News and Views

Cough: A Marker of Disease Progression in Fibrotic Interstitial Lung Disease

A study published online March 27, 2024 in the *American Journal of Respiratory and Critical Care* Medicine suggests that cough severity tends to worsen over time in patients with both idiopathic pulmonary fibrosis (IPF) and non-IPF fibrotic interstitial lung disease (ILD), irrespective of whether they receive ILD-targeted therapy[1].

A team of researchers from Australia and Canada focused on assessing the prevalence rates and longitudinal change in cough in patients with fibrotic ILD. They also examined the associations between cough severity and other demographic and clinical factors as well as implications of severity of cough on the overall management and prognosis. This study included 1,061 patients with IPF and 2,825 patients with non-IPF fibrotic ILD from the prospective multicenter Canadian Registry for Pulmonary Fibrosis. The 100 mm-Cough Severity Visual Analog Scale (VAS) was used to assess cough severity at baseline. Participants with IPF tended to be older, male, smokers (current or past) and had heart diseases.

The study findings indicate that patients with IPF generally experienced higher baseline cough severity compared to those with non-IPF fibrotic ILD (median 24 vs. 20 mm). The severity of cough was associated with gastroesophageal reflux disease in both cohorts. Worse cough severity also had significant adverse implications for health-related quality of life at baseline, a larger annualized decrease in DLCO (diffusing capacity of the lungs for carbon monoxide), disease progression and transplant-free survival in both IPF and non-IPF fibrotic ILD patients.

Additionally, the IPF patients showed a larger annualized increase in cough severity compared to the non-IPF fibrotic ILD patients (2.2 vs. 1.1 mm, respectively) indicating that cough severity may worsen more rapidly in IPF patients. Interestingly, there was no significant difference in worsening cough over time based on ILD-targeted therapy or lung function decline status.

To conclude, it is indeed common for patients with IPF and non-IPF fibrotic ILD to experience cough, though cough may be more pronounced in IPF patients. The level of cough severity reported by patients can have prognostic implications on various aspects of their health, including health-related quality of life, disease progression, and overall survival in fibrotic ILD. Monitoring and addressing cough severity in these patients can play a crucial role in managing their condition and improving their outcomes and quality of life.

Reference

1. Khor YH, et al; CARE-PF Investigators. Epidemiology and prognostic significance of cough in fibrotic interstitial lung disease. Am J Respir Crit Care Med. 2024;210(8):1035-44.

Benefits of Risk Factor Modification: It is Never Too Late to Act

Absence of five major cardiovascular risk factors (hypertension, hyperlipidemia, abnormal weight [underweight or overweight/obesity], diabetes, and smoking) at 50 years of age can extend life expectancy by more than a decade in both men and women. Controlling high blood pressure and quitting smoking in middle age also made a significant impact. These findings from a study by the Global Cardiovascular Risk Consortium involving over 2 million participants was published March 30, 2025 in the *New England Journal of Medicine*[1].

This global study, involving 2,078,948 participants from 133 cohorts in 39 countries, examined how the presence of five traditional cardiovascular risk factors affects the lifetime risk of cardiovascular disease (CVD) and all-cause mortality. The analysis enrolled individuals at age 50, and assessed their estimated life expectancy and years lived free of CVD or death up to 90 years of age based on the presence or absence of these five risk factors.

Results showed that men with all five risk factors at age 50 had a 38% lifetime risk of CVD, while this risk was 24% in women with all five risk factors. When participants with none of the risk factors and those with all the risk factors were compared, it was found that women gained 13.3 additional years free of CVD and 14.5 years free of death. Men gained 10.6 years free of CVD and 11.8 years free of death. Control of high blood pressure between ages 55 and 60 was associated with the most additional CVD-free years. Smoking cessation in the same age range contributed the most additional years free of death.

This study illustrates the high burden of traditional cardiovascular risk factors in middle-aged individuals and reemphasizes the impact of primary prevention.

Equally important, it bolsters the benefits of secondary prevention even when started at midlife. Cardiovascular risk assessment at age 50 therefore is important to mitigate risk factors, if present, and improve health outcomes with tailored interventions. It is never too late to act.

Reference

1. Global Cardiovascular Risk Consortium; Magnussen C, et al. Global effect of cardiovascular risk factors on lifetime estimates. N Engl J Med. 2025 Mar 30.

Start Combination Lipid Therapy Early after MI for Better Outcomes

Adding ezetimibe to statins within the first 12 weeks after the index myocardial infarction (MI) had fewer major adverse cardiovascular events (MACE) compared to those in whom the combination therapy was started late, according to findings from a Swedish study published April 22, 2025 in the *Journal of the American College of Cardiology*[1,2].

This study examined data of 35,826 statin-naïve patients hospitalized for MI between 2015 and 2022 and discharged on statins from the SWEDEHEART registry. Their median age was 65 years and 26% were women. The aim was to investigate the impact of early (within 12 weeks of discharge) versus delayed (from 13 weeks to 16 months after discharge) initiation of combination lipid-lowering therapy (statins + ezetimibe) on cardiovascular outcomes (MACE or cardiovascular death). Out of the total study group, 6,040 (16.9%) received early combination therapy, 6,495 (18.1%) received late combination therapy, and 23,291 (65.0%) received no ezetimibe. More than 98% were on high-intensity statins. Those who did not receive ezetimibe were older, had more comorbidities, and had lower baseline low-density lipoprotein (LDL) cholesterol.

After nearly 4 years of follow-up, 2,570 patients experienced a MACE, including 440 cardiovascular-related deaths. The incidence of MACE at 1 year in the early, late, and no ezetimibe arms was 1.79, 2.58, and 4.03 per 100 patient-years, respectively. Compared with early combination therapy, the weighted risk differences in MACE for late combination therapy were 0.6% at 1 year, 1.1% at 2 years, and 0.7% at 3 years, with a hazard ratio (HR) of 1.14 at 3 years. In the no ezetimibe group, the risk difference was 0.7%, 1.6%, and 1.9%, respectively, with a HR of 1.29 at 3 years. For cardiovascular death, the HRs were 1.64 and 1.83 in the late combination and no ezetimibe arms.

European guidelines recommend a stepwise approach to initiating lipid-lowering therapy in all patients with atherosclerotic CVD, including those presenting with acute coronary syndrome or undergoing percutaneous coronary intervention, to achieve the recommended lipid targets[3].

The study concluded that adding ezetimibe to lipid-lowering therapy, whether started early or later, led to more patients achieving LDL cholesterol levels below 55 mg/dL. However, reductions in MACE were greater with early combination therapy compared to delayed initiation of combination therapy. Conversely, patients who did not receive ezetimibe were at the highest risk of experiencing MACE and cardiovascular death. These findings support the immediate initiation of combination therapy as standard practice in post-MI patients.

References

1. Leosdottir M, et al. Early ezetimibe initiation after myocardial infarction protects against later cardiovascular outcomes in the SWEDEHEART Registry. J Am Coll Cardiol. 2025;85(15):1550-64.
2. American College of Cardiology. SWEDEHEART Registry: Early ezetimibe combination therapy may reduce CV risk post MI. Dated Apr 16, 2025. Available at: https://www.acc.org/Latest-in-Cardiology/Journal-Scans/2025/04/16/17/09/SWEDEHEART-Registry. Accessed Apr 22, 2025.
3. Koskinas KC, et al. Lipid-lowering therapy and percutaneous coronary interventions. EuroIntervention. 2021;16(17):1389-403.

PRISm: A Precursor to Chronic Obstructive Lung Disease

Preserved ratio impaired spirometry (PRISm) is associated with the development of airway obstruction within a decade, regardless of smoking status, with similar odds of disease progression among nonsmokers, former smokers, and current smokers, according to a retrospective study published online March 7, 2025, in the journal *Chest*.[1].

This study, part of the OLIN COPD cohort, aimed to determine the relationship between smoking clinical features, smoking habits, spirometric patterns, especially PRISm and future development of airway obstruction, a characteristic feature of COPD. The study retrospectively analyzed data from 902 patients with airway obstruction (forced expiratory volume in 1 second/vital capacity [FEV1/VC] ratio <0.70) and 819 matched controls without airway obstruction (FEV1 to VC ratio ≥0.70). All of them had undergone prior clinical evaluations 10.5 years earlier before inclusion in the OLIN COPD study.

PRISm, characterized by a normal FEV1/VC ratio but reduced FEV1, was more prevalent among those who later developed airway obstruction (18.6%) a decade later than controls (13.4%). Greater percentage of patients (45.1%) were current smokers than controls (18.2%); whereas the percentage of former smokers (stopped smoking at least 12 months previously) was comparable between the two groups (31.8% vs 34.9%, respectively). Patients also reported significantly more respiratory symptoms (chronic productive cough 3 months in a year, any wheeze in the last 12 months, or dyspnea) (78.0%) at baseline than controls (44.3%).

Examination of factors associated with having airway obstruction revealed that current smoking had the highest overall risk with adjusted odds ratio (aOR) of 4.1, but former smokers (aOR 1.5), and those with PRISm alone were also at elevated risk (aOR 3.5).

PRISm findings were independently associated with future development of airway obstruction regardless of smoking status, with aOR of 2.9 in current smokers, 3.8 in former smokers, and 3.7 in never-smokers (<1 cigarette/day for 1 year). Having PRISm alone increased the likelihood of airway obstruction by fourfold (aOR 4.87), whereas the combination of PRISm with a restrictive spirometric pattern raised the odds by approximately threefold (aOR 2.92). The aOR for restrictive spirometric pattern alone, without concomitant PRISm findings, was 0.48. These findings highlight PRISm as a vital early spirometric pattern that precedes COPD and necessitates clinical attention not only among smokers, but also in nonsmokers, who are generally not regarded as high-risk due to their non-smoking status. Patients with PRISm that transitioned into airway obstruction were more symptomatic and showed a more rapid decline in FEV1 vis-a-vis PRISm that did not transition into airway obstruction. Identifying PRISm through spirometry should be a part of COPD assessment. This would enable earlier intervention, closer monitoring, and initiation of preventive measures, such as pulmonary rehabilitation, or targeted anti-inflammatory therapies.

Reference

1. Backman H, et al. Preserved ratio impaired spirometry is an important risk factor for development of COPD, also in those who do not smoke. Chest. 2025 Mar 8:S0012-3692(25)00274-0.

Prepregnancy Body Weight and Future Heart Health

In healthy pregnant women, a prepregnancy BMI in the overweight or obese range nearly doubled the risk of gestational diabetes (GDM) and hypertensive disorders of pregnancy or HDP (gestational hypertension and pre-eclampsia), which were linked to the emergence of multiple cardiovascular risk factors by midlife. These findings were published in the *Journal of the American College of Cardiology*[1].

Researchers from Northwestern University, Chicago and The Ohio State University, Ohio conducted this study to evaluate whether adverse pregnancy outcomes mediate the relationship between prepregnancy body mass index (BMI) and development of CVD risk factors in midlife. The analysis included 4,269 pregnant women, mean age 30 years, who were enrolled in the Hyperglycemia and Adverse Pregnancy Outcomes Follow-Up Study (HAPO FUS) at mean gestation age of 28 weeks (ranging from 24 to 32 weeks) and who had no history of prepregnancy hypertension or diabetes. The follow-up duration after delivery was 11.6 years.

Results showed that around 10.6% participants had prepregnancy obesity, while 21.7% had overweight and 67.7% had normal prepregnancy BMI. About 13.8% had GDM and 10.7% had new-onset HDP. BMI, as calculated by self-reported prepregnancy weight, was within normal range in 67.7%, overweight in 21.7%.

At follow-up conducted at a mean age of 41.7 years, participants with prepregnancy obesity had significantly higher mean arterial pressure (MAP) by 7.0 mmHg, triglyceride levels by 28.5 mg/dL, and hemoglobin A1c (HbA1c) by 0.3% compared to those with a normal prepregnancy BMI. Mediation analysis revealed that GDM accounted for 24.6% of the association between prepregnancy obesity and HbA1c, while new-onset HDP mediated 12.4% of the association between obesity and MAP. In addition, GDM was associated with greater likelihood of developing hypertension (aOR 1.72), type 2 diabetes (aOR 7.01), and diabetes or prediabetes by midlife (aOR 4.30) compared with those who did not have GDM. Similarly, new-onset HDP was also significantly associated with a higher likelihood of hypertension (aOR 3.05), type 2 diabetes (aOR 1.88), and midlife diabetes or prediabetes (aOR 1.44) than in those with a normotensive pregnancy.

These findings highlight the critical role of prepregnancy health in determining long-term cardiovascular outcomes. Pregnancy and reproductive history should be integrated into cardiovascular risk assessment, at midlife or even earlier. Promoting a healthy body weight and lifestyle behaviors prior to conception may help prevent pregnancy complications and also reduce the risk of future CVD.

Reference

1. Borrowman JD, et al. Prepregnancy adiposity, adverse pregnancy outcomes, and cardiovascular disease risk in midlife. J Am Coll Cardiol. 2025;85(15):1536-46.