

KEEP Results Show Promise of New Equation

BY RICHARD M. KIRKNER

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY OF HYPERTENSION

NEW YORK – Boosting patient awareness and use of a new equation for measuring glomerular filtration rate are showing early signs of being the cornerstones to the prevention of chronic kidney disease among people at risk for the disease, according to preliminary results from the National Kidney Foundation's nationwide screening initiative.

The Kidney Early Evaluation Program (KEEP) has enrolled 150,000 people so far, making it the nation's largest perpetual chronic kidney disease screening program, according to Dr. Joseph Vassalotti, chief medical officer of the National Kidney Foundation and a faculty member at Mount Sinai School of Medicine, New York.

The point is to identify "individuals in the community with kidney disease along with the risk factors that go with it," said Dr. George Bakris, professor of medicine at the University of Chicago Medical Center and a former KEEP principal investigator.



All of the participants have some stage of kidney disease or hypertension and are referred to the registry by physicians. Enrollment is voluntary and participants complete a questionnaire and undergo a medical evaluation that includes standard panels plus testing for calcium, phosphorus, and parathyroid hormone. The program does not accept people who have had a kidney transplant or are on dialysis, he said.

VITALS

Major Finding: KEEP data have shown an uptick in overall blood pressure control among patients with early-stage kidney disease or hypertension, from 45% at the initial screening to 49% at re-screening.

Data Source: Preliminary results from the National Kidney Foundation's screening initiative.

Disclosures: KEEP is funded by Amgen, Abbott, Siemens, Astellas, Genzyme, Fresenius Medical Care, Pfizer, Nephroceuticals and the LifeScan unit of Johnson & Johnson. Panel participants disclosed affiliations with a variety of device and pharmaceutical companies.

Under the program, a new method for estimating glomerular filtration rate (eGFR), known as the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, has been used. This equation is more accurate in determining kidney function than is the Modification of Diet in Renal Disease (MDRD) Study equation, said Dr. Lesley Stevens of Tufts Medical Center, Boston.

The point is to identify persons 'in the community with kidney disease along with the risk factors that go with it.'

DR. BAKRIS

"The use of the CKD-EPI equation more accurately reflects measured GFR and results in a lower prevalence of eGFR below 60 mL/min per 1.73 m²," said Dr. Stevens, a KEEP

committee member. As a result, there are fewer false positives and "ultimately, fewer tests and lower costs," she said.

According to Dr. Stevens, the equation has been validated in two clinical studies (Am. J. Kidney Dis. 2010;55:648-59 and Am. J. Kidney Dis. 2010;55:660-70).

One of the goals of KEEP is to determine factors that help slow the slide into chronic kidney disease, as well as

the loss of kidney function over time, Dr. Vassalotti said.

"Multiple trials on systolic blood pressure show that untreated hypertension results in a loss of 10-12 mL/min per 1.73 m² eGFR a year," he said. "In individuals with blood pressure in the target range, the annual loss is approximately 2-3 mL/min per 1.73 m²."

By educating participants and fostering their engagement with local clinicians, KEEP can impact care."

Managing blood pressure early in kidney disease is critical because as eGFR declines, hypertension becomes more difficult to control, Dr. Vassalotti said.

Thus, self-reported hypertension is one of the qualifiers for KEEP enrollment, he said. He cited early data from KEEP that showed prevalence, awareness and treatment of hypertension increased with stage of chronic kidney disease, but that didn't necessarily translate to control with severe disease. Among those with stage 3 disease, only 82% were undergoing treatment, compared with 92% of those with stage 4 disease. However, 38% of the stage 3 group had systolic blood pressure below 140 mm Hg, while only 35% of the stage 4 group did (Am. J. Med. 2008; 121:332-40).

KEEP data have shown an uptick in overall blood pressure control, from 45% at the initial screening to 49% at re-

screening, Dr. Vassalotti said, and even some improvement in control without medication. "But I wouldn't overstate this."

The project involves merging data with the National Death Index and the United States Renal Data System to track survival and chronic kidney failure outcomes, respectively. Future goals include additional data links with Medicare Parts B and D to gain clarity on morbidity and medication use, Dr. Vassalotti said. "Preliminary longitudinal data show that community screening appears to influence hypertension despite progression of chronic kidney disease," he said.

Patient awareness is the cornerstone of hypertension management, noted Dr. Adam Whaley-Connell of the University of Missouri. "Awareness has a very important role in not only understanding blood pressure

'Community screening appears to influence hypertension despite progression' of CKD.

DR. VASSALOTTI

control, especially in the context of the early stages of kidney disease, but in improving kidney related patient outcomes," he said.

However, Dr. Whaley-Connell noted that awareness of kidney disease, particularly in its early stages, "is alarmingly low." He noted that KEEP data on awareness reflect that of National Health and Nutrition Examination Survey and other chronic kidney disease cohort studies:

Only about 5% of those with stages 1-3 are aware of their disease. "Roughly 95% of individuals entering into the screening program are unaware they have chronic kidney disease," Dr. Whaley-Connell said. ■



Two ARB-Based Regimens Found Equivalent in OSCAR

BY CAROLINE HELWICK

FROM THE ANNUAL MEETING OF THE AMERICAN COLLEGE OF CARDIOLOGY

NEW ORLEANS – Treatment with high doses of an angiotensin II receptor blocker or combined treatment with an ARB and a calcium channel blocker provided equal protection against cardiovascular events in elderly hypertensive patients, in a Japanese study presented at the meeting.

There were some differences, however. Greater blood pressure lowering was achieved with the combination, though in diabetic patients cardiovascular outcomes were more likely to be improved with high-dose ARBs, reported Dr. Hisao Ogawa of Kumamoto (Japan) University.

The OSCAR (Olmesartan and Calcium Antagonists Randomized) study enrolled 1,164 high-risk elderly hypertensive patients at 134 centers throughout Japan from 2005 to 2007. Patients had hypertension uncontrolled on standard-dose monotherapy with the ARB olmesartan and had at least one of the following cardiovascular conditions: type 2 diabetes, cardiac disease, vascular disease, renal dysfunction, or cerebrovascular disease.

Patients were randomized to receive either high-dose olmesartan 40 mg/day (n = 578) or a calcium channel blocker (CCB) combined with olmesartan 20 mg/day (n = 586). The primary end point was a composite of fatal and nonfatal cardiovascular events, including coronary artery disease, heart failure, cerebrovascular disease, other arteriosclerotic disease, diabetic complications, and the deterioration of renal function as well as noncardiovascular death.

At 36 months' follow-up, in the intention-to-treat analysis, blood pressure was adequately controlled by both treatment approaches, but the combination reduced blood pressure to significantly lower levels, compared with the ARB. With combination ARB/CCB, mean systolic levels were lower by 2.4 mm Hg, and mean diastolic levels were lower by 1.7 mm Hg, both significant differences.

However, no significant differences were seen between the arms in the composite end point, with 58 events occurring with high-dose ARB treatment and 48 occurring with the combination ARB/CCB. While risk was increased by 31% with the high-dose ARB, the difference was not statistically significant, Dr. Ogawa reported.

Subgroup analyses did reveal differences between the treatments. For patients with preexisting cardiovascular disease, those randomized to the combination therapy had significantly fewer cardiovascular events or deaths than those in the monotherapy group: 34% and 51%, respectively, for a 63% increased risk, he said.

Conversely, in the subgroups of patients with only diabetes and no other evidence of cardiovascular disease, the combination therapy group was at greater risk. Events occurred in 14 patients compared with 7 patients, for a 48% reduced risk with high-dose ARBs, though this was not statistically significant.

"There was a significant treatment-by-subgroup interaction for the primary end points between the patients with and those without cardiovascular disease [only diabetes]," he said. "The OSCAR study suggests that the relative effect of the two therapies depends on the presence of cardiovascular disease or type 2 diabetes."

The study was funded by the Japan Heart Foundation. Dr. Ogawa has received grant support from Astellas, AstraZeneca, Bayer, Boehringer Ingelheim, Daiichi Sankyo, Eisai, Kowa, Kyowa Hakko Kirin, Merck, Novartis, Pfizer, Sanofi-Aventis, Schering-Plough, and Takeda. ■