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Comparison of estimated GFR and measured GFR in prospective living kidney donors

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Abstract
Purpose The aim of this study was to examine the usefulness of three GFR-estimating equations (eGFR) compared with measured GFR (mGFR) in potential living kidney donors.
Methods We compared the performance of the MDRD, CKD-Epi and Cockcroft–Gault equations with mGFR measured using ^{51}Cr-EDTA in 508 consecutive potential living kidney donors. Each equation was assessed for bias, precision and accuracy compared with mGFR, and the sensitivity and specificity for the identification of donors with mGFR < 80 mL/min/1.73 m^2 was evaluated.
Results Two hundred and forty-four subjects were male, 398 Caucasian, 60 Afro-Caribbean and 50 from other ethnic groups. Median age and mGFR were 44.1 year and 91.7 mL/min/1.73 m^2, respectively. Spearman correlation coefficients between eGFR and mGFR were in the range $R_s = 0.520$–0.593. Median bias (eGFR–mGFR) for the MDRD, CKD-Epi and Cockcroft–Gault equations were -1.0 ($p = 0.98$), $+8.8$ ($p < 0.0001$) and $+11.1$ ($p < 0.0001$) mL/min/1.73 m^2, respectively. Significant differences in bias between Afro-Caribbean and Caucasian subjects were found. The sensitivity (specificity) for the MDRD, CKD-Epi and Cockcroft–Gault equations for identifying subjects with mGFR < 80 mL/min/1.73 m^2 was 60 (83), 39 (95) and 44 % (95 %), respectively.
Conclusions The level of agreement between mGFR and all three eGFR values was poor, with the MDRD equation performing best. We conclude that reliance on creatinine-based eGFR values is unsatisfactory for the evaluation of potential living kidney donors.

Keywords Glomerular filtration rate · Kidney transplantation · Living donor · Estimated GFR · Measured GFR

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Introduction

Over the last 5–10 years, reliance on serum creatinine concentration (SCr) as an index of renal function has been superseded by the numerical manipulation of SCr to calculate an estimated glomerular filtration rate (eGFR) for the assessment of kidney function [1–4]. This has now become the main approach to screening for chronic kidney disease (CKD), and as a result, it is less common for physicians to request a measured GFR (mGFR) based on the evaluation of plasma clearance. While the introduction of eGFR is without doubt a significant advance, it is critically dependent on the formulaic manipulation of SCr and how applicable this may be to the population being studied [5].

In individuals with normal renal function, performance of the eGFR equations is frequently sub-optimal with low overall accuracy when results are compared with mGFR [6–13]. The two most widely used equations, the modification of diet in renal disease (MDRD) and the Cockcroft–Gault (CG), were both derived from populations with

reduced GFR [1–3]. Recently, a new equation was reported by the Chronic Kidney Disease Epidemiology Collaboration (CKD-Epi), which was developed in a large data set derived from several different populations, including renal patients as well as healthy individuals [4]. The CKD-Epi equation was developed to provide better precision and accuracy than other formulas in patients with normal GFR.

In potential living kidney donors, the accurate measurement of GFR and the prediction of the likely fall in GFR following donation of a kidney are of paramount importance for the safe selection of kidney donors. Current guideline statements from national and international bodies recommend that it is preferable not to accept kidneys from younger donors with GFR < 80 mL/min/1.73 m^2 [14–17]. However, with respect to which method should be employed to evaluate GFR, the guidelines are confusing and contradictory, in particular whether the use of eGFR or mGFR is best practice. All the guidelines call for more clinical evidence, both cross-sectional and long-term follow-up. This uncertainty reflects the present lack of evidence whether any of the currently available eGFR formulas that estimate GFR from SCr measurements is robust enough for safe clinical use.

The aim of this study was to examine the clinical utility and performance of the MDRD, CKD-Epi and CG equations in the setting of prospective living kidney donation, alongside mGFR measurements using ^{51}Cr-ethylenediaminetetraacetic acid (^{51}Cr-EDTA), a GFR tracer widely used in the UK [18] that gives plasma clearance measurements consistent with the renal clearance of inulin [19]. The findings will help inform best clinical practice.

Materials and methods

Measurements of mGFR in 508 consecutive potential living kidney donors were taken using ^{51}Cr-EDTA plasma clearance as previously described [20]. All subjects gave written informed consent for investigations that included SCr and mGFR. In 60 subjects with low or borderline mGFR for donation (56–90 mL/min/1.73 m^2), the ^{51}Cr-EDTA investigation was repeated and used to evaluate the precision error expressing the clinical repeatability of the mGFR measurements [21, 22]. The median difference between the dates of the repeat ^{51}Cr-EDTA investigations was 31 days (range 13–93 days).

The method of measuring SCr was the same throughout the study and is traceable to the NIST Isotope Dilution Mass Spectrometry (IDMS) standard. Our centre has participated in the UK National External Quality Assessment Service (UK NEQAS) for SCr since 2007. The UK NEQAS coefficient of variation (CV) for the laboratory analysis of SCr using the Roche enzymatic method is <3.5 %. The median difference between the dates of the mGFR and SCr measurements was 25 days (range 0–272 days) with 87 % of measurements within 90 days.

eGFR calculations

eGFR was calculated using the MDRD [3], CG [1] and CKD-Epi [4] equations using the following formulas with SCr in mg/dL and body weight in kg.

$$\text{MDRD} = 175 * (\text{SCr})^{-1.154} * (\text{Age})^{-0.203} * 0.742\,(\text{if female}) * 1.212\,(\text{if black})$$

$$\text{Cockcroft}-\text{Gault} = (140 - \text{Age}) * \text{body weight}/(72 * \text{SCr}) * 0.85\,(\text{if female})$$

eGFRs calculated using the CG equation were standardised to a BSA of 1.73 m^2 using the Haycock formula [23].

The CKD-Epi equation is gender- and race-specific and is stratified by SCr levels. For white and other races except black, the equations are as follows:

$$\begin{aligned}
&\text{Female with SCr} \le 0.7: \quad \text{eGFR} = 144 * (0.993)^{\text{Age}} * (\text{SCr}/0.7)^{-0.329}\\
&\text{Female with SCr} > 0.7: \quad \text{eGFR} = 144 * (0.993)^{\text{Age}} * (\text{SCr}/0.7)^{-1.209}\\
&\text{Male with SCr} \le 0.9: \quad \text{eGFR} = 141 * (0.993)^{\text{Age}} * (\text{SCr}/0.9)^{-0.411}\\
&\text{Male with SCr} > 0.9: \quad \text{eGFR} = 141 * (0.993)^{\text{Age}} * (\text{SCr}/0.9)^{-1.209}
\end{aligned}$$

For black subjects, the equations are the same except that for black females, the multiplying coefficient is 166 instead of 144, and for black males, the coefficient is 163 instead of 141.

For each equation, the precision error of the eGFR measurements expressing their clinical repeatability was assessed from replicate measurements of SCr in the same group of 60 subjects who had repeat ^{51}Cr-EDTA studies. The median difference between the dates of the repeat SCr measurements was 50 days (range 1–314 days).

Statistical analysis

Bias, precision and accuracy were measured to evaluate the performance of each equation following the methods recommended by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative [24]. GFR measurements using ^{51}Cr-EDTA were used as the reference method against which the eGFR findings were compared. As well as the entire group ($n = 508$), separate analyses were performed for the subgroups with mGFR < 80 mL/min/1.73 m^2 ($n = 84$) and mGFR ≥ 80 mL/min/1.73 m^2 ($n = 424$). Bias was expressed as the median difference after subtracting mGFR from eGFR. Precision was expressed as the interquartile range (IQR) of the differences. Accuracy was expressed as the percentage of estimates within 30 % (p_{30}) of mGFR, and also as the root

Table 1 Characteristics of the study population

No.	508
Age (years)	44.1 (18.5–84.1)
Age stratification (years)	
<30	72 (14.2 %)
30–39	111 (21.9 %)
40–49	179 (35.2 %)
50–59	96 (18.9 %)
60–69	40 (7.9 %)
70+	10 (2.0 %)
Race and gender	
Caucasian female	205 (40.4 %)
Caucasian male	193 (38.0 %)
Afro-Caribbean female	32 (6.3 %)
Afro-Caribbean male	28 (5.5 %)
Other female	27 (5.3 %)
Other male	23 (4.5 %)
Height (m)	1.70 (1.48–2.01)
Weight (kg)	76.4 (45.1–138.0)
Body surface area (m^2)	1.90 (1.39–2.81)
Body mass index (kg/m^2)	25.8 (16.8–39.9)
Systolic BP (mmHg)[a]	125 (81–191)
Diastolic BP (mmHg)[a]	74 (46–102)
Serum creatinine (μmol/L)	72 (38–139)
mGFR (mL/min/1.73 m^2)	91.7 (38.6–166.7)
eGFR	
MDRD (mL/min/1.73 m^2)	90.1 (46.9–172.0)
CKD-Epi (mL/min/1.73 m^2)	100.8 (50.6–151.6)
CG (mL/min/1.73 m^2)	102.9 (48.9–195.2)

Values for continuous variables expressed as median (range). Values for categorical variables expressed as number (percentage)

BP blood pressure, *CG* Cockcroft–Gault, *CKD-Epi* Chronic Kidney Disease Epidemiology Collaboration, *eGFR* estimated GFR; *GFR* glomerular filtration rate, *MDRD* Modification of Diet in Renal Disease, *mGFR* measured GFR

[a] BP data available for 180 subjects

mean standard error (RMSE). Confidence intervals (CIs) for the IQR and RMSE were calculated using the bootstrap method. CIs for bias and p_{30} were assessed using the binomial distribution. The Wilcoxon matched-pairs signed rank test was used to compare the bias of each of the GFR estimates against mGFR. The McNemar test was used to compare p_{30} values of the CKD-Epi and CG equations against the MDRD equation. Effects of gender and ethnicity were examined using the Mann–Whitney test. The eGFR equations were also assessed by their sensitivity, specificity, PPV and NPV for the identification of subjects with mGFR < 80 mL/min/1.73 m^2. Precision errors derived from repeated measurements were expressed as the coefficient of variation (CV). A p value <0.05 was considered statistically significant.

Results

Demographic data for 508 consecutive prospective living kidney donors who underwent assessment at Guy's and St Thomas' NHS Foundation Trust between January 2008 and September 2012 are listed in Table 1. Median age was 44.1 (range 18–84) years. Two hundred and forty-four subjects (48.0 %) were male, 398 subjects (78.3 %) were Caucasian, 60 (11.8 %) were Afro-Caribbean and 50 (9.8 %) were from other ethnic groups. Median mGFR measured using ^{51}Cr-EDTA plasma clearance was 91.7 (range 38.6–166.7) mL/min/1.73 m^2. After age adjustment using a fractional polynomial equation derived in potential living kidney donors [20], there was no significant difference in median mGFR between either men or women ($p = 0.93$) or between Caucasian and Afro-Caribbean subjects ($p = 0.96$). Precision errors derived from repeat measurements in a group of 60 subjects with low or borderline mGFR for donation were mGFR 9.7 %; MDRD eGFR 9.8 %; CKD-Epi eGFR 6.8 %; and CG eGFR 8.6 %.

The performance of the MDRD, CKD-Epi and CG equations compared with mGFR is summarised in Tables 2 and 3. Scatter and Bland–Altman plots [25] of the eGFR equations against mGFR are shown in Fig. 1. The Spearman correlation coefficients between eGFR and mGFR were in the range $R_s = 0.520$–0.593. In Fig. 1, the percentage of the variance in the three eGFR versus mGFR scatter plots explained by the precision errors ranged between 51 and 54 %.

Of the three equations, the MDRD formula had the least bias compared with mGFR with a median difference of −1.0 (95 % CI −2.3–0.8) mL/min/1.73 m^2 that was not statistically significantly different from zero (Fig. 2a; Table 2). In comparison, the median bias of the CKD-Epi equation [8.8 (95 % CI 6.9–10.0) mL/min/1.73 m^2] and CG equation [11.1 (95 % CI 9.2–13.0) mL/min/1.73 m^2] was both highly statistically significantly different from zero ($p < 0.0001$). The MDRD formula also showed the least bias for the subgroups with mGFR < 80 mL/min/1.73 m^2 and mGFR ≥ 80 mL/min/1.73 m^2 (Table 2).

When the effect of gender was examined, there was no statistically significant difference in bias (Δbias) between Caucasian men and women for the MDRD (Δbias = +1.1 mL/min/1.73 m^2, $p = 0.87$), CKD-Epi (Δbias = −1.8 mL/min/1.73 m^2, $p = 0.29$) or the CG (Δbias = −1.8 mL/min/1.73 m^2, $p = 0.31$) equations. Similarly, there were no statistically significant gender differences between Afro-Caribbean subjects.

When the effect of ethnicity was examined, highly statistically significant differences in bias were found between Afro-Caribbean and Caucasian men and Afro-Caribbean and Caucasian women for both the MDRD (Fig. 2b) and CKD-Epi equations (Men: MDRD equation: Δbias = +14.4 mL/min/1.73 m^2, $p = 0.010$;

Table 2 Performance of the MDRD study, CKD-Epi and CG equations compared with mGFR

	All subjects ($n = 508$)	mGFR < 80 ($n = 84$)	mGFR ≥ 80 ($n = 424$)	mGFR < 80 versus mGFR ≥ 80 p value
Bias: median difference, eGFR–mGFR (95 % CI)[a]				
MDRD study	−1.0 (−2.3–0.8); $p = 0.25$	5.4 (1.9–9.5); $p = 0.001$	−2.2 (−4.0 to –0.4); $p = 0.011$	<0.0001
CKD-Epi	8.8 (6.9–10.0); $p < 0.0001$	11.9 (9.5–15.0); $p < 0.0001$	7.3 (5.9–9.4); $p < 0.0001$	0.004
Cockcroft–Gault	11.1 (9.1–12.9); $p < 0.0001$	10.0 (5.3–14.3); $p < 0.0001$	11.2 (9.1–13.0); $p < 0.0001$	0.92
Precision: IQR of the difference (95 % CI) [range]				
MDRD study	19.5 (17.4–21.2) [119.1]	15.6 (13.2–21.2) [86.0]	18.6 (16.6–21.5) [119.1]	0.32
CKD-Epi	17.5 (16.2–18.9) [92.7]	18.4 (12.2–22.7) [70.3]	17.2 (15.6–19.3) [85.6]	0.72
Cockcroft–Gault	22.5 (19.8–24.2) [122.6]	19.0 (13.7–26.1) [102.9]	22.9 (20.2–24.9) [122.5]	0.31
Accuracy: p_{30} (95 % CI)[b]				
MDRD study	93 (90–95) %	90 (82–96) %	94 (91–96) %	0.30
CKD-Epi	89 (86–92) %; $p = 0.0015$	75 (64–84) %; $p = 0.0002$	92 (89–94) %; $p = 0.19$	<0.0002
Cockcroft–Gault	82 (78–85) %; $p < 0.0001$	74 (63–83) %; $p = 0.0026$	84 (80–87)%; $p < 0.0001$	0.030
Accuracy: RMSE (95 % CI)				
MDRD study	16.1 (15.1–17.1)	14.7 (12.5–16.9)	16.3 (15.2–17.4)	0.091
CKD-Epi	16.3 (15.3–17.3); $p = 0.39$	18.4 (15.7–21.2); $p = 0.019$	15.8 (14.8–16.9); $p = 0.25$	0.043
Cockcroft–Gault	21.2 (19.9–22.5); $p < 0.0001$	22.4 (19.0–25.8); $p < 0.0001$	20.9 (19.5–22.3); $p < 0.0001$	0.22

Units of eGFR and mGFR are millilitres per minute per 1.73 m^2

CI confidence interval, *CKD-Epi* Chronic Kidney Disease Epidemiology Collaboration, *eGFR* estimated GFR, *GFR* glomerular filtration rate, *IQR* interquartile range, *MDRD* Modification of Diet in Renal Disease, *mGFR* measured GFR, p_{30} percentage of estimates within 30 % of mGFR; *RMSE* root mean standard error

[a] Wilcoxon matched-pairs signed rank test was used to compare the bias of each of the GFR estimates against mGFR

[b] McNemar test was used to compare p_{30} values of the CKD-Epi and CG equation GFR estimates against the MDRD equation

Table 3 Sensitivity, specificity, positive predictive value and negative predictive value for each eGFR equation to identify potential living kidney donors with mGFR < 80 mL/min/1.73 m^2

eGFR equation	Sensitivity	Specificity	Positive predictive value	Negative predictive value
MDRD	50/84 (60 %)	353/424 (83 %)	50/121 (41 %)	353/387 (91 %)
CKD-Epi	33/84 (39 %)	404/424 (95 %)	33/53 (62 %)	404/455 (89 %)
CG	37/84 (44 %)	404/424 (95 %)	37/57 (65 %)	404/451 (90 %)

Numbers of subjects in numerator and denominator for the calculations of sensitivity, specificity, PPV and NPV (% in brackets)

CG Cockcroft–Gault, *CKD-Epi* Chronic Kidney Disease Epidemiology Collaboration, *eGFR* estimated GFR, *GFR* glomerular filtration rate, *MDRD* Modification of Diet in Renal Disease, *mGFR* measured GFR

CKD-Epi equation: Δbias = +15.1 mL/min/1.73 m^2, $p = 0.011$; Women: MDRD equation: Δbias = +16.5 mL/min/1.73 m^2, $p < 0.0001$; CKD-Epi equation: Δbias = +15.6 mL/min/1.73 m^2, $p < 0.0001$). In contrast, no significant ethnicity differences were found for the CG equation.

For the entire group and the subgroup with mGFR ≥ 80 mL/min/1.73 m^2, the CKD-Epi equation had the smallest interquartile range, although none of the differences from the MDRD equation were statistically significant. For all three groups, the MDRD equation had the best accuracy when expressed in terms of p_{30} (Table 2).

Table 3 lists the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of each eGFR equation to identify subjects with mGFR < 80 mL/min/1.73 m^2. Of 84 subjects with mGFR measurements below this threshold, the sensitivity figures show that 60 % had a MDRD, 39 % a CKD-Epi and 44 % a CG eGFR < 80 mL/min/1.73 m^2 consistent with the findings of the mGFR study. Of 424 subjects with mGFR ≥ 80 mL/min/1.73 m^2, the specificity figures show that 83 % had a MDRD, 95 % a CKD-Epi and 95 % a CG eGFR above threshold consistent with the mGFR findings.

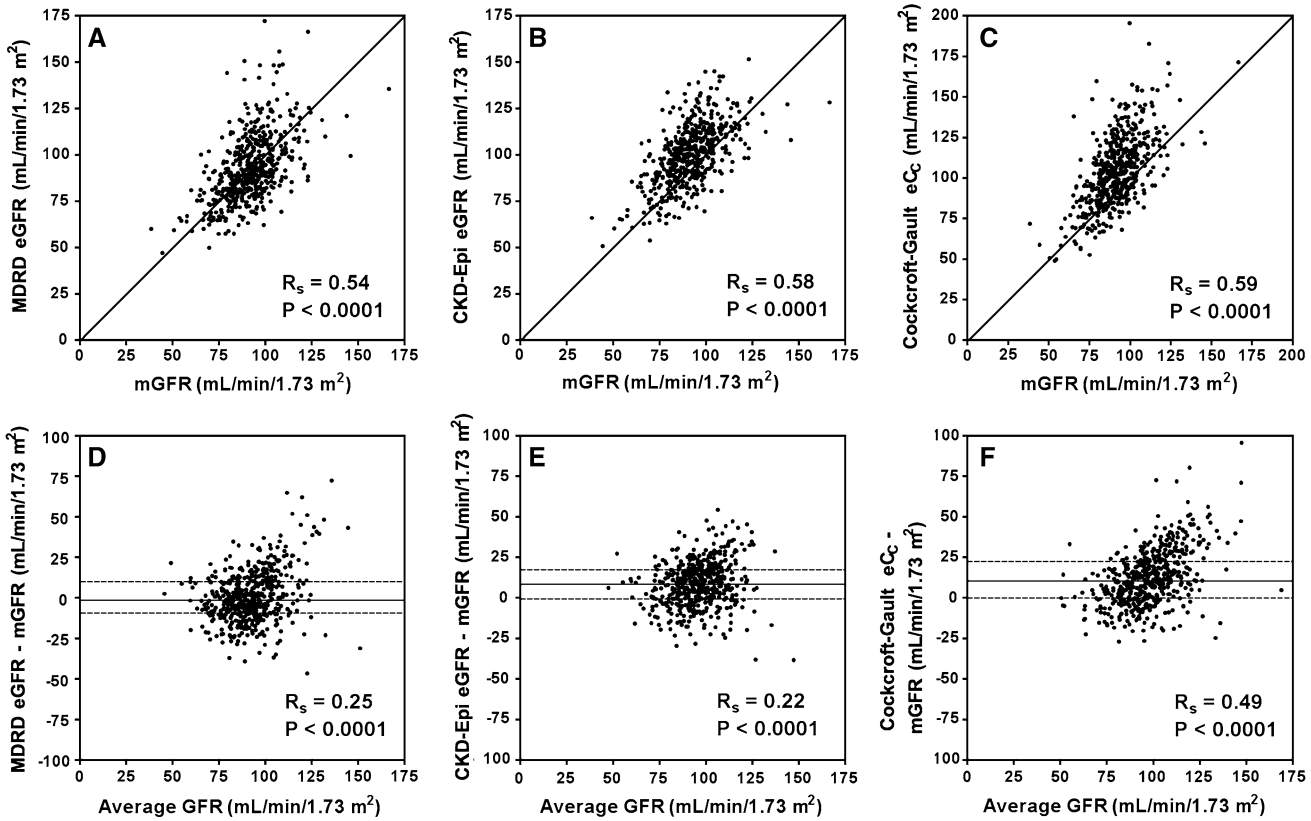

Fig. 1 Scatter plots of estimated eGFR calculated using **a** MDRD equation, **b** CKD-Epi serum creatinine-based equation, **c** CG equation plotted against mGFR determined using ^{51}Cr-EDTA. *Diagonal solid lines* are the lines of identity. All data are shown in millilitres per minute per 1.73 m^2. R_s values are the Spearman correlation coefficient and *p* values their statistical significance. **d–f** Bland–Altman plots [25] drawn for each of the above three scatter plots. *Horizontal lines* indicate median bias (*solid line*) and the 25th and 75th percentiles of the bias (*dashed lines*)

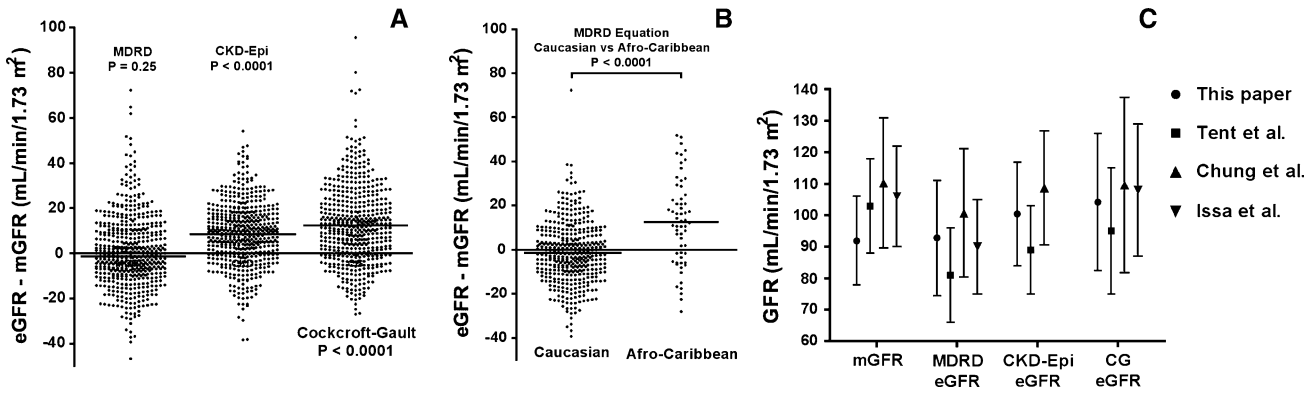

Fig. 2 **a** Bias plots (eGFR–mGFR) for the MDRD, CKD-Epi and CG equations for all 508 subjects in the study. *Horizontal bars* show the median bias for each eGFR equation. **b** Bias plots for the MDRD equation for Caucasian and Afro-Caribbean subjects plotted separately. **c** Comparisons of mGFR and eGFR derived from three equations MDRD equation, CKD-Epi equation, CG equation for the present study and three similar studies performed in potential living kidney donors [6–8]. *Data points* show the mean and SD

Discussion

This study reports on a large group of potential living kidney donors selected by current clinical and other criteria [15]. The use of ^{51}Cr-EDTA plasma clearance to measure GFR has been validated against inulin clearance [19], and our data are in close agreement with measurements at other UK transplant centres [20, 26]. Our ^{51}Cr-EDTA data also

performed well when assessed by the quality assurance index of extracellular fluid volume normalised to body surface area (BSA) proposed by Peters [26, 27]. Moreover, our mGFR precision error of 9.7 % is in good agreement with the previous findings [21, 22].

Examination of the scatter and bias plots showed substantial discordance between eGFR and mGFR results in individual donors as evidenced by the poor correlations and large residuals seen in some subjects. The precision errors expressing the repeatability of the mGFR and eGFR measurements accounted for 50 % of the variance in Fig. 1. However, even after allowing for these errors, a substantial degree of discordance remained, with the other 50 % of the variance likely to reflect the inherent differences between mGFR and eGFR measurements attributable to the effects of difference between subjects in muscle mass and dietary protein intake.

In this study that used ^{51}Cr-EDTA to measure mGFR, the MDRD equation had the least bias and best accuracy. This was also true when the subjects were divided into subgroups with mGFR < 80 mL/min/1.73 m^2 and mGFR $\geq$ 80 mL/min/1.73 m^2. In contrast, the CKD-Epi and CG equations both had substantial bias and poorer accuracy for all three groups. A comparison of the differences in bias between men and women showed no significant gender difference for any of the eGFR equations for either Caucasian or Afro-Caribbean subjects. In contrast, when the effect of ethnic origin was examined, Afro-Caribbean men and women were found to have biases around 15 mL/min/1.73 m^2 greater than their Caucasian counterparts when eGFR was calculated using the MDRD or CKD-Epi equations. Poggio et al. [9] reported a similar finding comparing MDRD eGFRs with mGFR measurements made using ^{125}I-iothalamate. Since there was no significant difference in age-corrected mGFR between the races, this large difference in bias suggests that the MDRD and CKD-Epi equations are inappropriate for the Afro-Caribbean subjects in our local population.

The poor concordance between eGFR and mGFR findings is confirmed by the sensitivity and specificity results. Among subjects with mGFR results below the threshold of 80 mL/min/1.73 m^2, 40 % had a MDRD, 61 % a CKD-Epi and 56 % a CG eGFR above threshold such that they would have been wrongly recommended for donation. Among subjects with an mGFR result above threshold, 17 % had a MDRD, 5 % a CKD-Epi and 5 % a CG eGFR below threshold such that they would have been wrongly rejected as suitable donors. In summary, the level of agreement between mGFR and all three eGFR equations was poor, with the MDRD equation faring least badly overall.

A number of previous studies have compared eGFR and mGFR findings in groups of potential living kidney donors [6–13]. Like the study reported here, they found scatter plots with poor correlations and significant levels of discordance in the identification of individuals with GFR below the safety threshold of 80 mL/min/1.73 m^2. For three of these studies, the mGFR methodology was judged consistent with the gold standard of inulin clearance, and the eGFR equations were identical to those studied here [6–8]. Figure 2c compares the findings of these three reports with those of the present study. The mean age of subjects in all four studies was in the range 40–49 years, so the effect of age difference on mean GFR is small and was neglected [20]. Mean mGFR was lowest for the ^{51}Cr-EDTA data reported here. The studies of Tent et al. and Issa et al. [6, 8] both evaluated mGFR using ^{125}I-iothalamate and found mean mGFRs 10 and 14 mL/min/1.73 m^2 higher than those reported here. The study of Chung et al. [7] used ^{99m}Tc-diethylenetriaminepentaacetic acid (^{99m}Tc-DTPA) and reported a mean mGFR 18 mL/min/1.73 m^2 higher than the present study. In contrast, the mean eGFR results from the present study were bracketed by those of the other three studies (Fig. 2c), while the Tent and Chung studies showed differences >20 mL/min/1.73 m^2 for the MDRD and CKD-Epi equations [6, 8].

From the results of the four studies shown in Fig. 2c, the achievement of better consistency between different centres in the measurement of both mGFR and eGFR is clearly an issue that requires greater attention. In the UK, an audit of GFR measurements undertaken in 2001 showed substantial differences between centres attributable to differences in methods of calculation [28]. Subsequently, the British Nuclear Medicine Society published guidelines on GFR measurements [18] and a recent study by Peters comparing results from 15 UK transplant centres showed greater consistency [26]. ^{51}Cr-EDTA is widely used as a GFR tracer in the UK and Europe, and ^{125}I-iothalamate in North America, and we were unable to find any studies that directly compared these two tracers. A systematic difference between them may explain our unexpected finding that the MDRD rather than the CKD-Epi equation showed the least bias.

Contemporary guidelines' statements on the measurement of native kidney function in prospective living donors undergoing donor evaluation are confusing and contradictory over whether the use of eGFR or mGFR is best practice [14–16]. It is evident that greater clarification is required with respect to the methods used to evaluate GFR. Any guideline for donor GFR must be based upon the premise that an individual in his or her lifetime will not develop clinically significant renal impairment as a result of unilateral nephrectomy. On this basis, the potential kidney donor must have sufficient kidney function prior to donation to have an adequate GFR at the age of 80 years, independent of the age at which he or she donated. We believe that our work shows the importance of accurate assessment of GFR based on ^{51}Cr-EDTA or a comparable

plasma clearance technique and that alternative methods based upon SCr concentration are not sufficiently accurate in this special clinical setting.

Our study has some limitations. There is low representation of those older than 60 years (around 10 %), and Afro-Caribbean and other ethnic minority races are under-represented. Also, we have not evaluated eGFR equations using cystatin C or the combination of plasma creatinine and cystatin C, which may be more reliable predictors of GFR. In 10 % of subjects, the dates of the SCr and mGFR investigations differed by more than 90 days. However, in this young and healthy population, there is no reason to think that significant changes in GFR occurred between the two measurements. Our study also has important strengths. It is based on a large homogeneous donor group of both genders with a wide age range and with good quality mGFR measurements.

In summary, our study shows the significant discordance that exists between mGFR and GFR estimates from SCr in potential living transplant donors. When GFR was measured using ^{51}Cr-EDTA, the MDRD equation showed the least bias and best accuracy. However, agreement was closest for Caucasian subjects, with Afro-Caribbean donors showing biases 15 mL/min/1.73 m^2 larger than Caucasian for both the MDRD and CKD-Epi equations. Although 50 % of the variance in the scatter plots between mGFR and eGFR was explained by precision errors, after allowance for these substantial discordance still remains between eGFR and mGFR measurements. Comparison of the results of this study with previous studies in potential living transplant donors shows clinically important differences in both the mean mGFR results and the mean eGFR results between different centres and suggests the need for greater attention to quality assurance for both types of measurement. In conclusion, we believe that our study shows that in the important clinical setting of living transplant donation reliance on mGFR over eGFR is best practice.

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