Guest Editorial

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Chronic Kidney Disease Screening: Don't Miss This Vital Opportunity

Chronic kidney disease (CKD) is one of the world's major public health problems, and the prevalence of kidney failure is rising steadily. In the United States alone, 20 million Americans have CKD, and an additional 20 million are at increased risk for developing the disease.[1]

A strong link exists between CKD and cardiovascular conditions. Not only is hypertension a significant risk factor for CKD, but CKD itself is an independent risk factor for cardiovascular disease (CVD). In fact, patients with CKD are more likely to die from CVD than to develop end stage renal disease. Furthermore, a diagnosis of CKD affects antihypertensive, lipid lowering, and other therapies.

If we, as clinicians, are to work toward halting the rising CKD epidemic, we must assume a more active role in diagnosing and managing the disease in its earliest stages. But while blood pressure (BP) is measured during nearly every clinic visit, CKD screening has not yet become as routine. This may be due, in large part, to the perception that CKD assessment is too time consuming and complex for clinicians struggling with the harried realities of modern medical practice.

Yet, is this perception accurate? For those of us practicing in the VA, at least, recent policies make CKD screening easier than ever.

CKD SCREENING

The two methods for detecting CKD involve either screening for proteinuria (through urinalysis) or calculating or estimating the glomerular filtration rate (GFR). In the seventh report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, CKD is defined as an estimated GFR (eGFR) of less than 60 mL/min/1.73 m^2 or the presence of clinical proteinuria (greater than 300 mg/day or 200 mg/g creatinine).[2]

Patients with hypertension should have a routine urinalysis.[2] If initial results indicate no macroalbuminuria, additional testing for microalbuminuria is optional—unless the patient is diabetic, in which case the procedure should be routine.[3] Microalbuminuria (between 30 and 300 mg/day) is a risk factor for progressive kidney disease and a strong risk factor for CVD,[4] even in individuals who do not have diabetes or hypertension.[5]

GFR calculation remains the most sensitive and specific means of assessing renal function. While measurement of inulin clearance is the most accurate way to determine GFR, the test is rarely performed because of its complexity and cost. Instead, measurement of serum creatinine (SCr) levels is used as a means of estimating GFR and the presence of CKD (defined as an SCr level greater than 1.5 mg/dL in men or greater than 1.3 mg/dL in women).[2]

When considered alone, however, SCr measurement may overestimate GFR by 10% to 40% in healthy people and underestimate the severity of renal impairment in individuals who are older, smaller, and frail.[3] In fact, small changes in SCr levels often represent large changes in the GFR. Additionally, such factors as muscle mass, diet, and certain medications affect SCr levels and can lead to errors in the assessment of renal function.[6] Furthermore, CKD often is present in people with normal SCr levels.[2] Relying solely on SCr levels as a measure of the GFR, therefore, can result in missed opportunities to identify patients with CKD.

Estimating GFR more accurately

Over the years, there have been numerous attempts to incorporate SCr measurements into mathematical equations for estimating GFR. These models, which take into account such factors as age, gender, ethnicity, and body size, along with SCr levels, are more accurate estimates of GFR than SCr levels alone.[3] For many years, the Cockcroft-Gault equation was used most commonly to calculate eGFR.[3] It more accurately reflects SCr clearance than eGFR, however, and was derived using a small sample of about 260 predominantly white, male patients.

More recently, the Modification of Diet in Renal Disease (MDRD) equation, which was based on data from about 1,600 patients with CKD from various backgrounds, has emerged as a more accurate means of estimating GFR.[6] This formula uses SCr levels along with age, gender, and ethnicity to determine eGFR as follows: eGFR = $186.3 \times (SCr)^{-1.154} \times (age)^{-0.203} \times (0.742$ if female) x (1.21 if black).[7] Although it does tend to underestimate eGFR in individuals with near normal renal function, the MDRD equation nevertheless has become, for all practical purposes, the new "gold standard" for detecting both early and late manifestations of impaired kidney function.

Recognizing how little time busy clinicians have to search for formulas or perform complex calculations, as well

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as the value of routine CKD screening, the VA has implemented a policy requiring the laboratory service of all of its hospitals to calculate and report the eGFR value, using the MDRD equation, whenever an SCr level is ordered.

CLINICAL IMPLICATIONS OF CKD DETECTION

Blood pressure goals

For patients who have neither diabetes nor CKD, the currently accepted BP goal is less than 140/90 mm Hg. In patients with CKD, however, a goal of less than 130/80 mm Hg is recommended.[2] Yet many VA clinicians are not aware of or do not heed the eGFR reported by the laboratory service, thus allowing patients with values above the CKD threshold—who require tighter BP control—to escape "under the radar."

Coronary disease

The burden of CVD among patients with CKD is substantial. Individuals with stage 3 CKD (eGFR less than 60 mL/min/1.73 m^2) have a 16% increase in CVD mortality while those with stage 4 or 5 CKD (eGFR less than 30 mL/min/1.73 m^2) have a 30% increase.[8] Using the MDRD equation to calculate eGFR for more than 40,000 high risk patients with hypertension enrolled in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), investigators found that 57% of patients had stage 2 CKD and almost one of every five patients had stage 3 or greater CKD[9]—findings that would not have been apparent from SCr levels alone. Compared to patients with stage 2 CKD, those with stage 3 or greater CKD were more likely to have had a previous myocardial infarction or stroke, have ischemic changes on electrocardiography (ECG), and have left ventricular hypertrophy (LVH) on ECG. And for every 10-mL/min/1.73 m^2 reduction in eGFR, individuals experienced a 6% increase in CVD risk and a 14% increase in the risk of LVH on ECG.[9]

The increased CVD risk in patients with CKD is due partly to the overlap of risk factors—such as age, hypertension, hyperlipidemia, diabetes, and physical inactivity—between the two conditions. A recent meta-analysis of clinical trials indicates that lipid lowering therapy preserves eGFR and decreases proteinuria in patients with CKD.[10] Although evidence suggests that patients with CKD have an expected 10-year coronary heart disease risk greater than 20%, CKD has not been included as a coronary risk equivalent in the Adult Treatment Panel III guidelines.[11] The Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines do, however, recognize CKD as a coronary risk equivalent and recommend a low-density lipoprotein (LDL) cholesterol goal of less than 100 mg/dL for these patients.[12]

Secondary hyperparathyroidism

Bone disease and disorders of calcium, phosphorus, and vitamin D metabolism are common comorbidities in CKD. As renal function declines, the kidneys lose their ability to excrete phosphorus. Phosphate retention inhibits the renal enzyme that allows the kidneys to convert vitamin D to its active metabolite, 1,24-dihydroxyvitamin D3.[13] In CKD, hyperphosphatemia, hypocalcemia, deficiency of the active form of vitamin D (calcitriol), and diminished expression of calcium and vitamin D receptors lead to partial resistance to the metabolic actions of parathyroid hormone (PTH), thus contributing to the hormone's excessive production.[14] And, as one study of 218 ethnically diverse patients with renal impairment and a variety of comorbidities found, higher PTH levels are associated significantly with increased CVD risk.[15]

The recently published K/DOQI Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney disease recommend that clinicians monitor PTH, calcium, and phosphorus levels at least every 12 months in people with stage 3 CKD and every three months in patients with stages 4 and 5 CKD.[16] These guidelines also provide target levels for serum calcium, phosphorus, and PTH in an effort to improve clinical outcome. Randomized controlled trials need to be conducted to evaluate the role of vitamin D and its analogues in improving the survival of patients with CKD.[17]

ENSURING EARLY CKD DETECTION

Each of the interventions discussed here represents a practical step toward improving global cardiovascular risk status in VA patients who may have unrecognized CKD.[18] It is particularly important for VA clinicians to utilize reports of eGFR regularly. Only through greater vigilance will an appropriate effort to prevent declining renal function and progression of CVD occur. ●

Author disclosures

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