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ORIGINAL RESEARCH

Prognostic Value of Impaired Spirometry in Patients with Myocardial Infarction: A Longitudinal Study of Two European Cohorts

Josefin Sundh[1,*], William AE Parker[2,3,*], Jonas Oldgren[4,5], Pontus Andell[6], Christian Reitan[7], Tomas Jernberg[7], Robin Hofmann[8], Moman A Mohammad[9], David Erlinge[9], Axel Åkerblom[4,5], Sofia Sederholm Lawesson[10], Kyriakos V Konstantinidis[11], Johan Lindbäck[5], Christer Janson[4], Anna Björkenheim[12], Nadir Elamin[2,3], Hannah McMellon[2,3], Bethany Moyle[2,3], Mehul Patel[13], Jad El Khoury[14], Raulin Surujbally[15], Stefan James[4,5,*], Robert F Storey[2,3,*]

[1]Department of Respiratory Medicine, Örebro University Hospital; Faculty of Medicine and Health, School of Medical Sciences, Örebro University, Örebro, Sweden; [2]Cardiovascular Research Unit, Division of Clinical Medicine, University of Sheffield, Sheffield, UK; [3]NIHR Sheffield Biomedical Research Centre, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK; [4]Department of Medical Sciences, Uppsala University, Uppsala, Sweden; [5]Uppsala Clinical Research Centre, Uppsala University, Uppsala, Sweden; [6]Department of Physiology and Pharmacology, Karolinska Institutet, and ME Cardiology, Karolinska University Hospital, Stockholm, Sweden; [7]Department of Clinical Science, Danderyd Hospital, Karolinska Institutet, Stockholm, Sweden; [8]Department of Clinical Science and Education, Division of Cardiology, Karolinska Institutet, Stockholm, Sweden; [9]Department of Cardiology, Clinical Sciences, Lund University, Skåne University Hospital, Lund, Sweden; [10]Clinical Department of Cardiology, Region Östergötland and Department of Health, Medicine and Caring Sciences, Linköping University, Linköping, Sweden; [11]Global Project, Respiratory and Immunology, BioPharmaceuticals R&D, AstraZeneca, Cambridge, UK; [12]Department of Cardiology, Faculty of Medicine and Health, Örebro University, Örebro, Sweden; [13]Clinical Development, Respiratory and Immunology, BioPharmaceuticals R&D, AstraZeneca, Cambridge, UK; [14]Global Medical Affairs, Global Medical Affairs, Cardiovascular, Renal & Metabolic Disease, BioPharmaceuticals Medical, AstraZeneca, Cambridge, UK; [15]Global Clinical Operations, Respiratory and Immunology, BioPharmaceuticals R&D, AstraZeneca, Cambridge, UK

*These authors contributed equally to this work

Correspondence: Josefin Sundh, Department of Respiratory Medicine, Örebro University Hospital, Örebro, Sweden, Email josefin.sundh@regionorebrolan.se

Purpose: The study aimed to investigate the associations between impaired spirometry such as obstructive pattern and preserved ratio impaired spirometry (PRISm) and occurrent cardiovascular events and deaths in patients with acute myocardial infarction.

Patients and Methods: Cohort study of 517 patients with age ≥40 years and ≥10 pack-years of smoking, hospitalized for myocardial infarction at eight sites in Sweden and the United Kingdom. The Vitalograph® COPD-6 device was used to assess the ratio of forced expiratory volume in 1 and 6 seconds (FEV_1/FEV_6) and FEV_1 as a percentage of the predicted value (FEV_1%pred). Obstructive pattern was defined as FEV_1/FEV_6 <0.7, PRISm as FEV_1/FEV_6 >0.7 and FEV_1%pred <80, and normal findings as FEV_1/FEV_6 ≥0.7 and FEV_1%pred ≥80. Follow-up data were obtained from national registers or follow-up visits. Multivariable Cox regression was used to analyze the associations of obstructive pattern and PRISm with the incidence of acute ischemic cardiovascular events or major adverse cardiovascular events (MACE), respectively, within one year.

Results: Obstructive pattern was found in 95 (18%), PRISm in 192 (37%) and normal spirometry in 230 (45%) patients. A cardiovascular event occurred in 21 (4%) and MACE in 28 (5%). Compared with normal spirometry, PRISm was independently associated with both new cardiovascular events (HR (95% CI) 3.44 (1.07–11.0)) and MACE (4.94 (1.63 to 15.0)), and obstructive pattern with MACE (3.87 (1.08–13.8)). Further adjustment for cardiac or COPD treatment did not substantially change the results.

Conclusion: About half of patients with acute myocardial infarction and a ≥10 pack-year smoking history have abnormal spirometry findings. Both obstructive pattern and PRISm are independently associated with increased risk for MACE within one year. We suggest that spirometry should be considered as a routine assessment in patients with smoking history and recent myocardial infarction.

Plain Language Summary:

- Impaired spirometry such as obstructive pattern as in chronic obstructive pulmonary disease (COPD) and preserved ratio impaired spirometry (PRISm) are associated with increased risk of mortality in the general population

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- The present study investigated the prevalence and associations of obstructive pattern and PRISm with and occurrent cardiovascular events and deaths in patients with acute myocardial infarction, in cohorts from Sweden and the United Kingdom
- We found that about half of patients with acute myocardial infarction and a ≥10 pack-year smoking history have abnormal spirometry findings
- In patients with acute myocardial infarction and a ≥10 pack-year smoking history, obstructive pattern and PRISm are both associated with increased one-year risk of occurrent acute ischemic cardiovascular events and cardiovascular deaths

Keywords: chronic obstructive pulmonary disease, COPD, obstructive pattern, preserved ratio impaired spirometry, PRISm, acute ischemic cardiovascular events, major adverse cardiovascular events, MACE

Introduction

Several large cohort studies have established chronic obstructive pulmonary disease (COPD) as an independent risk factor for cardiovascular disease and mortality.[1–4] Patients with a history of myocardial infarction represent a high-risk group in whom coexisting COPD has consistently been associated with increased morbidity and mortality.[5]

COPD is considered in patients with respiratory symptoms and/or a history of exposure to risk factors, and is confirmed by spirometry demonstrating an obstructive pattern with low ratio of forced expiratory volume in one second to forced vital capacity (FEV_1/FVC).[6] Another type of abnormal lung function pattern that has gained increasing interest is preserved ratio impaired spirometry (PRISm). In PRISm, the FEV_1/FVC ratio is normal but FEV_1 is decreased.[7] PRISm is a heterogeneous condition that may include both a restrictive pattern of similarly reduced FEV_1 and FVC, and pre-COPD where FEV_1 is low but FVC is normal. Patients with PRISm often experience respiratory symptoms and functional limitations, and transitions to COPD over time have been reported in 25% of cases.[8]

The prognostic significance of PRISm compared with obstructive and normal spirometry results has been investigated in several population-based studies where PRISm was associated with higher risks of incident cardiovascular disease as well as all-cause and cardiovascular mortality.[8–15] In the selected population of patients with a previous myocardial infarction, a single study has been published, reporting a higher all-cause mortality risk.[16] However, data on the associations of PRISm and obstructive pattern with the risk of future cardiovascular events in patients with newly diagnosed myocardial infarction are lacking.

We previously reported that the Vitalograph® COPD-6 device may be used to identify patients at risk of underlying respiratory disease among those hospitalised for myocardial infarction, demonstrating a prevalence of significant obstructive pattern of around 20% in patients with acute myocardial infarction and a ≥10 pack-year smoking history.[17] The aim of the present study was to explore the patterns of abnormal spirometry findings in the same cohort and to test our hypothesis that obstructive pattern and PRISm were associated with increased risk of new cardiovascular events and deaths within one year.

Materials and Methods

Study Design and Data Collection

This was a cohort study of 517 patients consecutively recruited at seven hospitals in Sweden from February 2022 to March 2023 and at one hospital in the United Kingdom from January to November 2022.[17] Inclusion criteria were ongoing hospitalization due to acute myocardial infarction, age ≥40, ≥10 pack years of smoking (regardless of current smoking status), and ability and willingness to provide written consent. Important exclusion criteria were current ischemic chest pain (eg. awaiting revascularization), acute pulmonary oedema, cardiogenic shock or other acute conditions in which forced respiratory manoeuvers could not be performed.

Baseline data on sex, age, comorbid diabetes, systolic blood pressure, current smoking status, body mass index (BMI) and relevant treatment at discharge in terms of beta-blockers, angiotensin-converting enzyme/angiotensin receptor inhibitors (ACE/AII-inhibitors), antiplatelet therapy (aspirin and $P2Y_{12}$ inhibitors), oral anticoagulants, statins, long-acting muscarinic antagonists (LAMA), long-acting beta-2-agonists (LABA) and inhaled corticosteroids (ICS), were obtained from clinical records and, in Sweden, also from the national quality register Swedish Web-system for

Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies (SWEDEHEART).[18] Follow-up data on cardiovascular events and mortality were obtained from the national Patient and Cause of Death registers (Sweden),[19,20] and from follow-up visits (United Kingdom).

Baseline information on lung function in both sub-cohorts was collected by performing microspirometry using the Vitalograph® COPD-6 device, which examines the ratio of forced expiratory volume in 1 and 6 seconds (FEV_1/FEV_6) and FEV_1 as percentage of the predicted value (FEV_1%pred).[21] The standard procedure includes three exhalations, with the best results of FEV_1/FEV_6, FEV_1 and FEV_6 saved in the device. An obstructive pattern is confirmed by establishing a FEV_1/FVC ratio below 0.7, and the COPD-6 device was originally developed as a screening instrument with ≥0.73 as a cut-off for ruling out obstructive disease.[22,23] However, as the maximum breath volume is usually exhaled in less than six seconds, several devices for FEV_1/FEV_6 assessment have also been proven valuable for COPD diagnosis, using FEV_1/FEV_6 <0.7 to define obstruction,[24–26] with very good correlation to ordinary spirometry.[27] In the present paper, baseline lung function data were used to further classify patients based on FEV_1/FEV_6 and FEV_1%pred as normal spirometry (defined as FEV_1/FEV_6 ≥0.7 and FEV_1%pred >80), PRISm (FEV_1/FEV_6 ≥0.7 and FEV_1%pred <80) and obstructive pattern (FEV_1/FEV_6 <0.7).[27]

A cardiovascular event was defined as an ischemic cardiovascular event consisting of a new myocardial infarction (fatal or non-fatal) (ICD-10, I21) or an ischemic stroke (I63), within one year. A cardiovascular death was defined as death due to any condition within ICD-10 chapter I within one year. Major adverse cardiovascular events (MACE) were defined as an ischemic cardiovascular event or cardiovascular death within one year.

Statistical Analysis

Patient characteristics were presented as mean and standard deviation for continuous variables (all approximately normally distributed) and as numbers and percentages for categorical variables. Crosstabulations with chi-square test and Kaplan-Meier curves were used to explore patient characteristics, cardiovascular events and MACE in patients with obstructive pattern, PRISm and normal spirometry. As a sub-analysis of the PRISm group, these patients were further divided into PRISm with restrictive pattern (ie, low FEV_6 in percentage of predicted (FEV_6%pred) as a proxy for low vital capacity in addition to low FEV_1%pred)[28] and PRISm with isolated low FEV_1%pred as a marker of pre-obstructive disease sometimes referred to as COPD 0.

Univariable and multivariable Cox regression, with adjustment for sex, age, comorbid diabetes and systolic blood pressure, used lung function pattern (in the three categories) as the explanatory variable, and all-cause death, cardiovascular events and MACE, respectively, as outcome variables. The models were repeated using obstructive pattern as the reference variable to allow a head-to-head analysis of obstructive pattern and PRISm, and with a binary variable of any pathological spirometry finding (obstructive pattern or PRISm) vs normal spirometry as the explanatory variable. The confounders were based on previous knowledge of risk factors for cardiovascular events and death. The main models were also repeated with further adjustment for relevant treatment at discharge as described above. Due to few missing data in the main model, complete case analysis was used. All analyses were performed using IBM SPSS version 26 (IBM Corporation, Armonk, NY, USA), and statistical significance was defined as a two-sided $p < 0.05$.

Ethics Approval and Consent to Participate

The study complies with the Declaration of Helsinki. The Swedish sub-study was approved by the Swedish Ethical Review Authority (Dnr 2021–05615-01), and the United Kingdom sub-study by the National Health Service Yorkshire & the Humber (Bradford/Leeds) Research Ethics Committee (Ref 22/YH/0015). All participants provided written informed consent.

Results

Patient characteristics were mostly similar in both sub-cohorts, with a mean age of 65 years and the majority being male (Table 1). The proportion of patients receiving oral anticoagulants was somewhat higher in Sweden, while current smoking and treatment at discharge with beta-blockers, antiplatelet therapy, LAMA and LABA were slightly more common in the UK (Table 1).

Table 1 Patient Characteristics, Treatments and Spirometry Results at Baseline, and Events at One-year Follow-Up, Distributed Over Sub-Cohorts

	Sweden	UK	All
Baseline characteristics			
Male sex, n (%)	229 (76)	159 (74)	388 (75)
Age, mean (SD)*	68 (10)	60 (10)	65 (11)
Systolic BP, mean (SD)*	147 (27)	123 (19)	137 (27)
Diabetes, n (%)	67 (22)	34 (16)	101 (20)
Current smoking, n (%)*	114 (38%)	124 (58%)	238 (46%)
BMI, n (%)			
<20	4 (1.5)	7 (4)	11 (2)
20.0–24.9	60 (22)	44 (24)	104 (23)
25.0–29.9	119 (44)	70 (37)	189 (41)
≥30	86 (32)	66 (35)	152 (33)
Treatment at discharge			
Beta-blockers, n (%)*	226 (75)	186 (87)	412 (80)
ACE/AII-inhibitors, n (%)	236 (78)	180 (84)	416 (81)
Antiplatelet therapy, n (%)*	279 (92)	213 (99)	492 (95)
Oral anticoagulants*	44 (15)	14 (7)	58 (11)
Statins, n (%)	272 (90)	203 (94)	475 (92)
LAMA, n (%)*	18 (6)	28 (13)	46 (9)
LABA, n (%)*	29 (10)	37 (17)	66 (13)
ICS, n (%)*	31 (10)	34 (16)	65 (13)
Spirometry pattern			
Normal, n (%)	137 (45)	93 (43)	230 (45)
PRISm, n (%)	111 (37)	81 (38)	192 (37)
Obstructive, n (%)	54 (18)	41 (19)	95 (18)
One year follow-up events			
MI, n (%)	10 (3)	5 (2)	15 (3)
CVL, n (%)	3 (1)	1 (1)	4 (1)
CV death, n (%)	7 (2)	1 (1)	8 (2)
All-cause death	12 (4)	5 (2)	17 (3)
CV events	13 (4)	6 (3)	19 (4)
MACE*	20 (7)	6 (3)	26 (5)

Note: Statistical differences between countries are indicated by an asterisk.
Abbreviations: ACE/AII-inihibitors, angiotensin converting enzyme/angiotensin II-receptor inhibitors; BMI, body mass index; BP, blood pressure; CV, cardiovascular; CVL, cerebrovascular lesion; ICS, inhaled corticosteroids; LABA, long-acting beta-2 agonists; LAMA, long-acting muscarinic antagonists; MACE, major adverse cardiovascular events; MI, myocardial infarction; PRISm, preserved ratio impaired spirometry; SD, standard deviation; UK, United Kingdom.

Obstructive pattern was found in approximately one-fifth of the merged population, while PRISm and normal spirometry were observed in about two-fifths each (Table 1). Within one year, a cardiovascular event occurred in 21 patients (4%) and the composite of MACE in 28 patients (5%) (Table 1). Total one-year mortality was 17 (3%) of whom 8 patients died from cardiovascular disease (Table 1).

The proportions of patients with current smoking, cardiovascular events and MACE were higher among those with PRISm and obstructive pattern than among patients with normal spirometry (Table 2 and Figure 1). Obesity was more frequent in patients with normal spirometry and PRISm compared with obstructive pattern (Table 2). The majority (94%) of the patients with PRISm, and all of the patients with both PRISm and MACE, had a restrictive pattern with both low FEV_1 and FEV_6. Among those with complete data on height and weight, BMI ≥30 was found in 40% of patients with restrictive PRISm compared with only 10% of patients with pre-obstructive pattern (COPD 0).

Table 2 Patient Characteristics and Outcomes Distributed Over Spirometry Pattern

	Normal Spirometry	PRISm	Obstructive	p-value
Male sex, n (%)	178 (77)	138 (72)	72 (76)	0.420
Age, mean (SD)	64 (11)	65 (11)	66 (10)	0.149
Systolic BP, mean (SD)	140 (26)	135 (27)	133 (26)	0.026
Diabetes, n (%)	38 (17)	48 (25)	15 (16)	0.054
Current smoking, n (%)	87 (38)	99 (52)	52 (55)	0.003
BMI, n (%)				0.001
<20	1 (1)	4 (2)	6 (7)	
20.0–24.9	39 (19)	39 (23)	26 (32)	
25.0–29.9	93 (46)	63 (37)	33 (40)	
≥30	70 (35)	65 (38)	17 (21)	
Beta-blockers	181 (79)	159 (83)	72 (76)	0.335
Antiplatelet therapy	219 (95)	181 (94)	92 (97)	0.633
Oral anticoagulants	18 (8)	26 (14)	14 (15)	0.087
Statins	210 (91)	177 (92)	88 (93)	0.906
ACE/AII inhibitors	188 (81)	148 (77)	82 (86)	0.175
LAMA	3 (1)	25 (13)	18 (19)	<0.001
LABA	16 (7)	33 (17)	17 (18)	0.002
ICS	19 (8)	28 (15)	18 (19)	0.017
CV events, n (%)	4 (2)	10 (5)	5 (5)	0.112
MACE, n (%)	4 (2)	15 (8)	7 (7)	0.009
CV death, n (%)	1 (0)	5 (3)	2 (2)	0.176
Death, all cause, n (%)	3 (1)	9 (5)	5 (5)	0.075

Abbreviations: ACE/AII inhibitors, angiotensin converting enzyme/angiotensin II receptor inhibitors; BMI, body mass index; BP, blood pressure; CV, cardiovascular; ICS, inhaled corticosteroids; LABA, long-acting beta-2-agonists; LAMA, long-acting muscarinic antagonists; MACE, major adverse cardiovascular events; PRISm, preserved ratio impaired spirometry; SD, standard deviation.

The risks of cardiovascular events and MACE were higher in both PRISm and with obstructive pattern compared with normal spirometry (Figure 2). In the multivariable Cox regression analyses, PRISm was independently and statistically significantly associated with MACE and cardiovascular events, and obstructive pattern with cardiovascular events (Table 3 and Figure 3). When the reference category was changed to obstructive pattern, no significant differences in the adjusted risk for CV events (HR (95% CI) 0.98 (0.33 to 2.91), p = 0.969) or MACE (1.28 (0.49 to 3.32), p = 0.617) were found for PRISm compared with obstructive pattern. Using the combined binary variable of obstructive pattern / PRISm vs normal spirometry, abnormal spirometry was independently associated with an increased risk for cardiovascular events (HR (95% CI) 3.46 (1.14 to 10.5) and MACE (4.58 (1.56 to 13.4).

Neither PRISm (HR (95% CI) 3.19 (0.86 to 11.9) nor obstructive pattern (2.00 (0.40 to 10.0) demonstrated an independent statistically significant association with all-cause mortality.

When the main Cox regression model was repeated with further adjustment for cardiac and COPD discharge treatment, the numerical risk estimates of cardiovascular events and MACE in patients with PRISm and obstructive pattern were only slightly reduced (Table 4). In this material, antiplatelet treatment was the therapy with a statistically significant association with a reduced risk of MACE (Table 4).

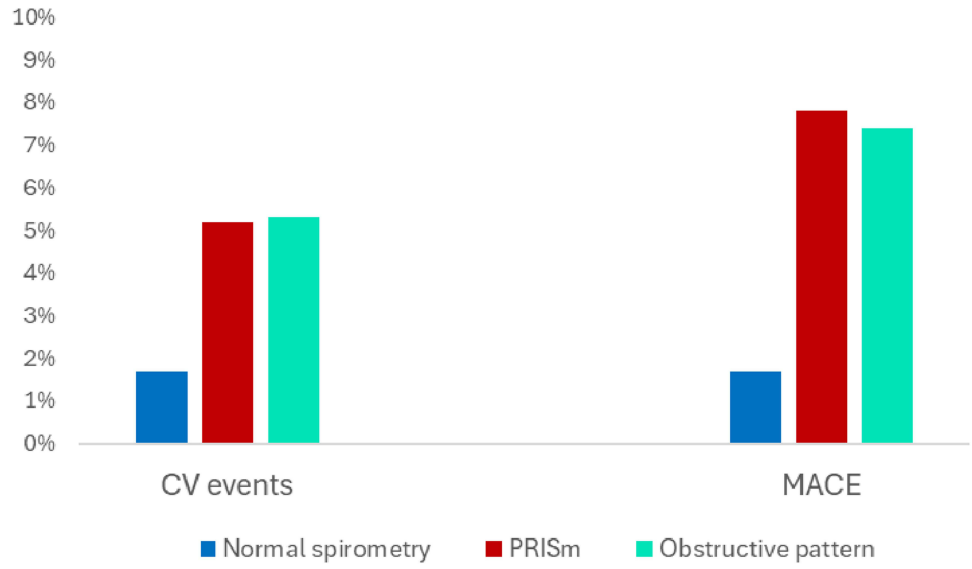

Figure 1 Proportions of CV events and MACE in different spirometry patterns.
Abbreviations: CV, cardiovascular; MACE, major adverse cardiovascular events; PRISm, preserved ratio impaired spirometry.

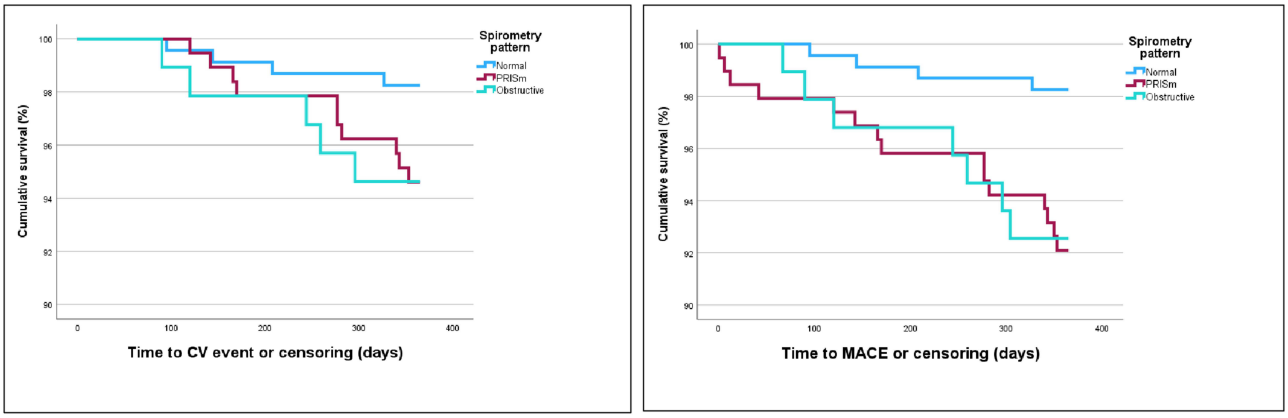

Figure 2 Kaplan-Meier curves of time to cardiovascular event and MACE in patients with obstructive, PRISm or normal spirometry patterns.
Abbreviations: CV, cardiovascular; MACE, major adverse cardiovascular events; PRISm, preserved ratio impaired spirometry.

Discussion

Main Findings

In this study of patients with a history of myocardial infarction and a ≥10 pack-year smoking history, impaired spirometry, whether consistent with an obstructive pattern or with PRISm, was associated with increased cardiovascular risk compared with those with normal spirometry. The associations remained robust in multivariable models adjusted for

Table 3 Results from Univariable and Multivariable Cox Regression, with Adjustment for Sex, Age, Diabetes and Systolic Blood Pressure

	CV Events		MACE	
	Unadjusted HR (95% CI)	**Adjusted HR (95% CI)**	**Unadjusted HR (95% CI)**	**Adjusted HR (95% CI)**
Spirometry pattern				
Normal	Ref	Ref	Ref	Ref
PRISm	3.12 (0.98–9.96)	3.44 (1.07–11.0)	3.12 (0.98–9.96)	4.94 (1.63–15.0)
Obstructive	3.16 (0.85–11.8)	3.51 (0.93–13.3)	3.16 (0.85–11.8)	3.87 (1.08–13.8)

(*Continued*)

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Table 3 (Continued).

	CV Events		MACE	
	Unadjusted HR (95% CI)	**Adjusted HR (95% CI)**	**Unadjusted HR (95% CI)**	**Adjusted HR (95% CI)**
Male sex	1.24 (0.41–3.73)	1.26 (0.41–3.84)	1.24 (0.41–3.73)	1.15 (0.45–2.90)
Age	1.02 (0.98–1.06)	1.01 (0.96–1.05)	1.02 (0.98–1.06)	1.03 (0.99–1.07)
Systolic BP	1.02 (1.00–1.03)	1.02 (1.00–1.04)	1.01 (1.00–1.03)	1.01 (1.00–1.03)
Diabetes	1.10 (0.36–3.30)	0.89 (0.29–2.72)	1.10 (0.36–3.30)	0.79 (0.30–2.13)

Abbreviations: BP, blood pressure; CI, confidence interval; CV, cardiovascular; HR, hazard ratio; MACE, major adverse cardiovascular events; PRISm, preserved ratio impaired spirometry.

baseline use of standard cardiac therapies and COPD inhaled treatments, underscoring the independent prognostic value in this high-risk group. Importantly, these prognostically significant findings were identified using a simple and feasible COPD-6 device for in-hospital screening.

Our results are consistent with several population-based studies, where COPD and PRISm have been reported as major prognostic risk factors for cardiovascular disease and mortality.[8–16] Our study extends previous knowledge of associations with all-cause and cardiovascular mortality in patients with myocardial infarction to include associations with cardiovascular events and MACE. As for all-cause mortality, we believe that the absence of a significant association with impaired spirometry could be due to low number of deaths in the present study.

Spirometry Patterns and Potential Underlying Conditions

As our study population had a clear tobacco exposure, we find it very reasonable to assume that an established obstructive pattern most likely is due to underlying COPD. As COPD is an established independent risk factor for heart disease,[1–4] this assumption is supported by our reported association of an obstructive pattern with a higher risk of MACE.

The relatively high prognostic importance of PRISm deserves further discussion. As described, PRISm is a heterogeneous condition that may include both a restrictive pattern of similarly reduced FEV_1 and FVC and the

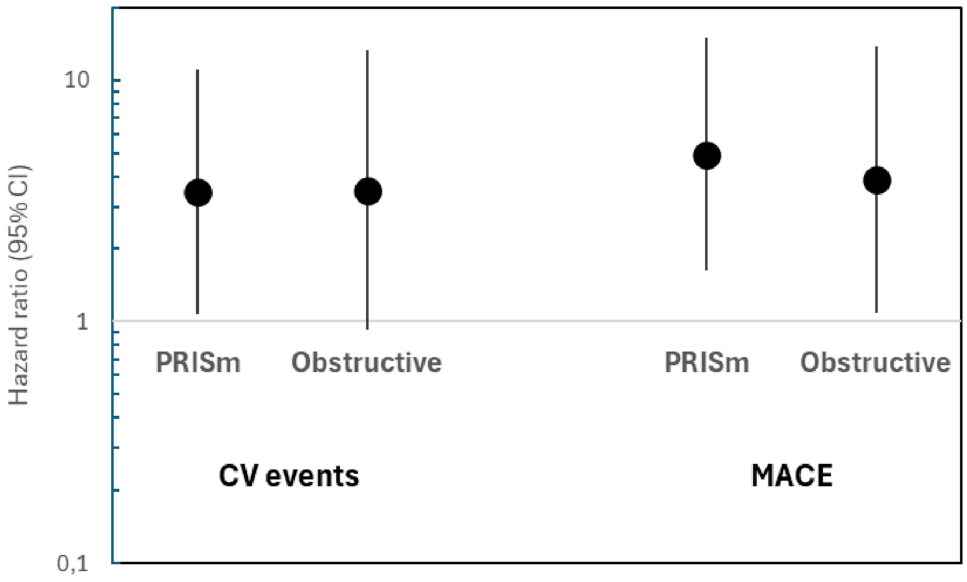

Figure 3 Associations of PRISm and obstructive spirometry with CV events and MACE. Results from Cox regression, respectively, with adjustment for sex, age, diabetes and systolic blood pressure.
Abbreviations: CI, confidence interval; CV, cardiovascular; MACE, major adverse cardiovascular events; PRISm, preserved ratio impaired spirometry.

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Table 4 Results from Univariable and Multivariable Cox Regression, with Adjustment for Sex, Age, Diabetes, Systolic Blood Pressure and Treatment

	CV Events	MACE
	Adjusted HR (95% CI)	**Adjusted HR (95% CI)**
Spirometry pattern		
Normal	Ref	Ref
PRISm	2.93 (0.86–9.96)	4.52 (1.44–14.2)
Obstructive	3.26 (0.82–12.9)	3.61 (0.97–13.4)
Male sex	1.57 (0.45–5.52)	1.71 (0.61–4.80)
Age	1.01 (0.96–1.06)	1.02 (0.98–1.07)
Systolic BP	1.02 (1.00–1.04)	1.02 (1.00–1.03)
Diabetes	1.00 (0.33–3.09)	0.80 (0.29–2.21)
Beta-blockers	0.50 (0.18–1.44)	0.52 (0.21–1.29)
ACE/AII-inhibitors	1.63 (0.26 to 7.37)	0.83 (0.30 to 2.26)
Antiplatelet therapy	0.17 (0.01 to 2.10)	0.15 (0.03 to 0.87)
Oral anticoagulants	0.28 (0.04 to 2.22)	0.66 (0.18 to 2.48)
Statins	0.80 (0.10 to 6.38)	0.36 (0.10 to 1.32)
LAMA	3.21 (0.41 to 25.0)	2.90 (0.46 to 18.4)
LABA	1.75 (0.14 −21.8)	1.12 (0.13 to 10.1)
ICS	0.40 (0.06–2.89)	0.57 (0.10–3.06)

Abbreviations: ACE/AII inhibitors, angiotensin converting enzyme/angiotensin receptor inhibitors;)BP, blood pressure; CI, confidence interval; CV, cardiovascular; HR, hazards ratio; ICS, inhaled corticosteroids; LABA, long-acting beta-2-agonists; LAMA, long-acting muscarinic antagonists; MACE, major adverse cardiovascular events; PRISm, preserved ratio impaired spirometry; SD, standard deviation.

condition sometimes referred to as pre-COPD or COPD 0, where FEV_1 is low but FVC is normal. Previous population-based studies have found both restrictive and obstructive spirometry patterns to be associated with all-cause as well as respiratory and cardiovascular mortality.[29,30] Restrictive patterns may be explained by intrapulmonary conditions such as pulmonary fibrosis, or by extrapulmonary conditions like obesity, thoracic deformations or neuromuscular diseases. In patients with acute myocardial infarction, secondary severe heart failure with fluid retention in the interstitial space may theoretically cause intrapulmonary restriction, but a detected PRISm with both reduced FEV_1 and FEV_6 would most likely be due to obesity.

In our study, the majority of the patients with PRISm had a restrictive pattern, and BMI ≥30 was much more common in patients with restrictive PRISm compared with patients with pre-COPD pattern with isolated low FEV1%pred. Thus, we speculate that the increased risk associated with PRISm in our study is driven by restrictive disease, probably most commonly due to metabolic syndrome with obesity, rather than solely pre-stage COPD. Heart failure with pleural effusion and interstitial fluid retention or interstitial lung disease were not exclusion criteria and could potentially have caused restriction in patients with normal or low BMI.

However, it is very important to keep in mind that in patients with COPD and a comorbid restrictive condition, the obstruction may be masked. If the vital capacity or FEV_6 is reduced both by higher residual volume due to emphysema (as part of COPD) and by reduced total lung capacity due to pulmonary or extrapulmonary restriction, the otherwise low ratio may be normalized. This means that we cannot exclude, especially in this setting with all patients having

a significant smoking history, that at least some of the patients with PRISm in our population had both COPD and restrictive disease, which would contribute to the increased risk.

Treatment Interventions

The fact that a majority of patients already had guideline-recommended treatment for secondary prevention after myocardial infarction at discharge from the initial hospitalization, may explain why differences in outcome events due to cardiovascular treatment at discharge were largely not found.

ICS has been suggested to reduce mortality in patients with COPD when used with long-acting bronchodilators, by decreasing the risk for both exacerbations and cardiovascular events.[31,32] Further adjustment for ICS usage did not reduce the estimates in our study, but we speculate that this may at least partly be due to low power with only a few patients using ICS.

Clinical Implication and Need for Further Research

We suggest that all patients with myocardial infarction and a smoking history should be considered for spirometry, and that patients with abnormal findings should be further referred to a pulmonologist or to a primary care physician. Further pulmonary investigation of patients with PRISm and no obvious untreated clinical heart failure could include body plethysmography and arterial blood gas analysis to identify obesity hypoventilation syndrome or overlap syndrome (COPD and obesity hypoventilation syndrome), which may require nocturnal home ventilation therapy, or computed tomography scanning to identify interstitial lung disease, which may warrant specific treatment.

The ongoing randomized controlled trial THARROS (clinicaltrials.gov nr NCT06283966) aims to investigate the utility of budesonide in combination with long-acting dual bronchodilators in preventing cardiorespiratory events in patients with COPD and comorbid cardiovascular disease or risk factors. However, future randomized controlled trials on the role of ICS in populations including PRISm are also warranted.

Strengths and Limitations

The major strengths of the study are the consecutive recruitment at multiple centers in two different countries, the longitudinal design and the completeness of follow-up data due to mandatory public health registers. Limitations include relatively limited power due to a small sample size, the absence of full spirometry or body plethysmography, lack of information on the potential confounder of occupational and environmental exposure to smoke, dust and gas, and some differences in data collection between countries. However, FEV_1/FEV_6 has been shown to correlate well with FEV_1/FVC (27), and the COPD-6 device is reliable for the diagnosis of obstructive disease.[24–26] As for event data collection, we believe the nature of our outcome events is fully captured by follow-up visits in secondary care or registers, as acute cardiovascular events are usually not managed outside hospitals.

Conclusion

About half of patients with acute myocardial infarction and a ≥10 pack-year smoking history have abnormal spirometry findings. Both findings of obstructive pattern and PRISm are independently associated with increased risk of MACE within one year. We suggest that spirometry should be considered a routine assessment in patients with a smoking history and a recent myocardial infarction.

Data Sharing Statement

Data cannot be made freely available as they are subject to secrecy in accordance with the Swedish Public Access to Information and Secrecy Act, but can be made available to researchers upon request, after approval from the Swedish Ethical Review Authority has been obtained: www.etikprovningsmyndigheten.se/en/.

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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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