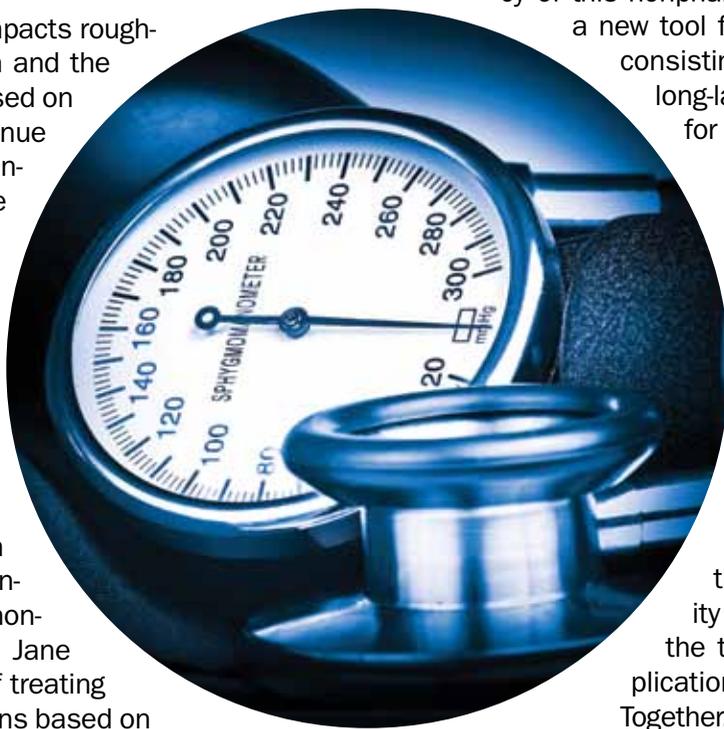


Hypertension: The Good, the Bad, and the Unknown

For this issue's focus on hypertension, we have assembled a small portfolio of articles describing recent provocative advances in the study of hypertension.

But first, the bad news. Hypertension impacts roughly 30 percent of the adult U.S. population and the majority of Americans aged 65 or older, based on NHANES surveys. The prevalence will continue to rise rapidly as the U.S. population continues to get older. Moreover, although there have been improvements over the past 10 years, less than 50 percent of patients under treatment for hypertension reach target for blood pressure control. A similar level of poor control is seen in hypertensive patients with chronic kidney disease (CKD), where hypertension is known to promote progression of kidney damage. Laura Svetkey and Crystal Tyson address the prevalence of hypertension in CKD, treatment goals, and the debates underlying choices in pharmacologic and non-pharmacologic therapies. In her piece, Jane Reckelhoff describes the potential risks of treating men and women with the same interventions based on her studies identifying gender-specific mechanisms underlying the pathogenesis of hypertension.

Among the obstacles to improving outcomes in patients with hypertension is the lack of new therapies. One could argue that there has not been a truly novel drug for hypertension since the development of ACE inhibitors in the 1980s, considering that angiotensin receptor blockers and renin inhibitors also target the renin-angio-



tensin system. In another article in our series, Svetkey and Tyson detail potentially good news regarding progress in developing a novel approach for hypertension treatment: renal nerve ablation. If ongoing prospective randomized controlled trials confirm the efficacy of this nonpharmacologic intervention, we would have a new tool for patients with resistant hypertension consisting of a single intervention with apparent long-lasting effects circumventing the need for daily medication dosing.

And now for the unknown. Jens Titze explains new concepts of sodium homeostasis whereby macrophages can regulate non-osmotic sodium storage in the skin to influence blood pressure responses to increased dietary salt intake. Finally, Steven Crowley summarizes the growing literature that supports a role for the immune system to regulate blood pressure and target organ damage in hypertension through effects on the vasculature and the kidney. This work raises the possibility of targeting inflammatory pathways in the treatment of hypertension and its complications.

Together, the articles in this series highlight opportunities to turn the bad news about hypertension into good news for our patients.

Thomas Coffman, MD, FASN, and Steven Crowley, MD, edited this special section of ASN Kidney News and are affiliated with the Division of Nephrology at Duke University Medical Center in Durham, NC.

Treatment of Hypertension in Patients with Chronic Kidney Disease

By Laura P. Svetkey and Crystal C. Tyson

Most people with chronic kidney disease (CKD) have high blood pressure. Treatment of hypertension in patients with CKD is considered critical to prevent CKD progression and related cardiovascular events. However, questions remain about the appropriate BP goal. Most evidence indicates there is no benefit of treating to a goal any lower than 140/90 mm Hg, but there is some suggestion that such a goal may be appropriate for patients with albuminuria. Given recent evidence that a lower goal in patients with diabetes (without CKD) actually increases risk, and the subsequent change in American Diabetes Association guidelines from 130/80 mm Hg to 140/80 mm Hg, it may be prudent to consider other factors—such as presence or absence of albuminuria and comorbid disease—in order to individualize BP management in patients with CKD.

The evidence is somewhat more clear-cut with regard to choice of antihypertensive medication: treatment with angiotensin converting enzyme (ACE) inhibitors (and possibly angiotensin receptor blockers [ARBs] as well) is more effective than other classes at slowing CKD progression, and possibly preventing incident heart failure.

However, no clinical outcomes trial has carried out head-to-head comparison between ACE inhibitors and ARBs, or between ACE inhibitors and diuretics. Most patients with CKD have some degree of volume-dependent hypertension, arguing for use of diuretic (specifically a loop diuretic if their eGFR is less than 30 mL/min/1.73 m²). Furthermore, many patients with CKD have resistant hypertension, a condition in which diuretic is critical for achieving BP control.

In addition, the evidence favoring ACE inhibitors or ARBs comes from studies comparing classes of agents for the initial treatment of hypertension (i.e., the first drug). Most patients with CKD require at least two antihypertensive medications to achieve goal BP. There is no clinical trial evidence to guide the choice of the second, third, fourth, or more medication.

Therefore, a reasonable strategy involves initial treatment with an ACE inhibitor (or an ARB) with a diuretic added as the second agent, or vice versa.

There is no evidence base to guide the use of non-pharmacologic antihypertensive therapy in patients with CKD. The effective lifestyle strategies for lowering BP (weight loss in the overweight/obese, DASH [Dietary Approaches to Stop Hypertension] dietary pattern, reduced sodium intake, physical activity, and moderation of alcohol intake) have not been tested

specifically in patients with CKD, but most are likely to be effective and safe in this population. The possible exception is the DASH dietary pattern, which is high in potassium, calcium, magnesium, and phosphorus. With an eGFR greater than 45 mL/min/1.73 m², excretion of these minerals is likely to be sufficiently preserved to comfortably recommend DASH; however, additional laboratory surveillance is prudent. Despite the fact that the BP-lowering effects and safety of DASH and other lifestyle interventions have not yet been tested in the setting of CKD, they are nonetheless “heart healthy” behaviors appropriate for any population with high cardiovascular risk.

Overall, when treating hypertension in patients with CKD the therapeutic goal should be to effectively lower BP while simultaneously slowing progression of disease and reducing cardiovascular risk. Blood pressure targets should be individualized, taking into account degree of albuminuria and presence of comorbidities. Using an ACE inhibitor (or ARB) and diuretic should be the cornerstones of drug therapy, and nonpharmacologic lifestyle strategies should be encouraged. ●

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