A Software Upgrade: CKD Testing in 2010

Software upgrades are routine for all of us. We take advantage of the creativity and knowledge of programmers and companies who identify new ways to enhance the delivery of work via our computers. We too in the kidney healthcare community are in the midst of a software upgrade. That upgrade is the new glomerular filtration rate (GFR) estimating equation developed by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI).[1] The CKD-EPI equation is the best available technology at present for serum creatinine–based chronic kidney disease (CKD) testing.[2]

With this upgrade, it is wise to reflect on our science regarding CKD prior to 2002. A sizeable emphasis of this effort was focused on mechanisms of progressive loss of kidney function and large-scale clinical trials examining the effect of kidney protective therapies. The Kidney Disease Outcomes Quality Initiative (KDOQI) CKD guideline[3] from the National Kidney Foundation (NKF) added much to this profile of CKD in a short period of time. The CKD guideline provided a common nomenclature related to CKD, something that had been lacking previously. It also provided a mode of communication regarding kidney function that could be uniformly applied across multiple care environments, particularly those where we as nephrologists were not present.

The cornerstone of the CKD guideline has been the definition and classification schema for CKD based on estimating equations that were derived from the Modification of Diet in Renal Disease (MDRD) Study.[4,5] The use of estimating equations to assess kidney function was not new. Indeed, a body of literature had evolved, in particular with regards to drug dosing, using the Cockcroft-Gault formula for creatinine clearance.[6] Other mathematical approaches to progressive changes in kidney function had been assessed too, such as the reciprocal of the serum creatinine[7] and the Nankivell estimating equation for kidney transplant function.[8]

The MDRD Study equation provided a more accurate standard for estimating kidney function compared with serum creatinine alone, the Cockcroft-Gault equation, or 24-hour urine collection for creatinine clearance. Yet, neither the original manuscript describing the MDRD Study equation nor the KDOQI CKD guideline workgroup held the MDRD Study equation up as a perfect standard. Indeed, the guideline itself does not endorse the MDRD Study equation as a single standard. In fact, the guideline laid out an objective to "evaluate the accuracy of prediction equations to estimate the level of GFR from serum creatinine."[3]

Constructive debate has evolved related to the accuracy of GFR estimating equations and their influence, be it overdiagnosis or underrecognition of CKD or appropriate or inappropriate intensification of treatment for CKD. The debate hinges on the fact that the CKD definition and classification schema and the MDRD Study equation have had a tremendous effect over the last 7 years. They have changed practice in a far shorter time frame than the average of 17 years that it usually takes to move something from research and development into regular practice.[9] For example, as of 2008, more than 80% of the highest-volume laboratories in the United States and more than 55% of all labs in the top quarter of high-volume clinical laboratories in the United States reported estimated GFR[10] and the general chemistry C-B survey from the College of American Pathologists indicated that estimated GFR reporting had increased from 20% of laboratories participating in the survey in 2005 to more than 80% of laboratories participating in the survey in 2009.[11]

Has the equation's pervasive availability facilitated or prompted additional research into CKD? Yes. The MDRD Study equation has become a staple of multiple clinical investigations[12-17] and prompted investigators to examine laboratory and testing variability.[18,19] This validation science is mandatory for improving the trustworthiness of our clinical data. The MDRD Study equation also has been used by investigators to determine prognostic implications of CKD,[20-25] the subject of a recent Controversies Conference

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0272-6386/09/5501-0004$36.00/0
doi:10.1053/j.ajkd.2009.11.005

sponsored by KDIGO (Kidney Disease: Improving Global Outcomes).[26] Finally, it has prompted the search for even greater accuracy in GFR estimation and CKD prognosis using different filtration markers, such as cystatin C.[27-32]

The science and observation that spawned the initial MDRD Study equation has yielded new projects including the recent results of CKD-EPI.[1] This large, multi-sample, multistudy approach led to the development of a more accurate serum creatinine–based GFR estimating equation that could be applied to multiple populations. The scientific rigor of the work represented a concerted effort to acknowledge many of the aforementioned concerns. It also remained focused on developing a cost-effective, straightforward clinical tool that could be used in multiple venues to more accurately detect CKD. The result was advancement in the science of estimating equations and a more precise and accurate estimating equation for clinical use.

The NKF has a stake in supporting the best available clinical science and its application to patient care as a patient-centered organization. The NKF strives to promote implementation of best practices, evidenced by its continued support of evidence-based guidelines for kidney healthcare. The CKD-EPI equation represents a similar evidence-based advancement. It is today the best available and least expensive serum creatinine–based measurement of kidney function in clinical practice and for clinical research purposes.

As such, the NKF will work through its organizational channels to implement the CKD-EPI equation in several ways, including: (1) determining how to most readily add the CKD-EPI equation to the GFR calculator on the NKF website (http://www.kidney.org/professionals/kdoqi/gfr_calculator.cfm), with information that allows individuals to compare between the GFR estimates computed using the CKD-EPI and the MDRD Study equations; (2) incorporating the CKD-EPI equation in the Kidney Early Evaluation Program (KEEP) in the near future, after developing an appropriate communication plan; (3) strongly supporting assessment of the CKD-EPI equation in other venues, in dialogue with other organizations and agencies such as the National Kidney Disease Education Program (NKDEP) and Centers for Disease Control and Prevention (CDC); (4) asking the newly restructured KDOQI leadership to provide a thoughtful assessment of how CKD-EPI should be further implemented in practice as the best available estimating equation to date; and (5) requesting the KDOQI and KDIGO leadership to help guide NKF in how best to implement the CKD-EPI equation in future commentaries and guidelines.

All new software has some unexpected glitches and we can expect the very same from the CKD-EPI equation. NKF will do its job to work with organizations to approach transition to the CKD-EPI equation and indeed work in partnership with those organizations for a future with potentially even more accurate estimating equations. We do not have to shy away from this upgrade (CKD-EPI equation). Let's see how it works, knowing we will have to experiment (new research) with how to optimize it for our purposes.

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ACKNOWLEDGEMENTS

Dr Becker is President of the National Kidney Foundation and Dr Vassalotti is Chief Medical Officer of the National Kidney Foundation.

Financial Disclosure: None.

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