News and Views

Targeting Treatable Traits in Obstructive Lung Diseases

Many patients with obstructive lung diseases have various combinations of treatable traits (TTs) necessitating the need for personalized management for better disease control, according to a recent study published in the *International Journal of Chronic Obstructive Pulmonary Disease*[1].

The aim of this study was to ascertain the prevalence of TTs and their co-existence in patients, aged ≥18 years, with obstructive lung diseases. In addition, the researchers also sought to examine the stability of these traits over time and whether management had any impact on these traits and clinical outcomes.

Data of 8,663 patients with asthma, 4,822 patients with chronic obstructive pulmonary disease (COPD), and 1,761 patients with asthma-COPD overlap attending primary care, obtained from the Dutch asthma/COPD service between 2007 and 2023, was analyzed retrospectively. Eight TTs were evaluated: insufficient inhaler technique, poor medication adherence, Type 2 eosinophilic inflammation, current smoking, obesity, physical inactivity, reversible airflow limitation, and anxiety and/or depression. Participants were followed up within 1 to 2 years of the study.

Overall, 83.3% of patients had ≥1, and 48.9% of patients had ≥2 TTs. Compared to patients with asthma (60.3%) or COPD (59.0%), more patients with asthma-COPD overlap had ≥2 TTs (79.9%). The most prevalent TT was insufficient inhaler technique (43.6%), followed by poor medication adherence at 40.3%, and blood eosinophilia at 36.9%. A significant reduction in the trait at follow-up (OR: 0.61) was noted among patients with blood eosinophilia, along with an improvement in health status following recommendation from the pulmonologist that the General Practitioner start or increase the dose of inhaled corticosteroids (ICS) compared to patients who did not receive this advice. No significant association between management advice and the exacerbation rate was noted at the follow-up visit.

This study demonstrated that TTs are common among COPD patients, with nearly half of the study group exhibiting at least 2 traits in various combinations. A thorough evaluation of the patient with a checklist of TTs by the primary care physician followed by a personalized, trait-targeted management may help improve management of obstructive airway diseases. As per the authors, "a TT approach is feasible to implement".

Reference

1. Lars Dijk, et al. Treatable traits in patients with obstructive lung diseases in a well-established asthma/COPD service for primary care. Int J Chron Obstruct Pulmon Dis. 2025;20:1189-201.

Radiological Clues to Pulmonary TB with Pleural Effusion on Chest CT

"Does the frequency of subpleural micronodules and interlobular septal thickening correlate with the presence of pleural effusion in patients with pulmonary tuberculosis (TB)?" Researchers from South Korea sought to find an answer to this research question in a retrospective single-center study, where they analyzed the presence of pleural effusion in patients with pulmonary TB in relation to CT scan findings[1]. The frequency of subpleural micronodules was examined. The distribution of micronodules (peribronchovascular, septal, subpleural, centrilobular, and random), as well as other CT scan findings such as large opacity (consolidation/macronodules), cavitation, tree-in-buds, bronchovascular bundle thickening, interlobular septal thickening, lymphadenopathy and pleural effusion were also analyzed. The patients were divided into two groups based on the presence of pleural effusion, and their clinicoradiologic findings were compared.

A total of 338 patients who had been diagnosed with pulmonary TB between January 2017 and November 2019 were enrolled for this study. Sixty patients were excluded from the study due to the presence of co-existing pulmonary diseases such as pneumonia, intrathoracic malignancy and metastasis, pulmonary edema, and severe old TB.

According to the findings published in the journal *Chest*, the frequency of subpleural nodules was significantly higher in patients with pulmonary TB and pleural effusion (69%) compared to those without effusion (14%). Similarly, interlobular septal thickening was also more common in the group with pleural effusion (81%) compared to the group without effusion (64%). Conversely, tree-in-buds were uncommon in patients with pulmonary TB and pleural effusion (29%) than in those without effusion (48%).

Based on the analysis of CT scan findings in patients with pulmonary TB, this study shows that subpleural nodules and septal thickening were more frequently observed in patients with pleural effusion versus those without pleural effusion. This suggests a potential correlation between the development of pleural effusion and TB involvement of the pulmonary lymphatics in the peripheral interstitium. However, further research and investigation is required to establish a definitive causal relationship between these factors.

Reference

1. Jung MK, et al. CT scan differences of pulmonary TB according to presence of pleural effusion. Chest. 2023; 164(6):1387-95.

CONFIDENCE in Combination Therapy for CKD and Type 2 Diabetes

Starting combination therapy with finerenone and empagliflozin results in a greater reduction in urinary albumin-to-creatinine ratio (UACR) over 6 months compared to monotherapy with either drug in patients with chronic kidney disease (CKD) and type 2 diabetes. These breakthrough findings from the multicenter CONFIDENCE (COmbinatioN effect of FInerenone anD EmpaglifloziN in participants with chronic kidney disease and type 2 diabetes using a UACR Endpoint) trial were recently published in the *New England Journal of Medicine*[1,2]. A high UACR is indicative of kidney disease. UACR <30 mg/g is considered normal or at goal.

The trial investigators randomized 800 patients with CKD, albuminuria, and type 2 diabetes in a 1:1:1 ratio to one of three treatment arms: 10 or 20 mg of finerenone once daily (with empagliflozin-matching placebo), 10 mg of empagliflozin once daily (with finerenone-matching placebo), or a combination of finerenone + empagliflozin. The mean age of the participants was 66 years and one-quarter of them were female. Patients were enrolled from 14 countries between July 2022 and August 2024.

At baseline, the estimated glomerular filtration rate (eGFR) was 30-90 mL/min/1.73 m^2 of body surface area, the UACR was 100 to ≤5,000 mg/g, and the mean glycated hemoglobin (HbA1c) was 7.3. The primary study outcome was the percentage change in UACR from baseline to 180 days. Safety outcomes were also assessed.

At baseline, the median UACR was similar across the three intervention groups (258 in the finerenone group, 261 participants in the empagliflozin group, and 265 in the combination-therapy group) at 579 (interquartile range, 292 to 1092). The mean eGFR was 54.2 mL/min/1.73 m^2 and the mean A1c was 7.3. About 28% of patients had a history of atherosclerotic cardiovascular disease (ASCVD), 16% had diabetic retinopathy, 4% had heart failure, ~23% were on glucagon-like peptide-1 receptor agonists (GLP-1RA) and 98.4% were taking angiotensin receptor blockers or angiotensin-converting enzyme inhibitors.

After 180 days, the combination therapy reduced UACR by 29% more than with finerenone alone (least-squares mean ratio, 0.71; $p < 0.001$) and by 32% more than with empagliflozin alone (least-squares mean ratio, 0.68; $p < 0.001$). The UACR was reduced by 52% in the combination therapy group at the end of the study (least-squares mean ratio 0.48). The reduction in UACR with combination therapy was rapid, with a >30% decline by Day 14 and a >40% decrease by Day 90.

UACR declined rapidly in the combination therapy group, with a reduction of over 30% from baseline seen within 14 days, which exceeded 40% after 90 days. During the 30-day washout period following treatment cessation, UACR levels rose but remained below baseline in both the finerenone and combination groups.

No unforeseen adverse events were reported in any group. Symptomatic hypotension, acute kidney injury, and hyperkalemia resulting in drug discontinuation were rare and had minimal clinical impact. Combination therapy was associated with a transient increase in serum potassium, with a mean rise of 0.27 mmol/L after 14 days, which returned to near baseline 30 days after treatment cessation. An early decline in both eGFR and systolic blood pressure was observed, but these changes generally rebounded after discontinuation of the study drugs.

This randomized trial provides clear compelling evidence for early and synergistic renoprotection by combining finerenone and empagliflozin in patients with CKD and type 2 diabetes, which may have potential for a paradigm change in clinical practice. Moreover, the combination therapy was well-tolerated. Hence, starting combination therapy at the very outset, instead of treading the traditional stepwise path, could significantly delay progression of CKD more effectively than with the use of either drug alone and optimize clinical outcomes.

References

1. Agarwal R, et al; CONFIDENCE Investigators. Finerenone with empagliflozin in chronic kidney disease and type 2 diabetes. N Engl J Med. 2025;393(6):533-43.
2. Available from: https://www.acc.org/Latest-in-Cardiology/Journal-Scans/2025/06/17/18/34/Finerenone-Plus-Empagliflozin. Dated June 17, 2025. Accessed Aug 7, 2025.

Genitourinary Complications of SGLT2i in Men with Type 2 Diabetes

Use of sodium-glucose cotransporter 2 inhibitors (SGLT2i) in men with type 2 diabetes is associated with a significantly elevated risk of phimosis, especially evident within the first year after treatment initiation, according to a study published July 30, 2025 in the journal *Diabetes Care*[1]. The risk was found to persist over 8 years of follow-up.

The researchers undertook this study to evaluate the likelihood of developing phimosis in men with type 2 diabetes initiating treatment with SGLT2i compared to those starting GLP-1RA. Adult Danish male patients taking metformin and initiated either SGLT2i or GLP-1RA between 2016 and 2021 were included in this population-based, active-comparator new-user cohort study. The short- and long-term risks of phimosis were assessed using weighted intention-to-treat analyses, with data drawn from population-based medical databases.

The study included a total of 32,486 men who were taking SGLT2i and 14,793 who were put on GLP-1RA. The median follow-up period was 4 years with a maximum of 8 years. At 1 year follow-up, the risk of phimosis was higher in participants on SGLT2i (0.9%) compared to those in the GLP-1RA group (0.5%) with a risk ratio of 1.88. At 8 years, the cumulative risk rose to 4.8% among those taking SGLT2Is versus 3.6% in GLP-1RA users. The 8-year risk ratio of 1.36.

These findings highlight the increased risk of phimosis associated with the use of SGLT2i vis-à-vis GLP-1RAs, both in the short-term and over long-term follow-up. This higher risk can be attributed to SGLT2i-induced glucosuria, which may create a favorable environment for infection and inflammation by disturbing the preputial microenvironment thereby increasing the risk of phimosis. Hence, patients receiving SGLT2i should be monitored for genital infections and also counseled about genital hygiene.

Reference

1. Ljungberg C, et al. Risk of phimosis associated with SGLT2i versus GLP-1RA: A Danish cohort study. Diabetes Care. 2025 Jul 30:dc250693.

Higher Muscle Mass Lowers Risk of Incident Type 2 Diabetes

New research published in the journal *Diabetes, Obesity and Metabolism* has linked greater muscle mass in women with lower risk of type 2 diabetes[1]. For men, this association was significant only among those with reduced muscle mass.

In this population-based cohort study, Chinese adults without a history of diabetes were enrolled from the WATCH (West chinA adulT health CoHort) database, a large health check-up-based database, between January 2010 and December 2020. The researchers used predicted skeletal muscle mass index (pSMI) to estimate skeletal muscular mass and measure the blood glucose variables. Self-reported history was evaluated to identify new-onset diabetes.

The objective of the study was to examine the sex-specific associations between the pSMI and incident type 2 diabetes. This retrospective study involved 47,885 adults with a median age of 40 years; 53.2% of the study group were women. After a median follow-up of 5 years, 1836 participants (5.3% of men and 2.1% of women) developed type 2 diabetes.

Results further showed that a higher pSMI in women was associated with a lower risk of incident type 2 diabetes with hazard ratio (HR) per standard deviation increment in pSMI of 0.79. In men, a nonlinear association between pSMI and incident type 2 diabetes was observed. Among men with pSMI ≤8.1 (indicative of lower muscular mass), a higher pSMI was associated with a lower risk of incident type 2 diabetes with HR of 0.58. However, there was no significant association between pSMI and incident diabetes (HR 1.08) for men with pSMI ≥8.1 (indicative of higher muscular mass).

To conclude, this study aimed to investigate whether there are differences in the relationship between pSMI and incident type 2 diabetes based on gender. It showed a gender difference in the association between skeletal muscle mass and incidence of type 2 diabetes. In women, a larger muscular mass was associated with a reduced risk of type 2 diabetes. This suggests that having more muscle mass may have a protective effect against developing type 2 diabetes in females. On the other hand, for men, this association was significant only among those with reduced muscle mass. This implies that in males, the relationship between muscular mass and the risk of type 2 diabetes is dependent on the initial muscle mass.

Reference

1. Liu D, et al. Sex-specific associations between skeletal muscle mass and incident diabetes: a population-based cohort study. Diabetes Obes Metab. 2024;26(3):820-8.

Unmasking Future Stroke Risk in Young Women Through Obstetric History

Women with a history of pregnancy complications such as pre-eclampsia, preterm birth, gestational diabetes,

miscarriage, and stillbirth are more likely to develop a stroke before the age of 50 years, according to a study published August 6, 2025, in the journal *Neurology*[1,2].

The objective of the study was to evaluate the association between pregnancy complications and the underlying causes of ischemic stroke in 1012 women aged 18 to 49 years. These included pre-eclampsia, preterm birth before 37 weeks, small-for-gestational-age (SGA) births, gestational diabetes and pregnancy loss, including miscarriage and stillbirth.

The analysis included data of 358 women who had a first ischemic stroke, confirmed by imaging, from the Observational Dutch Young Symptomatic StrokE studY (ODYSSEY), and 714 women without stroke from the Pregnancy and Infant Development (PRIDE) study.

Results showed that over half of the women (51%) who had a stroke had at least one complication during pregnancy compared to 31% of those without a stroke. Young women who experienced an ischemic stroke at a median age of 28 years were more likely to have a history of hypertensive disorders of pregnancy, SGA infants, preterm birth, gestational diabetes, stillbirth, and miscarriage, compared to women, median age 29 years, without ischemic stroke.

Women with a history of stillbirth had nearly a fivefold increased risk of experiencing a stroke. Those with a history of pre-eclampsia were around four times more likely to have a stroke, while the risk was increased threefold among women who had preterm births or delivered SGA infants. Ischemic stroke likely due to large artery disease was more common in women with a history of hypertensive disorders of pregnancy, SGA, and preterm birth compared with women with a cryptogenic stroke.

These findings therefore suggest that women with a history of pregnancy complications are at high risk of experiencing an ischemic stroke, specifically atherosclerotic stroke. However, this study only denotes an association and not causality.

An advisory from the American Heart Association (AHA) and the American College of Obstetricians and Gynecologists (ACOG) recognizes adverse pregnancy outcomes as a cardiovascular disease risk factor and suggests that these can be used to identify women who are at an increased risk for ASCVD, "even in those for whom the conditions resolve after delivery". The Advisory further notes that these risk factors are often not assessed during standard ASCVD risk assessment[3].

"Pregnancy complications may be an early warning sign of stroke risk, even before age 50", write the authors. Obstetric history, therefore, should be a part of evaluation of stroke risk. Awareness of this association may help clinicians to identify at-risk patients who could benefit from early preventive measures and targeted cardiovascular care, even at a young age.

References

1. Verburgt E, et al. History of pregnancy complications and the risk of ischemic stroke in young women. Neurology. 2025;105(5):e214009.
2. American Academy of Neurology Press release. Available at: https://www.aan.com/PressRoom/Home/PressRelease/5275. Dated Aug. 6, 2025. Accessed August 8, 2025.
3. Brown HL, et al; American Heart Association and the American College of Obstetricians and Gynecologists. Promoting risk identification and reduction of cardiovascular disease in women through collaboration with obstetricians and gynecologists: a presidential advisory from the American Heart Association and the American College of Obstetricians and Gynecologists. Circulation. 2018;137:e843-52.

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