Kidney Medicine

Combined Albuminuria and Estimated GFR Laboratory Reporting Affects Primary Care Management of CKD

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According to the Centers for Disease Control and Prevention (CDC), chronic kidney disease (CKD) affects 37 million American adults who experience high rates of cardiovascular events and are at risk for kidney failure, and among those who develop kidney failure, 5-year mortality is 50% worse than for most cancers.[1] The original definition and stratification of CKD published in 2002 by the US Kidney Disease Outcomes Quality Initiative (KDOQI) transformed practice worldwide by promoting the adoption of estimated glomerular filtration rate (eGFR) reporting rather than reporting serum creatinine level alone and by increasing kidney disease recognition and management upstream from nephrologist services.[2] The international Kidney Disease: Improving Global Outcomes (KDIGO) 2012 clinical practice guideline for CKD evaluation and management,[3] endorsed in the United States by KDOQI,[4] updated the previous work based on an impressive amount of epidemiology to include a cause-GFR-albuminuria (C-G-A) CKD definition and classification system to optimize risk stratification based on eGFR and urinary albumin-creatinine ratio (uACR).[3,4]

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Unfortunately, recent assessments of US population-level care for individuals with eGFRs < 60 mL/min/1.73 m^2 reveal that <50% undergo uACR testing,[5-7] only 12% to 20% carry a CKD diagnosis,[6,7] almost 50% have hypertension that is not controlled,[6] ~40% have diabetes that is not controlled,[6] only ~30% use statins to reduce cardiovascular events,[6] and <40% are using angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs).[6] Although these data predominantly represent primary care delivery, nephrology care has also been suboptimal, with short durations of nephrology services before dialysis initiation and limited preparation for kidney replacement therapy reflected by high rates of hemodialysis catheter use at initiation and low rates of both home dialysis and preemptive kidney transplant.[5] In sum, there is considerable room for improvement in the care of individuals with CKD by primary care clinicians and nephrologists alike.

Primary Care Interpretation of CKD Test Reporting

The impact of clinical practice guideline implementation in primary care is important to nephrology, particularly for improving care coordination and for quality improvement and population health interventions. In this issue of *Kidney Medicine*, Hallan et al[8] present a novel randomized vignette study of 249 primary care physicians (218 in Norway plus 31 in the United States) at various levels of training and experience, showing that more detailed laboratory reporting and level of clinical experience are correlated with a greater likelihood of making a correct interpretation of the clinical scenario and suggesting the appropriate treatment plan. The methodology randomly assigned professionals to 6 vignettes, each with 4 potential answers, from a broad range of 18 CKD scenarios. There were 3 laboratory reporting formats: minimal data showed only dichotomous reporting of high or low serum creatinine levels and dipstick proteinuria, KDOQI 2002 showed CKD stage based on eGFR, and KDIGO 2012 showed risk for CKD-related complications (low, moderate, high, or very high) based on both eGFR and uACR strata.

There were successive increases in the correct assessment across the 3 laboratory reporting categories, with 47.9% for minimal data, 59.2% for KDOQI 2002, and 67.7% for KDIGO 2012. Specific improvements in clinical interpretation were seen for both the KDOQI 2002 methodology and the KDIGO 2012 methodology (odds ratio [OR], 1.57; $P < 0.001$; and OR, 2.28; $P < 0.001$, respectively) as compared to minimal data. Similarly, there was a stepwise significant improvement in clinical interpretation found with both the KDOQI 2002 and the KDIGO 2012 methodology (OR, 1.45; $P = 0.005$; and OR, 2.28; $P < 0.001$, respectively) as compared with minimal data. In addition, there was a nominally significantly greater effect by clinical experience with OR of 1.10 per year of additional experience; $P = 0.002$. Even with additional years of clinical experience, few practitioners had prior nephrology rotations, ranging from 7% to 10% among trainees and 12% of general practitioners. Although this difference was not statistically significant, low exposure to nephrology limits the recognition and incorporation of kidney disease clinical practice guidelines.

In addition to this study, the published literature on the effect of clinician interpretation of eGFR reporting as compared to serum creatinine level reporting suggests incremental benefits with eGFR reporting as recommended by the 2002 KDOQI guideline in the context of heterogenous study design. These benefits include a modest increase in albuminuria/proteinuria testing, increased CKD diagnosis, avoidance of nonsteroidal anti-inflammatory drugs, increased use of ACE inhibitors or ARBs, and

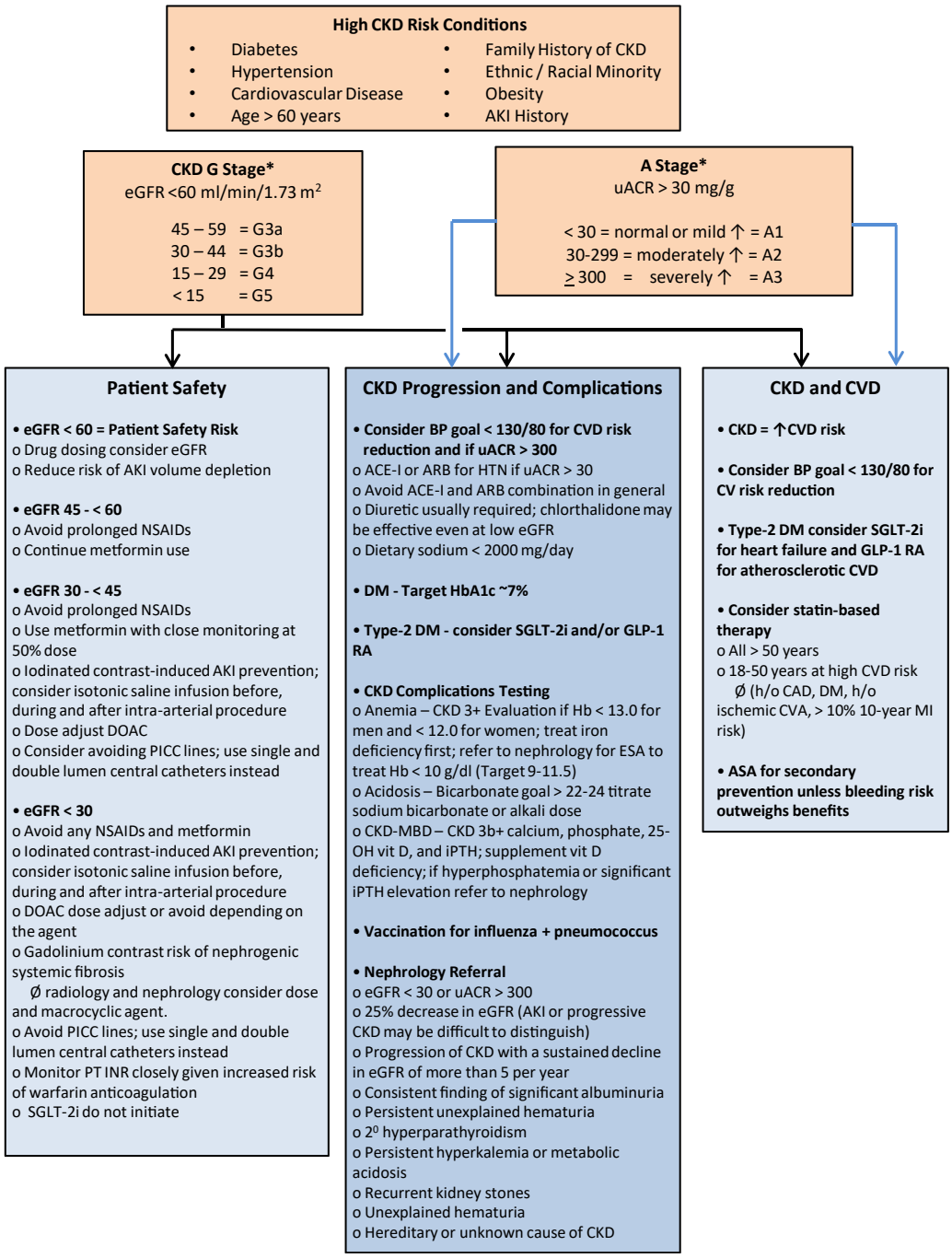

Figure 1. Schematic that summarizes a practical approach to the detection and management of chronic kidney disease (CKD) for primary care practitioners,[12] updated to incorporate recent editorial commentary[13,14] and clinical practice guidelines for type 2 diabetes.[19] *Confirmed for 3 or more months. Abbreviations: 25(OH)D, 25-hydroxyvitamin D; ACE-I, angiotensin-converting enzyme inhibitor; ACR, albumin-creatinine ratio; AKI, acute kidney injury; ARB, angiotensin receptor blocker; ASA, acetylsalicylic acid/aspirin; A stage, albuminuria category; BP, blood pressure; CAD, coronary artery disease; CKD-MBD, chronic kidney disease–mineral and bone disorder; CV, cardiovascular; CVA, cerebrovascular accident; CVD, cardiovascular disease; DM, diabetes mellitus; DOAC, direct oral anticoagulant; eGFR, estimated glomerular filtration rate; ESA, erythropoiesis-stimulating agent; GLP-1 RA, glucagon-like peptide 1 receptor agonist; G stage, glomerular filtration rate category; Hb, hemoglobin; HbA1c, glycated hemoglobin; h/o, history of; HTN, hypertension; iPTH, intact parathyroid hormone; MI, myocardial infarction; NSAID, nonsteroidal anti-inflammatory drug; PICC, peripherally inserted central catheter; PT INR, prothrombin time international normalized ratio; SGLT-2i, sodium-glucose cotransporter 2 inhibitor; uACR (UACR), urine albumin-creatinine ratio; vit, vitamin. Adapted from Vassalotti et al[12] with permission from Elsevier.

increased referral for nephrology services.[9,10] The KDIGO 2012 guideline essentially validated the classification from 2002 with added detail for the C-G-A classification. The emphasis on the addition of albuminuria to risk stratification in the KDIGO 2012 guideline is the most notable aspect of the vignettes by Hallan et al. Two of the 6 vignettes emphasize severe albuminuria (uACR > 300 mg/g) as both a strong predictor of cardiovascular risk and high-level evidence for use of either ACE-inhibitor or ARB therapy for hypertension, regardless of the presence of diabetes.[3,4]

In 2017 in the United States, ~33% of the CKD population received little or no nephrology care and only 32.6% were treated by specialists for more than 1 year before initiation of dialysis or kidney transplant.[5] Accordingly, 2 of the 6 vignettes explore knowledge of the indications for nephrology consultation (confirmed eGFR < 30 mL/min/1.73 m^2 or rapid CKD progression defined by annualized eGFR loss > 5 mL/min/1.73 m^2),[3,4] highlighting that improved reporting could increase appropriate and timely nephrology referral. Unfortunately, the vignettes are unable to address additional barriers to optimal CKD care coordination revealed in US clinician surveys, including lack of timely and adequate information exchange, unclear roles and responsibilities between primary and nephrology care, and variable access to nephrologists.[11]

Limitations are described comprehensively by the investigators, including the distinction between knowledge applied in a vignette and real-world practice. Ironically, by far the most significant limitation not addressed by the authors in assessing the utility of the C-G-A classification is that clinicians cannot interpret tests that they do not order. In recent years in the United States, annual uACR testing is <50% for diabetes and <10% for hypertension in both the Medicare 5% and commercial insurance Optum Clinformatics data sets,[5] supporting the need for interventions to improve targeted albuminuria testing. Where this study is of critical importance is that clinicians are unlikely to order tests that they are not sure how to interpret, suggesting that low rates of albuminuria testing may simply reflect an underappreciation of the utility of the results. Accordingly, an important innovation not considered in this analysis is disseminating distilled clinical practice guidelines that would be more readily used in primary care management (Fig 1).[12-14]

The utility of evaluating the minimal data reporting that consists of only serum creatinine level in contemporary practice in the United States is limited because a College of American Pathologists international sample showed that 89% of laboratories reported eGFR in 2017, although most of the laboratories surveyed were in North America.[15] Adoption of eGFR reporting in Norway is likely similar. A major challenge for primary CKD care is the heterogeneity of the condition, not only in terms of cause, but also with respect to severity. The authors have focused on albuminuria modification of the earlier KDOQI 2002 with the C-G-A classification incorporated into the KDIGO 2012 guideline, but unfortunately do not explore the impact of the CKD cause on management. The absence of a clear cause of CKD in many individuals is an important consideration for primary care evaluation and management and an indication for nephrology input.[3,4]

CKD is a heterogenous state, such that people with only slightly low eGFRs without elevated uACRs may have only small management and prognostic implications, whereas people with very low eGFRs and/or severely elevated uACRs may be at critical risk for adverse events and require multidisciplinary interventions to address the substantial risk for hospitalization, cardiovascular events, kidney failure, and mortality. The authors miss an opportunity to use the vignettes to investigate the controversy regarding the distinction between loss of eGFR with normal aging versus disease among seniors with eGFRs of 45 to 60 mL/min/1.73 m^2 in the absence of albuminuria (CKD G3a, A1). Areas for consideration in this setting would be the potential role of cystatin C testing, patient safety factors including limiting nephrotoxins and addressing the risk for major surgery perioperative acute kidney injury, as well as the absence of evidence to support ACE-inhibitor or ARB use solely for kidney risk reduction.[3,4] Of course, only so much can be addressed in 6 clinical vignettes. The authors address the interaction between CKD as a major risk condition for acute kidney injury and medication management that considers the level of eGFR. Practitioners performed poorly on the acute kidney injury risk reduction strategy recognition.

CKD Primary Care Initiative

CKDintercept primary care clinician engagement of the National Kidney Foundation (NKF) includes a Laboratory Engagement Initiative to simplify primary care clinician ordering of kidney tests and a harmonized KDIGO 2012 reporting scheme for the tests defined by the kidney profile (eGFR plus uACR) that has been recognized by the US Choosing Wisely initiative.[16,17]

The NKF also developed the Kidney Health Evaluation for adults with diabetes electronic clinical quality measure to recommend the same testing in collaboration with the National Committee for Quality Assurance and Physician Consortium for Performance Improvement for broad implementation.[18] Testing and recognition of albuminuria will aid in the selection of patients who need additional interventions beyond the current ACE-inhibitor or ARB paradigm, including novel kidney and cardiovascular protective therapies such as sodium-glucose cotransporter-2 inhibitor and/or glucagon-like peptide 1 receptor agonists in type 2 diabetes.[19,20]

The NKF has advanced CKD payment model proposals to the Centers for Medicare & Medicaid Services that incentivize primary care and nephrology practitioners to deliver evidence-based interventions and foster care coordination. A quality improvement project implementing

primary care population health for diabetes and hypertension with interventions based on eGFR and uACR risk stratification showed reduced hospitalization, decreased 30-day readmissions, and select medical per-patient per-month cost containment in a commercial health insurance plan's patient-centered medical home model.[21] This quality improvement project is a prime example of translating guidelines into implementation protocols that can be incorporated with modification to local practice by others to affect population health.

Last, on the basis of the CDC's definitions and reported prevalence of diabetes and hypertension,[1] the NKF is promoting the 1 in 3 kidney risk public awareness campaign in support of the Advancing American Kidney Health Initiative in partnership with the US Department of Health and Human Services and the American Society of Nephrology. Although there is much that needs to be done for the CKD population, the study by Hallan et al shows how reporting risk has the potential to improve primary care, both through delivery of risk-specific interventions to slow the progression and treat the complications of CKD and through appropriate and timely nephrology referral.

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REFERENCES

1. Centers for Disease Control and Prevention. Chronic kidney disease surveillance system. http://www.cdc.gov/ckd. Accessed January 22, 2020.
2. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis*. 2002;39(suppl 2):S1-S266.
3. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl*. 2013;3:1-150.
4. Inker LA, Astor BC, Fox CH, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. *Am J Kidney Dis*. 2014;63(5):713-735.
5. US Renal Data System. *2019 USRDS Annual Data Report: epidemiology of kidney disease in the United States*. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2019.
6. Tummalapalli SL, Powe NR, Keyhani S. Trends in quality of care for patients with CKD in the United States. *Clin J Am Soc Nephrol*. 2019;14:1142-1150.
7. Szczech LA, Stewart RC, Su HL, et al. Primary care detection of chronic kidney disease in adults with type-2 diabetes: the ADD-CKD Study (awareness, detection and drug therapy in type 2 diabetes and chronic kidney disease). *PLoS One*. 2014;26:9(11):e110535.
8. Hallan SI, Rifkin DE, Potok OA, et al. Physicians' recognition and management of kidney disease: a randomized vignette study evaluating the impact of the KDIGO 2012 CKD classification system. *Kidney Med*. 2020;2(3):258-266.
9. Wei L, MacDonald TM, Jennings C, et al. Estimated GFR reporting is associated with decreased nonsteroidal anti-inflammatory drug prescribing and increased renal function. *Kidney Int*. 2013;84(1):174-178.
10. Kagoma YK, Weir MA, Iansavichus AV, et al. Impact of estimated GFR reporting on patients, clinicians, and health-care systems: a systematic review. *Am J Kidney Dis*. 2011;57(4):592e601.
11. Greer RC, Liu Y, Cavanaugh K, et al. Primary care physicians' perceived barriers to nephrology referral and co-management of patients with CKD: a qualitative study. *J Gen Intern Med*. 2019;34(7):1228-1235.
12. Vassalotti JA, Centor R, Turner BJ, et al. National Kidney Foundation Kidney Disease Outcomes Quality Initiative. Practical approach to detection and management of chronic kidney disease for the primary care clinician. *Am J Med*. 2016;129(2):153-162.e7.
13. Thavarajah S, Knicely DH, Choi MJ. CKD for primary care practitioners: can we cut to the chase without too many shortcuts? *Am J Kidney Dis*. 2016;67(6):826-829.
14. Kramer HJ, Townsend RR, Griffin K, et al. KDOQI US commentary on the 2017 ACC/AHA hypertension guideline. *Am J Kidney Dis*. 2019;73(4):424-458.
15. Miller WG, Jones DRG. Estimated glomerular filtration rate; laboratory implementation and current global status. *Adv Chronic Kidney Dis*. 2018;25(1):7-13.
16. Miller WG, Bachmann LM, Delanghe JR, et al. Optimal use of biomarkers for chronic kidney disease. *Clin Chem*. 2019;65(8):949-955.
17. American Society for Clinical Pathology. Choosing Wisely, an initiaitive of the ABIM Foundation. http://www.choosingwisely.org/clinician-lists/ascp-serum-creatinine-to-test-for-ckd/. Accessed February 11, 2020.
18. National Kidney Foundation. Kidney health evaluation measure for adults with diabetes. https://www.kidney.org/sites/default/files/nkf-kidney-health-evaluation-measure-worksheet.pdf. Accessed February 11, 2020.
19. American Diabetes Association. 9. Pharmacologic approaches to glycemic treatment: standards of medical care in diabetes-2020. *Diabetes Care*. 2020;43(suppl 1):S98-S110.
20. Kliger AS, Brosius FC. Diabetic Kidney Disease Task Force of the American Society of Nephrology. Preserving kidney function instead of replacing it. *Clin J Am Soc Nephrol*. 2020;15(1):129-131.
21. Vassalotti JA, DeVinney R, Lukasik S, et al. CKD quality improvement intervention with PCMH integration: health plan results. *Am J Manag Care*. 2019;25(11):e326-e333.