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Original Article

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Assessment of Kidney Function in Living Kidney Donors: Single-center Experience from A Developing Country

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ABSTRACT

Background: In Bosnia and Herzegovina, the most common type of kidney transplant is from living donors. No national guidelines exist for assessing living donors, nor clear consensus among relevant guidelines on the best kidney donor function evaluation method.
Methods: We performed a retrospective-observational study in 170 potential donors between 1999 and 2020. We used the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) and Modification of Diet in Renal Disease (MDRD) formulas to estimate glomerular filtration rate (eGFR), a web-based calculator for predicting GFR below 80 mL/min/1.73 m^2, and creatinine clearance (CrCl) as well as measured GFR (mGFR) through diethylenetriamine pentaacetic acid (DTPA) renogram.
Results: MDRD, CKD-EPI, and a web-based calculator had similar abilities to detect potential donors with GFR <80 mL/min/1.73 m^2, with CKD-EPI performing the best but not statistically significant. MDRD and CKD-EPI formulas identified all potential donors with GFR<80 mL/min/1.73 m^2 at cutoff values of 98.5 mL/min/1.73 m^2 and 103.5 mL/min/1.73 m^2, respectively. The web-based calculator achieved a sensitivity of 100% in detecting donors with GFR<80 mL/min/1.73 m^2 at a cutoff point of >2.5% and a specificity of 24.20%. CrCl achieved a sensitivity of 100% at cutoff value <90.57 mL/min/1.73 m^2, identifying all the donors with GFR<80 mL/min/1.73 m^2 with the specificity of 62.14%, and provided the most significant reduction in the need for mGFR (56.6%).
Conclusion: eGFR-based screening done on 2 separate occasions or combined with CrCl is sufficient for most potential donors because the mGFR is likely between those values. mGFR with an exogenous marker is needed for borderline cases and selected groups.
Keywords: Kidney Transplantation, Glomerular Filtration Rate, Living Kidney Donation.

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INTRODUCTION

Kidney transplantation from a living donor (LKD) is considered the optimum treatment for most patients with established kidney failure as it offers superior outcomes[1] and also cost savings when compared to dialysis. In developing countries, the lack of resources required for a deceased-transplant program is another key driver for LKD. Evaluation of the kidney function of potential donors is of paramount importance for minimizing risks of donation, including the long-term risk of kidney failure in the donor which in a developing country constitutes an even more devastating outcome compared to elsewhere. Bosnia and Herzegovina is a good example of a developing country where LKD is available while the deceased-transplant program is not sufficiently developed.[2] The underlying causes include shortages of funding and infrastructure and also a lack of educational resources for the general public, which leads to erroneous beliefs around organ donation.[2]

The utility value of the glomerular filtration rate (GFR) in assessing overall kidney function in everyday clinical

practice is well established.[3] It can be estimated (estimated glomerular filtration rate- eGFR) through the use of several formulas or assessed from clearance and serum measurements of endogenous and exogenous markers (measured GFR- mGFR).[4,5] Even though in restricted resource circumstances, eGFR would be the most convenient option, this approach is not usually considered precise enough to base a decision for or against kidney donation on this test alone.[6-8] Both eGFR and mGFR may significantly differ from "true" GFR due to various reasons with proven systematic (bias) and random (imprecision) errors.[4-7,8] The Kidney Disease Improving Global Outcomes (KDIGO) guidelines currently recommend the mGFR as a confirmatory test. However, most of the current guidelines, including the KDIGO guidelines, are somewhat vague on which method should be used, resulting in a lack of uniformity between centers.[6-11] The availability of mGFR technology also varies hugely between countries[8] and access to this test is limited in many countries, including Bosnia and Herzegovina. Overall, no clear consensus exists on the threshold of GFR for donation, standard methods for mGFR, and accuracy of eGFR methods (Table 1).[10,11]

Recently, a web-based calculator (available from http://ckdepi.org/equations/donor-candidate-GFR-calculator/) has been developed for predicting the probability that GFR measurement value would be lower than determined thresholds.[6,12] It was based on probabilities calculated from large non-donor cohorts, but its clinical usefulness was also confirmed in a cohort of potential living kidney donors.[6,12] This tool, even though recommended by the KDIGO guidelines and occasionally mentioned in recent relevant literature, did not so far gain widespread use nor was retested in other populations and settings. This is despite the fact that it is inexpensive and simple to use and may therefore have great utility especially in resource-poor countries, by avoiding costly and time-consuming procedures and identifying the potential donors who are likely to benefit from mGFR tests.[6,12]

MAIN POINTS

- mGFR might be safely avoided in apparently healthy donors and with negative family history unless CKD-EPI <104 OR web-based posttest 90 probability > 2/2,5%, calculated on 2 separate occasions.
- Since most guidelines recommend the use of criteria calibrated for age, mGFR would not also be required if age adjusted eGFR in reference range (2 SD below mean for age.
- eGFR-based screening will be sufficient for most donors calculated on 2 separate occasions or combined with CrCl because the mGFR will likely be between those values.
- If eGFR and CrCl diverge, try to detect the reason and repeat the supposed incorrect method.
- For borderline cases with too low eGFR and acceptable CrCl, additional mGFR testing would be helpful.
- mGFR could be required for a selected group- young donors, especially blood-related, relatively young females planning pregnancy, and whenever separate GFR is needed.

Shortage of funding, trained personnel and technical infrastructure often renders mGFR unavailable in many low- and most middle-income countries, including Bosnia and Herzegovina. The only mGFR technology that is available in our own center is Tc-99m diethylenetriamine pentaacetic acid (DTPA) renogram, which is not the preferred method of mGFR according to current guidelines and therefore rarely used in recent publications around assessment of donors in LKD. The absence of national LKD guidelines in our country compounds this problem further. This situation prompted us to test all available methods of eGFR and compare them with locally available methods of mGFR and the aforementioned web-based tool to find the most convenient but safe way of evaluating potential living kidney donors at sight and similar settings.

MATERIAL AND METHODS

Patients

We carried out an observational, retrospective cohort study of potential adult living kidney donors evaluated at the Department for Nephrology, Dialysis, and Transplantation between September 1999 and October 2020. All potential donors evaluated (223) were considered for inclusion. We excluded only those potential kidney donors who did not consent and were missing mGFR data (n=53). All evaluated potential kidney donors (170) gave written consent, and University Clinical Center Tuzla Ethics Committee approved our study (approval number 02-09/2-32/23; date: May 10, 2023).

Estimation and measurement of GFR

GFR was measured by Tc-99m diethylenetriamine pentaacetic acid (DTPA) kidney dynamic imaging (Gates' method). Before the procedure, potential kidney donors were adequately hydrated and intravenously injected with f millicurie of 99mTc DTPA bolus. Images were acquired from the posterior aspect with a General Electric Dual Head SPECT Gamma Camera. Patients' age, height, and weight data were entered into XELERIS Software, which provided an automatic calculation of GFR that was subsequently adjusted for body surface area calculated using DuBois Formula.[13] CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) and MDRD (Modification of Diet in Renal Disease) formulas were used for the estimation of GFR before potential kidney donation.[14,15] Concentrations of serum creatinine were determined by the Jaffe method on Advia, Beckman Colter, and Siemens Dimension hematology analyzers at the central laboratory of our clinical center. CrCl values were also measured at the central laboratory of our clinical center using serum and urine creatinine concentration values and 24-hour urine volume (collected at our department), and they were adjusted for body surface area.

Web-based Application for Prediction of mGFR <80 mL/min/1.73 m^2

We used a web-based application developed by Huang et al and tested by Gaillard et al for the determination of the probability

Table 1. Relevant Guidelines on Living Kidney Donor Function Assessment

Guideline	GFR Assessment	GFR-Based Criteria
British Transplantation Society (2018)	mGFR in everyone after initial screening using eGFR	Provides age and sex-specific GFR criteria
KDIGO (2017)	eGFR, followed by confirmation with mGFR, CrCl, or eGFR	Donor candidates with GFR ≥90 ml/min per 1.73 m^2 should be considered acceptable, and those with GFR ≤60 ml/min per 1.73 m^2 should be excluded. The decision to approve donor candidates with GFR 60-89 mL/min per 1.73 m^2 should be individualized based on demographic and health profile about the transplant program's acceptable risk threshold.
OPTN (2021)	mGFR or 24-hour CrCl	No specific recommendations were provided.
Canadian KPD Protocol (2015)	eGFR on 2 separate occasions, followed by 24-hour CrCl on 2 separate occasions, or mGFR	Provides age-specific criteria.
ERBP (2013)	eGFR; mGFR when more exact knowledge of GFR is needed or where there is doubt regarding the accuracy of eGFR	Recommends age-dependent GFR cutoffs, such that the GFR of the remaining kidney will be >37.5 mL/min per 1.73 m^2 when the donor reaches age 80.
CARI (2010)	eGFR, at least on 2 separate occasions, or CrCl; mGFR if there is doubt regarding the accuracy or eGFR or CrCl	Recommends against accepting kidneys from donors with GFR <80 mL/min per 1.73 m^2.
Amsterdam Forum (2005)	eGFR or CrCl; mGFR may be used in patients with borderline GFR determination	GFR <80 mL/min/1.73 m^2 or body-surface area-adjusted GFR <2 SD below normal based on age and sex generally preclude donation; Noted successful Tx from some, usually elderly living donors with GFR as low as 65-70 mL/min/1.73 m^2. Need for individualization in donors with GFR <80 mL/min/1.73 m^2.

Table adopted from Nettika Garg et al.[11]
mGFR, measured GFR; KDIGO, Kidney Disease: Improving Global Outcomes; CrCl, creatinine clearance; OPTN, Organ Procurement and Transplantation Network; KPD, kidney paired donation; ERBP, European Renal Best Practice; CARI, Caring for Australians and New Zealanders with Kidney Impairment; eGFR, estimated GFR; GFR, glomerular filtration rate.

that the mGFR is lower than 80 mL/min/1.73 m^2, a clinically relevant reference value to contraindicate donation since it is accepted as longstanding practice in our center.[6,12] For this purpose, we calculated the sensitivity and specificity of posttest 90 and posttest 80 (probability of mGFR lower than 90 and 80 mL/min/1.73 m^2, respectively). We also measured the sensitivity and specificity of MDRD and CKD-EPI formulas in detecting potential living kidney donors having mGFR lower than 80 mL/min/1.73 m^2. Cystatin C measurement was unavailable in our central laboratory and was not included in posttest probability calculations.

Statistical Analysis

We used Excel and IBM SPSS Statistics Version 23 (IBM SPSS Corp.; Armonk, NY, USA) for data processing, the area under the curve for measuring overall diagnostic accuracy, and the Bland Altman plot for analyzing the agreement of different methods. We also used binary logistic regression to predict the relationship between predictors and outcome variables.

RESULTS

We analyzed 170 participants who completed the survey, 68 (40%) male and 102 (60%) female participants. Their characteristics are summarized in Table 2.

Diagnostic Performance of the Web-Based Application in Detecting mGFR <80 mL/min/1.73 m^2

We measured the sensitivity and specificity of posttest probabilities calculated with a web-based application for detecting mGFR <80 mL/min/1.73 m^2; the results are shown in Table 3 and Figure 1. Posttest 90 achieved a sensitivity of 100% with a cutoff point of >2.5%. This means that posttest 90 would detect 100% of donors with GFR <80 mL/min/1.73 m^2 with specificity of 24.20%. By testing mGFR only in those potential donors who were flagged as positive and not testing the negative ones, a reduction of 22.35% in the number of GFR measurements could be achieved. Posttest 80 achieved a maximum sensitivity of 92.31% and could not positively detect all donors with GFR <80 mL/min/1.73 m^2.

Diagnostic Performance of MDRD and CKD-EPI in Detecting mGFR Lower Than 80 mL/min/1.73 m^2

We measured the sensitivity and specificity of eGFR for detecting mGFR <80 mL/min/1.73 m^2; the results are shown in Table 4 and Figure 2. MDRD with a cutoff of <98.5 mL/min/1.73 m^2 achieved a sensitivity of 100%, meaning that it could identify all the donors with mGFR lower than 80 mL/min/1.73 m^2 with a specificity of 26.11%. By testing MDRD only in those potential donors who are flagged as positive and not

Table 2. Study Population Characteristics

Characteristics	All	Male	Female
n (%)	170	68 (40.0%)	102 (60.0%)
Age, years mean (SD)	50.47 (10.45)	51.19 (10.97)	49.99 (10.11)
Body weight, kg, mean (SD)	77.05 (12.85)	82.35 (11.95)	73.52 (12.25)
Body height, cm, mean (SD)	168.12 (9.16)	176.59 (6.10)	162.47 (5.93)
mGFR mL/min/1.73 m^2, mean (SD)	105.96 (19.96)	101.12 (19.57)	109.18 (19.66)
MDRD mL/min/1.73 m^2, mean (SD)	87.36 (17,93)	87.32 (16.42)	87.39 (18.97)
CKD-EPI mL/min/1.73 m^2 Mdn (IQR)	94.0 (19)	92.5 (16)	95.0 (22)

CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; IQR, interquartile range; Mdn, median; MDRD, Modification of Diet in Renal Disease; mGFR, measured GFR; SD, standard deviation.

testing the negative ones, a reduction of 24.11% in the number of GFR measurements could be achieved. Using CKD-EPI with a cutoff of <103.5 mL/min/1.73 m^2 achieved a sensitivity of 100%, meaning that it could identify all the donors with mGFR lower than 80 mL/min/1.73 m^2 with a specificity of 27.39%. By testing mGFR only in those potential donors who are flagged as positive and not testing the negative ones, a reduction of 25.29 % in the number of GFR measurements could be achieved.

Diagnostic performance of CrCl in detecting mGFR lower than 80 mL/min/1.73 m^2

In a subgroup of potential donors who had CrCl measured (n=113), we analyzed the sensitivity and specificity of CrCl for detection of mGFR <80 mL/min/1.73 m^2, and the results are shown in Table 5 and Figure 3. Using CrCl with a cutoff of <90.57 mL/min/1.73 m^2 achieved a sensitivity of 100%, meaning

Table 3. Diagnostic Performance of Web-based Application in Detection of mGFR Lower than 80 mL/min/1.73 m^2

	Posttest Below 90	Posttest Below 80
AUC (95% CI)	0.754 (0.611-0.896)	0.695 (0.522-0.867)
Maximum sensitivity (95% CI)	100% (75.29-100)	92.31% (63.97-99.81)
Cutoff for 100% sensitivity	>2.5%	N/A
Specificity (95% CI)	24.20% (17.73-31.67)	25.48% (18.87-33.04)
Possible reduction of GFR measurements (%)	38 (22.35%)	N/A

AUC, area under curve; CI, confidence interval; GFR, glomerular filtration rate.

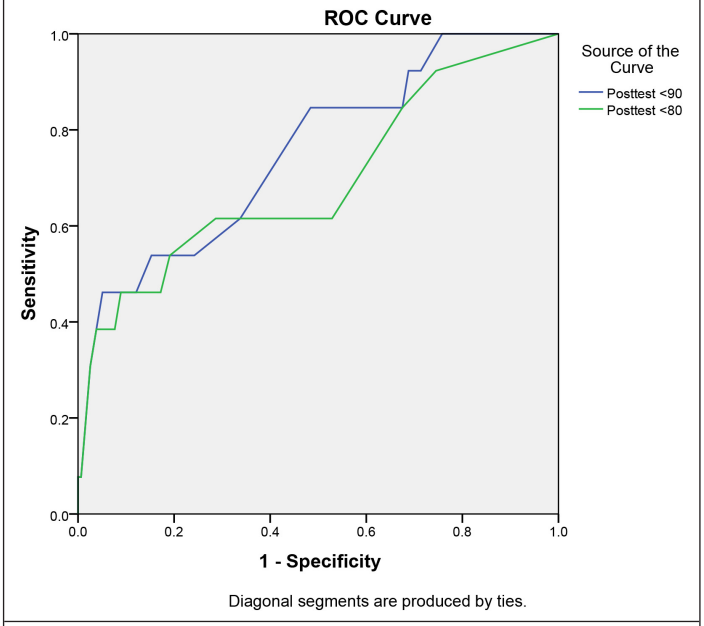

Figure 1. Posttest 80 and posttest 90 ROC curves for identifying potential donors with mGFR <80 mL/min/1.73 m^2.

it could identify all the donors with mGFR lower than 80 mL/min/1.73 m^2 with a specificity of 62.14%. By testing mGFR only in those potential donors who are flagged as positive and not testing the negative ones, a reduction of 56.6% in the number of GFR measurements could be achieved.

Reduction in mGFR Testing Between Web-Based Application, MDRD, and CKD-EPI

Potential reductions in mGFR testing in the group of 170 potential donors using a web-based application, MDRD, and CKD-EPI were n = 38 (22.35%), n = 41 (24.11%), and n = 43 (25.29%), respectively. Differences in testing reduction between web-based application, MDRD, and CKD-EPI were insignificant (P = .815). The difference in testing reduction

Table 4. Diagnostic Performance of MDRD and CKD-EPI in the Detection of mGFR Lower than 80 mL/min/1.73 m^2

	MDRD	CKD-EPI
AUC (95% CI)	0.766 (0.631-0.902)	0.767 (0.636-0.897)
Maximum sensitivity (95% CI)	100% (75.29-100)	100% (75.29-100)
Cutoff for 100% sensitivity	<98.5 ml/min/1.73m^2	<103.5 ml/min/1.73m^2
Specificity (95% CI)	26.11% (19.44-33.72)	27.39% (20.58-35.07)
Possible reduction of GFR measurements (%)	41 (24.11%)	43 (25.29%)

AUC, area under curve; CI, confidence interval; CKD-EPI, - Chronic Kidney Disease Epidemiology Collaboration; MDRD, Modification of Diet in Renal Disease.

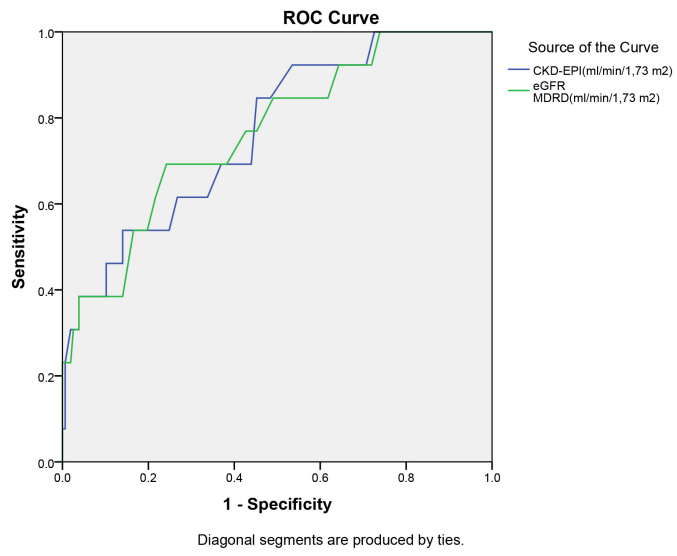

Figure 2. MDRD and CKD-EPI ROC curves for identifying potential donors with mGFR<80 mL/min/1.73 m^2. CKD-EPI- Chronic Kidney Disease Epidemiology Collaboration; MDRD- Modification of Diet in Renal Disease; eGFR- Estimated glomerular filtration rate.

between web-based application and CKD-EPI was insignificant (*P* = .89). In the subgroup of potential donors (n = 113) with measured CrCl, the measurement reduction was n = 64 (56.6%). Potential reduction in GFR measurements using CrCl as a screening method was significantly higher than all other methods (*P* < .001).

Agreement between mGFR and MDRD

Calculated eGFR MDRD showed a significant mean difference compared to mGFR (*P* < .001), systematically underestimating measured GFR with a constant mean bias of −18.59 mL/min/1.73 m^2 (95% CI −21.59 to −15.59). Linear regression analysis did not reveal significant proportional bias (*P* = .121) (Figure 4). Limits of agreement show wide intervals, which could not be considered clinically acceptable for evaluating kidney function.

Table 5. Diagnostic Performance of Creatinine Clearance in the Detection of mGFR Lower Than 80 mL/min/1.73 m^2

	Creatinine Clearance
AUC (95% CI)	0.768 (0.674-0.862)
Maximum sensitivity (95% CI)	100% (69.15-100)
Cutoff for 100% sensitivity	<90.57 mL/min/1.73 m^2
Specificity (95% CI)	62.14% (52.04-71.51)
Possible reduction of GFR measurements (%)	n = 64 (56.6%)

AUC, area under curve; CI, confidence interval.

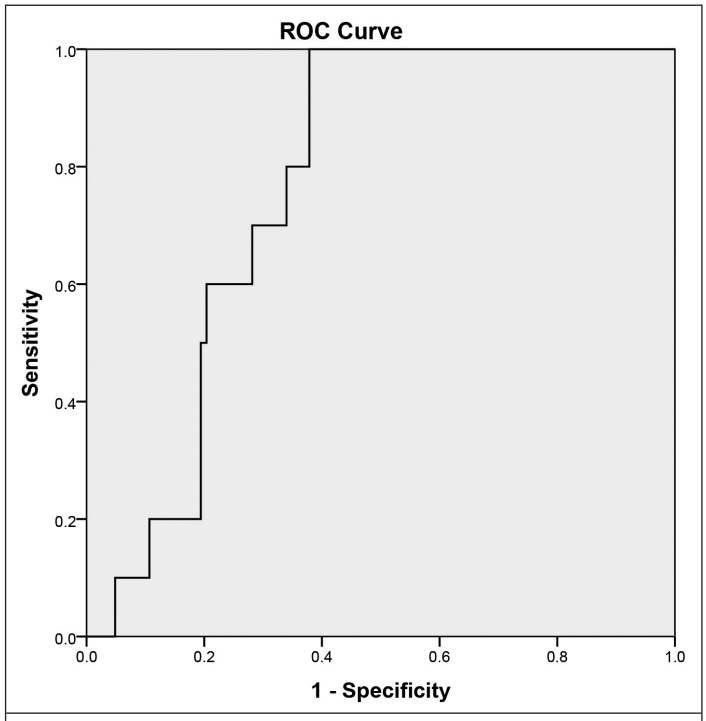

Figure 3. Creatinine clearance ROC for identifying potential donors with mGFR <80 mL/min/1.73 m^2.

Agreement between mGFR and CrCl

CrCl compared to mGFR showed a mean difference of -1,89 (95% CI -9.76 to 5.97) without significant systemic bias compared to mGFR (p=0.63). Linear regression analysis revealed significant proportional bias (p<0.001) (figure 5). Limits of agreement show

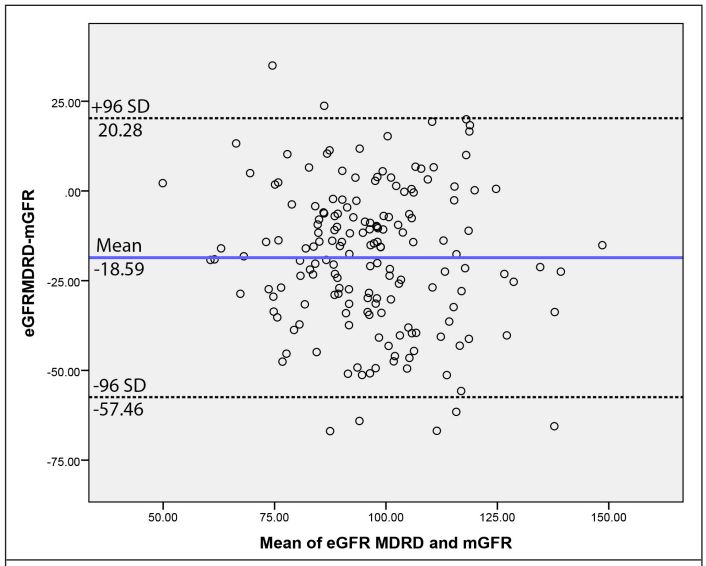

Figure 4. Bland–Altman plot showing agreement between eGFR MDRD and mGFR. The dotted lines represent the Lower and Upper limits of the agreement. eGFR, Estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease; mGFR, Measured glomerular filtration rate.

wide intervals, which could not be considered clinically acceptable for evaluating kidney function.

DISCUSSION

We have evaluated 3 strategies of estimating GFR: CKD-EPI and MDRD plus a web-based calculator for predicting mGFR, together with CrCl as one method of mGFR against other mGFR methods-DTPA renogram-the only available method of exogenous marker mGFR in our center and our country in general. According to our knowledge, the aforementioned web-based application was not retested since Gaillard et al first tested it in a cohort of living donors after Huang et al derived the tool from large cohorts.[6,12] We intended to find which of the 3 eGFR methods or CrCl provides the most significant reduction in the need for additional mGFR by DTPA renogram.

eGFR and Web-based Application and Their Combination

MDRD, CKD-EPI, and web-based calculator with posttest 90 strategy had similar abilities to detect potential living kidney donors with mGFR <80 mL/min/1.73 m^2 with CKD-EPI performing the best (but not statistically significant) among these methods of eGFR.

One of the intentions of the authors interested in this problem-solving was that with the use of multiple markers combined, we might compute the estimates, which may then approach the accuracy of mGFR. The fact that eGFR formulas show similar diagnostic performance to the posttest 90 strategy is probably because these 3 strategies are based on analysis of similar parameters: age, sex, ethnicity, and plasma creatinine, and although different in their nature and the method of calculation, they are all based on the kidney metabolism of creatinine and therefore not independent indicators/predictors of actual GFR.

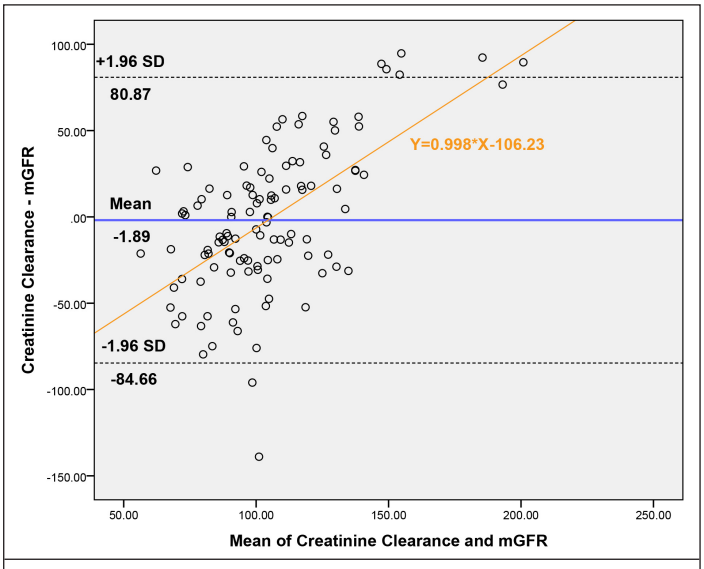

Figure 5. Bland Altman plot showing agreement between creatinine clearance and mGFR. The dotted lines represent the Lower and Upper limits of agreement. The orange line represents the proportional bias regression line. mGFR- Measured glomerular filtration rate.

Therefore, we would not recommend combining different eGFR formulas with web-based applications to increase the detection of GFR <80 mL/min/1.73 m^2, at least not on the same occasion, using 1 creatinine measurement. We recommend using these different strategies but inputting creatinine measured on at least 2 different occasions.

The specificity of both eGFR formulas and web-based calculators was low in our study and in the study of Gaillard et al, who also proved similar performance of both eGFR formulas and web-based applications.[6] So, these cannot be used without due caution of wrongly excluding potential adequate donors.[6,11] Results from our and the study mentioned above both show that if the calculated GFR values, including web-based tool, are high enough (threshold accepted by the given center), GFR measurement methods could be avoided,[6,11] especially if confirmed on 2 separate occasions with one or combination of those estimates, and no other medical concerns.

24-h Creatinine Clearance

In our study, CrCl performed the best, providing the most significant reduction in the need for additional mGFR by DTPA renogram in our cohort of potential donors. Traditionally, the accuracy of CrCl is thought to be hampered by possible errors in 24-hour urine collection; however, in our center, urine collection is performed in a hospital setting and with well-trained personnel, so the possibility of some technical error is minimal. Our results showed that 24-hour CrCl had the most significant diagnostic performance in the detection of mGFR lower than 80 mL/min/1.73 m^2 and the most significant reduction in the need for mGFR using an exogenous marker and with the highest and respectful specificity, compared to all available methods of estimating GFR here tested.

The real-world data show that 24-hour CrCl is one of the mainstays for evaluating kidney function in potential donors, even in some resource-rich countries, even though it is often questioned as a reliable tool for this purpose.[7,16,17] Major limitations of CrCl are susceptibility to technical errors due to inaccurate urine collections and overestimation of mGFR because of distal tubular creatinine secretion. The accuracy of 24-hour CrCl was recently tested in a study by Neetika et al, and it was concluded that using conventional equations for estimation of CrCl collection accuracy, 43% of collections would have been deemed inaccurate, mostly under-collected.[17] The authors recommend using the equations developed by Ix et al—CER4 formula as the preferred method for assessment of the accuracy of timed urine collections while assessing CrCl in potential donors, for it showed more reliability in their study.[18] Also, in the absence of the availability of a measured GFR, based on their results, the eGFR-CrCl average was the best surrogate in all populations except blacks.

Mandelbrot et al surveyed the United States living kidney transplant programs in 2007 and found that 90% used 24-hour CrCl.[16] Similar results showed a survey conducted in 28 transplant centers in Argentina—78.5% of them used 24-hour CrCl to assess kidney function in potential donors.[17] Ebert et al provided a review of large studies on assessing the kidney function in potential donors underlying the rising trend of measurement of GFR and poor reliability of eGFR, with a call for mGFR to become standard for estimating kidney function in potential donors. However, it is important to stress that the authors referred to the aforementioned USA survey in which, if analyzed—the most frequent measurement method was actually 24-hour CrCl.[16,17,19]

In a study conducted on multiple cohorts in transplant centers in the Netherlands, authors hypothesized that if the donor screening is based on mGFR, it would lead to a greater acceptance rate of donors who had lower eGFR before the donation, compared to screening based on eGFR.[20] Authors recommended 24-hour CrCl and/or eGFR as sufficient in the donor selection process for most potential donors since they did not find that mGFR elevated the acceptance rate of potential donors.[20] It is essential to say that the authors also did not find any difference in eGFR 5 years post-donation between centers with eGFR and mGFR-based screening pre-donation.[20] Authors speculated that introducing age-adapted thresholds of pre-donation eGFR introduced in their national living kidney donor guidelines in 2008 might have contributed to a more similar position of different centers towards uniformity in donor selection.[20]

In recent literature, growing attention has been paid to the importance of age-adapted GFR thresholds.[11,17,21] Using absolute single cutoff values for GFR without age adaptation could lead to the wrongful classification of potential living kidney donors.[11,17,21] For example, according to the KDIGO guidelines and recommended absolute cutoff values of ≤ 60 mL/min/1.73 m^2 and ≥90 mL/min/1.73 m^2 for rejection and acceptance of potential living kidney donors, there is a possibility that younger candidates could be inappropriately accepted and older candidates inappropriately rejected even though their GFR is suitable for their age.[11]

To additionally support the case of eGFR and web-based application as relatively reliable tools for assessing kidney function in potential donors, it is important to underline that in our study, the only available and the reference method of mGFR—DTPA renogram—has rather relevant drawbacks according to the recent literature. As a method of radionuclide measurement of GFR, DTPA renogram is generally considered less valuable and accurate than urinary and plasma clearance procedures.[8] Furthermore, Sovery et al, who performed a comprehensive systematic review on the subject in 2014, concluded that only the urinary clearance of 99mTc DTPA and plasma and urinary clearance of 125I-iothalamate, 51Cr-ethylenediaminetetraaceti c acid (EDTA), and Iohexol are adequate for GFR measurement.[22] A study by Xie et al from 2013 directly compared the kidney dynamic imaging method and CKD-EPI.[23] The authors found that in the subgroup with higher GFR, the 2 methods mentioned above performed similarly; however, in the subgroup with lower GFR, CKD-EPI had better performance, and the conclusion was that both methods could be used for GFR determination, but CKD-EPI was more accurate.[23]

Finally, we acknowledge that the ultimate decision on whether a potential donor is suitable for donation or not remains challenging and has become more difficult overall with an increasing proportion of donors who are elderly or have co-morbidity. Meticulous workup before LKD explains the results of some studies that showed that the survival of living donors is not different, perhaps even longer, compared to non-donors.[24,25] Our data provide some solution to the dilemma of donor assessment in a resource-deplete environment but do not provide an easy answer to the difficulty of donor assessment overall. Therefore, close attention should be paid to other factors impacting the remaining kidney function after donation, such as obesity, smoking, age, and family history of kidney diseases.[11,26] For obvious reasons, overcoming these includes additional challenges in a developing country. Thorough evaluation before the LKD is essential to identify those factors, make recommendations to address or modify them, and provide all the information to the potential donors to help them with risk-informed decision-making.[10,26]

Our study has strengths and weaknesses. We included a sizeable number of potential donors and it was limited to 1 center. We provide contemporary data on assessment of donors from a developing country where studies are often small. Another strength of our study is that only 1 method was used for mGFR, i.e., DTPA. The limitations of this study are firstly due to its retrospective nature. Furthermore, our reliance on DTPA renogram for mGFR limits the applicability of our findings to other centers where more sophisticated approaches to mGFR are available. We emphasize that DTPA is the only technology that is available to us for this purpose. We acknowledge that this method may not be the gold standard and there are more accurate methods available, but unfortunately, we do not have access to them. However, our study's experience and recommendations can be valuable for other centers that face similar challenges. Also, irrespective of the limitations of DTPA we emphasize the advantage of using DTPA renogram as it allows for the measurement of split kidney function.

CONCLUSION

Assessment of potential donors is a challenge in developing countries, representing a compromise between what is locally available on one side and what is considered mandatory in wealthy health economies on the other. Our findings suggest that for many potential donors, it may not be necessary to use

an exogenous marker for mGFR. In a resource-deplete environment, measuring CrCl is a safe, widely available, and cost-effective method to assess GFR in potential donors. However, in cases where eGFR and CrCl differ significantly in a way one method makes the potential donor eligible for kidney donation while the other method shows the donor as ineligible, or where either result falls in the borderline range, we recommended using a method of mGFR with an exogenous marker that is locally available. In such cases, a DTPA renogram may be used, which is valuable in clinical practice as it enables the measurement of split renal function. Further studies should now study the long-term outcomes with our approach and thereby confirm its safety overall.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of University Clinical Center Tuzla (date: May 10th 2023 number: 02-09/2-32/23)

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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