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Letter to the Editor

LETTER TO THE EDITOR

Estimating glomerular filtration rate with cystatin C: a systematic comparison of the new EKFC and the CKD-EPI equation

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To the Editor,

Serum cystatin C has been proposed as a superior biomarker of renal function compared with creatinine in chronic kidney disease (CKD), since its levels are less affected by patient characteristics such as muscle mass [1, 2]. Current KDIGO guidelines suggest using cystatin C measurements for confirmatory testing in specific circumstances where eGFR based on serum creatinine is less accurate [3].

Recently, the European Kidney Function Consortium (EKFC) published a new cystatin C–based equation for estimating glomerular filtration rate (eGFR) [4]. They demonstrated superior accuracy compared with the cystatin C–based Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) eGFR equation (CKD-EPI eGFRcys) [5, 6] in large cohorts from Europe, the USA and Africa.

To illustrate the numerical discrepancies between these two formulas and their impact on kidney function categorization, we have created a series of contour plots (Fig. 1). The methodology has been described in detail before [7, 8]. The formulas are shown in the Supplementary data. As in a topographical map, absolute (Fig. 1A) and relative differences (Fig. 1B) between the formulas are demonstrated by isolines within a coordinate system defined by age (x-axis; 18–92 years) and CKD-EPI eGFRcys values (y-axis; 1–105 mL/min/1.73 m^2).

CKD is classified according to eGFR thresholds of 15, 30, 45, 60 and 90 mL/min/1.73 m^2 into kidney function categories of G5, G4, G3b, G3a, G2 and G1, respectively [3]. Using the same coordinate system of age and CKD-EPI eGFRcys values as above, we can illustrate all areas where the numerical differences of the two formulas would lead to discordant eGFR categorization (Fig. 1C).

We wish to emphasize that our analyses are purely mathematical and do not assess the performance of the two formulas in predicting measured GFR. They also do not contain any epidemiological information. Instead, we are focusing on the implications for individual patients when using the EKFC eGFRcys equation instead of CKD-EPI eGFRcys.

For most patients with CKD-EPI eGFRcys values <60 mL/min/1.73 m^2, EKFC eGFRcys values are consistently higher (green areas in Fig. 1). The higher EKFC results are maximal for patients 40 years of age, but the absolute differences are <9 mL/min/1.73 m^2 for females and lie below 6 mL/min/1.73 m^2 for males. With CKD-EPI eGFRcys values >60 mL/min/1.73 m^2, older females and males as well as younger males show generally lower EKFC eGFRcys results than with CKD-EPI eGFRcys (red areas in Fig. 1). With CKD-EPI eGFRcys values >75 mL/min/1.73 m^2, EKFC eGFRcys results can be more than 10 mL/min/1.73 m^2 lower in older adults.

Areas where these differences lead to discordant classification of chronic kidney disease categories are shown in Fig. 1C. For CKD stages 3, 4 and 5, using the EKFC eGFRcys equation instead of CKD-EPI eGFRcys will downgrade some patients to a less severe CKD category (green areas in Fig. 1C). For young males and older adults of both sexes, some patients with CKD-EPI eGFRcys >90 mL/min/1.73 m^2 will end up in CKD stage 2 when using EKFC eGFRcys (red areas in Fig. 1C). Since the number of older adults with such high CKD-EPI eGFRcys results is very small, i.e. <5% of individuals older than 80 years in the USA [9], using the EKFC eGRcys equation instead of CKD-EPI eGFRcys will generally result in identical or less severe kidney function categorization.

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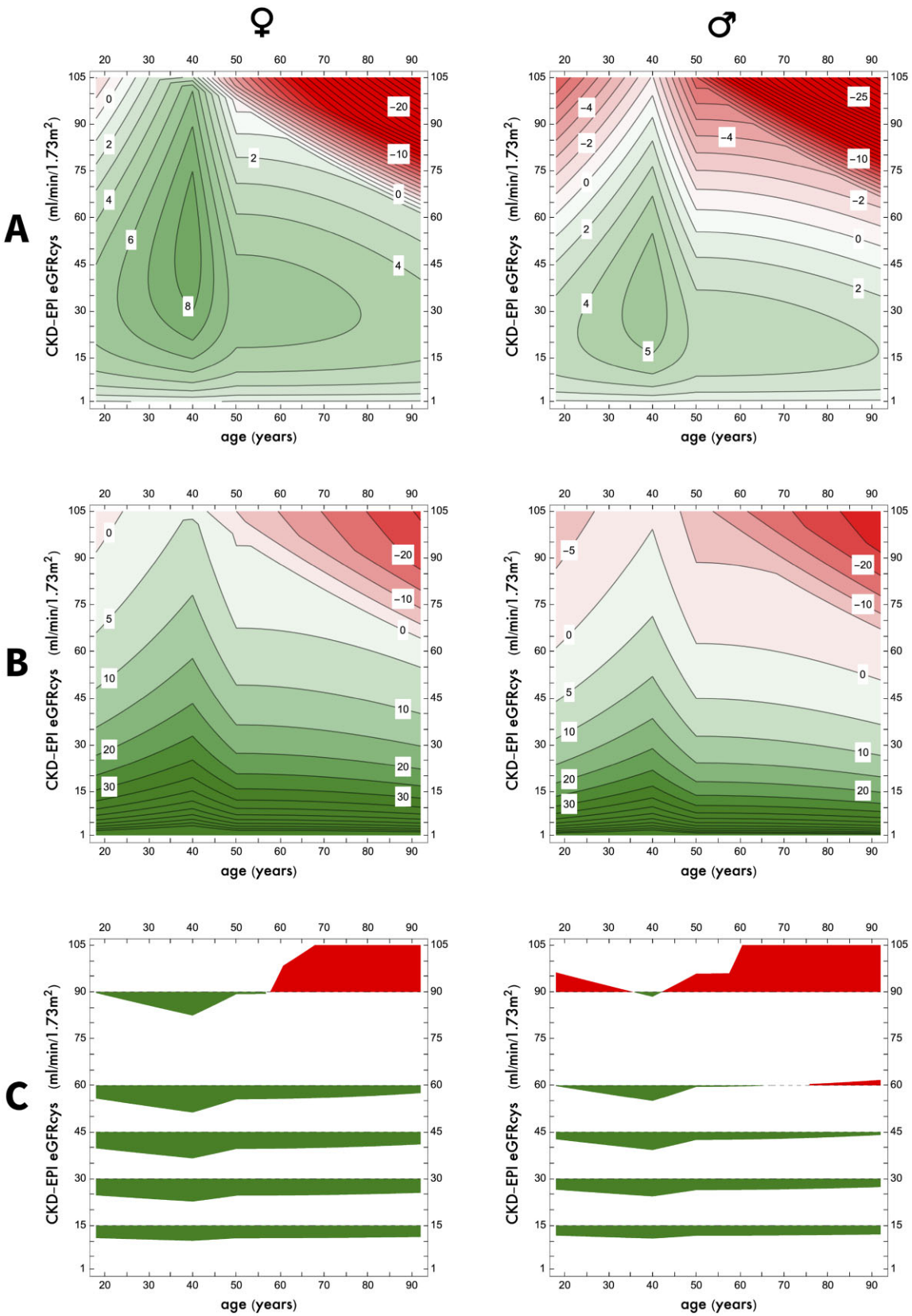

Figure 1: Differences between the EKFC and CKD-EPI cystatin C–based eGFR equations as a function of age (x-axis, 18–92 years) and CKD-EPI eGFRcys values (y-axis, 1–105 mL/min/1.73 m^2) for females and males. (**A**) Contour plot of absolute differences (EKFC minus CKD-EPI). Contours are drawn for every 1 mL/min/1.73 m^2 difference. (**B**) Contour plot of relative differences in % of CKD-EPI eGFRcys [100*(EKFC minus CKD-EPI)/CKD-EPI]. Contours are drawn for every 5% difference. (**C**) Region plots showing discordant CKD stages between the two equations. Areas where the CKD stage according to EKFC eGFRcys was higher than that according to CKD-EPI eGFRcys (i.e. eGFR was worse) are shaded red, and areas where the CKD stage was lower (i.e. eGFR was better) are shaded green. In the white areas, CKD stages are the same with both equations.

SUPPLEMENTARY DATA

Supplementary data are available at *ckj* online.

CONFLICT OF INTEREST STATEMENT

None declared.

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