Is the new Mayo Clinic Quadratic (MCQ) equation useful for the estimation of glomerular filtration rate in type 2 diabetic patients?

Néstor Fontseré, MD, PhD, Jordi Bonal, MD, PhD, Isabel Salinas, MD, PhD, Manel Ramírez de Arellano, MD, Jose Rios, Ferran Torres, MD, PhD, Anna Sanmartí, MD, PhD, Ramón Romero, MD, PhD.

Corresponding author’s contact information:
Néstor Fontseré, MD, PhD.
E-mail: 34989nfb@comb.es


This is an uncopyedited electronic version of an article accepted for publication in Diabetes Care. The American Diabetes Association, publisher of Diabetes Care, is not responsible for any errors or omissions in this version of the manuscript or any version derived from it by third parties. The definitive publisher-authenticated version will be available in a future issue of Diabetes Care in print and online at http://care.diabetesjournals.org.
**Objective:** The aim of present study was to test the MCQ against isotopic GFR, compared with the MDRD and CG in DM2.

**Research design and Methods:** According to the values obtained with iothalamate, renal function of 118 DM2 patients was divided in hyperfiltration (26), normal (56) and CKD stages 3-4 (36). ANOVA, Bland-Altman and Lin’s coefficient (Re) to study accuracy.

**Results:** In hyperfiltration and normal function groups, all the prediction equations significantly underestimated the value obtained with isotopic GFR (P<0.05). In the CKD, all the equations also presented significant differences with the isotopic method. However, MDRD had a bias of -5.3 (Re 0.452), CG -0.2 (Re 0.471) and the MCQ -4.5 (Re 0.526).

**Conclusions:** The MCQ and prediction equations proved inaccurate (excessive underestimation) in DM2 patients with hyperfiltration or normal renal function. In CKD, the results obtained provided no evidence of superiority of the MCQ over the MDRD or CG.
According to current epidemiologic data, type 2 diabetes is considered to be one of the most frequent causes of end-stage chronic renal disease and inclusion in renal substitution programs (1,2). In previous study, our group evaluated the accuracy of different prediction equations for the ambulatory follow-up of a cohort of DM2 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 have 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 CKD (n = 320) (4). However, only 13% of their 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 GFR, compared with the recommended MDRD and Cockcroft-Gault (CG), in DM2 patients with a wide range of GFR (15-209 ml/min/1.73m²), particularly in hyperfiltration and normal renal function.

RESEARCH DESIGN AND METHODS

Study Population: The study was conducted in 118 Caucasian DM2 patients (63 women; 57.2 ± 9.7 years and HbA1c 7.3 ± 2%). According to the values obtained with isotopic GFR, patients were divided into three study subgroups: hyperfiltration [GFR > 140 ml/min/1.73m² (26 patients)]; normal renal function [GFR 140-90 ml/min/1.73m² (56 patients)] and CKD stages 3-4 [GFR 59-15 ml/min/1.73m² (36 patients)].

Study Design and Method: Isotopic GFR was measured by a single-shot clearance technique using an intravenous injection of 30-50 µCi 125I-iothalamate corrected for body surface area of 1.73m² (6).

In each study subgroup, the isotopic GFR was compared with those of the following prediction equations: MDRD (7), CG (8) and MCQ (4).

MCQ: \[ \text{exp} \left[ 1.911 + 5.249 / \text{SCr (mg/dl)} - 2.114 / \text{SCr}^2 - 0.00686 \times \text{age} - 0.205 \right \] if female.

All serum creatinine measurements were performed in the same laboratory and determined by the Jaffé alkaline picrate method (normal SCr range: 0.6-1.5 mg/dl), calibrated using the SET point calibrator T13-1291 Bayer Corporation® (Barcelona, Spain).

Statistical Analysis: ANOVA was used to determine significant differences (P<0.05 with Bonferroni adjusted for three contrast tests). The Bland-Altman method (9,10) [fig. 1] and Lin’s coefficient (Rc) (11) were used to study accuracy. The SAS v 9.1 software (SAS Institute Inc., Cary, N.C., USA) was used for statistical analysis.

RESULTS

Mean value 125I-iothalamate GFR was 96.3 ± 50.9 ml/min/1.73m². In the hyperfiltration group (aged 49.6 ± 8.5 yrs (31-62); 13 women) mean isotopic GFR was 159.5 ± 18.8 ml/min/1.73m² and mean SCr value 79.3 ± 21.7 µmol/l. In this group, the prediction equations 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/1.73m² (Rc 0.034), with CG -62.0 ml/min/1.73m² (Rc 0.015) and with MCQ equation -50.9 ml/min/1.73m² (Rc 0.045).

In normal renal function group (56 ± 8.2 yrs (31-69); 37 women) mean isotopic GFR was 115.6 ± 14.1 ml/min/1.73m² and mean SCr of 88.7 ± 14.8 µmol/l. In this group, all prediction equations and MCQ were inaccurate, compared with the isotopic GFR and differed statistically...
The MCQ equation in DM2 patients

and significantly (P<0.05). Bias obtained with the MDRD was -46.5 ml/min/1.73m² (Rc 0.025), CG -41.4 ml/min/1.73m² (Rc 0.013) and MCQ equation -23.2 ml/min/1.73m² (Rc 0.040).

In the CKD stages 3-4 group (64.1 ± 8.0 yrs (45-84); 13 women) mean isotopic GFR was 31.2 ± 10.8 ml/min/1.73m² and mean SCr of 249.0 ± 91.5 µmol/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/1.73m² (Rc 0.452), CG –0.2 ml/min/1.73m² (Rc 0.471) and MCQ equation –4.5 ml/min/1.73m² (Rc 0.526).

DISCUSSION

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 and CG formula.

The validity of GFR-predictive equations must be verified in the diabetic population, as both equations (MDRD and CG) were developed from the results of non-diabetic subjects with CKD.

Despite yielding statistically-significant differences, in hyperfiltration and normal renal function situations, MCQ presents a mean and standard deviation closer to those of the isotopic method and a lower bias and confidence intervals in the estimation of renal function. In this respect, recent results (12) concluded that the MDRD equations values in considerably higher rates of estimated GFR classes 2 and 3 compared to the MCQ equation, while MDRD and MCQ were comparable in classes 4 and 5. In patients with normal serum creatinine, 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 since 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. One recent study (15), recommended the use of serum cystatin C (100/Cys C) 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 or CG formula.
REFERENCES


Figure 1.

(a) MDRD + 125I-iothalamate/2 (ml/min/1.73m²)

(b) CG + 125I-iothalamate/2 (ml/min/1.73m²)

(c) MCQ + 125I-iothalamate/2 (ml/min/1.73m²)