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Response to Previous Letter to the Editor

Estimated Glomerular Filtration rate (eGFR): A Serum Creatinine-based Test for the Detection of Chronic Kidney Disease and its Impact on Clinical Practice

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To the Editor,

We appreciate the interesting comment raised by Jain et al.[1] concerning the review on estimated Glomerular Filtration Rate (eGFR) and its implication on clinical practice.[2] They question the need for developing specific eGFR equations for each population including those in the Middle East that may be related to racial variation in body composition. The comparison of six equations by Jain et al.[1] should inspire future studies.[3,4] However, the issue, though valid, is subject to practical pitfalls when utilising its application.

All publications implementing the MDRD and CKD.EPI equations do not include correction factors for weight or race, and preserving a factor of 1.212 only to African Americans when using MDRD and none when using CKD.EPI. The increase of multi cultural communities does not ease deriving and validating different equations for the different populations. For our community in the Middle East, only serum creatinine, age and sex are currently utilised for calculating the eGFR by the aforementioned equations, and the non-requirement for including weight or height has contributed in the widespread acceptance of these equations by both pathologists and clinicians. In our practice, using serum-creatinine based eGFR reporting has eased and improved the awareness of the clinicians towards the interpretation of renal function test in screening and management of different diseases. While few requestors are aware about the reference ranges for serum creatinine, however almost all are familiar with the eGFR ranges in healthy subjects and in different stages of chronic kidney diseases (CKD).[5] Despite the concern about the increasing patients' referral to nephrologists based on eGFR diagnosis of CKD, the overall concept is fulfilling the eGFR use as a screening test for early detection of renal impairment which is better than serum creatinine alone for this task.

From our own experience of using eGFR.MDRD reporting since 2006, I would like to add two comments. First, our preliminary feedback for the agreement between the GFR isotope-based method and eGFR.MDRD, particularly when screening donors for kidney transplants, seems to be satisfactory to use it in the renal function profile. A comparison study is underway for analysing this relationship. Second, there are two versions of MDRD equation. The equation described originally by Levey et al.[6] uses the constant factor 186 in the calculation (traditional MDRD186) as follows: eGFR (mL/min/1.73m^2) = 186 (S.Cr in µmol/l × 0.011312)$^{-1.154}$ × (age)$^{-0.203}$ × (0.742 if female) × (1.212 if African/American Black). This factor was then recommended by the same authors to be re-expressed using a constant of 175 for MDRD (revised MDRD175), for creatinine measurement standardized against Isotope Dilution-Mass Spectrometry (ID-MS) reference method.[7] We continued using the traditional MDRD186 based on our feedback from using the different approaches for GFR measurement, the interpretive data from daily practice as well as, most importantly, the increasing publications pointing to the revised MDRD175 in underestimating the GFR and over-diagnosing CKD, especially stage 2. For such limitation, the CKD.EPI was derived and recommended by Levey et al.[8] to overcome this underestimation in eGFR. From 2009, many authors pointed to the underestimation of eGFR when using MDRD175 particularly when started to compare it with the new CKD.EPI.[2] Carter et al.[9] in a large cohort study in UK, reported a median GFR.CKD-EPI that was significantly higher than median GFR.MDRD175 (82 *vs.* 76 mL/min/1.73m^2, p<0.0001) with an overall mean bias of 5.0%.

Since 2006, when we introduced eGFR reporting in Oman, we observed mathematically that MDRD175 provides eGFR values nearly 5% lower than MDRD186 (about 3-5 mL/min/1.73 m^2 for CKD stage 1-2, 1.5-3.0 mL/min/1.73 m^2 for CKD stage 2-3, and <1.5 mL/min/1.73 m^2 for CKD stage 4-5), and so using MDRD186 may minimize or overcome the underestimation of eGFR by MDRD175. Recently, we have compared the different eGFR equations in Omani diabetic population attending different Primary Care Centres in the Muscat region. We observed a very good agreement between CKD.EPI and MDRD186 with almost no differences in their abilities for classifying the different stages of CKD. Of the diabetics screened (n=607), 57%, 57.5% and 47.1% had eGFR >90 mL/min/1.73m^2 while 32.5%, 33.6% and 40.5% had eGFR 60-89 mL/min/1.73m^2 based on CKI.EPI, MDRD186 and MDRD175 respectively. The median eGFR in these diabetics was 93.7, 93.9 and 88.3 mL/min/1.73m^2 using CKD.EPI, MDRD186, and MDRD175, respectively. The median eGFR was lower when using MDRD175 with many subjects in normal or stage 1 CKD based on CKD.EPI or MDRD186 were mis-classified as CKD stage 2 based on MDRD175 (unpublished data).[10] Therefore, our recommendation is towards using MDRD186 version (for MDRD equation) which appears to be more comparable and representative to CKD.EPI than MDRD175 regardless of the standardization issue.[5] Unfortunately, the majority of publications still favor MDRD175 when referring to the MDRD equation as a chain of citations that lack the strong clinical judgment. Chudleigh et al.[11] in their patients series with GFR (mean±SD) based on the gold standard method 51Cr-EDTA plasma clearance of 114.9±22.4 mL/min/1.73m^2 reported eGFRs of 94.7±22.0 using MDRD175

and 89.9±19.0 using MDRD186 (CKD.EPI equation was not available at that time). This study lacks the mathematical support by providing data that to our surprise were oppositely presented and interpreted (in tables and text) to conclude favorness of MDRD175 instead of MDRD186.[11] The numerical results cannot be explained mathematically as simply using the factor of 186 will always result in higher values than when using 175 in both MDRD equations which consist of similar numerical components!

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