Findings

Serum T50 Test Reflects CAC Progression Risk in CKD

A new serum test of calcification propensity provides useful information on the severity and progression of coronary artery calcification (CAC) in patients with chronic kidney disease, reports the American Journal of Kidney Diseases.

The prospective study included patients with stage 2 to 4 CKD, mean age 57.5 years, enrolled in the Chronic Renal Insufficiency Cohort (CRIC) study. Serum calcification propensity was measured as the transformation time from primary to secondary calciprotein particles (T50), with lower T50 values reflecting a higher calcification propensity. The analysis included baseline samples from 1274 patients and follow-up samples (average 3 years) from 780 patients.

On baseline CT scans, 65% of patients had CAC. Median T50 value was 321 minutes. Lower T50 values (higher calcification propensity) were associated with a wide range of factors: non-Hispanic black race/ethnicity, history of cardiovascular disease and diabetes, higher blood pressure, and lower kidney function.

In multivariable-adjusted models, T50 was unrelated to the presence of CAC. However, among patients with prevalent CAC, lower T50 was linked to increased CAC severity: a 21% increase in severity per 1-standard-deviation decrease in T50.

During follow-up, 20% of patients developed incident CAC while 19% had progression (annual increase of 100 Agatston units or more) of baseline CAC. On adjusted analysis, T50 was unrelated to the development of new CAC, but was significantly associated with CAC progression. For each 1-standard-deviation decrease in T50, the risk of CAC progression increased by 28%.

Coronary artery calcification is common in patients with CKD and is associated with increased cardiovascular risks. By evaluating the transformation from primary to secondary calciprotein particles, the T50 test might provide a useful marker of CAC and the associated risks.

This study finds that a lower serum T50, indicating increased calcification propensity, is associated with greater CAC severity and an increased risk of CAC progression in patients with CKD. The T50 test does not appear to reflect prevalent CAC. Noting that further studies are needed to establish causality, the investigators conclude, “These findings provide valuable insights into the development of calcification and atherosclerosis in patients with CKD and highlight potential pathways for risk stratification and therapeutic intervention” [Bundy JD, et al. Serum calcification propensity and coronary artery calcification among patients with CKD: The CRIC (Chronic Renal Insufficiency Cohort) Study. Am J Kidney Dis 2019; https://doi.org/10.1053/j.ajkd.2019.01.024].

Moderate Sodium plus High Potassium Yields Lowest Mortality

The risks of cardiovascular events and mortality are lowest with the combination of moderate sodium intake and higher potassium intake, concludes an international prospective cohort study in the British Medical Journal.

The “Prospective Urban Rural Epidemiology” (PURE) study enrolled more than 103,000 adults, aged 35 to 70, from 628 urban and rural communities in low-, middle-, and high-income countries. Twenty-four-hour urinary sodium and potassium excretion were estimated (as surrogates for intake) from morning fasting urine samples.

During a median follow-up of 8 years, 6.1% of patients died or experienced a cardiovascular event. Risks of these outcomes were assessed for participants with low, moderate, and high sodium excretion (less than 3 mg/d, 3 to 5 mg/d, and over 5 mg/d, respectively) and those with high versus low potassium excretion (greater versus equal or less than the median of 2.1 g/d).

Very few individuals—0.002% of the study population—met the World Health Organization target of sodium excretion combined with potassium excretion greater than 3.5 g/d. Risk of the combined outcomes was lowest for individuals...
with moderate sodium excretion (3 to 5 g/d) plus higher potassium excretion, who comprised 21.9% of the study population. Compared to this group, hazard ratios were 1.23 for the combination of low sodium/low potassium excretion and 1.21 for high sodium and low potassium excretion. These groups accounted for 7.4% and 13.8% of the study cohort, respectively.

Among participants with higher potassium excretion, hazard ratios were 1.19 for those with low sodium excretion (3.3% of the cohort) and 1.18 for those with high sodium excretion (29.6% of the cohort). The increased cardiovascular risk associated with high sodium excretion was attenuated by potassium excretion above the median.

Current dietary recommendations for adults include a very low sodium intake and high potassium intake. Reported associations with mortality vary for sodium, while most studies report a linear reduction in mortality with higher potassium intake. A very small percentage of the population meets current recommendations for low sodium intake and high potassium intake, this international study suggests. The risk of cardiovascular events and mortality appears lowest with a combination of moderate sodium intake and high potassium intake, found in about 22% of the PURE study cohort. The researchers conclude: “The J-shaped association of sodium intake with mortality and cardiovascular events does not lend support to the current WHO recommendation to consume low sodium diets (<2.0 g/day), and it also argues against use of the sodium/potassium ratio” O’Donnell M, et al. Joint association of urinary sodium and potassium excretion with cardiovascular events and mortality: prospective cohort study. BMJ 2019; 364:l7723.

Higher eGFR Linked to Higher Mortality in Pediatric Dialysis Patients

Exposure to high doses of nonsteroidal anti-inflammatory drugs (NSAIDs) shows a modest but significant association with kidney disease in a military population, reports a study in the open-access journal JAMA Network Open.

The retrospective analysis included data on more than 764,000 US Army soldiers on active duty from 2011 through 2014. Eighty-six percent of participants were men, median age was 27 years. Dispensing and dose of prescription NSAIDs were evaluated for association with incident diagnoses of acute kidney injury (AKI) and chronic kidney disease (CKD).

The participants received a total of 1.6 million distinct NSAID prescriptions during the observation period: mean 2.1 prescriptions per person. Nearly two-thirds of personnel had no NSAID prescriptions in the previous 6 months. About 18% were dispensed 1 to 7 mean total daily defined doses (DDDs) per month, while 16% received more than 7 DDDs. There were a total of 2356 AKI outcomes, affecting 0.9% of participants; and 1634 CKD outcomes, affecting 0.2% of participants.

Participants with 7 or more DDDs per month had significant increases in both kidney disease outcomes: adjusted hazard ratio 1.2 for both AKI and CKD. At this level of exposure, there were 17.6 additional cases of AKI and 30.0 additional cases of CKD per 100,000 exposed individuals. Obese individuals were at significantly increased risk of both outcomes: adjusted hazard ratio 1.5 for AKI and 1.6 for CKD. The hazards were more than doubled for individuals with a history of hypertension and rhabdomyolysis. For diabetes, the hazard ratio was 1.8 for both outcomes.

Most studies of NSAID associations with kidney disease have focused on older adults or patients with chronic diseases. There has been little concern about the renal effects of these widely used medications in young, healthy adults. Some studies have suggested a possible increase in kidney disease risk among NSAID users engaging in endurance exercise.

This large study of Army personnel finds “modest but statistically significant” associations between high doses of NSAIDs and the risk of acute and chronic kidney disease outcomes. “Dosage reduction represents an approach that may decrease associated kidney disease outcome rates,” the researchers write. They also note the contribution of modifiable factors such as body mass index and hypertension [Nelson DA, et al. Association of nonsteroidal anti-inflammatory drug prescriptions with kidney disease among active young and middle-aged adults. JAMA Netw Open 2019; 2 (2):e187896. doi:10.1001/jamanetworkopen.2018.7896].