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LETTER

Prediction of mortality rate in type 2 diabetes: estimated glomerular filtration rate underestimates the true rate

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Abbreviations

eGFR	estimated glomerular filtration rate
iGFR	isotopic glomerular filtration rate
MDRD	Modification of Diet in Renal Disease

To the Editor: In their paper published in *Diabetologia* [1], Bruno et al. assessed whether a reduction in estimated glomerular filtration rate (eGFR), calculated using the abbreviated Modification of Diet in Renal Disease (MDRD) study equation [2], predicted mortality in type 2 diabetes. Although an eGFR of <60 ml min^{-1} 1.73 m^{-2} was associated with a twofold increase in the mortality rate, further analyses using smaller eGFR categories (15–29, 30–44, 45–59 ml min^{-1} 1.73 m^{-2}) revealed that this was due to the increased risk in patients with eGFR values between 15 and 29 ml min^{-1} 1.73 m^{-2}, with hazard ratios even suggesting a benefit for the non-proteinuric, moderate renal failure strata. To investigate whether this unexpected finding was due to the inaccuracy of the abbreviated MDRD equation in estimating GFR, we compared eGFR values with GFR values determined by ^{51}Cr-labelled EDTA clearance (isotopic GFR [iGFR]) in a group of volunteers, stratifying the results as per Bruno et al. [1].

In total, 128 patients with type 2 diabetes (age 67±9 years, BMI 28.8±4.8, HbA_{1c} 8.5±1.6% [data presented as means ± SD], 53 women) gave informed consent to participate in this study, which was conducted in accordance with the Declaration of Helsinki. In the group as a whole, iGFR was 54.5±32.7 ml min^{-1} 1.73 m^{-2}. Although the eGFR (48.2±18.8 ml min^{-1} 1.73 m^{-2}) showed a strong correlation with i-GFR (r=0.80, p<0.001), it underestimated it (p<0.001). The comparisons of eGFR and iGFR for each eGFR stratum as defined by Bruno et al. are shown in Table 1.

In the group as a whole, most of the subjects (55.5%) were wrongly classified by the MDRD-estimated GFR in the four GFR strata. This suggests that the majority of patients followed by Bruno et al. would have been classified in other strata if measured GFR rather than eGFR values had been used. In particular, many patients in the 45–60 and 60–89 ml min^{-1} 1.73 m^{-2} eGFR intervals, who had hazard ratios of <1.00 for all-cause and cardiovascular mortality in the paper [1], would have been in higher GFR strata. Although it is the best predictor of GFR in diabetic patients with renal insufficiency [3], the MDRD equation is well known to underestimate GFR values at the upper end of the normal range [4]. This explains the high proportion of patients with chronic kidney disease in the population

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Table 1 Comparison between eGFR (MDRD equation) and iGFR (^{51}Cr-labelled EDTA clearance) in 128 patients with type 2 diabetes, stratified according to eGFR

	eGFR (ml min^{-1} 1.73 m^{-2})			
	15–29	30–44	45–59	60–89
n	26	32	38	32
eGFR	23±4	38±5	51±4	74±8
iGFR	22±9	39±14	58±10	92±31
Correlation between iGFR and eGFR				
r value	0.42	0.55	0.05	0.41
p value	0.03	0.001	0.73	0.01
p value for the difference between iGFR and eGFR	p=0.39	p=0.86	p=0.055	p=0.001
Percentage of iGFR values in the correct eGFR stratum (%)	57	37	39	46

studied by Bruno et al. (34.3%), the majority of whom were women, a finding previously reported by other investigators [5]. The bias and inaccuracy of the MDRD equation probably explain the unexpected results obtained when it is applied to epidemiological studies. For example, O'Hare et al. reported a reduced mortality rate in non-diabetic patients with moderate reductions in GFR (50–59 ml min^{-1} 1.73 m^{-2}) after the age of 65 years [6]. Inverse relationships between renal function and cardiovascular risk factors have also been reported in the general population, depending on which equation is used to predict GFR [7]. As mentioned by Bruno, further studies with measured GFR rather than eGFR will be necessary to fully establish whether there is a link between a moderate reduction in renal function and the outcome of patients with diabetes.

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Duality of interest The authors declare that there is no duality of interest associated with this manuscript.

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