggested potential causal relationships between fasting blood glucose and lung function, and between lung function, fasting insulin, and proinsulin. Other research has detected a significant correlation between the genetic predisposition to T2D and a reduction in FEV1 and FVC, along with an increase in the FEV1/FVC ratio.[88]

The mechanisms by which T2D could lead to PRISm may encompass lung parenchymal damage due to oxidative stress caused by diabetes, subsequently resulting in pulmonary fibrosis and structural alterations.[89] In patients with T2D, additional contributing factors may include microvascular changes in the alveolar capillaries and pulmonary arterioles, chronic low-grade inflammation, autonomous nervous system dysfunction of the respiratory muscles, and a reduction in elastic recoil due to pulmonary collagen glycation.[90–94]

Relationship Between PRISm and Hypertension

While the physiological mechanisms between the respiratory and cardiovascular systems remain not fully elucidated, mounting evidence suggests that chronic systemic and pulmonary inflammation plays a pivotal role in this interplay. Several studies have illuminated a conspicuous link between lung function and cardiovascular diseases.[95–101] Research has shown a connection between declines in FEV1 and arteriosclerosis.[102] The Framingham study highlighted a negative correlation between FVC and risks of cardiovascular diseases and mortality, which was particularly pronounced in women. Additional research has revealed a relationship between declines in lung function, notably reductions in FVC and FEV1, with coronary artery disease and hypertension,[95,96,99] with the most pronounced reductions in FEV1 and FVC noted among those with stage 3 hypertension.[83] Moreover, hypertension coupled with low FEV1 has been linked to elevated risks of, and mortality rates from cardiovascular diseases.[97,99] However, some studies have reported a negative correlation between hypertension and a decline in lung function.[95,96,101]

The pressing question remains whether it is hypertension itself that causes a reduction in lung function, thus triggering PRISm, or whether the effects originate from the antihypertensive medications. It is challenging to differentiate between the two in observational studies. One theory posits that chronic hypertension might lead to left ventricular dysfunction, increasing left atrial pressures. In turn, this may raise pulmonary arterial pressures and lead to pulmonary interstitial oedema, thereby impacting lung compliance, elevating the functional residual capacity, and ultimately causing reductions in FEV and FVC. Pertaining to antihypertensive medications, β-blockers, even those with relatively higher cardiac selectivity, might induce bronchospasm, exacerbating respiratory issues, especially among asthmatics.[103,104] Furthermore, other categories of antihypertensive drugs, such as diuretics, calcium channel blockers, and ACE inhibitors, may also have adverse effects on lung function.

In summary, diabetes impacts lung function mainly through microvascular changes, chronic inflammation, autonomic neuropathy, and the loss of pulmonary elasticity due to collagen glycation. Hypertension affects lung function by compromising left ventricular function and augmenting pulmonary interstitial oedema and pulmonary arterial pressures, thereby impacting lung compliance and function. Moreover, antihypertensive drugs, particularly β-blockers, can intensify changes in respiratory function and may be linked to a decline in lung function, consequently affecting PRISm. However, US research has shown that, while the prevalence of PRISm has remained stable over the past half-century, that of obesity and diabetes has been rising,[34] indicating divergent long-term trends and suggesting that a direct causal relationship may not necessarily exist between obesity, diabetes, and PRISm. Therefore, whether the associations of obesity, diabetes, and hypertension with PRISm are mediated through shared metabolic pathways or other systemic processes requires further exploration in future studies. Such studies will help to elucidate the mechanisms underpinning worsened outcomes in PRISm and optimise the management and treatment of these patients to enhance their lung function and overall health.

Prevention and Treatment of PRISm

Although the current literature on PRISm primarily focuses on epidemiology, aetiology, and its relationships with other diseases, there remain no established guidelines for the diagnostic evaluation and management of PRISm. Treatment for

PRISm subtypes may include anti-inflammatory and bronchodilator therapies for airway-predominant types, and pulmonary rehabilitation and appropriate nutritional support for emphysema-predominant types.[32,33] Bronchodilators can improve airway constriction by relaxing the airway smooth muscles, thereby alleviating symptoms and enhancing respiratory function.[12] Anti-inflammatory drugs and inhaled corticosteroids help maintain or increase airway dilation due to their anti-inflammatory and anti-allergic effects.[105] Moreover, while biologics have shown potential efficacy in the treatment of PRISm, there is a lack of definitive research confirming their therapeutic effects. Future treatment strategies should delve deeper into targeted drug therapies and the potential application of immunosuppressants. Quitting smoking has also been shown to improve the prognosis of patients with PRISm as it can significantly reduce the risk of mortality and the progression of airflow limitation (AFL).[5,56] Additionally, regular medical check-ups and proactive physical exercise are crucial measures for enhancing the quality of life of such patients.[8] When diagnosing PRISm, physicians must exercise caution to avoid misdiagnosing patients with PRISm as having COPD, which is especially common among elderly patients and smokers. Indeed, it has been reported that such misclassifications result in up to 82% of patients continuing to inappropriately use inhaled corticosteroids and bronchodilators for treatment.[34,58]

Outlook

While PRISm has an estimated global prevalence of approximately 10% and is gaining increasing recognition, it often goes unnoticed or misdiagnosed in the real world. This is largely due to its clinical heterogeneity and the fact that its early symptoms tend to be subtle, potentially overlooked, or confused with other common respiratory diseases.[106] Additionally, many patients do not routinely undergo pulmonary function tests until symptoms become pronounced, leading to missed early diagnostic opportunities. Moreover, the definition of PRISm may be somewhat ambiguous as it primarily relies on specific parameters from lung function tests, such as the FEV1/FVC ratio and the predicted FEV1. This definition can overlap with many other respiratory issues, making it difficult for doctors to identify PRISm clearly in daily practice.[34] Therefore, enhancing the early recognition and diagnosis of PRISm, strengthening education and training on PRISm, and encouraging regular lung function screenings are vital to reduce its prevalence and improve patient outcomes. Quitting smoking is also crucial for lowering the mortality risk associated with PRISm and preventing its progression to COPD.

PRISm exhibits unique radiological characteristics in different populations, which can be used to reduce the rates of COPD progression and improve the precise diagnosis, evaluation, and prognosis of PRISm, allowing for more personalised treatment approaches. Additionally, CT findings of centrilobular emphysema may serve as an indicator to identify high-risk individuals among smokers with PRISm. However, whether bronchodilators can improve gas retention and prevent the progression of patients with PRISm with CLE to COPD requires further research.

Lung function is closely related to various physiological and pathological states. Obesity, diabetes, and hypertension have significant impacts on adults. Future studies need to delve deeper into the potential relationships between PRISm and these comorbidities to decide how to better manage and treat these patients, with the aim to enhance their pulmonary function status and optimise their overall health. In summary, maintaining good lung function and cardiovascular health is of paramount importance for patients with diabetes and hypertension.

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Conclusions

This review aims to comprehensively explore the multifaceted characteristics of PRISm, including its epidemiology, aetiology, comorbid relationships, radiographic presentation, disease progression and prognosis. However, the methodological limitations of narrative reviews, particularly potential selection bias, may limit our findings and conclusions. Future research should use systematic review methods to more comprehensively and objectively evaluate PRISm, thereby facilitating a deeper understanding and development of management strategies.

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