EDITORIAL

Eliminating chronic kidney disease… as a diagnosis

Vinay Prasad[1], Adam Cifu[2]

1 Medical Oncology Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, United States
2 Section of General Internal Medicine, Department of Medicine, University of Chicago, Pritzker School of Medicine, Chicago, Illinois, United States

Chronic kidney disease (CKD) is both a new diagnosis and an old disease. The same patient who, a decade ago, would have been told of an elevated creatinine now has CKD. Recognition of CKD has grown as glomerular filtration rate (GFR) reporting became standard in diverse clinical settings and countries around the world. Indeed, the diagnosis of CKD carries a sobering prognosis. Based on population data, patients with a GFR of 45 to 59 ml/min/1.73 m^2 have a 17% higher mortality than those with normal renal function, after adjusting for comorbidities. Patients with a GFR of less than 15 ml/min/1.73 m^2 have an all-cause mortality 5 times that of controls.[1] Although CKD surely confers an increased risk, has our changed nomenclature and increasing awareness improved the lives of our patients? While it seems rational that identifying patients at high risk and recommending focused and proactive management should improve outcomes, there is no evidence that this is the case. Instead, the diagnosis of CKD prompts referrals,[2] but has not been shown to improve the morbidity or mortality to improve the morbidity or mortality for these patients.

Category definitions of CKD (stages, 1–5) were proposed in 2002 by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) and adopted in 2004. In current practice, a diagnosis of CKD prompts an evaluation for the cause of the disease and the extent of its consequences. Regarding causes, common diagnostic studies include imaging of the kidney (looking for anatomical etiologies), urinalysis, complement levels (used to screen for collagen vascular disease), hepatitis C antibodies, antineutrophil cytoplasmic antibody testing (to diagnose vasculitis), and serum and urine electrophoresis (myeloma). Renal biopsy is advised if an etiology remains elusive. Regarding consequences, testing typically includes screening for microalbuminuria and hypercholesterolemia (given elevated cardiovascular risk), complete blood count (anemia), and calcium and phosphate testing.[3]

Our current practice of diagnosis, evaluation, and management of CKD would be reasonable if performing most of these interventions for all patients with CKD improved outcomes beyond our previous standard of care. That standard was performing some of these tests for the few patients whose CKD progressed rapidly or to a later stage. Currently, there is no evidence that this is the case.[4]

First, consider testing for the consequences of CKD. Regarding cholesterol screening, a meta-analysis failed to show an overall mortality benefit for primary prevention with statins among patients with CKD.[5] One study[6] did find that the combination of ezetimibe and simvastatin could improve atherosclerotic event rates for patients with kidney disease; thus, whether increased cholesterol screening is beneficial remains a contentious issue.[7,8] For microalbuminuria, randomized trials suggest that angiotensin-converting enzymes may slow the rate of renal decline, but these studies have not told us whether this is a property of the class of drugs or whether this is simply related to appropriate blood pressure (BP) control,[9] which we should strive for regardless of CKD. But, more importantly, progression of renal disease is merely a numerical value, and not a patient-centered outcome. No randomized controlled trial has shown that angiotensin-converting enzyme inhibitors (ACEIs), given to patients with CKD, avert future end-stage renal disease (which ultimately affects only 2% of CKD patients) or improves mortality. A meta-analysis by Jafar et al.[10] did show that ACEIs can prevent future ESRD, which occurred in 7.4% vs. 11.6% of patients, respectively (P = 0.002). However, this analysis included placebo controlled trials, and the mean systolic and diastolic pressures were higher in the control group (systolic higher by 4.5 mmHg (95% confidence interval [CI], 3.0–6.1 mmHg) and diastolic higher by 2.3 mmHg (95% CI, 1.4 to 3.2 mm Hg).[10] Although the authors reported that the beneficial effect of

Correspondence to:
Vinay Prasad, MD, Medical Oncology Branch, National Cancer Institute, National Institutes of Health, 10 Center Dr. 10/12N226, Bethesda, MD 20892, United States, phone: +1-219-229-0170, fax: +1-301-402-1608, e-mail: vinayak.prasad@nih.gov
Received: September 20, 2013.
Revision accepted: January 16, 2014.
Published online: January 23, 2014.
Conflict of interest: none declared.
Pol Arch Med Wewn. 2014; 124 (1-2): 7-9

ACEIs on ESRD persists after adjustment for baseline variables and the differences blood pressure over the trial, such a conclusion requires assumptions that could be avoided if one compared only studies of 2 active drugs where similar BP was achieved in both arms. We maintain that it remains unclear whether the benefit of these drugs on ESRD is a property of this particular class of medications or merely the result of better BP control. Finally, consider anemia associated with renal impairment. Every randomized trial to date has shown that use of exogenous erythropoietin is associated with worse mortality at any hemoglobin target (than a lesser one), and no study has shown that some erythropoietin is superior to no erythropoietin. Finally, treating an elevated calcium–phosphate product with calcium-binding agents has been a moving target (what counts as elevated?) and has never shown improvement in hard outcomes in any randomized trial.

If diagnosing CKD does not alter how we should manage its consequences, an argument must be made that identifying the cause of CKD is itself valuable. If the benefits of diagnosing the etiology of CKD are limited to identifying reversible causes in a small subset of patients, then this must be weighed against the burden of evaluating all patients, with the requisite downside of false-positive test results and cost. For instance, if performing renal ultrasonography among 100 patients with CKD identifies 1 woman with fibromuscular dysplasia, or if 1 renal biopsy among 20 finds intrinsic renal disease amenable to medical treatment, this must be weighed against the numerous ultrasound findings of dubious significance, and the real risks of renal biopsy. Decision analyses might suggest an answer to this question, but given the complexity of the CKD work-up, even a well-done analysis would be prone to error. Instead, we can only answer this question with a randomized trial testing either screening for CKD or routine GFR reporting and powered for the endpoint of overall mortality.

The last consequence of diagnosing CKD is the recommendation of the KDOQI guidelines[11] that all patients with CKD be referred to a nephrologist. Proponents point out that CKD often occurs among patients with numerous comorbid conditions, requiring numerous medications, where specialist management may be helpful. But it is unclear how these patients are different from those already cared for by primary care providers. Frequent monitoring of the GFR is another oft-cited reason for nephrological follow-up, but it is unsure whether this intervention affords any benefit, and, even if it did, why a primary care provider could not perform more frequent blood work. Observational studies do suggest that early and frequent specialist referral is associated with improved mortality[12]; however, such results are confounded by socioeconomic factors. Given the undeniable associations between economic, social factors, access to care and renal disease, randomized studies are required to accept such a bold claim.

Given the considerations we have raised here, we submit that the rise of CKD is less of a public health strategy, and more akin to disease mongering. Disease mongering is the broadening of diagnostic categories to increase the utilization of medical resources with no evidence of the corresponding health benefit.[13] The KDOQI guidelines have been uniquely cited as having a dubious relationship with industry, with most committee members having some financial conflict of interest.[14] The management of CKD involves the use of many costly medications—the phosphate binder, sevelamer, costs 4 to 5 dollars per pill—taken for an indefinite and often lengthy period of time. That all these efforts do little to improve health is an ongoing tragedy in need of remedy.

One particularly unfortunate consequence of our efforts to report CKD is that many patients now labeled with the condition are the very oldest persons. A study by Hemmelgarn et al.[2] found that universal CKD reporting in Alberta, Canada significantly increased the rate of nephrologist referral among those greater than 86 years old, 1 of 2 groups predominantly responsible for the increase in referrals. These patients had numerous comorbidities and thus face numerous competing causes of death. It is unclear that an additional diagnosis benefits these patients.

To address these concerns, we propose 2 solutions. First, physicians should not make a diagnosis of CKD for patients who do not need it. When patient already warrants treatment for hypertension, diabetes, and coronary artery disease, the diagnosis of CKD does not alter management. Early referral to a nephrologist has not prospectively shown any improvement in outcomes, and we do not advocate it. Second, and more generally, new diagnostic categories should not be broadly adopted, lacking evidence that they improve outcomes. Updated 2012 guidelines do recognize some of the limitations of earlier guidelines, and now classify CKD by cause, glomerular filtration rate, and albuminuria.[15] However, the central challenges identified here remain. The real lesson of CKD is that it is cheap, easy, and satisfying to report estimated GFR, but it is also complicated, costly, and probably does not help patients.

REFERENCES

1 Go AS, Chertow GM, Fan D, et al. Chronic Kidney Disease and the Risks of Death, Cardiovascular Events, and Hospitalization. N Engl J Med. 2004; 351: 1296-1305.

2 Hemmelgarn BR, Manns BJ, Lloyd A, et al.; Alberta Kidney Disease Network. Relation between kidney function, proteinuria, and adverse outcomes. JAMA. 2010; 303: 423-429.

3 Matuszkiewicz-Rowińska J. KDIGO clinical practice guidelines for the diagnosis, evaluation, prevention, and treatment of mineral and bone disorders in chronic kidney disease. Pol Arch Med Wewn. 2010; 120: 300-306.

4 Stompor T, Olszewski A, Kierzkowska I. Can we prolong life of patients with advanced chronic kidney disease: what is the clinical evidence? Pol Arch Med Wewn. 2011; 121: 88-93.

5 Strippoli GFM, Navaneethan SD, Johnson DW, et al. Effects of statins in patients with chronic kidney disease: meta-analysis and meta-regression of randomised controlled trials. BMJ. 2008; 336: 645-651.

6 Baigent C, Landray MJ, Reith C, et al.; SHARP Investigators. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial. Lancet. 2011; 377: 2181-2192.

7 Ritz E. Should all patients with chronic kidney disease take a statin? A commentary to a meta-analysis of randomized control trials. Pol Arch Med Wewn. 2008; 118: 541-542.

8 Piecha G, Adamczak M, Ritz E. Dyslipidemia in chronic kidney disease: pathogenesis and intervention. Pol Arch Med Wewn. 2009; 119: 487-492.

9 Giatras I, Lau J, Levey AS. Effect of angiotensin-converting enzyme inhibitors on the progression of nondiabetic renal disease. a meta-analysis of randomized trials. Angiotensin-Converting-Enzyme Inhibition and Progressive Renal Disease Study Group. Ann Intern Med. 1997; 127: 337-345.

10 Jafar TH, Schmid CH, Landa M, et al. Angiotensin-converting enzyme inhibitors and progression of nondiabetic renal disease: a meta-analysis of patient-level data. Ann Intern Med. 2001;135: 73-87.

11 K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. 2002; 39: S1-S266.

12 Avorn J, Bohn RL, Levy E, et al. Nephrologist care and mortality in patients with chronic renal insufficiency. Arch Intern Med. 2002; 162: 2002-2006.

13 Moynihan R, Henry D. The fight against disease mongering: generating knowledge for action. PLoS Med. 2006; 3: e191.

14 Coyne DW. Influence of industry on renal guideline development. Clin J Am Soc Nephrol. 2007; 2: 3-7.

15 KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. 2012. http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf. Accessed January 14, 2014.