News and Views

Temporal Patterns of Cardiovascular Risk after COPD Exacerbations

Chronic obstructive pulmonary disease (COPD) patients with severe exacerbations are at a high immediate risk of experiencing cardiovascular events, within 1 to 14 days post-exacerbation. Conversely, patients with moderate exacerbations were at highest risk 14 to 30 days following the acute exacerbation event. The risk remained elevated 1 year later irrespective of the severity of exacerbation. These findings from a population-based study from the UK were published April 15, 2024 in the *American Journal of Respiratory and Critical Care Medicine*[1].

This study investigated the temporal relationship between exacerbations of COPD and new-onset nonfatal cardiovascular events. Data for COPD patients in England was sourced from the Clinical Practice Research Datalink Aurum primary care database from 2014 to 2020. Information about various individual and composite cardiovascular events such as acute coronary syndrome, arrhythmia, heart failure (HF), ischemic stroke, and pulmonary hypertension was determined from the linked hospital data. The index date was defined as the occurrence of the first COPD exacerbation; for those without exacerbations, it was defined as the date of eligibility for the trial.

Out of the 213,466 patients assessed, 146,448 (68.6%) reported at least one exacerbation. Over half (~56%) of these had moderate exacerbations, while ~13% had severe exacerbations. A total of 40,773 cardiovascular events occurred during the course of the study.

Analysis revealed an immediate period of heightened cardiovascular risk within 1 to 14 days after any exacerbation as indicated by the adjusted hazard ratio (aHR) of 3.19. The elevated cardiovascular risk declined progressively but persisted beyond the immediate post-exacerbation period, with an aHR of 1.84 after 1 year.

The risk was highest within 14 days after a severe exacerbation with aHR of 14.5. In patients with moderate exacerbations, the risk was highest after 14 to 30 days with aHR of 1.94.

Patients were nearly 13 times more likely to develop arrhythmia within 2 weeks of a severe exacerbation with aHR of 12.7. The likelihood of HF was also elevated almost ninefold with aHR of 8.31.

To conclude, cardiovascular events after moderate exacerbations occur a little later than after severe exacerbations. By demonstrating the differences in the timing of cardiovascular events following moderate and severe COPD exacerbations, this study highlights significant increases in cardiovascular risk following exacerbations. The extended duration of heightened cardiovascular risk beyond 1 year, regardless of exacerbation severity, underscores the chronic impact of COPD exacerbations on cardiovascular health.

This emphasizes the ongoing need for being vigilant and proactively monitor and proactive manage cardiovascular risk in COPD patients, even in the absence of acute exacerbations. The authors also note "*post-exacerbation intervention approaches should include the management of cardiopulmonary risk to reduce the risk of COPD and cardiovascular events in the short and long terms*".

Reference

1. Graul EL, et al. Temporal risk of nonfatal cardiovascular events after chronic obstructive pulmonary disease exacerbation: a population-based study. Am J Respir Crit Care Med. 2024;209(8):960-72.

Impact of Diabetes Duration and Glycemic Control on Heart Failure Risk in Type 2 Diabetes

Increased levels of glycated hemoglobin (HbA1c), fluctuations in HbA1c, and a history of severe hypoglycemia are all significant risk factors for HF in patients with type 2 diabetes, suggests a study published September 13, 2024 in the journal *Diabetes, Obesity and Metabolism*[1].

This study from Australia systematically reviewed longitudinal studies investigating the association of glycemic risk factors such as HbA1c, HbA1c variability, hypoglycemia, and diabetes duration with HF in patients with type 2 diabetes. The objective was to explore the link between these factors and the risk of HF in these patients.

The final analysis included 40 studies involving 4,102,589 participants. Analysis showed a 15% increased risk of HF for each 1% increase in HbA1c, a 2% increased risk for each additional year of diabetes and a 43% increased risk for individuals with a history of severe hypoglycemia. A 20%-26% increased risk of HF was observed for each unit increase in the metrics of HbA1c

variability (HbA1c standard deviation, coefficient of variation, and average successive variability). All included studies scored high in the risk of bias assessment indicating that issues such as selection bias, confounding factors, and reporting bias might have influenced the results. Results from Egger's test showed the presence of publication bias suggesting that studies reporting strong associations between HbA1c levels and HF risk were more likely to be published, while those with negative or weaker findings might have been underreported or not reported. After adjusting for publication bias, a 14% increased risk of HF per percentage point increase in HbA1c was observed on trim-and-fill analyses.

This study has highlighted the contribution of glycemic risk factors and duration of diabetes to the increased risk of HF in patients with type 2 diabetes. Early intervention and proactive management of these risk factors to achieve stable glycemic levels, reducing HbA1c variability and avoiding severe hypoglycemic episodes may minimize the risk and improve patient outcomes.

Reference

1. Tabesh M, et al. The association of glycaemic risk factors and diabetes duration with risk of heart failure in people with type 2 diabetes: a systematic review and meta-analysis. Diabetes Obes Metab. 2024;26(12):5690-700.

Placenta *In Situ* Management of Placenta Accreta Spectrum Disorders

Most women with placenta accreta spectrum (PAS) disorder who were managed with placenta left *in situ* did not develop infection or bleeding necessitating hysterectomy, as per findings from a single-center study published in *Obstetrics & Gynecology*[1].

This retrospective cohort study planned to investigate maternal outcomes when the placenta was left *in situ* in women with PAS as an alternative to cesarean hysterectomy for either planned uterine preservation or planned delayed hysterectomy later. The study was conducted from January 2015 to October 2024. The outcomes examined were risk of infection, significant bleeding culminating in hysterectomy, rates of blood transfusion, and serious maternal morbidity.

The study included 180 patients who had been diagnosed with PAS antenatally. Of these, 50 were planned for leaving the placenta *in situ*. Cesarean hysterectomy was performed in 7 (14%) due to antepartum or intraoperative hemorrhage, while 43 (86%) were successfully managed by leaving the placenta *in situ*. Among the 43 patients in whom the placenta was left *in situ*, 5 (12%) needed a hysterectomy due to bleeding, and 4 (9%) developed endometritis. No venous thromboembolism or maternal deaths occurred. Twenty-nine of this subgroup were planned for uterine preservation, and 14 for delayed hysterectomy. Leaving the placenta *in situ* was successful with a median time to placental expulsion or resorption of 17 weeks in 13 (45%) out of the 29 patients planned for uterine preservation. Sixteen (55%) eventually underwent interval hysterectomy, either for clinical indications or patient preference.

Women who underwent successful uterine preservation experienced significantly lower estimated blood loss (700 vs. 1,950 mL), transfusion rates (31% vs. 73%), and blood transfusions exceeding 4 units (8% vs. 47%) compared with patients who underwent interval hysterectomy. Five women subsequently conceived, with no recurrence of placenta previa or PAS. Analyses comparing patients by planned procedure - planned uterine preservation versus planned interval hysterectomy - revealed no significant differences in median estimated total blood loss, the proportion requiring blood transfusion, or transfusion volumes exceeding 4 units.

Based on these findings, the study concluded that leaving the placenta *in situ* may be a feasible and safe alternative to cesarean hysterectomy in selected PAS cases, particularly for women wanting uterine preservation. Most patients in this group did not develop complications such as infection or bleeding requiring hysterectomy. While these results may be used in counseling patients, this is an observational study. And, proper selection of patients for this approach is essential. The authors also caution that the small sample size necessitates cautious interpretation, as this could have precluded detection of rare but potentially serious complications.

Reference

1. Amro FH, et al. Leaving placenta in situ for management of placenta accreta spectrum disorder. Obstet Gynecol. 2025;145(6):683-9.

Cardiovascular Outcomes in COPD: Prognostic Role of Frailty

Chronic obstructive pulmonary disease (COPD) patients with greater frailty levels are at significant risk of experiencing major adverse cardiovascular events (MACE) in a decade, according to a study published in the *International Journal of Chronic Obstructive Pulmonary Disease*[1].

This study investigated the long-term impact of frailty on the risk of MACE, defined as a composite of acute coronary syndrome, HF, and stroke, in 1,527 Japanese patients with COPD. For this the researchers used data,

between 2013 and 2023, from the Sado-Himawari Net electronic health record system in Sado City, Niigata Prefecture, Japan. The participants were categorized into four groups based on the hospital frailty risk score (HFRS): no-frailty (HFRS = 0), low frailty (HFRS >0 and <5), intermediate frailty (HFRS ≥5 and <15), and high frailty (HFRS ≥15).

During the 10-year follow-up, nearly one-quarter (23.8%) of COPD patients experienced MACE, with acute coronary syndrome occurring in 7.4%, HF in 10.2%, and stroke in 12.8% of cases. MACE occurred more frequently among those with HFRS ≥15 points.

In multivariable analysis, COPD was associated with MACE as follows: no-frailty versus low HFRS (HR, 1.47 [95% CI, 1.01-2.14], $p < 0.05$), intermediate HFRS (HR 2.00 [1.34-2.97], $p < 0.001$), and high HFRS (HR 2.62 [1.50-4.59], $p < 0.001$) during a 10-year follow-up. Similar relationships were observed even after adjusting for the severity of airflow limitation and COPD exacerbation. After adjusting for variables like age, sex, inhaled treatments, comorbidities, COPD exacerbations, and severity of airflow limitation, the HRs were 1.47 for low frailty, 2.00 for intermediate frailty, and 2.62 for high frailty compared to the no-frailty group. These associations were statistically significant.

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2025 Report highlights that frailty is more prevalent in individuals with COPD and can help identify patients at risk of poor outcomes. The five components of frailty are exhaustion, slowness, weakness, low physical activity, and unintended weight loss[2].

The findings of the present study indicate frailty as an independent predictor of cardiovascular risk in COPD patients. While cardiovascular diseases are common in COPD patients, they are often "underdiagnosed and undertreated". Evaluation of frailty could help clinicians to stratify the cardiopulmonary risk and guide early implementation of preventive strategies using a multidisciplinary approach. Hence, frailty assessment should be a part of routine management of COPD patients.

References

1. Hamada K, et al. Impact of frailty on major adverse cardiovascular events in chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis. 2025;20:3111-22.
2. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2025 Report.

Risk Factors for Renal Dysfunction in Newly Diagnosed Type 2 Diabetes

Nearly 13% of patients who have been newly diagnosed with type 2 diabetes develop a rapid decline in kidney function within 3 years, suggests a new study published recently in the *European Journal of Internal Medicine*[1].

In this study, Giuseppina Tiziana Russo, from the Department of Clinical and Experimental Medicine at the University of Messina, Italy, and co-researchers undertook to examine the prevalence of rapid estimated glomerular filtration rate (eGFR) decline in patients with newly diagnosed type 2 diabetes. They also sought to identify factors that contribute to the decrease in eGFR. Data for the study was obtained from the Associazione Medici Diabetologi (AMD), the Italian Association of Clinical Diabetologists Annals initiative. Rapid eGFR decline was defined as an annual decrease in eGFR >5 mL/min/1.73 m^2.

The study included 105,163 participants, including 57.7% males, who had been diagnosed with type 2 diabetes between January 2010 and December 2019. Their baseline eGFR was >30 mL/min/1.73 m^2. Of these, 13,587 (12.9%) showed a rapid decline in eGFR at the 3-year follow-up, "most without kidney function impairment at baseline", note the authors. Age, female gender, HbA1c, smoking, high baseline eGFR, retinopathy, and albuminuria were found to be independent predictors of a faster decline in eGFR.

This study has shown that a significant number of patients with newly diagnosed type 2 diabetes had a rapid decline in eGFR, which is a predictor of end-stage renal disease (ESRD) and mortality. Also, several factors were associated with the faster decline. Early identification of these patients is vital as they require more intensive observation and treatment to slow down the progression of renal disease. "Given the association between dynamic changes in eGFR and the risk of ESRD or death, we suggest to include this variable in the definition of chronic kidney disease (CKD)", conclude the authors.

Reference

1. Russo GT, et al; AMD Annals Study Group. Prevalence and clinical determinants of rapid eGFR decline among patients with newly diagnosed type 2 diabetes. Eur J Intern Med. 2024;130:123-9.

Mitigating CKD Risk in Obesity Through Joint Risk Factor Control

Optimal control of six key modifiable risk factors reduced the risk of CKD in persons with obesity by

almost half, according to a study published in the journal *Diabetes, Obesity and Metabolism*[1].

Rui Tang, from the Department of Epidemiology, School of Public Health and Tropical Medicine, Tulane University, New Orleans and colleagues conducted this study to explore how comprehensive management of multiple risk factors could reduce the elevated risk of CKD in individuals with obesity. They analyzed control of risk factors in 97,538 participants with obesity at baseline and compared them with 97,538 age- and sex-matched, normal-weight control participants without CKD from the UK Biobank. Joint risk factor control was evaluated by assessing six major CKD risk factors: blood pressure, smoking status, A1c, low-density lipoprotein cholesterol (LDL-C), albuminuria, and levels of physical activity. The participants were followed until the endpoints of the study, which were occurrence of CKD, death or the end of the follow-up period.

Over a median follow-up period of nearly 11 years, there were 3,954 cases of incident CKD among participants with obesity and 1,498 in matched participants without obesity. Analysis of risk factor revealed that 2,487 participants with obesity had two risk factors under joint control; 12,720 had three risk factors under control, 32,388 had four risk factors under control, 36,988 had five risk factors under control, and 15,381 six risk factors under combined control. Participants with ≤2 risk factors under control were taken as the reference group.

After controlling for confounding variables, the aHR of controlling ≤2 risk factors in persons with obesity was 2.11; for three risk factors, the aHR was 1.28; for four, it was 1.23; for five it was 1.22 and for all six factors, it was 0.99.

In participants with obesity, joint risk factor control was associated with a gradual reduction in the risk of developing CKD. Optimal control of each additional risk factor resulted in an 11% reduction in the risk of CKD risk with HR of 0.89, while optimal control of all six major risk factors led to a 49% decrease in CKD risk (HR 0.51). Moreover, in individuals with obesity who achieved successful control of all six risk factors, the increased risk of CKD typically linked to obesity was effectively eliminated, making their risk comparable to that of normal-weight control participants.

The protective effect of the degree of joint risk factor control was more robust in men than in women, in individuals with a lower healthy food score versus those with a higher score, and among diabetes medication users compared to nonusers.

This study has demonstrated an inverse association between collective control of all six risk factors and CKD risk in a cumulative manner among individuals with obesity. All these risk factors are modifiable. A joint management strategy targeted at attaining optimal control of these risk factors can significantly and effectively offset the heightened risk of CKD typically linked to obesity.

Reference

1. Tang R, et al. Degree of joint risk factor control and incident chronic kidney disease among individuals with obesity. Diabetes Obes Metab. 2024;26(11):4864-74.

Ocular Surface Changes in Type 2 Diabetic Nephropathy

More than half of patients with type 2 diabetic nephropathy have dry eye disease, suggests a study from Vietnam published May 6, 2024 in the journal *Clinical Ophthalmology*[1]. Advanced age, high HbA1c levels and decreased eGFR were also identified as factors that were independently associated with dry eye disease.

A total of 338 individuals, consisting of 169 patients with type 2 diabetic nephropathy and 169 patients with type 2 diabetes but without renal complications as a control group, were included in this cross-sectional study. All subjects were evaluated for Ocular Surface Disease Index (OSDI) via a questionnaire and test fluorescein tear-film break-up time (TBUT). Patients with OSDI scores <13 and TBUT values ≤10 seconds were diagnosed with dry eye. The aim of this cross-sectional study was to determine the prevalence of dry eye among patients with type 2 diabetic nephropathy and also identify factors potentially associated with dry eye in these patients.

The prevalence of dry eye among type 2 diabetic nephropathy patients was found to be significantly higher than the control group, with rates of 55.6% versus 37.3%, respectively. They had higher OSDI scores but lower TBUT than the type 2 diabetes alone group.

The type 2 diabetic nephropathy patients with dry eye were older and had a longer duration of diabetes. They also had a higher percentage of participants with hypertension, peripheral nerve complications, anemia including insulin users compared with those without dry eye in the group. This subgroup also had higher levels of plasma glucose, HbA1c, urea, creatinine and high-sensitivity C-reactive protein.

Advanced age, high HbA1c level and decreased eGFR were identified as independent factors associated with dry eye in type 2 diabetic nephropathy patients.

This study highlights dry eye as a common condition in patients with type 2 diabetic nephropathy compared to those with type 2 diabetes mellitus without renal complications. The authors note, "*kidney complications and eye complications often go together, and 'renal-retinal syndrome' originates from this coincidence*". It further elucidates on potential risk factors contributing to a better understanding of ocular complications in this population.

Reference

1. Tran Tat T, et al. Dry eye and some related factors in patients with type 2 diabetic nephropathy: a cross-sectional study in Vietnam. Clin Ophthalmol. 2024:18:1217-24.

Predicting Exacerbation Risk in Bronchiectasis

Bronchiectasis patients with no or minimal exacerbations, but who are severely symptomatic, are at an increased risk of future exacerbations, according to a study of more than 9,000 patients, reported in *The Lancet Respiratory Medicine*[1].

Oriol Sibila from the Department of Respiratory, Hospital Clinic, University of Barcelona, and colleagues conducted this observational study to assess whether daily symptoms could independently predict future exacerbations in patients with bronchiectasis and if symptom burden could help identify participants eligible for macrolide therapy. Data from 9,466 participants with bronchiectasis, median age 68 years; 60.9% women, from the multicenter European Bronchiectasis Registry (EMBARC) were analyzed, and findings were validated through a post-hoc pooled analysis of three randomized controlled trials of macrolides treatment in bronchiectasis (BLESS, BAT, EMBRACE) in 341 participants.

The symptoms were measured using the Quality-of-Life Bronchiectasis Questionnaire Respiratory Symptoms Score (QoL-B-RSS) at baseline and at 1 year follow-up. The score ranged from 0 to 100 with high scores indicative of mild symptoms.

QoL-B-RSS includes nine questions related to respiratory symptoms such as congestion, cough, sputum production, sputum color, wheeze, shortness of breath during daily activity, chest pain, shortness of breath while talking, and nocturnal cough.

Findings revealed a median Bronchiectasis Severity Index (BSI) score of 7. *Pseudomonas aeruginosa* was detected in the sputum of 2,041 patients (21.6%) within 12 months of baseline.

Both previous exacerbations and symptoms were found to be independent risk factors for future exacerbations. Each additional exacerbation increased the risk for future such events by 11% (rate ratio [RR] 1.11 per additional exacerbation). Each 10-point reduction in symptom score (QoL-B-RSS) increased the risk by 10%.

Of note, patients with no previous exacerbations but high symptom scores experienced similar exacerbation risks (RR 1.55) during 1-year of follow-up as those with ≥3 prior exacerbations and average symptom scores (RR 1.58; QoL-B-RSS 60-70). A similar pattern was seen in the post-hoc analysis of the three randomized controlled trials, the macrolide-treated as well as the placebo groups. The number-needed-to-treat (NNT) to prevent one exacerbation with long-term macrolide therapy was comparable between patients with frequent prior exacerbations and average symptom scores (NNT = 1.45) and those with few prior exacerbations but high symptom scores (NNT = 1.43).

Current guidelines recommend long-term macrolide therapy only for patients who experience frequent exacerbations. However, this study indicates that symptom burden, independent of prior exacerbation history, is strongly predictive of future exacerbations. Patients with no or minimal exacerbations but high symptoms are at comparable risk to those with frequent exacerbations and average symptoms. They could benefit equally from macrolide treatment similar to patients with a high baseline exacerbation frequency. Therefore, risk stratification and therapeutic decision-making in bronchiectasis should routinely include assessment of symptoms. "Treating patients with high symptom burden is likely to reduce disease activity and prevent the progression to the frequent exacerbator stage", note the authors.

Reference

1. Sibila O, et al. Symptoms, risk of future exacerbations, and response to long-term macrolide treatment in bronchiectasis: an observational study. Lancet Respir Med. 2025;13(10):911-20.

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