Wider Use of Intensive Blood Pressure Control Could Save Lives

Chicago—Wider use of intensive control of systolic blood pressure could save the lives of as many as 32,145 individuals with chronic kidney disease each year, estimated a study presented at Kidney Week 2016.

Lowering systolic blood pressure to 120 mm Hg or less was found to reduce deaths by 27% compared to standard blood pressure control after an average follow-up of 3.26 years in the Systolic Blood Pressure Intervention Trial (SPRINT). The SPRINT trial enrolled 9361 adults age 50 or older at high risk of cardiovascular disease. Participants were randomized to either intensive blood pressure control (≤ 120 mm Hg) or standard blood pressure control (≤140 mm Hg). The trial excluded individuals with diabetes, stroke, polycystic kidney disease, and several other characteristics (SPRINT Research Group. *N Engl J Med* 2015; 373:2103–2116).

Now, Tisha Joerla Tan, MD, of Loyola University Medical Center, and her colleagues have used data from the National Health and Nutrition Examination Survey (NHANES), an annual nationally representative survey of the US population, to estimate how many US individuals would benefit if the tight blood pressure control were applied to those who meet the criteria used in the SPRINT trial. The analysis included adults age 50 or older with a systolic blood pressure between 130 and 180 mm Hg depending on how many antihypertensives they were taking, and one or more risk factors for cardiovascular disease. Individuals with diabetes, a history of stroke, proteinuria greater than 1g/day, heart failure, or an estimated glomular filtration rate (eGFR) <20 mL/min/1.73 m^2 were excluded from the analysis.

About 18 million US adults met SPRINT criteria and Dr. Tan and her colleagues estimated that applying intensive blood pressure control to these individuals would prevent about 100,000 deaths each year. The researchers also estimated the number of deaths that could be prevented among adults with eGFRs between 20 and 59 mL/min/1.73 m^2.

"Our analyses also showed that more than 4 million adults with stage 3–4 chronic kidney disease meet SPRINT criteria, and intensive systolic blood pressure lowering was projected to prevent 32,800 deaths per year in this group," said Dr. Tan in a press release.

The SPRINT trial has demonstrated that intensive lowering of blood pressure can provide cardiovascular benefits and reduce deaths, said George Thomas, MD, director of the Center for Blood Pressure Disorders at the Cleveland Clinic in Ohio. But he also noted it is important to remember that patients with uncontrolled hypertension on multiple medications, diabetes, past strokes, or with severe kidney disease were excluded. And NHANES doesn't provide all the information needed to determine all SPRINT exclusion criteria, he said.

"Additionally, the risks of intensive therapy need to be kept in mind," he said. "It is not possible to predict who would experience a benefit and who would experience harm."

Patients who were intensively treated in the SPRINT trial had higher rates of hypotension, syncopal events, electrolyte abnormalities, and acute kidney injury compared with the standard group, explained Dr. Thomas. Additionally, it may be more difficult to monitor for potential adverse events in practice than in the trial.

"Patients in the trial were very closely followed and blood pressure measurements were done with an automated device following a very strict protocol for measurement," Dr. Thomas said. "In real-world practice, this

may not happen and the adverse events may potentially be higher."

Longer-term data from the SPRINT trial on quality of life, neurologic effects, and long-term kidney outcomes in intensively treated patients may help clinicians decide who might benefit from tighter blood pressure control, Dr. Thomas said.

In the meantime, he recommended that clinicians carefully measure patients' blood pressure, and closely monitor patients whose blood pressure is being tightly controlled. This monitoring should include kidney function and electrolyte levels. "Pros and cons of intensive therapy need to be discussed with patients, and blood pressures goals should be individualized rather than taking a one size fits all approach," Dr. Thomas said.

"Intensive Blood Pressure Lowering Will Prevent Over 100,000 Deaths Annually" (Abstract 2229)

Smoking Counteracts the Benefit of Medications for Kidney Disease

Smoking may partly counteract the benefits of treatment with angiotensin converting enzyme inhibitors (ACE inhibitors) for patients with chronic kidney disease (CKD), according to a study presented at Kidney Week 2016.

Smoking has been linked to worsening kidney decline, but the exact mechanisms are unclear, according to lead author Bethany Roehm, MD, of Tufts Medical Center in Boston.

"The importance of smoking as a renal risk factor is highlighted by the fact that its negative effects have been shown in subjects of the general population and in patients with primary or secondary renal disease," said Stephan R. Orth, MD, PhD, FASN, of the Dialysis Center in Bad Aibling, Germany (Hallan SI and Orth SR. *Kidney Int* 2011; 80:516–523).

One of the reasons it is difficult to pinpoint how smoking contributes to kidney disease exacerbation is that cigarette smoke is made up of more than 4000 chemicals, Orth said, but it is "sensible to assume that several of these components act as nephrotoxic potpourri."

To further study smoking's effects, Roehm and her colleagues enrolled 216 patients with early CKD who were taking ACE inhibitors; 108 were smokers and 108 were nonsmokers. All of the smokers were given a smoking cessation intervention, but 83 continued to smoke and 25 quit. All of the patients were followed for 5 years after starting ACE inhibitors. At enrollment, patients in all groups had comparable estimated glomerular filtration rate (eGFR) and systolic and diastolic blood pressures. But urinary 8-Iso/cr was higher in the continuing smokers and those who later quit.

Those who never smoked and those who quit had slower worsening of their kidney function, according to Dr. Roehm and her colleagues. After 1 year of taking ACE inhibitors, the nonsmokers had lowered their alb/cr to 395 ± 143 compared with 420 ± 148 ($p<0.01$) at initiation. In quitters these levels didn't change significantly from their entry levels, (356 ± 178 vs. 367 ± 160, $p=0.15$). But continuing smokers saw increases in alb/cr (453 ± 152 vs 426 ±138, $p<0.01$). Continuing smokers also had higher urinary 8-iso/cr (3.6 ± 0.8) than nonsmokers (1.6 ± 0.3, $p<0.01$) and quitters (1.6 ± 0.3, $p<0.01$). At 5 years, eGFRs were also lower in the continued smokers (54.9 ± 5.6 mL/min) than in the nonsmokers (66.8 ± 5.8 mL/min) and quitters (64.1 ± 5.6 mL/min) with a p value <0.01.

Dr. Roehm and her colleagues concluded that ongoing smoking was counteracting the typical decrease in protein excretion seen in patients treated with ACE inhibitors likely owing to oxidative stress.

"It has practically become dogma that if you have a patient with high blood pressure and CKD that you start them on an ACE inhibitor, and we are often comforted as clinicians that we are doing something to help slow progression of their kidney disease in doing this," said Dr. Roehm. "But our data suggest that in smokers this may not be the case, and our study underscores the importance of doing all we can as clinicians to encourage our patients to stop smoking."

The study shows ACE inhibitors alone are not enough to counteract smoking's affects, said Orth.

"The results are absolutely in line with what we know about the renal effects of smoking in patients with nephrosclerosis and other renal diseases," he said. "The newest aspect is that ACE inhibition is not able to fully protect from the adverse renal effects of smoking."

But cessation strategies can make a big difference. "The benefit of quitting smoking was particularly impressive due to the fact that eGFR at the end of the study [for quitters] did not differ from never-smokers," Orth said.

Studies that show how nephrologists can boost cessation rates would be useful, said Orth.

"Nephrologists should be aware that smoking cessation strategies in smokers with a diseased kidney are part of their therapeutic armamentarium," he said.

"Cigarette Smoking Partially Negates the Kidney Protective Effect of ACE Inhibition in Stage 2, Non-Diabetic, Hypertension-Associated CKD" (Abstract 2784)