Findings

Modestly Reduced eGFR Associated with Adverse Outcomes in Young Adults

Modest reductions in kidney function in younger adults are associated with later increases in risk of cardiovascular disease, kidney failure, and death, reports a study in *BMJ*.

The population-based cohort study included linked Ontario, Canada, health care data on 8.7 million adults (aged 18–65 years; mean age, 41.3 years). All had at least one outpatient estimated glomerular filtration rate (eGFR) value with no history of kidney diseases. Modest reductions in kidney function were identified, based on age-specific eGFR reference levels: 100–110 mL/min/1.73 m^2 at aged 18–39 years, 90–100 mL/min/1.73 m^2 at aged 40–49 years, and 80–90 mL/min/1.73 m^2 at aged 50–65 years. Associations with all-cause mortality, any cardiovascular event, and kidney failure were assessed.

In the study sample, the mean index eGFR value was 104.2 mL/min/1.73 m^2, and the median follow-up was 9.2 years. Based on age-specific cutoffs, modest reductions in eGFR were found in 18.0% of patients aged 18–39 years, 18.8% of those aged 40–49 years, and 17.0% of those aged 50–65 years.

"Modest eGFR reductions were consistently associated with higher rates of adverse outcomes," the researchers write. At an eGFR between 70 and 80 mL/min/1.73 m^2, hazard ratios for adverse outcomes were 1.42 in participants aged 18–39 years, 1.13 for those aged 40–49 years, and 1.08 for those aged 50–65 years. Incidence rates were 4.39, 9.61, and 23.4 per 1000 person-years, respectively. Associations were significant for all three types of adverse events.

The effects of age on eGFR and the associated clinical risks are unclear, specifically at values above the 60 mL/min/1.73 m^2 cutoff for CKD. Thus, there is limited evidence to guide the management of younger adults with early reductions in eGFR.

The new analysis links modest age-specific reductions in eGFR to increased risks of adverse clinical outcomes. The risks appear more prominent in adults aged 18–39 years, beginning at index eGFR values under 80 mL/min/1.73 m^2. The researchers conclude: "These findings suggest a role for more frequent monitoring of kidney function in younger adults to identify individuals at risk to prevent chronic kidney disease and its complications" [Hussain J, et al. Associations between modest reductions in kidney function and adverse outcomes in young adults: Retrospective, population based cohort study. *BMJ* 2023; 381:e075062. doi: 10.1136/bmj-2023-075062]. ■

Population Screening for CKD: Is It Cost-Effective Now?

In the era of sodium-glucose cotransporter-2 (SGLT2) inhibitor therapy, population-wide screening for albuminuria to identify chronic kidney disease (CKD) would be a cost-effective practice, suggests a study in the *Annals of Internal Medicine*.

The researchers designed a decision analytic Markov cohort model of CKD progression among U.S. adults aged 35 years or older. Cost-effectiveness analysis focused on the impact of screening for albuminuria from a health care sector perspective, with and without adding SGLT2 inhibitors to the standard of care for CKD. Data for the analysis came from the National Health and Nutrition Examination Survey, Centers for Medicare & Medicaid Services databases, and published studies including the Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease (DAPA-CKD) trial.

One-time screening with the addition of SGLT2 inhibitors at aged 55 years increased costs from $249,000 to $259,000 and increased quality-adjusted life-years (QALYs) from 12.61 to 12.72, for an incremental cost-effectiveness ratio of $86,300 per QALY gained. This screening strategy reduced the incidence of kidney failure requiring dialysis or transplantation by 0.29 percentage points while increasing life expectancy from 17.29 to 17.45 years.

Other strategies were also cost-effective. One-time screening between aged 35 and 75 years avoided dialysis or transplantation in 380,000 people. For a strategy of screening every 10 years up to aged 75 years, cost per QALY gained was less than $100,000. In sensitivity analyses, costs per QALY were affected by the estimated effectiveness and costs of SGLT2 inhibitors.

Trials have demonstrated the efficacy of SGLT2 inhibitor therapy in patients with CKD, with and without diabetes. This new treatment appears capable of altering the natural history of CKD, suggesting that it should be included in cost-effectiveness analyses of CKD screening.

"Screening adults for albuminuria to identify CKD could be cost-effective in the United States," the researchers conclude. In contrast to studies performed before the availability of SGLT2 inhibitor therapy, "[B]oth one-time and periodic screening for CKD represent very good value in every age group when SGLT2 inhibitors are included in treatment [Cusick MM, et al. Population-wide screening for chronic kidney disease: A cost-effectiveness analysis. *Ann Intern Med* 2023; 176:788–797. doi: 10.7326/M22-3228]. ■

Similar Outcomes with Different Glucose-Lowering Drugs in Type 2 Diabetes

In patients with type 2 diabetes, four different classes of glucose-lowering medications produce similar kidney outcomes at 5 years' follow-up, according to a clinical trial report in *JAMA Internal Medicine*.

The randomized "Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness" (GRADE) trial enrolled 5047 patients with type 2 diabetes at 36 U.S. centers. Approximately two-thirds of patients were men. The mean age was 57.2 years; hemoglobin A1c (HbA1c), 7.5; duration of diabetes, 4.2 years; and estimated glomerular filtration rate (eGFR), 94.9 mL/min/1.73 m^2.

Patients were assigned to receive insulin glargine, glimepiride, liraglutide, and sitagliptin, added to metformin. Treatment continued until HbA1c exceeded 7.5%, at which point insulin therapy was started. At 5 years, the chronic eGFR slope and a composite outcome of kidney disease progression were compared among treatment groups, along with secondary outcomes.

There was no significant difference in the mean chronic eGFR slope: –2.03 mL/min/1.73 m^2 per year with sitagliptin, –1.92 with glimepiride, –2.08 with liraglutide, and –2.02 with insulin glargine. Rates of the composite kidney disease outcome were 10.6%, 12.4%, 12.0%, and 11.9%, respectively. Albuminuria progression accounted for 98.4% of composite outcome events.

Secondary outcomes were also similar among treatments, including incident eGFR reductions to less than 60 mL/min/1.73 m^2. No treatment-related adverse kidney events occurred.

Among patients with type 2 diabetes, free of baseline kidney diseases, 5-year kidney outcomes are comparable with various classes of glucose-lowering medications. The authors discuss their findings in the context of randomized trials of the different types of drugs [Wexler DJ, et al. Comparative effects of glucose-lowering medications on kidney outcomes in type 2 diabetes: The GRADE randomized clinical trial. *JAMA Intern Med* 2023; 183:705–714. doi: 10.1001/jamainternmed.2023.1487]. ■

How Does AKI Affect Risk of CKD Progression?

Once other characteristics are taken into account, patients with chronic kidney disease (CKD) who are hospitalized with mild to moderate acute kidney injury (AKI) have only a small, additional risk of CKD progression, reports a study in the *Annals of Internal Medicine*.

The analysis included 3150 patients with CKD, drawn from the Chronic Renal Insufficiency Cohort (CRIC) study. The occurrence of "hospitalized AKI" was assessed, defined as at least a 50% increase in inpatient serum creatinine (SCr). The main outcome of interest was kidney function trajectory, with the estimated glomerular filtration rate (eGFR) based on the SCr or cystatin C level.

Over a median of 3.9 years' follow-up, AKI episodes occurred in 433 patients: a rate of 13.7%. Severity was grade 1 or 2 in 92% of cases. Episodes of AKI were associated with reductions in eGFR: –2.30 based on SCr and –3.61 based on cystatin C.

However, after adjustment for other factors, including baseline eGFR and proteinuria, the associated declines in eGFR were much smaller: –0.38 based on SCr and –0.15 based on cystatin C, with overlapping confidence intervals. By both methods, there was a possibility of no effect on changes in the eGFR slope.

Studies have linked AKI to more rapid loss of kidney function, leading to trials of interventions to reduce AKI severity. However, studies of the association between AKI and subsequent changes in eGFR have had important limitations, including inadequate controls for differences between patients with and without AKI.

The new analysis of patients with CKD suggests that mild to moderate episodes of AKI have little or no effect on worsening subsequent kidney function, after adjustment for other variables. "Our results suggest that much of the kidney disease observed after AKI may already be present before AKI," the researchers write [Muiru AN, et al. Risk for chronic kidney disease progression after acute kidney injury: Findings from the Chronic Renal Insufficiency Cohort study. *Ann Intern Med*, published online ahead of print July 11, 2023. doi: 10.7326/M22-3617; https://www.acpjournals.org/doi/10.7326/M22-3617]. ■