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Medicine Update

PROGNOSTIC SIGNIFICANCE OF NORMOALBUMINURIA IN DIABETIC KIDNEY DISEASE

Type 2 diabetes patients with incident albuminuria show more than double the risk of progression of diabetic kidney disease (DKD), as per a study reported in the *Journal of Diabetes and its Complications*[1]. On the other hand, older age, poor glycemic control, presence of cardiovascular comorbidities, and use of diuretics among those with normoalbuminuria were predictive of disease progression.

This retrospective cohort study sought to elucidate the prognosis of normoalbuminuric DKD and to identify risk factors associated with disease progression. A total of 24,558 patients with type 2 diabetes and no baseline albuminuria at Seoul National University Hospital, South Korea were enrolled for the study. The participants were categorized into two groups: normoalbuminuria (no albuminuria until estimated glomerular filtration rate [eGFR] dropped below 30 mL/min/1.73 m^2) and incident albuminuria (albuminuria developed before eGFR decline <30).

After propensity score matching, 6575 patients per group were analyzed, over a median follow-up of 139 months (maximum up to 21 years). The risk of progression of DKD, defined as >50% eGFR decline or development of end-stage kidney disease, was higher in the incident albuminuria group, with an adjusted hazard ratio (aHR) of 2.39. Among those with normoalbuminuria, risk factors for disease progression were older age, poor glycemic control, cardiovascular comorbidities, and use of diuretics, whereas metformin and statin therapy were found to be protective.

While normoalbuminuria usually indicates a favorable prognosis in type 2 diabetes, a percentage of patients remains at risk for progression of kidney disease; "some experience a significant decline in kidney function without developing albuminuria. These patients are categorized as having a reduced eGFR with normoalbuminuria", write the authors. These findings underline the importance of monitoring that also focuses on factors such as metabolic control, cardiovascular health, and medication use and not just albuminuria alone, when evaluating prognosis.

Reference

1. Kim J, et al. Clinical outcomes of and risk factors for normoalbuminuric diabetic kidney disease. J Diabetes Complications. 2025;39(10):109154.

AIRWAY MUCUS PLUG BURDEN AND RISK OF ACUTE EXACERBATIONS IN COPD

Do airway mucus plugs predict the likelihood of moderate to severe acute exacerbations in patients with chronic obstructive pulmonary disease (COPD)?

A prospective cohort study from China set out to examine this association with 194 COPD patients. The mucus plugs detected on CT scans were divided into three groups based on the number of pulmonary segments affected (range 0–18): none (0), mild (1–3), and extensive (≥4). Patients were followed for up to 2 years to determine the incidence of moderate-to-severe acute COPD exacerbations.

At the start of the study, 22% of patients had no mucus plugs, 35% had plugs in 1-3 segments, and 43% had plugs in ≥4 segments. Within 1 year, 30% of

patients experienced at least one moderate to severe acute exacerbation, with incidence rates being 12% in participants without mucus plugs, 25% in those with 1-3 segments affected, and 44% in those with ≥4 segments affected.

Further analysis showed that each one-point increase in mucus plug score corresponded to an 8.3% higher risk of exacerbation (incidence rate ratio 1.08). Multivariate Cox regression demonstrated significantly increased hazards for patients with ≥4 mucus plugs (HR 5.02) or 1-3 plugs (HR 2.32) compared with those with none. These findings remained consistent among the 150 patients who completed 2 years of follow-up.

This study demonstrates that airway mucus plugs are strong predictors of future moderate to severe exacerbations in COPD patients. The incidence of exacerbations increased proportionally with the mucus plug burden. Hence, detection of mucus plugs on CT scans can potentially serve as a biomarker for risk stratification and help choose the best management strategy for the patient.

Reference

1. Li X, et al. Association between airway mucus plugs and risk of moderate-to-severe exacerbations in patients with COPD: Results from a Chinese prospective cohort study. Chest. 2025;168(3):627-38.

IMPACT OF NOCTURNAL HYPOXEMIC BURDEN ON RENAL OUTCOMES IN TYPE 2 DIABETES

Nocturnal hypoxemic burden (NHB) is a novel prognostic marker for progression of chronic kidney disease (CKD) in type 2 diabetes, suggests a new study published in the journal *Cardiovascular Diabetology*[1]. A team of researchers from Germany and Australia investigated if NHB, measured as cumulative time with oxygen saturation below 90% (T90), was associated with incident very high-risk CKD in patients with type 2 diabetes. A total of 857 participants, mean age 65 years, were included in the study. The median duration of diabetes was 9.0 years; the median eGFR 82 mL/min/1.73 m^2).

Data of participants from the DIACORE sleep-disordered breathing sub-study was analyzed for the present study. Very high-risk CKD was classified according to KDIGO risk classification:

- eGFR <30 mL/min/1.73 m^2 regardless of urinary albumin-to-creatinine ratio (uACR)
- eGFR <45 mL/min/1.73 m^2 and uACR >30 mg albumin/g creatinine
- eGFR <60 mL/min/1.73 m^2 and uACR >300 mg/g.

During follow-up, 72 patients (8.4%) developed very high-risk CKD. Patients in the highest T90 quartile (quartile 4) had a significantly greater incidence of progression (15.0%) compared to those in the lower quartiles (quartiles 1-3) (6.2%).

Patients in the highest quartile of T90 had nearly threefold greater likelihood of developing very high-risk CKD compared to low NHB with odds ratio (OR) of 2.96, even after adjustment for other risk factors for CKD prognosis such as age, sex, adiposity, hypertension, medication use, HbA1c, diabetes duration, baseline eGFR, and hemoglobin (OR 2.96).

This study highlights the importance of screening type 2 diabetes patients for nocturnal hypoxemia. The authors call for further studies to validate these findings, nevertheless these findings suggest that targeted interventions to reduce T90 may be a new "clinically meaningful prevention target".

Reference

1. Driendl S, et al. Nocturnal hypoxemic burden is associated with worsening prognosis of chronic kidney disease in patients with type 2 diabetes. Cardiovasc Diabetol. 2025;24(1):354.

DIAGNOSIS OF DEMENTIA IS DELAYED BY AN AVERAGE OF 3 YEARS

The average time to diagnosis (TTD) of all types of dementia is 3.5 years, with younger age at onset and having frontotemporal dementia associated with even longer diagnostic intervals. These findings from a new meta-analysis were recently published in the *International Journal of Geriatric Psychiatry*[1].

Olubunmi Kusoro, from the Faculty of Brain Sciences, Division of Psychiatry, University College London, and colleagues conducted a systematic review of quantitative studies addressing the average TTD of dementia as well as factors associated with its duration. A total of 13 studies involving 30,257 participants were identified following a comprehensive search of the MEDLINE, EMBASE, PsychINFO, and CINAHL databases for relevant studies published up to December 2024. The age at onset of these participants ranged from 54 to 93 years.

TTD was defined as the period from first symptom onset, as reported by patients or caregivers using interviews or medical records, to the point of formal diagnosis.

Meta-analysis of 10 studies revealed that the mean TTD across all dementia types was 3.5 years, supported by moderate-quality evidence. A subgroup analysis

of six studies showed that the TTD in young-onset dementia was 4.1 years, with moderate quality of evidence. While the factors influencing TTD varied, two showed consistent association with a longer diagnostic delay: younger age at onset and the presence of frontotemporal dementia.

According to the authors, this study has for the first time quantified TTD in dementia and highlights the longer delays in diagnosis, which hamper timely optimal care. It is important to identify various factors - sociodemographic, disease specific, and health care specific - contributing to a longer TTD in dementia. "Development of interventions that aim to reduce the diagnostic interval in dementia are urgently needed", conclude the authors.

Reference

1. Kusoro O, et al. Time to diagnosis in dementia: a systematic review with meta-analysis. Int J Geriatr Psychiatry. 2025;40(7):e70129.

HYPERTENSION CONFERS THE HIGHEST MORTALITY RISK IN MASLD

Metabolic dysfunction-associated steatotic liver disease (MASLD) is defined by the presence of hepatic steatosis together with one or more of five cardiometabolic risk factors: overweight/obesity, impaired fasting glucose/type 2 diabetes, high blood pressure, hypertriglyceridemia, and low high-density lipoprotein (HDL) cholesterol[1].

A study published online September 17 in the journal *Clinical Gastroenterology and Hepatology* has found that the cardiometabolic risk factors of high blood pressure, glucose intolerance, and low HDL cholesterol are associated with the greatest risk for mortality[2].

Researchers from the University of Southern California Keck School of Medicine, Los Angeles investigated the association of specific cardiometabolic risk factors with all-cause mortality among US adults with MASLD. Data of 21,872 participants with MASLD sourced from NHANES III (1988-1994) and continuous NHANES (1999-2018) was linked to mortality records through 2019. The inclusion criteria were adults aged 20 years or older with a Fatty Liver Index (FLI) >60 and minimum one cardiometabolic risk factor (with a median of three risk factors). The mean age was 50 years, and over half (53%) were male. The mean body mass index (BMI) was 33.6 kg/m^2.

Almost all (99.5%) participants were overweight/obese; 55% had glucose intolerance, 58% were hypertensive, 67% had raised triglycerides, while 40% had low HDL.

In an adjusted analysis of individual risk factors, hypertension was found to significantly increase the risk of death by ~40% with aHRs of 1.39. Glucose intolerance raised mortality risk by 26% (aHR 1.26) and low HDL cholesterol by 15% (aHR 1.15). Overweight/obesity graded by BMI revealed greater risk for mortality with higher BMIs; the highest risk was seen for BMI >45 (aHR 1.64) compared to those with a BMI 25-30 kg/m^2. For BMI 35-40 kg/m^2, the aHR was 1.18 and for BMI 40-45 kg/m^2, the aHR was 1.55. Additionally, in age-adjusted analysis, presence of each additional metabolic risk factor increased mortality risk by 15% (aHR 1.15).

This study shows that while all cardiometabolic risk factors increased the mortality risk in patients with MASLD, each contributed differently to the risk. The strongest predictors of all-cause mortality were hypertension and glucose intolerance. But a surprising observation was the association of high blood pressure with a greater risk of death than diabetes, contrary to common perception. "Knowing which aspects of MASLD might lead to poorer outcomes can help us offer patients the best possible care", note the authors[3].

References

1. Park H, et al. Impact of cardiometabolic risk factors on hepatic fibrosis and clinical outcomes in MASLD: a population-based multi-cohort study. JHEP Rep. 2025;7(6):101388.
2. Dukewich M, et al. Differential effects of cardiometabolic risk factors on all-cause mortality in us adults with metabolic dysfunction-associated steatotic liver disease (MASLD). Clin Gastroenterol Hepatol. 2025:S1542-3565(25)00758-X.
3. Keck Medicine USC Newsroom. Dated September 18, 2025. Available at: https://news.keckmedicine.org/three-deadliest-risk-factors-of-a-common-liver-disease-identified-in-new-study/. Accessed October 1, 2025.