

Difference in Respiratory Function Between GOLD Stage I and Preserved Ratio Impaired Spirometry as Assessed by Impulse Oscillometry and Spirometry

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Purpose: Preserved ratio impaired spirometry (PRISm) is heterogeneous, and its physiological relationship to early COPD remains unclear. We compared respiratory-mechanical patterns between non-restrictive PRISm (NrP) and GOLD stage 1 COPD (GOLD 1) using impulse oscillometry (IOS) and spirometry and explored longitudinal changes in a trackable subset.

Patients and Methods: We retrospectively analyzed 1,139 adults who underwent post-bronchodilator spirometry in 2013; IOS was available for a subset. PRISm was defined by $FEV_1/FVC \geq LLN$ with $\%FEV_1 < 80\%$. GOLD 1 was defined per GOLD criteria ($FEV_1/FVC < 0.70$; $\%FEV_1 \geq 80\%$). Longitudinal analyses were restricted to individuals with >10 pack-years, IgE <170 U/L, eosinophils $<300/\mu L$, and ≥ 2 examinations to minimize Th2-high asthma confounding.

Results: Among PRISm cases, 18 met NrP criteria, and 127 met GOLD 1 criteria; IOS was available for all 18 NrP and for 39 GOLD 1 participants cross-sectionally. IOS indicated greater peripheral airway dysfunction in NrP than in GOLD 1, with higher R5–R20 and Fres and more negative X5, despite relatively preserved spirometric indices. In the longitudinal subset (39 GOLD 1; 8 NrP), annual changes in spirometry and IOS exhibited wide variability and did not differ meaningfully between groups. These analyses were limited by small NrP sample size and incomplete IOS availability.

Conclusion: PRISm and GOLD 1 demonstrated distinct respiratory-mechanical patterns despite partially overlapping spirometric profiles. IOS identified peripheral airway abnormalities in PRISm that were not evident on spirometry, suggesting potential value for characterizing early or atypical airway dysfunction. However, sample-size limitations and major confounding factors—including age, smoking status, and bronchodilator exposure—preclude causal inference. Findings should be considered descriptive and hypothesis-generating. Larger prospective studies with balanced treatment exposure and comprehensive imaging and lung-volume assessment are needed to clarify the clinical relevance of IOS patterns in PRISm.

Plain Language Summary: Some people have breathing problems that do not fit neatly into common categories such as asthma or chronic obstructive pulmonary disease (COPD). One such pattern is called preserved ratio impaired spirometry (PRISm). People with PRISm have reduced overall lung performance, even though a standard breathing test may still appear relatively normal.

In this study of patients attending a respiratory clinic, we used a gentle, non-invasive test that measures how air moves through the small airways during quiet breathing. Compared with people who had very mild COPD, individuals with PRISm showed differences in these measurements, suggesting altered airway mechanics, even when standard lung tests appeared less impaired.

These findings suggest that PRISm may involve different airway characteristics rather than simply representing an early stage of COPD. Tests that assess breathing during normal, relaxed breathing may provide additional information alongside standard lung tests and help doctors better understand and monitor this heterogeneous condition.

Keywords: small airway disease, peripheral airway mechanics, airway resistance, early detection, lung function decline, phenotypic heterogeneity

Introduction

Preserved ratio impaired spirometry (PRISm) is a spirometric pattern characterized by a preserved post-bronchodilator FEV₁/FVC ratio with reduced FEV₁.¹

Although described in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) reports, PRISm is not incorporated into the American Thoracic Society/European Respiratory Society (ATS/ERS) pulmonary-function interpretation framework, in which reduced FEV₁ with a preserved ratio prompts further lung-volume assessment to distinguish non-specific ventilatory patterns from true restriction.²

Accordingly, PRISm represents an operational spirometric category rather than a fully defined physiological entity and is recognized as a heterogeneous condition.^{3–5}

Epidemiologic studies have shown that individuals with PRISm have higher all-cause and cardiovascular mortality than those with normal spirometry,^{4,6–9} and that longitudinal trajectories vary, with some individuals progressing to chronic obstructive pulmonary disease (COPD) while others revert to normal spirometry.^{4,5,10}

These divergent outcomes suggest that PRISm does not uniformly represent a “pre-COPD” state but instead encompasses multiple physiological patterns. However, the contribution of small-airway dysfunction—an aspect incompletely captured by conventional spirometry—remains insufficiently characterized.¹¹

Impulse oscillometry (IOS) measures respiratory system resistance and reactance during quiet tidal breathing and provides effort-independent indices related to airway caliber and elastic properties.^{12,13}

Although the anatomical specificity of individual IOS indices remains debated, frequency-dependent resistance and reactance-related parameters are commonly interpreted as reflecting distal airway mechanics and have been applied to detect early or subtle airway abnormalities in asthma and early COPD.^{13–17}

Despite increasing interest in PRISm, most prior studies have focused on epidemiologic outcomes rather than respiratory mechanics.^{3,6–8,18,19}

Direct assessments of peripheral airway dysfunction in PRISm using IOS are limited, and longitudinal evaluations combining spirometry and IOS are particularly scarce.^{16,20}

Moreover, physiological distinctions between PRISm and GOLD stage 1 COPD (GOLD 1)—two spirometric patterns with partially overlapping features—remain poorly defined from a respiratory-mechanical perspective.^{3–5}

Accordingly, the aim of this study was to describe and explore cross-sectional and longitudinal respiratory-mechanical characteristics of PRISm compared with GOLD 1 using spirometry and IOS. We sought to characterize functional differences rather than establish causality or define fixed phenotypes, with the goal of generating hypotheses regarding small-airway involvement in PRISm and informing future prospective studies.

Methods

Study Design and Population

We conducted a retrospective observational study of consecutive adults evaluated at the Nippon Medical School Respiratory Care Clinic between January 5 and December 29, 2013. A total of 1,139 individuals underwent post-bronchodilator spirometry during the study period; impulse oscillometry (IOS) was obtained at the same visit as part of routine functional assessment.

At that time, bronchodilator testing was routinely performed when airway disease was clinically suspected. However, a small number of patients whose presentation clearly suggested parenchymal restriction or who were unable to complete repeated maneuvers (eg, frailty) did not undergo post-bronchodilator spirometry. Individuals without post-bronchodilator measurements were therefore excluded from GOLD-based comparisons, an operational approach that may introduce selection bias.

Written informed consent was waived; details are provided in the section Ethics approval and informed consent.

Spirometric Classification

Post-bronchodilator spirometry was used for all analyses. Abbreviations are as follows: FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; LLN, lower limit of normal; TLC, total lung capacity.

PRISm was defined according to the spirometric description used in the GOLD reports, namely a preserved FEV₁/FVC ratio with reduced FEV₁, while recognizing that PRISm is not incorporated into the formal ATS/ERS pulmonary-function interpretation framework, which recommends lung-volume assessment to distinguish true restriction from a non-specific ventilatory pattern.^{1,2}

Accordingly, the present classifications represent operational spirometric categories aligned with prior epidemiological studies.^{3–5}

Participants were categorized as follows:

- Normal: FEV₁/FVC $\geq$ LLN with %FEV₁ $\geq$ 80% and %FVC $\geq$ 80%.
- PRISm: FEV₁/FVC $\geq$ LLN with %FEV₁ $<$ 80%.
- Restrictive ventilatory defect: FEV₁/FVC $\geq$ LLN with %FVC $<$ 80% (TLC not routinely available).
- Obstructive ventilatory defect: FEV₁/FVC $<$ LLN.
- Mixed ventilatory defect: FEV₁/FVC $<$ LLN with %FVC $<$ 80%.

Within PRISm, restrictive PRISm (rP) and non-restrictive PRISm (NrP) were defined by %FVC $<$ 80% and $\geq$ 80%, respectively. Because TLC was not uniformly measured, these subgroups should be interpreted as FVC-based operational categories rather than physiological classifications.²¹

For comparisons with early COPD, GOLD 1 was defined according to GOLD criteria as FEV₁/FVC $<$ 0.70 with %FEV₁ $\geq$ 80% after bronchodilation.¹

Thus, obstructive disease was defined using a fixed-ratio threshold, whereas PRISm and restrictive patterns were defined using LLN-based criteria. This mixed approach follows prior epidemiological practice but does not constitute a unified physiological framework; group labels should therefore be interpreted descriptively.^{2,4,5}

Analysis Plan

We conducted the following analyses:

- I. Descriptive comparisons of clinical characteristics and spirometry across Normal, PRISm, and other ventilatory patterns;
- II. Exploratory contrasts within PRISm (rP vs NrP);
- III. A primary descriptive comparison between NrP and GOLD 1 COPD for clinical features, spirometry, and IOS; and
- IV. Longitudinal analyses in a trackable subset with ≥ 2 examinations.

To reduce confounding by Th2-high or asthma-dominant phenotypes, longitudinal analyses were restricted to individuals with > 10 pack-years of smoking, total immunoglobulin E (IgE) < 170 U/L, and blood eosinophils < 300 cells/ μ L. This restriction was intended to improve internal validity at the expense of sample size and generalizability.¹⁶

Imaging analyses using the percentage of low-attenuation area below -950 Hounsfield units (%LAA-950) on inspiratory computed tomography (CT) obtained within ± 6 months were descriptive. Expiratory CT was not routinely available. All spirometric and IOS values were post-bronchodilator.

Spirometry

Respiratory function was measured using a CHESTAC-8900 system (Rev. 1.6; Chest M.I. Co., Ltd., Tokyo, Japan) in accordance with ATS/ERS standards and Japanese Respiratory Society (JRS) guidelines.^{22,23}

Measured parameters included FVC, FEV₁, FEV₁/FVC, maximal mid-expiratory flow (MMF), and forced expiratory flow at 50% of FVC (FEF50 [V50]), expressed as percent predicted for the Japanese population.

After baseline spirometry, patients inhaled 200 μ g of salbutamol, and repeat testing was performed 15–20 minutes later. All analyses were based on post-bronchodilator values.

Impulse Oscillometry

Respiratory impedance was measured using the MostGraph-22 system (Rev. 1.2; Chest M.I. Co., Ltd., Tokyo, Japan) in accordance with established technical recommendations.^{12,13}

With a nose clip and cheek support, patients breathed quietly at tidal volume for approximately 30 seconds in the seated position. IOS was performed before spirometry to minimize the influence of forced expiratory maneuvers on peripheral-airway tone.^{12,13}

Measurements were repeated until quality criteria were met (≥ 3 technically acceptable recordings; coefficient of variation for $R5 \leq 10\%$), and the mean of acceptable measurements was analyzed.¹³

The following whole-breath indices were evaluated: $R5$, $R20$, $R5-R20$, $X5$, resonant frequency (F_{res}), and area of low reactance (ALX).

Clinical Features and Serology

We collected demographic and clinical variables including age, sex, body mass index (BMI), smoking status (current, former, or never) and cumulative exposure (pack-years). Laboratory data included peripheral white blood cell count, eosinophils, hemoglobin, total IgE, Krebs von den Lungen-6 (KL-6), surfactant protein-D (SP-D), blood glucose, lipid parameters, and B-type natriuretic peptide (BNP). These variables were considered potential contributors to between-group physiological differences and longitudinal change.

Chest CT Acquisition and Assessment

Non-contrast, supine, full-inspiration chest CT was acquired using a GE Discovery CT750 HD scanner. The helical series reconstructed at 1.25-mm slice thickness with a high-spatial-frequency lung kernel was analyzed; 2.5-mm axial images were not used. Examinations indicating pneumonia or acute exacerbation were excluded. Expiratory CT was not routinely obtained.

Emphysema burden was quantified as the percentage of low-attenuation area below -950 HU ($\%LAA-950$) and reviewed for plausibility by a blinded thoracic radiologist. Prior histopathologic studies have demonstrated that small-airway involvement may precede emphysema development.¹¹

Interstitial abnormalities and airway findings (eg, bronchial wall thickening, bronchiectasis) were recorded descriptively in accordance with ATS/ERS/JRS/ALAT guidance.²⁴

Statistical Analysis

The primary outcome was $R5-R20$, representing frequency-dependent peripheral airway resistance. Secondary outcomes included $X5$, F_{res} , ALX , and spirometric indices.

Group differences between NrP and GOLD 1 COPD were summarized using Hedges' g with 95% confidence intervals. Welch's t -tests were used for hypothesis testing, with Mann-Whitney U -tests performed as robustness checks. To account for multiple comparisons, Benjamini-Hochberg false discovery rate (FDR) correction was applied within prespecified families (IOS and spirometry).

For longitudinal analyses, annual slopes were estimated using simple linear regression. Given the small number of NrP participants with longitudinal IOS data, slope comparisons were considered exploratory. Sensitivity analyses excluded extreme outliers using Tukey's fences. All analyses were performed using JMP version 14.2 (SAS Institute Inc., Cary, NC). Continuous variables are presented as mean (SD), and categorical variables as n (%).

Ethics Approval and Informed Consent

The protocol was approved by the Nippon Medical School Hospital Ethics Committee (approval No. B-2024-861). The committee waived the requirement for written informed consent on the grounds that this was a minimal-risk, retrospective review of existing records with no interventions or additional costs to patients, and that obtaining consent from all individuals evaluated in 2013 would be impracticable; therefore, an opt-out procedure (public notice with an

opportunity to decline participation) was implemented. All data were de-identified before analysis. The study adhered to the Declaration of Helsinki and relevant national guidance.

Results

Study Population

A total of 1,139 individuals underwent post-bronchodilator spirometry during the study period.

Of these, 71 (6.2%) met criteria for PRISm, 127 (11.1%) met criteria for GOLD 1, and 459 (40.3%) had normal spirometry.

The flow of patient selection, including IOS availability and longitudinal follow-up, is shown in [Figure 1](#), and baseline characteristics are summarized in [Table 1](#).

Main Cross-Sectional Comparison: NrP Vs GOLD 1 (Primary Analysis; [TABLE 2](#))

Among 71 PRISm cases, 18 were classified as non-restrictive PRISm (NrP) of these, 8 had analyzable IOS and comprised the NrP subgroup for the primary comparison with 39 GOLD 1 patients.

Impulse Oscillometry (Primary Outcomes)

Across all IOS indices, NrP demonstrated higher small-airway resistance and more negative reactance compared with GOLD 1. Effect sizes were moderate to large, and differences in R5–R20, X5, Fres, and ALX remained significant after FDR adjustment ([Table 2](#)). These findings suggest possible differences in small-airway mechanics, although interpretation should remain cautious due to sample-size limitations.

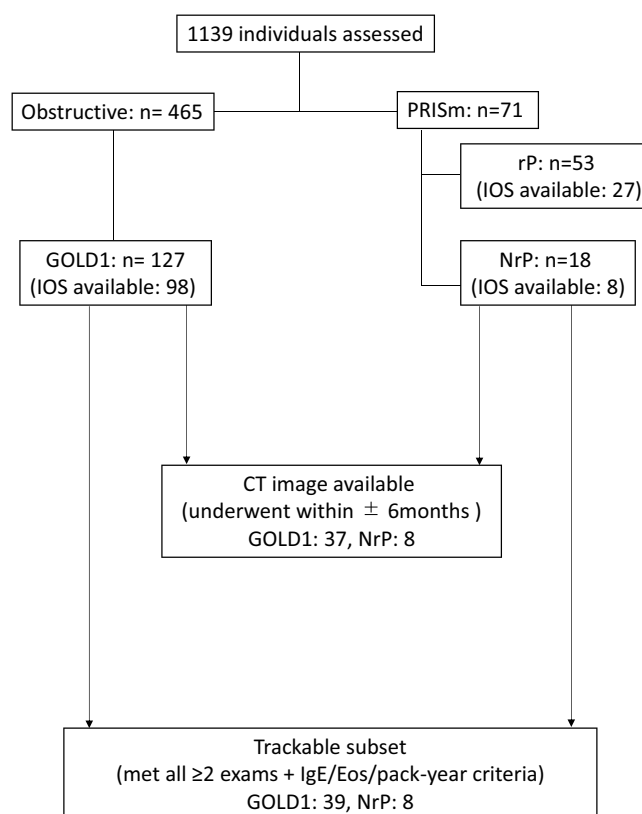


Figure 1 Flow of participant classification and data availability of 1139 individuals who underwent post-bronchodilator spirometry, 71 met criteria for PRISm and 465 for obstructive impairment (including 127 GOLD 1 cases). “IOS available” indicates participants for whom paper charts containing oscillometry tracings remained retrievable. Inspiratory chest CT performed within ± 6 months of the index visit was available for 37 GOLD 1 and 8 non-restrictive PRISm (NrP) participants and was used for exploratory descriptive analyses only. The trackable subset comprised GOLD 1 ($n = 39$) and NrP ($n = 8$) participants who had ≥ 2 examinations and met pre-specified IgE, eosinophil, and pack-year criteria; longitudinal IOS was collected only in this subset.

Table 1 Baseline Characteristics and Spirometric Parameters in Normal, PRISm, and GOLD I Groups

Variable	Normal (n=452)	PRISm (n=71)	GOLD I (n=126)	p-value
Age, years	62.4 ± 13.9	67.2 ± 15.1	70.5 ± 10.8	5.99×10 ⁻⁹
BMI, kg/m ²	22.8 ± 4.0	20.3 ± 4.5	22.7 ± 2.7	2.06×10 ⁻⁶
FEV ₁ , L	2.65 ± 0.76	1.77 ± 0.62	2.44 ± 0.58	<0.0001
FEV ₁ /FVC, %	79.1 ± 5.9	82.8 ± 8.9	64.0 ± 4.5	<0.0001
FEV ₁ (% predicted), %	100.9 ± 12.6	66.6 ± 11.8	92.1 ± 10.3	<0.0001
FVC (% predicted), %	104.0 ± 12.6	66.0 ± 15.6	114.7 ± 12.1	<0.0001
Sex, male, n (%)	258 (57.1)	51 (71.8)	103 (81.7)	7.31×10 ⁻⁷
Current, n (%)	33 (7.3)	8 (11.3)	7 (5.6)	2.04×10 ⁻⁶
Former, n (%)	227 (50.2)	40 (56.3)	97 (77.0)	
Never, n (%)	192 (42.5)	23 (32.4)	22 (17.5)	

Notes: Data are presented as mean (SD) or n (%). P-values from one-way ANOVA (continuous variables) and χ^2 -test (categorical variables) compare differences across the three groups. Smoking status categories (current, former, never) are analyzed as a single categorical variable.

Abbreviations: PRISm, preserved ratio impaired spirometry; GOLD, Global Initiative for Chronic Obstructive Lung Disease; BMI, body mass index; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; %FEV₁/FVC, percent predicted values.

Table 2 Cross-Sectional Comparison of Baseline Impulse Oscillometry and Spirometry Between GOLD I and Non-Restrictive PRISm (Trackable Subset)

Variable	GOLD I (n=39)	NrP (n=8)	p-value (MWU)
A. Demographics			
Age, yr	68.9 (10.4)	59.1 (8.1)	0.017
Current smoking, %	5.1	50.0	<0.001
Pack-years,	56.2 (27.8)	40.9 (12.8)	0.142
BMI, kg/m ²	23.4 (2.3)	25.3 (3.4)	0.068
Any maintenance therapy, n (%)	33 (84.6)	3 (37.5)	<0.01
B. Impulse oscillometry (Primary outcomes)			
R5–R20 (kPa s L ⁻¹)	0.34 (0.33)	0.70 (0.39)	0.047
X5 (kPa s L ⁻¹)	−0.46 (0.40)	−1.04 (0.36)	0.001
Fres (Hz)	8.3 (3.5)	11.8 (2.2)	0.009
ALX (kPa s L ⁻¹)	2.49 (2.87)	5.41 (2.40)	0.003

(Continued)

Table 2 (Continued).

Variable	GOLD I (n=39)	NrP (n=8)	p-value (MWU)
C. Spirometry (Secondary outcomes)			
FEV ₁ (%pred), %	91.76 (10.00)	76.80 (1.56)	<0.001
FEV ₁ /FVC, %	63.19 (4.98)	75.10 (3.18)	0.004
V50 (%pred), %	44.75 (13.45)	61.70 (12.48)	0.012
MMF (%pred), %	46.77 (13.98)	54.10 (12.00)	0.151

Notes: Data represent baseline (initial-visit) values from participants with retrievable IOS records and ≥ 2 examinations meeting pre-specified criteria (trackable subset: GOLD I = 39; NrP = 8). Only baseline values are shown; longitudinal changes are presented separately in [Figures 2 and 3](#). P-values are from Mann–Whitney *U*-tests (continuous variables), except for categorical variables, which use the χ^2 -test.

Abbreviations: NrP, non-restrictive PRISm; IOS, impulse oscillometry; R5–R20, frequency dependence of resistance; X5, reactance at 5 Hz; Fres, resonant frequency; ALX, low-frequency reactance area; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; MMF, maximal mid-expiratory flow; V50, expiratory flow at 50% of FVC.

Spirometry (Secondary Outcomes)

NrP showed higher FEV₁/FVC and %V₅₀ but lower %FEV₁ compared with GOLD I, with %MMF showing a non-significant trend ([Table 2](#)). These results illustrate a dissociation between effort-dependent spirometry and effort-independent IOS.

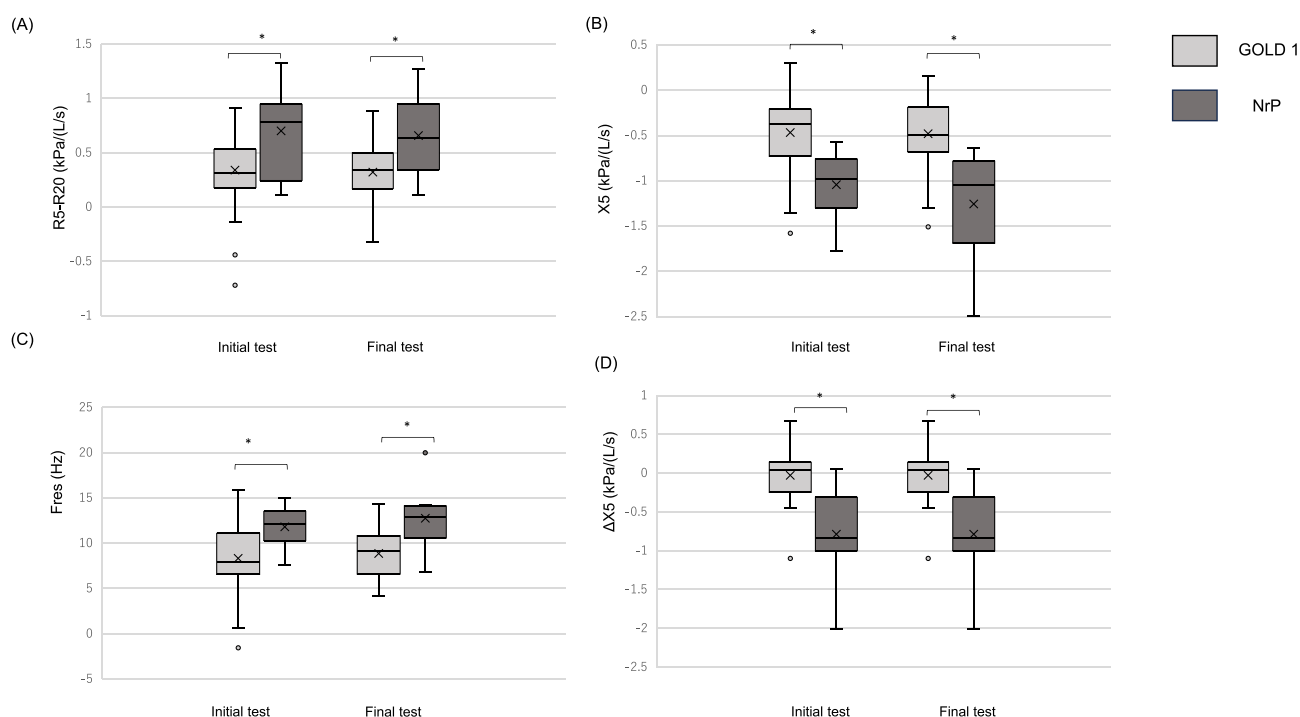


Figure 2 Cross-sectional comparison of impulse oscillometry indices between non-restrictive PRISm (NrP) and GOLD I COPD in the trackable subset at the initial and final tests. Panels show (A) R5–R20, (B) X5, (C) Fres, and (D) ΔX5. R5–R20, X5, and ΔX5 are expressed in kPa/(L/s), and Fres in Hz. Box-and-whisker plots show median, IQR, and outliers; cross symbols (x) indicate the mean value. * $p < 0.05$ between groups (Mann–Whitney *U*-test). All values are post-bronchodilator.

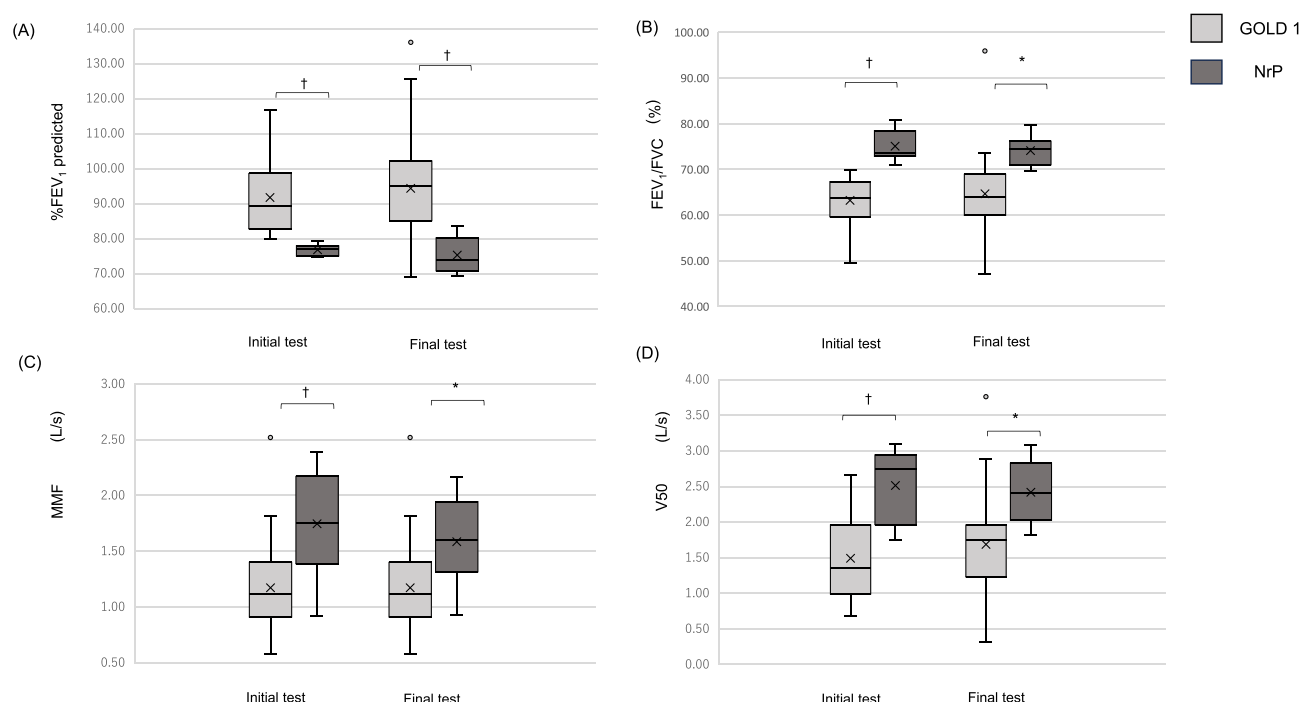


Figure 3 Cross-sectional comparison of spirometric indices between non-restrictive PRISm (NrP) and GOLD 1 COPD in the trackable subset at the initial and final tests. Panels show (A) %FEV₁ predicted, (B) FEV₁/FVC, (C) MMF, and (D) V50. MMF and V50 are expressed as measured values (L/s) to visualize distributional differences between groups. Box-and-whisker plots show median, IQR, and outliers; cross symbols (x) indicate the mean value. * $p < 0.05$, † $p < 0.001$ between groups (Mann-Whitney U-test). All values are post-bronchodilator.

CT Imaging (Descriptive)

Inspiratory CT was available for 37 GOLD 1 and 8 NrP patients. NrP exhibited lower emphysema burden across lobes on a descriptive basis. Given the small and imbalanced samples and the use of inspiratory-only CT, these observations should be interpreted cautiously.

Treatment Exposure (Potential Confounder)

Maintenance bronchodilator therapy (LABA/LAMA) was common in GOLD 1 but infrequent in NrP, with 62.5% of NrP receiving no maintenance treatment. This treatment imbalance represents a potential confounder in interpreting physiological differences.

Exploratory Comparison Within PRISm: Restrictive vs Non-Restrictive (TABLE 3; Descriptive Only)

Among PRISm patients, 53 were classified as restrictive PRISm (rP) and 18 as NrP.

To avoid definition-driven contrasts, FVC-dependent indices were excluded.

rP tended to be older, had lower BMI, and showed a higher frequency of interstitial abnormalities on CT, whereas NrP exhibited an airway-dominant physiological profile.

These analyses were exploratory, descriptive, and not powered for inference.

Longitudinal Changes (Trackable Subset) (Figures 2 and 3)

A total of 8 NrP and 39 GOLD 1 patients met criteria for longitudinal follow-up.

Median follow-up duration was 3.1 and 4.9 years, respectively.

Table 3 Exploratory Comparison of Baseline Characteristics, Pulmonary Function, and Serologic Features Between Restrictive and Non-Restrictive PRISm

Variables	rP (n=53)	NrP (n=18)	p-value
A. Baseline characteristics			
Age, yr	71.2 (13.2)	55.5 (13.8)	<0.001
BMI, kg/m ²	19.2 (3.7)	22.8 (4.3)	0.004
pack-years	35.6 (43.8)	22.9 (30.0)	0.26
A. Pulmonary function			
FEV ₁ /FVC, %	85.30 (8.7)	75.36(3.0)	<0.001
DLCO, mL/min/mmHg	9.87 (4.7)	19.61(5.6)	<0.001
MMF (%pred), %	83.82 (36.8)	56.42(14.1)	<0.001
V50 (%pred), %	81.4 (34.3)	62.6 (13.2)	0.001
A. Serology			
KL-6, U/mL	470.33 (408.8)	374.93 (171.5)	0.009
SP-D, ng/mL	98.78 (124.6)	64.72 (54.7)	0.003
A. CT image findings			
Interstitial abnormalities, n (%)	29 (54.7)	1 (5.6)	<0.001

Notes: Data are shown as mean (SD) or n (%). P-values are from Mann–Whitney *U*-tests for continuous variables and Fisher's exact tests for categorical variables (Fisher's exact test was used because of small expected cell counts). Because rP/NrP classification was based on FVC thresholds rather than lung volumes, observed differences may partly reflect operational definitions rather than intrinsic physiological subtypes. CT findings are descriptive and based on available inspiratory scans only. These comparisons are exploratory with no adjustment for multiplicity.

Abbreviations: PRISm, preserved ratio impaired spirometry; rP, restrictive PRISm; NrP, non-restrictive PRISm; BMI, body mass index; DLCO, diffusing capacity of the lung for carbon monoxide; MMF, maximal mid-expiratory flow; V50, expiratory flow at 50% of FVC; KL-6, Krebs von den Lungen-6; SP-D, surfactant protein-D; CT, computed tomography.

Impulse Oscillometry

Initial and final IOS distributions are shown in [Figure 2](#). Baseline differences persisted at the final visit, although annual slopes were exploratory due to small sample size.

Spirometry

Initial and final spirometry distributions are shown in [Figure 3](#). Annualized change in FEV₁ did not differ materially between groups, with wide variability in NrP and heterogeneous slopes in GOLD 1.

Discussion

In this retrospective observational study, we compared respiratory-mechanical characteristics of preserved ratio impaired spirometry (PRISm) with those of GOLD 1 COPD using post-bronchodilator spirometry and impulse oscillometry (IOS), with additional exploratory longitudinal analyses in a trackable subset. The prevalence of PRISm in our clinical cohort was 6.2%, lower than that reported in population-based studies (approximately 10%–15%), which likely reflects differences in study setting and case mix, as our cohort consisted of patients presenting for clinical evaluation rather than asymptomatic individuals identified through health screening programs.^{3,7–9}

Differences Between Restrictive and Non-Restrictive PRISm

Previous studies have proposed subclassifying PRISm based on the presence or absence of a restrictive spirometric pattern, with non-restrictive PRISm (NrP) reported to be more closely associated with smoking exposure and subsequent development of COPD than restrictive PRISm (rP).^{4,6,21} In our cohort, rP and NrP differed in several clinical and physiological characteristics.

However, because total lung capacity was not routinely measured, rP and NrP were defined using forced vital capacity thresholds, representing operational rather than physiological subgroups. Consequently, some between-subtype differences may reflect this definitional constraint rather than intrinsic biological distinctions. The relatively high proportion of rP observed in our cohort (>70%) further underscores the potential influence of classification criteria and study context. Given the small sample size and documented instability of PRISm classification over time, rP–NrP comparisons in this study should be interpreted as exploratory and hypothesis-generating.^{4,5}

Comparison Between Non-Restrictive PRISm and GOLD 1 COPD

The primary focus of this study was the comparison between NrP and GOLD 1 COPD. Despite partially overlapping spirometric profiles, clear differences in respiratory-mechanical indices were observed. NrP demonstrated less expiratory flow limitation on spirometry, while IOS consistently showed greater abnormalities in indices commonly interpreted as reflecting peripheral airway mechanics, including higher R5–R20, more negative X5, and elevated Fres and ALX.

These findings highlight a dissociation between spirometric and oscillometric assessments in NrP. Spirometry, which depends on forced expiratory maneuvers, may underestimate airway dysfunction when expiratory capacity is relatively preserved. In contrast, IOS, performed during tidal breathing, may detect subtle abnormalities in airway mechanics that are not evident on spirometry.^{12,13}

Although inspiratory CT demonstrated a lower emphysema burden in NrP compared with GOLD 1 COPD, IOS abnormalities were more pronounced in NrP. CT and IOS capture complementary physiological domains—parenchymal structure and airway mechanics, respectively—and prior histopathologic studies suggest that small-airway abnormalities may precede emphysematous destruction detectable on CT.¹¹

Importantly, these contrasts should be interpreted descriptively. Differences in age, smoking status, and bronchodilator treatment between groups represent major sources of residual confounding, and the modest sample size precluded multivariable adjustment. While key IOS findings were directionally consistent across statistical approaches, they do not establish disease-intrinsic or causal distinctions between NrP and early COPD.

Longitudinal Findings

In exploratory longitudinal analyses, annual rates of change in spirometric and IOS indices did not differ materially between NrP and GOLD 1 COPD. Declines in FEV₁ were modest in both groups, with greater variability in NrP. Given the very small number of NrP participants with longitudinal IOS data, these findings should be interpreted with caution and viewed as hypothesis-generating.

The absence of clear between-group differences in annualized change does not negate the cross-sectional physiological contrasts observed at baseline. Rather, it underscores the heterogeneity and dynamic nature of early airway disease and highlights the need for adequately powered prospective studies with standardized follow-up and comprehensive physiological assessment.^{4,5}

Limitations and Future Directions

Several limitations warrant consideration. PRISm is not incorporated into the formal ATS/ERS pulmonary-function interpretation framework, and our classifications were based on operational spirometric definitions. Total lung capacity and expiratory CT were not routinely available, limiting assessment of true restriction and air trapping. IOS data were available for only a subset of PRISm participants, and longitudinal analyses were restricted to a very small number of cases, precluding adjusted analyses.

Despite these limitations, IOS findings were directionally consistent across analyses. Future prospective studies incorporating lung-volume measurements, expiratory CT or parametric response mapping, and prespecified IOS endpoints will be required to determine whether IOS-defined abnormalities in PRISm predict subsequent functional decline or clinical outcomes.

Conclusion

In this exploratory analysis, PRISm and GOLD 1 COPD demonstrated different respiratory-mechanical patterns despite partially overlapping spirometric profiles. Whereas spirometry suggested relatively preserved expiratory flow in PRISm, IOS revealed abnormalities consistent with peripheral airway involvement. These observations underscore the physiological heterogeneity of PRISm and suggest that effort-independent measures such as IOS may complement spirometry in characterizing early or atypical airway dysfunction.

However, these findings should be interpreted cautiously. Group differences were influenced by small sample sizes, incomplete IOS availability, and major imbalances in age, smoking status, and bronchodilator exposure—factors that preclude causal or phenotypic inference. The present results therefore remain descriptive and hypothesis-generating.

Prospective, adequately powered studies with standardized treatment exposure, balanced comparison groups, and comprehensive imaging and lung-volume assessment are needed to clarify the clinical significance of IOS-derived mechanical patterns in PRISm and to determine their role in predicting progression or long-term outcomes.

Abbreviations

PRISm, preserved ratio impaired spirometry; GOLD, Global Initiative for Chronic Obstructive Lung Disease; NrP, non-restrictive PRISm; rP, restrictive PRISm; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; IOS, impulse oscillometry; R5–R20, frequency-dependent resistance; X5, reactance at 5 Hz; Fres, resonant frequency; ALX, low-frequency reactance area; %LAA–950, percentage of low-attenuation area below –950 HU.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Statement of Ethics

This study was performed in accordance with the Declaration of Helsinki and approved by the ethics committee of Nippon Medical School Hospital (approval number: B-2024-861). Although patient's consent was waived because this was a minimal risk retrospective study, we used an opt-out system for patients to declare whether or not they wish to participate.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article, gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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