Predictive Factors for CKD; Renal Denervation

Q Quite a few of my teenage patients are overweight. I know they are at risk for diabetes, but does their weight also affect their kidneys? Isn't diabetes the main cause of kidney failure?

The number one cause of chronic kidney disease (CKD) in the United States and worldwide is diabetes, but it is certainly not the only risk factor. Studies have shown a link between obesity and CKD; even in the absence of kidney disease, obesity may cause glomerular dysfunction and an increase in glomerular size.[1]

Obesity during adolescence has been identified as a strong predictor of CKD in adulthood. Other diseases and conditions that, if present in adolescence, indicate future risk for kidney disease include diabetes, hypertension, inflammation, and proteinuria.

A recent Swedish study followed patients from adolescence to adulthood to identify markers that would predict later kidney disease. In this study, the most predictive factor of kidney failure in adulthood was proteinuria in adolescence (odds ratio, 7.72). These results may be limited by the homogeneity of the predominantly white, male study population, but the extensive follow-up period, which "highlights the long natural history" of kidney disease, is one strength of this study.[2]

Based on these and other findings, you know that if your teenage patients have proteinuria, they are much more likely to develop kidney failure as an adult. Yet, in the US, the American Academy of Pediatrics and the US Preventive Services Task Force do not recommend urine screening for asymptomatic children.[3]

Interestingly, however, a survey of pediatric practices revealed that 58% of pediatricians screen adolescents with urinalysis, even if they are asymptomatic.[4] In other words, they ignore the guidelines. If they did not, we would likely miss what is possibly the most important predictive factor for kidney failure in adults. **—TAH**

Q I've heard a lot of references to "renal denervation" and its use for resistant hypertension. What is it? Does it work? Is it common in the US?

Renal denervation is a minimally invasive endovascular procedure that ablates (or disrupts) the renal nerves in and around the renal arteries with radiofrequency energy.[5] Renal denervation has been approved in the US and other countries and is being used clinically in Europe, Canada, and Australia.[6]

It is thought that renal denervation interrupts the efferent and afferent signals that stimulate the renin-angiotensin-aldosterone system (RAAS) and regulate whole-body sympathetic nervous system activity.[5] Similar to surgical sympathectomy, renal denervation should theoretically lower blood pressure. However, Ezzahti et al found that renin levels did not decrease in patients following renal denervation.[7]

Drug-resistant hypertension is defined as blood pressure that remains greater than 140/90 mm Hg despite treatment with three or more antihypertensive medications, including a diuretic.[8] Patients with resistant hypertension have increased cardiovascular risk.[9] Clinical trials of renal denervation have focused on treatment of resistant hypertension, in the hope of reducing the associated morbidity and mortality.

Results of the Symplicity HTN-3 trial, which assessed the safety and efficacy of renal denervation, were anxiously awaited, since prior trials yielded mixed results. Although the Symplicity HTN-1 and Symplicity HTN-2 studies demonstrated a possible benefit of renal denervation to lower office-measured blood pressure, other studies did not show a decrease in BP in patients who had undergone renal denervation.[6,7] These

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early trials, however, were small and did not randomize patients to a sham procedure.[10]

The Symplicity HTN-3 trial included 535 patients at 88 centers in the US. Patients were randomly assigned to receive either renal denervation plus baseline antihypertensive medications or a sham procedure plus baseline antihypertensive medications.

The researchers found that the sham procedure was just as effective as the "true" renal denervation in decreasing systolic blood pressure in patients with resistant hypertension.[10] In other words, renal denervation did not demonstrate efficacy for this purpose.

In response to the results of this well-designed trial, the FDA has halted approval to perform renal denervation in patients with resistant hypertension in the US. However, clinical investigation will continue among subgroups of hypertensive patients or separate populations.

Despite a lack of efficacy, renal denervation does appear to be well tolerated, as evidenced by safety data from Symplicity HTN-3. **—JK** **CR**

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