

# Is the New Mayo Clinic Quadratic Equation Useful for the Estimation of Glomerular Filtration Rate in Type 2 Diabetic Patients?

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**OBJECTIVE** — To test the Mayo Clinic Quadratic (MCQ) equation against isotopic glomerular filtration rate, compared with the Modification of Diet in Renal Disease (MDRD) and the Cockcroft-Gault formulas, in type 2 diabetes.

**RESEARCH DESIGN AND METHODS** — Based on values obtained with iothalamate, 118 type 2 diabetic patients were divided into three groups according to renal function: hyperfiltration (26), normal function (56), or chronic kidney disease (CKD) stages 3–4 (36). ANOVA, the Bland-Altman procedure, and Lins coefficient (Rc) were performed to study accuracy.

**RESULTS** — In the hyperfiltration and normal function groups, all prediction equations significantly underestimated the value obtained with isotopic glomerular filtration rate ( $P < 0.05$ ). In the CKD group, all equations also presented significant differences with the isotopic method. However, MDRD had a bias of  $-5.3$  (Rc 0.452), Cockcroft-Gault formula  $-0.2$  (Rc 0.471), and the MCQ  $-4.5$  (Rc 0.526).

**CONCLUSIONS** — The MCQ and prediction equations proved inaccurate (excessive underestimation) in type 2 diabetic patients with hyperfiltration or normal renal function. With regard to CKD, the results obtained provided no evidence of superiority of the MCQ over the MDRD or the Cockcroft-Gault formula.

*Diabetes Care* 31:2265–2267, 2008

According to current epidemiologic data, type 2 diabetes is considered one of the most frequent causes of end-stage chronic renal disease and inclusion in renal substitution programs (1,2). In a previous study, our group evaluated the accuracy of different prediction equations for the ambulatory follow-up of a cohort of type 2 diabetic patients (3). From the results obtained, it can be concluded that the application of these equations is inadequate in situations of normal renal function and hyperfiltration. Recently, the Mayo Clinic group has developed a new Mayo Clinic Quadratic (MCQ) equation based on

the results of both healthy subjects ( $n = 580$ ), who had an iothalamate clearance test specifically for kidney donor evaluation, and patients with chronic kidney disease (CKD) ( $n = 320$ ) (4). However, only 13% of 320 patients with CKD were diabetic, and the validity of the MCQ for patients outside the Mayo Clinic has been questioned (5).

The aim of the present study was to test the MCQ against isotopic glomerular filtration rate (GFR), compared with the recommended MDRD and Cockcroft-Gault formulas, in type 2 diabetic patients with a wide range of GFR (15–209 ml/min per  $1.73 \text{ m}^2$ )—particularly in

those with hyperfiltration or normal renal function.

## RESEARCH DESIGN AND METHODS

The study was conducted in 118 Caucasian type 2 diabetic patients (63 women; mean  $\pm$  SD age  $57.2 \pm 9.7$  years and A1C  $7.3 \pm 2\%$ ). According to the values obtained with isotopic GFR, patients were divided into three study subgroups: hyperfiltration (GFR  $>140$  ml/min per  $1.73 \text{ m}^2$ , 26 patients); normal renal function (GFR 90–140 ml/min per  $1.73 \text{ m}^2$ , 56 patients); and CKD stages 3–4 (GFR 15–59 ml/min per  $1.73 \text{ m}^2$ , 36 patients).

Isotopic GFR was measured by a single-shot clearance technique using an intravenous injection of 30–50  $\mu\text{Ci}$   $^{125}\text{I}$ -iothalamate corrected for body surface area of  $1.73 \text{ m}^2$  (6). In each study subgroup, the isotopic GFR was compared with those of the following prediction equations: MDRD (7), Cockcroft-Gault (8), and MCQ (4). The equation for MCQ calculation is as follows:

$$\begin{aligned} &\exp [1.911 + 5.249/\text{SCr} (\text{mg/dl}) \\ &\quad - 2.114/\text{SCr}^2 - 0.00686 \times \text{age} \\ &\quad - 0.205 \text{ if female}] \end{aligned}$$

where exp is exponent and SCr is serum creatinine. All serum creatinine measurements were performed in the same laboratory and determined by the Jaffé alkaline picrate method (normal range 0.6–1.5 mg/dl), calibrated using the SET-point Calibrator T13-1291 (Bayer, Barcelona, Spain).

## Statistical analysis

ANOVA was used to determine significant differences ( $P < 0.05$  with Bonferroni adjusted for three contrast tests). The Bland-Altman procedure (9,10) (Fig. 1) and Lins coefficient (Rc) (11) were used to study accuracy. SAS software (version 9.1; SAS Institute, Cary, NC) was used for statistical analysis.

**RESULTS** — Mean  $^{125}\text{I}$ -iothalamate GFR was  $96.3 \pm 50.9$  ml/min per  $1.73 \text{ m}^2$ . In the hyperfiltration group (aged

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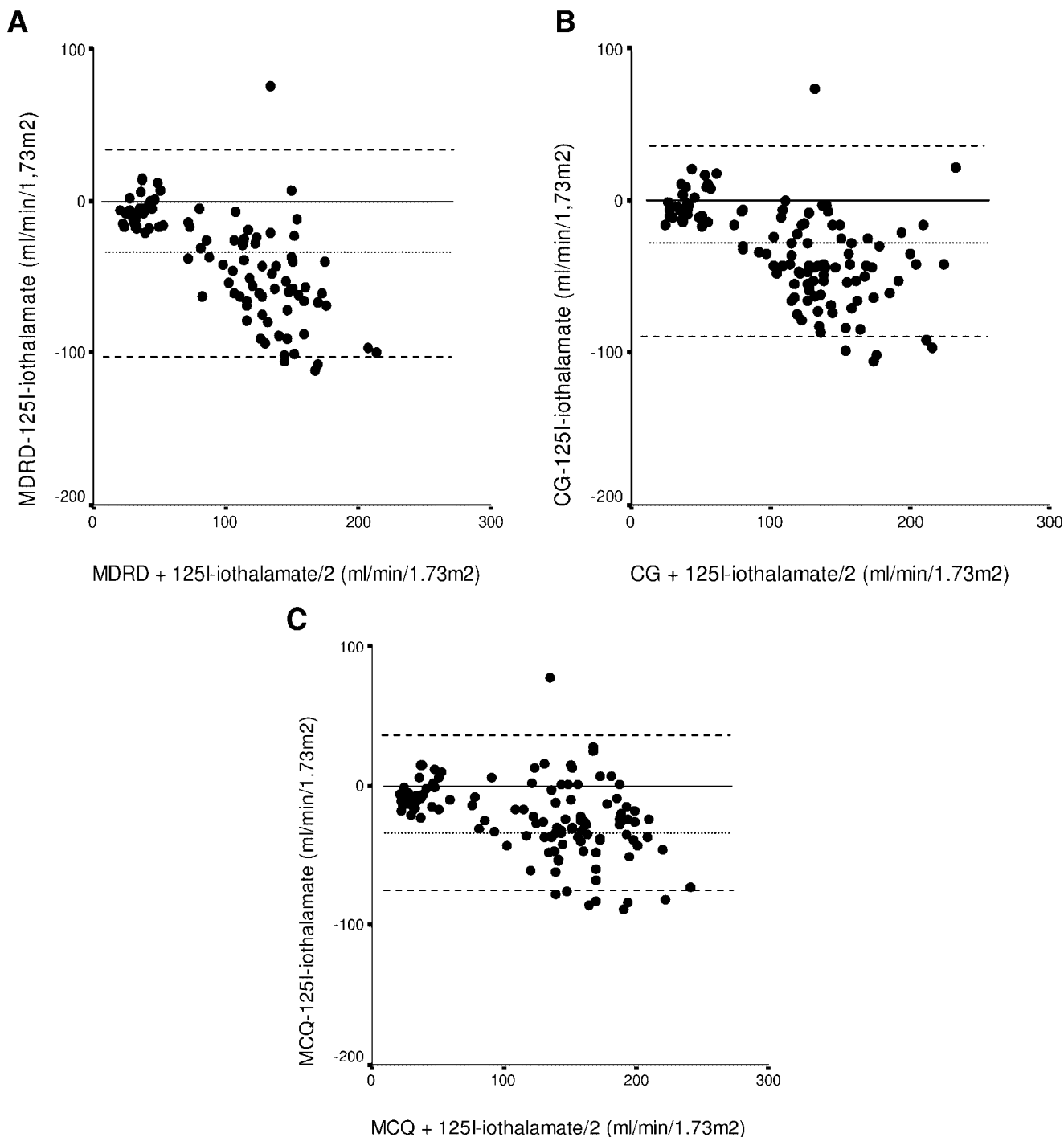
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Received 28 May 2008 and accepted 29 August 2008.

Published ahead of print at <http://care.diabetesjournals.org> on 3 October 2008. DOI: 10.2337/dc08-0958.

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**Fig. 1**

49.6 ± 8.5 years [range 31–62]; 13 women), mean isotopic GFR was 159.5 ± 18.8 ml/min per 1.73 m<sup>2</sup> and SCr 79.3 ± 21.7 μmol/l. In this group, the prediction equations that included MCQ were inaccurate compared with isotopic GFR and differed statistically and significantly (*P* < 0.05). Bias obtained with the MDRD was -83.1 ml/min per 1.73 m<sup>2</sup> (Rc 0.034), with the

Cockcroft-Gault formula -62.0 ml/min per 1.73 m<sup>2</sup> (Rc 0.015) and the MCQ equation -50.9 ml/min per 1.73 m<sup>2</sup> (Rc 0.045).

In the normal renal function group (56 ± 8.2 years [range 31–69]; 37 women), mean isotopic GFR was 115.6 ± 14.1 ml/min per 1.73 m<sup>2</sup> and SCr 88.7 ± 14.8 μmol/l. In this group, all prediction equations and MCQ were inaccurate

compared with the isotopic GFR and differed statistically and significantly (*P* < 0.05). Bias obtained with the MDRD was -46.5 ml/min per 1.73 m<sup>2</sup> (Rc 0.025), with the Cockcroft-Gault formula -41.4 ml/min per 1.73 m<sup>2</sup> (Rc 0.013) and the MCQ equation -23.2 ml/min per 1.73 m<sup>2</sup> (Rc 0.040).

In the CKD stages 3–4 group (64.1 ± 8.0 years [range 45–84]; 13

women), mean isotopic GFR was  $31.2 \pm 10.8$  ml/min per  $1.73 \text{ m}^2$  and SCr  $249.0 \pm 91.5 \mu\text{mol/l}$ . In this group, the prediction equations and MCQ also presented significant differences compared with isotopic GFR ( $P < 0.05$ ). However, bias obtained with the MDRD was  $-5.3$  ml/min per  $1.73 \text{ m}^2$  (Rc 0.452), with the Cockcroft-Gault formula  $-0.2$  ml/min per  $1.73 \text{ m}^2$  (Rc 0.471) and the MCQ equation  $-4.5$  ml/min per  $1.73 \text{ m}^2$  (Rc 0.526).

**CONCLUSIONS**— According to our results, the application of these equations is inadequate in situations of hyperfiltration and normal renal function. In the CKD stages 3–4 group, the results obtained presented no evidence of superiority of the MCQ equation over the MDRD equation and Cockcroft-Gault formula. The validity of GFR predictive equations must be verified in the diabetic population, as both equations (MDRD and Cockcroft-Gault) were developed from the results of nondiabetic subjects with CKD.

Despite yielding statistically significant differences, in hyperfiltration and normal renal function situations, MCQ presents a mean  $\pm$  SD closer to those of the isotopic method and lower bias and CIs in the estimation of renal function. In this respect, a recent study (12) concluded that the MDRD equation results in considerably higher rates of estimated GFR for CKD classes 2 and 3 compared with the MCQ equation, whereas MDRD and MCQ were comparable in CKD classes 4 and 5. In patients with normal Scr, the MDRD equation underestimated the iothalamate GFR; thus, its limitation in clinical practice may give rise to a misclassification of renal function stage. In contrast to Rigalleau et al. (13), we believe the MCQ equation offers no advantage over conventional prediction equations because it excessively underestimates GFR (high bias and low precision).

As in previous studies (14,3), we

showed the hyperfiltration situation, with a greater slope for GFR compared with normal filters, to be a marker of poor evolution and worse renal function deterioration in type 2 diabetic patients. In these situations that limit the use of prediction equations, new markers of renal function are required. In this respect, one recent study (15) recommended the use of serum cystatin C (100/cystatin C, expressed as milligrams per liter) to diagnose early renal function decline and develop interventions for protecting renal function while it is normal or even elevated.

In conclusion, our results showed the MCQ and conventional prediction equations to be inaccurate (excessive underestimation) in type 2 diabetic patients with hyperfiltration or normal renal function. In CKD stages 3–4, the results obtained presented no evidence of superiority of the MCQ equation over the MDRD equation or Cockcroft-Gault formula.

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