New innovations in clinical science

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A variety of recent studies highlight new and innovative research efforts that could help improve individuals' kidney health. Below are the findings of some of these studies, which are being presented at ASN Kidney Week 2013 November 5-10 at the Georgia World Congress Center in Atlanta, GA.

In one study*, Linda Fried, MD, FASN (VA Pittsburgh Healthcare System) and her colleagues examined the effects of combination therapy with two types of blood pressure–lowering drugs: angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB). The combination is known to decrease protein excretion in the urine, which is a marker of kidney dysfunction, but its safety and impact on progression of kidney disease is uncertain. In this latest study, 1148 patients with type 2 diabetes who had moderately decreased kidney function were treated with the ARB losartan and then randomized to receive the ACE inhibitor lisinopril or placebo.

- After a midpoint follow-up of 2.2 years, significant kidney function decline occurred in 152 patients in the monotherapy arm and 132 in the combination arm. There was no benefit on mortality or cardiovascular events.
- "The study was stopped early by the data monitoring committee as they concluded that the risks of combination therapy outweighed a small possible benefit on progression of kidney disease, though not statistically significant," said Dr. Fried. The main risks were a 1.7-fold higher risk of acute worsening of kidney function and a 2-fold higher risk of elevated potassium

levels in the blood. Individuals on combination therapy also had a higher rate of hospital admissions.

*Additional data from this study are available in the following Late-Breaking Posters: Risk and Severity of Hyperkalemia with Combined Angiotensin Antagonism in Diabetic Nephropathy – The VA-NEPHROND Study (SA-PO1089); and Acute Kidney Injury (AKI) Associated with Combined Angiotensin Antagonism in Patients with Diabetic Nephropathy – A Secondary Analysis of the VA NEPHRON-D Study (SA-PO1096).

Another team led by Rajiv Agarwal, MD, MBBS, FASN (VA Medical Center in Indianapolis) conducted a clinical trial to assess the safety and efficacy of an ACE inhibitor–based antihypertensive treatment compared with a β-blocker-based antihypertensive treatment. Two hundred patients on hemodialysis who had hypertension and thickened heart muscles were randomized to the ACE inhibitor lisinopril or the β-blocker atenolol, each administered three times weekly after dialysis.

- Blood pressure improved over time in both groups, and no statistical difference between drugs was noted.
- An independent data safety monitoring board recommended termination of the study due to safety concerns. Serious cardiovascular events occurred in 14 patients in the atenolol group and 26 patients in the lisinopril group. Hospitalizations for heart failure and other causes were worse in the lisinopril group.

"Contrary to the original hypothesis, the trial found that among kidney dialysis patients with hypertension and thickening of heart muscles, atenolol-based antihypertensive therapy may be superior to lisinopril-based therapy in preventing cardiovascular disease such as heart failure and heart attacks as well as all-cause hospitalizations," said Dr. Agarwal.

Afshin Parsa, MD, FASN (University of Maryland School of Medicine) and his colleagues designed a study to investigate why African Americans are at increased risk for kidney failure, or end stage renal disease (ESRD), compared with European Americans. They focused on variants of the apolipoprotein L1 (APOL1) gene that have been associated with the development of kidney diseases in African Americans. The APOL1 gene creates a protein that is a component of HDL cholesterol. The researchers examined the effects of APOL1 variants on chronic kidney disease (CKD) progression in the African American Study of Kidney Disease and Hypertension (AASK) and the Chronic Renal Insufficiency Cohort Study (CRIC), which together enrolled more than 3600 patients.

- In AASK, which enrolled only African Americans, kidney failure occurred in 58% of participants in the APOL1 risk group and 37% in the APOL1 non-risk group.
- In CRIC, kidney function decline was greater among African Americans in the APOL1 risk group, but it was similar among African Americans in the APOL1 non-risk group and European Americans.
- APOL1 risk variants were associated with faster CKD progression and ESRD in patients with and without diabetes.
- Tight regulation of blood pressure did not impact the APOL1-related increase in CKD progression.

The findings provide direct evidence that African Americans with established CKD have a faster kidney function decline and increased rates of kidney failure compared with whites, and that APOL1 risk variants increase CKD progression in African Americans. "The next step of our research will be directed towards delineating which pathways may relate to the APOL1-genotype mediated increase in CKD progression, with the goal of identifying potential targets for treatment," said Dr. Parsa

Finally, Amit Garg, MD, PhD (London Health Sciences Centre, in Ontario) and his team designed a study to see if interventions to reduce the risk acute kidney injury (AKI) in hospitalized patients might preserve long-term kidney function. AKI, an abrupt decline in kidney function, is an increasingly prevalent and potentially serious condition following heart surgery; it occurs because the kidneys are deprived of normal blood flow during the procedure. Within the CORONARY trial, investigators assessed kidney function in 2932 patients from 63 sites in 16 countries who were randomly assigned to coronary-artery bypass grafting (CABG) either with a beating-heart technique (off-pump) or with cardiopulmonary bypass (on-pump).

- Off-pump vs on-pump CABG reduced the risk of AKI (17.5% vs 20.8%); however, there was no significant difference between the two groups in the loss of kidney function after one year (17.0% vs. 15.3%).

"The findings emphasize that an intervention that reduces the risk of mild AKI may not necessarily improve long-term kidney function," the researchers concluded.

More information: Combined Angiotensin Inhibition for Treatment of Diabetic Nephropathy: VA Nephron D (Abstract 5780)
APOL1 Risk Variants, Race, and Progression of Chronic Kidney Disease (Abstract 5828)
Acute Kidney Injury from Off-Pump or On-Pump Coronary Bypass Grafting and Kidney Function One Year Later (Abstract 5812)

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