Comparison of 2 Methods for the Calculation of Estimated Glomerular Filtration Rate

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DOI: 10.1309/42G9KLF13R78VNWK

Abstract

Background: Due to limitations of reference methods, it is recommended to estimate glomerular filtration rate (GFR) by serum creatinine-based equations. The purpose of this study was to assess the correlation between the Modification of Diet in Renal Disease (MDRD) formula and the new "Mayo Clinic Quadratic" (MCQ) equation.

Methods: Cumulative results for serum creatinine were retrospectively analyzed in 8,388 outpatients.

Results: A significant correlation was observed between the MDRD and MCQ estimates; however, a greater disparity of values, and a less satisfactory correlation, was observed between the 2 equations in subjects with MDRD estimates of GFR >60 mL/min per 1.73 m^2. The prevalence of subjects with abnormal GFR values was also significantly different when calculated with either formula.

Conclusion: Our results support the hypothesis the new MCQ equation may be a step toward accurately estimating GFR when the diagnosis of chronic kidney disease is unknown.

Chronic kidney disease, a major public health problem whose prevalence is constantly increasing worldwide, is traditionally diagnosed and monitored by assessment of the glomerular filtration rate (GFR).[1,2] Traditionally, GFR cannot be measured by direct means, but it can be assessed by measuring the urinary clearance of exogenous filtration markers, such as inulin, iohexol, iothalamate, or creatinine clearance calculation.[1] Due to difficulty in use, expense, radiation exposure, and radionuclide regulatory requirements, the urinary clearance of exogenous filtration markers has limited use in the routine laboratory and is typically confined to the research setting.[1] Therefore, it is now recommended to estimate GFR by equations based on serum creatinine,[1-3] and the currently-recommended algorithm is that developed and validated from the Modification of Diet in Renal Disease (MDRD) Study.[1] However, since this formula systematically underestimates GFR, and may erroneously categorize some healthy persons as having kidney disease, a new "Mayo Clinic Quadratic" (MCQ) equation was developed.[4] Although this new equation aimed to represent a step toward a more accurate estimation of GFR when the diagnosis of chronic kidney disease is unknown, it was not developed in a general population sample and lacked adequate representation of elderly patients. The purpose of this study was to assess the correlation between MDRD and MCQ estimates of GFR in the general population.

Materials and Methods

Results of serum creatinine tests, which were performed on consecutive adult outpatients referred by general practitioners for routine blood testing over the past year, were retrieved from the database of our laboratory information system at the University Hospital of Verona. Venous blood from outpatients was routinely collected in the morning on fasting subjects. The study population was homogenous for either ethnic origin (Caucasian) and geographic residence (Northern Italy). Serum creatinine was measured on a Roche/Hitachi Modular System P (Roche Diagnostics GmbH, Mannheim, Germany) by creatinine Jaffé rate blanked and compensated assay. The GFR was estimated by the MDRD formula, as modified by Levey and colleagues for methods traceable to the serum creatinine reference system, and the MCQ equation, according to the following formulas:

MDRD Equation

$$GFR = 175 \times (\text{serum creatinine}^{-1.154}) \times (\text{age}^{-0.203}) \times 1.212 \text{ (if black)} \times 0.742 \text{ (if female)},$$

which does not require a body weight variable because it normalizes GFR for a standard body surface area of 1.73 m^2.[5,6]

MCQ Equation

$$GFR = \exp(1.911 + (5.249/\text{serum creatinine}) - (2.114/\text{serum creatinine}^2) - 0.00686 \times \text{age} - 0.205 \text{ (if female)});$$

if serum creatine is <71 µmol/L, it is replaced by 71 µmol/L.[4]

Measures of performance include percentage bias of MCQ versus MDRD estimates of GFR by Bland-Altman plots, linear regression analysis, and χ^2 tests. Statistical analyses were performed using the SPSS version 12.0 (SPSS, Chicago) and the level of statistical significance was set at $P<0.05$. Data is presented as geometric mean and 95% confidence interval (CI).

Results

Cumulative results for serum creatinine levels were retrieved for 8,388 outpatients over a 1-year period (M/F=5,546/2,842; age range: 21 to 79 years). The mean

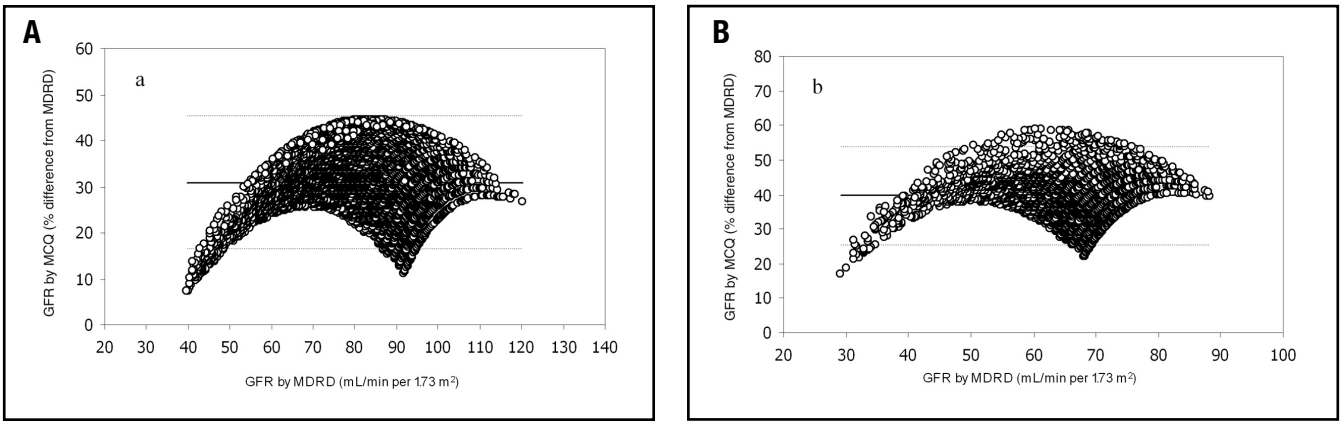

Figure 1_Linear regression analysis of Modification of Diet in Renal Disease (MDRD) and "Mayo Clinic Quadratic" (MCQ) estimates of glomerular filtration rate (GFR) in a general population of male (**A**) and female (**B**) outpatients.

values (95% CI) of creatinine, MDRD-estimated GFR, and MCQ-estimated GFR were 82 µmol/L (72 to 126 µmol/L), 73 mL/min per 1.73 m^2 (44 to 102 mL/min per 1.73 m^2) and 99 mL/min per 1.73 m^2 (56 to 137 mL/min per 1.73 m^2), respectively. A highly significant correlation was observed between the MDRD and MCQ estimates in the entire study population (females: y=1.39x+0.28, r = 0.945, *P*<0.001; males: y=1.35x-2.64, r=0.956, *P*<0.001) (**Figure 1**). However, a greater dispersion of values (**Figure 2**) and a less satisfactory correlation was observed between the 2 equations in subjects with MDRD estimates of GFR >60 mL/min per 1.73 m^2 (females: y=1.57x-12.2, r = 0.840, *P*<0.001 and males: y=1.25x-5.85, r = 0.922, *P*<0.001). The overall prevalence of subjects with values <60 mL/min per 1.73 m^2 was also significantly different when calculated by the MDRD and MCQ formulas in either gender (females: 31% versus 5%, *P*<0.001; males: 10% versus 3%, *P*<0.001).

Discussion

The determination of serum creatinine is the most widely used and commonly accepted measure of renal function in clinical medicine. Regardless of its widespread use, the accuracy of estimating GFR on the basis of the serum creatinine concentration only is limited, because it is affected by several factors, including body mass, gender, and age.[1] In an attempt to circumvent these limitations, a variety of formulas have been developed, which also take into account age, sex, and body size in their calculation. Among these formulas, the MDRD and MCQ equations are widespread, since they are supposed to compensate for the major drawbacks of serum creatinine determination and adequately correlate with GFR measured by the reference method.[1] Nevertheless, little information is available on the correlation of GFR as estimated by either formula to the best of our knowledge. The results of this epidemiological analysis attest that the application of the MDRD formula to the general population, including elderly patients, may substantially overestimate the prevalence of chronic kidney disease as compared with the new MCQ equation, regardless of reexpression of the MDRD Study equation according to the standardized serum creatinine assay.[6] Although the 2 equations may provide different information on renal function in the range of normal GFR values, which prevents their interchangeable use,

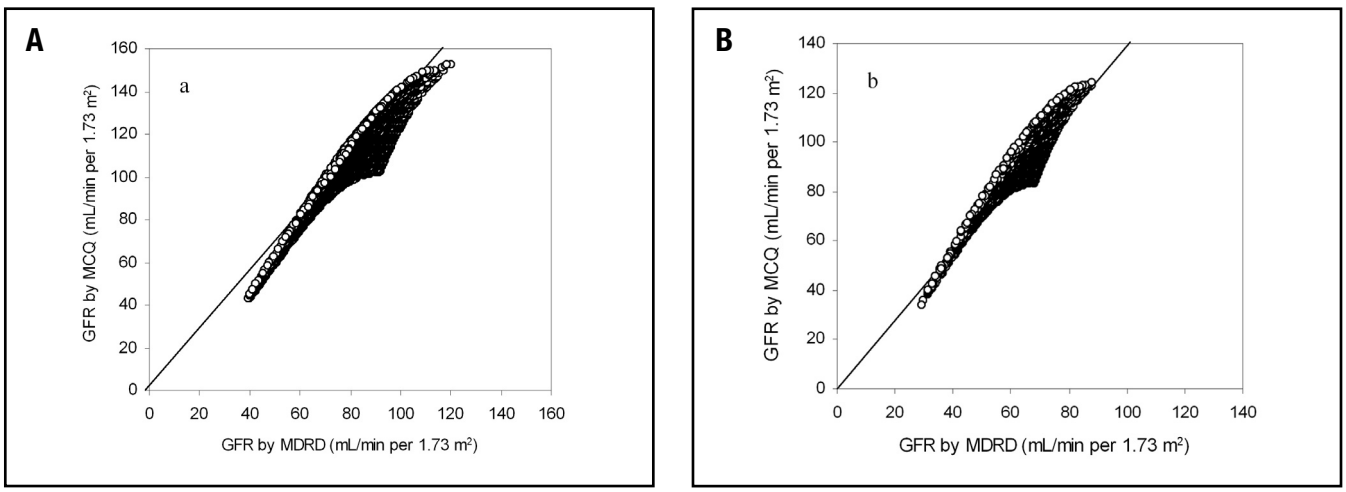

Figure 2_Bland-Altman plots of Modification of Diet in Renal Disease (MDRD) and "Mayo Clinic Quadratic" (MCQ) estimates of glomerular filtration rate (GFR) in a general population of male (**A**) and female (**B**) outpatients. The differences are expressed as a percentage bias. Solid lines are drawn at the mean difference and dashed lines are drawn at the mean difference ±1.96 times the standard deviation of the difference.

our results support the hypothesis that the new MCQ equation may be a step toward accurately estimating GFR when the diagnosis of chronic kidney disease is unknown.[4] We are aware this study has a major limit since we could not evaluate GFR by a reference method; however, the results provided by the MDRD equation are based on GFR values measured by iothalamate clearance and it has been validated in a large epidemiological study. Therefore, it performs similarly to the reference methods and it is currently recommended as a reliable surrogate.[1] LM

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