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Original

Comparative analysis of different nuclear medicine techniques in evaluation of renal function

Aleksandra Peshevska[1], Tanja Makazlieva[1], Venjamin Majstorov[1], Lambe Barandovski[2], Irena Rambabova-Bushljetik[3], Daniela Miladinova[1]

[1]Faculty of Medicine Institute of Pathophysiology and Nuclear Medicine, University Ss Cyril and Methodius, Skopje, North Macedonia
[2]Institute of Physics at the Faculty of Natural Sciences and Mathematics, University Ss Cyril and Methodius, Skopje, Macedonia
[3]University Clinic of Nephrology, Skopje, North Macedonia

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Abstract

Introduction: Nuclear medicine (NM) methods play an important role in the evaluation of renal function in a wide range of clinical indications. The aim of our study was to evaluate the correlation between measured GFR (mGFR) obtained by the three-plasma sample slope-intercept NM method (TPSM) — reference method vs. estimated GFR (eGFR) using Fleming's single plasma sample method (SPSM) at 120 min, 180 min, and 240 min and correlation of reference method with eGFR with camera-based Gates' protocol.

Material and methods: A total of 82 subjects (33 male/49 female) with a mean age of 54.87 ± 15.65 years were included and mGFR value was obtained by the three-plasma sample slope-intercept NM method and eGFR was obtained with Fleming's single sample method. eGFR was also quantified with the camera-based Gates' protocol after *i.v.* application of [^{99m}Tc]Tc-DTPA.

Results: Our study revealed a very strong positive significant correlation between all three SPSMs with the TPSM as the reference method. Between the Gates' method and the TPSM in the group of patients with mGFR ≥ 61–84 mL/min/1.73 m^2 and mGFR ≥ 84 mL/min/1.73 m^2, a moderate positive statistically significant correlation was obtained.

Conclusions: The SPSM method shows a very strong correlation with the reference and low bias in all three groups of patients and can be routinely used for GFR estimation.

KEY words: GFR, [^{99m}Tc]Tc-DTPA, plasma sampling, slope-intercept method, Fleming's single sample method, Gates method

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Introduction

Nuclear medicine (NM) methods play an important role in the evaluation of renal function [1–3]. Nuclear nephrology uses different methods with the possibility of different quantifications to obtain functional parameters [4, 5]. Glomerular filtration rate (GFR) is important for the evaluation of renal function and different formulas have been developed to estimate with sufficient precision the kidney function in patients. GFR quantification is possible by using various methods, but an ideal substance is one that is freely filtered through the glomeruli without additional tubular secretion and reabsorption occurring. Inulin clearance is considered the gold standard for measuring GFR, but the need for continuous infusion, multiple blood samples, and urine collection as well as the cost of the tracer are obstacles to routine clinical implementation [6]. Radionuclide-based techniques allow for rapid and reliable measurement of GFR from plasma samples taken after intravenous administration of a bolus of radionuclide-labeled tracer. [^{99m}Tc]Tc-DTPA has become a standard GFR tracer in Europe and in the United States and has been recommended by the British Nuclear Medicine Society (BNMS), International Scientific Committee of Radionuclides in Nephrourology (ISCORN), and European Association of Nuclear Medicine (EANM) [5, 6]. The nuclear medicine method for evaluation of GFR using [^{99m}Tc]Tc-DTPA as radiopharmaceutical is an established methodology and there are two techniques: camera-based Gates' protocol and plasma sampling method [2]. Nuclear medicine methods are also unique non-invasive methods that assess the relative renal split function, expressed as a percentage [1, 2]. Different techniques of GFR measurement

Correspondence to: Tanja Makazlieva,
Faculty of Medicine Institute of Pathophysiology and Nuclear Medicine,
University Ss Cyril and Methodius, St. Mother Tereza, 17,
1000 Skopje, North Macedonia,
e-mail: tmakazlieva@medf.ukim.edu.mk

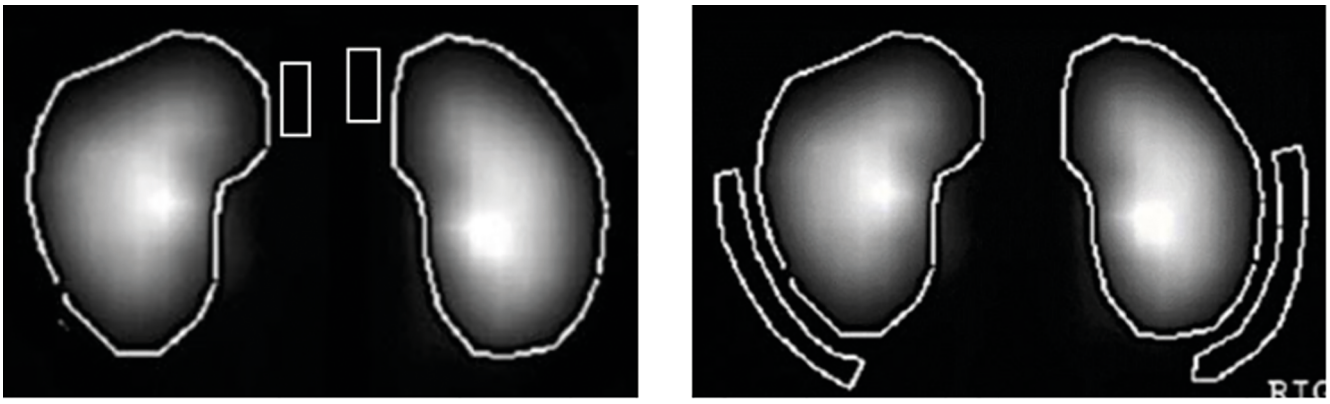


Figure 1. Background region of interest used for eGFR calculation using Gates' method; (**A**) $Gates_{ROI1}$; (**B**) $Gates_{ROI2}$

can be used with only one, two, or more blood samples taken from a patient at specific time points after the *i.v.* application of a radiopharmaceutical. The most accurate is the multi-sample technique which involves taking blood at 5, 10, 15, 30, 45, 60, 120, 180, and 240 minutes after application. Once the plasma time dependence curve is obtained, the GFR is determined as the ratio of the applied activity to the area under the curve [7]. The aim of our study was to evaluate the correlation between measured GFR (mGFR) obtained by the three-blood sample slope-intercept NM method (reference method) *vs.* eGFR using Fleming's single sample method at 120 min, 180 min, and 240 min and the correlation of the reference method with estimated (eGFR) with camera-based Gates' protocol.

Material and methods

The study included 82 patients, 33 male, and 49 female, with a mean age of 54.87 ± 15.65 years (18–80 years). The mean height was 167.39 ± 8.70 cm (152–190 cm) and the mean weight was 78.22 ± 16.05 kg (44–113 kg). All patients were divided into three groups according to mGFR value. The first group comprised patients with mGFR < 60 mL/min/1.73 m^2 (31 patients), the second one with mGFR 61–84 mL/min/1.73 m^2 (27 patients), and the third group with mGFR ≥ 85 mL/min/1.73 m^2 (24 patients). In all patients, mGFR was evaluated using the standard reference three-plasma sample method (TPSM) and eGFR was obtained with Fleming's single sample method and was also quantified with the camera-based Gates' protocol after *i.v.* application of [^{99m}Tc]Tc-DTPA. Subjects preparation for NM examinations included good hydration by oral fluid intake of approximately 10 mL/kg body weight 30 minutes prior to tracer administration. Subject preparation for NM methods was performed according to Fleming's et al. [7] published guidelines. The study was approved by the Ethics Committee of the Faculty of Medicine at Ss. Cyril and Methodius University in Skopje, and a written consent was obtained from all subjects enrolled in the study.

Nuclear medicine methods: dynamic renal scan and Gates' protocol for quantification of eGFR and plasma sampling method for evaluation of mGFR using [^{99m}Tc]Tc-DTPA

Dynamic renal scintigraphy was performed with a Siemens gamma camera, model E.Cam Signature Series using software syngo VD20K SL11P274, from where the data were transferred to the workstation with the software esoft 3.5 and processed by the Gates' method. Before the start of the acquisition, the activity of the full syringe was measured, containing the dose of [^{99m}Tc]Tc-DTPA (111–185 MBq), and then carefully *i.v.* applied, with accurate recording of the time of application/administration of the radiopharmaceutical. The subjects were scanned in a supine position with a camera placed posteriorly. Dynamic acquisition with 2 s frames for 60 s renal perfusion phase was made, followed by renal function assessment phase with 60 s frames during 20 min. The regions of interest (ROIs) were plotted around the kidneys and also for the background activity. The residual activity was measured in the empty syringe at the end of the acquisition. Camera-based eGFR was quantified using the Gates' protocol with two different ROIs for the background activity: infrarenal background regions of interest (ROI1) and subrenal background regions of interest (ROI2) (Fig. 1).

Determination of GFR by plasma sampling method with [^{99m}Tc]Tc-DTPA

Blood samples (7 mL) were drawn from the veins of the contralateral arm, from the radiopharmaceutical injection site, at 120, 180, and 240 min. after administration of [^{99m}Tc]Tc-DTPA for the renal dynamic scan. Blood samples were centrifuged at 1000 g/10 minutes and 1 mL of plasma was transferred in two separate test tubes, allowing measurement of the activity in duplicate for each patient, and at the same time a standard was prepared. Activity from the plasma samples and standard samples were measured in a well gamma counter and were expressed as counts per minute. In order to be able to calculate GFR, it was necessary to convert the values of relative activity into plasma tracer concentration expressed as a percentage of injected dose per liter (%/L). mGFR was obtained using the slope-intercept plasma sample method. The resulting mGFR was normalized on the body surface area and corrected for the omitted measurement of activity in the early phase after the application of the tracer, using the Brochner-Mortensen correction method [7]. According to Fleming's formula, eGFR was quantified using a single plasma sample method (SPSM) at 120 min ($SPSM_{120}$), then only activity from the plasma sample at 180 min ($SPSM_{180}$) and for plasma sample collected at 240 min ($SPSM_{240}$) [7].

Table 1. Mean GFR ± SD and the mean percentage error ± SD for all the methods

GFR interval		GFR_{120min}	GFR_{180min}	GFR_{240min}	GFR_{ROI1}	GFR_{ROI2}
< 60 (mL/min/1.73 m²)	Mean GFR ± SD	30.35 ± 16.99	32.90 ± 18.14	34.90 ± 19.34	14.74 ± 11.71	31.16 ± 17.89
	Mean percentage error ± SD	41.01 ± 39.57	26.37 ± 31.55	20.28 ± 26.80	65.18 ± 21.22	28.09 ± 36.34
60–84 (mL/min/1.73 m²)	Mean GFR ± SD	67.70 ± 8.89	70.22 ± 7.86	72.63 ± 8.67	38.63 ± 15.81	60.56 ± 20.45
	Mean percentage error ± SD	6.76 ± 5.69	2.18 ± 1.56	3.42 ± 3.84	46.43 ± 17.45	23.70 ± 15.94
≥ 85(mL/min/1.73 m²)	Mean GFR ± SD	93.46 ± 8.64	93.92 ± 7.44	96.17 ± 7.22	53.57 ± 12.13	76.81 ± 14.50
	Mean percentage error ± SD	3.67 ± 1.35	3.35 ± 1.87	3.05 ± 2.73	44.31 ± 10.47	20.93 ± 13.11

Statistical analyses

Statistical analyses were performed using STATISTICA 8, version 6. All data were expressed as mean ± standard deviation of the mean (SD). Correlation analyses were performed between reference method TPSM and $SPSM_{120}$, $SPSM_{180}$, $SPSM_{240}$, and Gates' method, using Pearson's correlation; p-values of ≤ 0.05, were considered significant. The percentage error for each measurement was assessed as (eGFR-mGFR/mGFR) ×100, where eGFR is GFR evaluated by one of the estimation methods. The agreement between different methods for GFR estimation with the reference method was tested using Bland-Altman plots analyses plotted with NCSS 2021 statistical software.

Results

In the group of patients with low eGFR values (< 60 mL/min/1.73 m²), the mean ± SD of the mGFR using the reference TPSM was 34.65 ± 17.65 mL/min/1.73 m²; in the group of patients with eGFR values from 60 to 84 mL/min/1.73 m² the mean mGFR ± SD was 70.56 ± 7.54 mL/min/1.73 m² and in the group of patients with normal eGFR values (≥ 85 mL/min/1.73 m²) the mean mGFR ± SD using the reference TPSM method was 97.00 ± 8.67 mL/min/1.73 m². The mean mGFR ± SD and the mean percentage error for all SPSM methods and eGFR with camera-based Gates' method using two different background ROIs are presented in Table 1.

Group of patients with low eGFR values (< 60 mL/min/1.73 m²)

The regression equations of $SPSM_{120}$, $SPSM_{180}$, $SPSM_{240}$, $Gates'_{ROI1}$ and $Gates'_{RO2}$ method against the TPSM were $1.4384 + 0.8346 \times x$, $-1.1205 + 0.9821 \times x$, $-2.2501 + 1.0724 \times x$, $-4.0795 + 0.5433 \times x$, $3.017 + 0.8124 \times x$, respectively (Fig. 2). There was a very strong positive significant correlation between each of the SPSM and the Gates' method with the TPSM (Tab. 2).

Bias ± 1.96·SD values (mL/min/1.73 m²) for $SPSM_{120}$, $SPSM_{180}$, $SPSM_{240}$, $Gates'_{ROI1}$ and $Gates'_{RO2}$ were −4.29 ± 17.84, −1.74 ± 10.69, 0.26 ± 8.39, −19.90 ± 20.91, −3.48 ± 22.30, respectively. The highest bias and mean percentage error were found in the $Gates'_{ROI1}$ method. For this group of patients, Bland-Altman plots are shown in Figure 3, and 95% limits of agreement values are presented in Table 3.

Group of patients with eGFR values (60–84 mL/min/1.73 m²)

The regression equations of $SPSM_{120}$, $SPSM_{180}$, $SPSM_{240}$, $Gates'_{ROI1}$ and $Gates'_{RO2}$ method against the TPSM were $-1.0946 + 0.9751 \times x$, $-1.3907 + 1.015 \times x$, $-2.978 + 1.0716 \times x$, $-48.8394 + 1.2397 \times x$, $-42.0442 + 1.4542 \times x$, respectively (Fig. 4). There was a very strong positive significant correlation between each of the three SPSMs with the TPSM (Tab. 2). Between the Gates' method with the TPSM, there was a strong positive significant correlation in both cases for background ROIs.

Bias ± 1.96·SD values (mL/min/1.73 m²) for $SPSM_{120}$, $SPSM_{180}$, $SPSM_{240}$, $Gates'_{ROI1}$ and $Gates'_{RO2}$ were −2.84 ± 9.97, −0.33 ± 3.61, 2.07 ± 6.39, −31.93 ± 25.72, −10 ± 35.15, respectively. Again, the highest bias and mean percentage error were found in the $Gates'_{ROI1}$ method. For this group of patients, Bland-Altman plots are shown in Figure 5, and 95% limits of agreement values are presented in Table 4.

Group of patients with normal eGFR values (≥ 85 mL/min/1.73 m²)

The regression equations of $SPSM_{120}$, $SPSM_{180}$, $SPSM_{240}$, $Gates'_{ROI1}$ and $Gates'_{RO2}$ method against the TPSM were $-2.1974 + 0.9861 \times x$, $13.4776 + 0.8293 \times x$, $24.4383 + 0.7395 \times x$, $-48.057 + 1.0613 \times x$, $13.3133 + 0.6631 \times x$, respectively (Fig. 6). There was a very strong positive significant correlation between each of the SPSMs with the TPSM (Tab. 2). Between the Gates' method with the TPSM when the infrarenal background was used, there was a moderate positive significant correlation. In the case of subrenal background ROIs, there was a positive insignificant correlation (Tab. 2).

Bias ± 1.96·SD values (mL/min/1.73 m²) for $SPSM_{120}$, $SPSM_{180}$, $SPSM_{240}$, $Gates'_{ROI1}$ and $Gates'_{RO2}$ were −3.54 ± 2.53, −3.08 ± 4.86, −0.83 ± 8.04, −42.19 ± 19.11, −18.95 ± 27.97, respectively. The highest bias and mean percentage error were in the $Gates'_{ROI1}$ method. For this group of patients, Bland-Altman plots are shown in Figure 7, and 95% limits of agreement values are presented in Table 5.

Discussion

GFR is an important parameter for estimation of the kidney function, so having an accurate and reproducible method for GFR estimation is essential. Inulin clearance which includes continuous inulin infusion with blood sampling is the known "gold standard" for GFR estimation, but this method is expensive and demanding to perform on a daily basis [6, 8]. Hence, an accurate method is needed that would be optimal regarding the implementation of the procedure, cost, and time.

Of the various NM methods for determination of the renal clearance of [^{99m}Tc]Tc-DTPA, the most relevant is the Biexponential fitting method which showed a strong correlation with the "gold

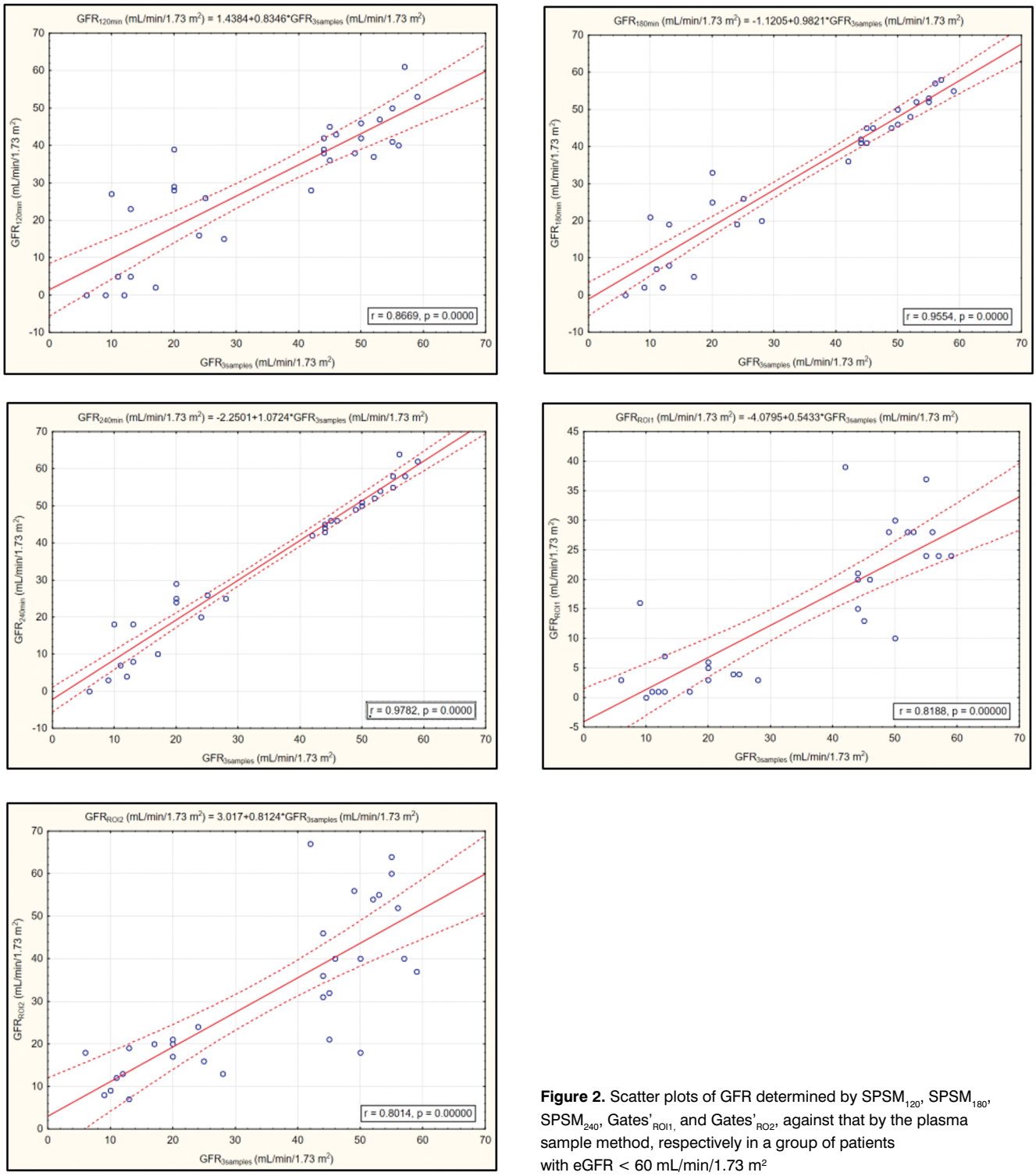
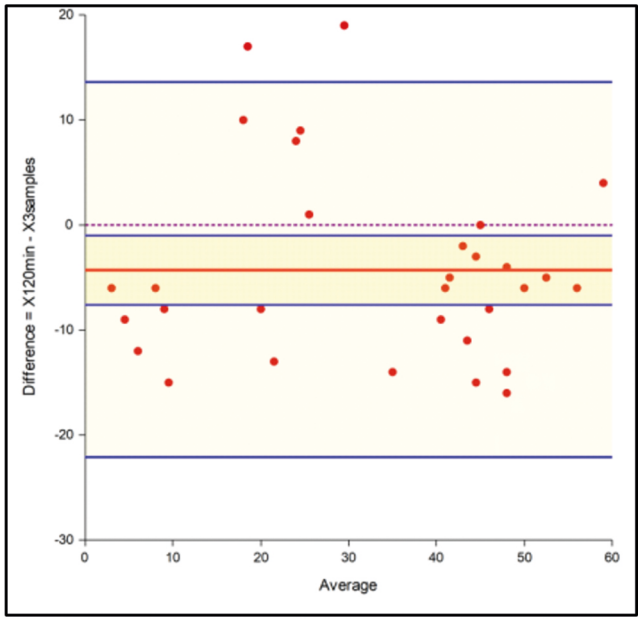


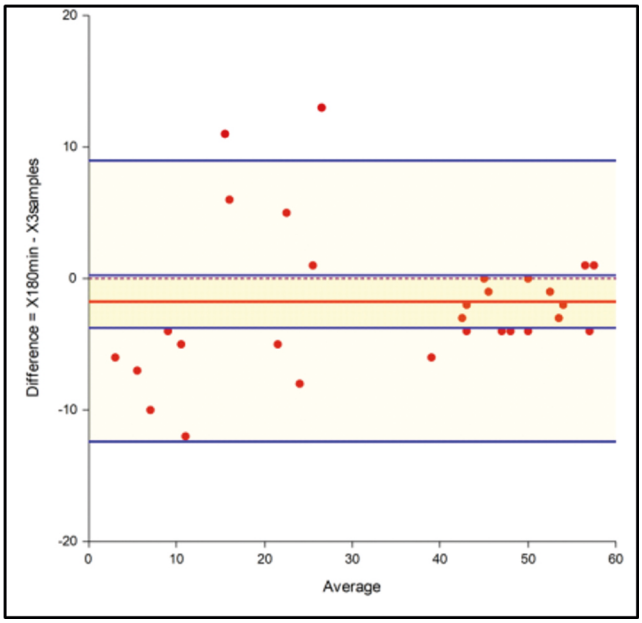
Figure 2. Scatter plots of GFR determined by $SPSM_{120}$, $SPSM_{180}$, $SPSM_{240}$, $Gates'_{ROI1}$, and $Gates'_{RO2}$, against that by the plasma sample method, respectively in a group of patients with eGFR < 60 mL/min/1.73 m²

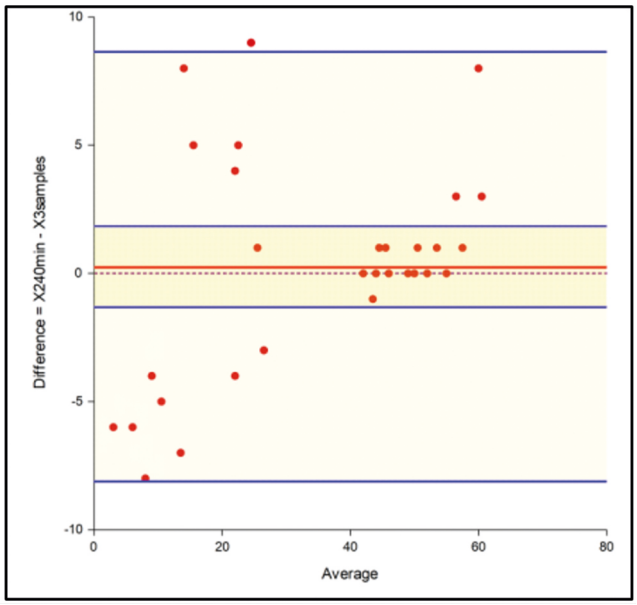
Table 2. Pearson's correlation coefficient between TPSM and the other methods

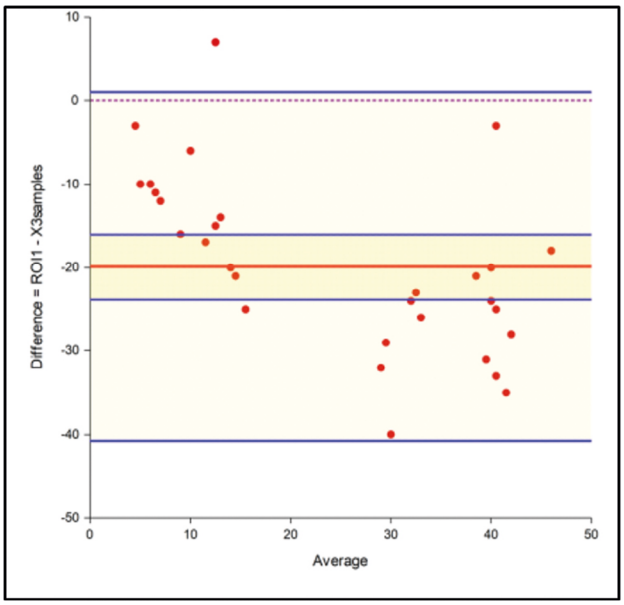
Pearson's correlation coefficient — TPSM *vs.* other methods						
GFR interval	< 60 (mL/min/1.73 m²)		60–84 (mL/min/1.73 m²)		≥ 85 (mL/min/1.73 m²)	
Method	r	p	r	p	r	p
$SPSM_{120}$	0.8669	0.0000	0.8274	0.0000	0.9894	0.0000
$SPSM_{180}$	0.9554	0.0000	0.9734	0.0000	0.9659	0.0000
$SPSM_{240}$	0.9782	0.0000	0.9317	0.0000	0.8879	0.0000
$Gates_{ROI1}$	0.8188	0.0000	0.5913	0.0012	0.6220	0.0026
$Gates_{ROI2}$	0.8014	0.0000	0.5361	0.0039	0.3251	0.1505

Gates — Gates' protocol; GFR — glomerular filtration rate; SPSM — single plasma sample method; TPSM — three-plasma sample slope-intercept method









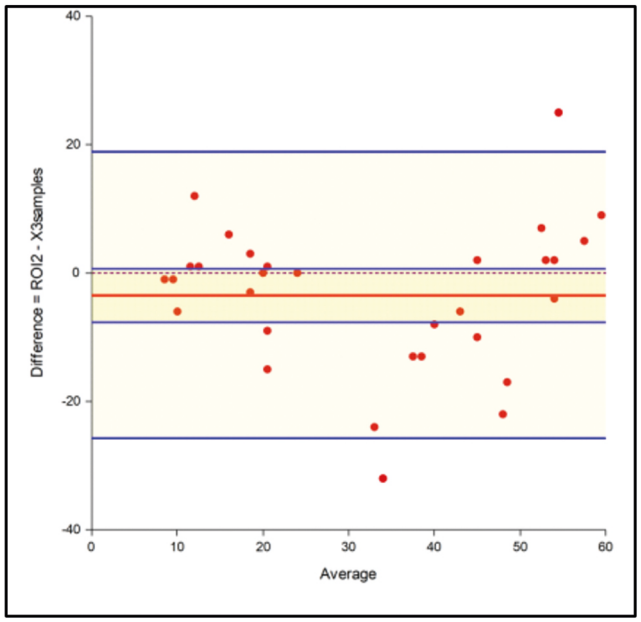


Figure 3. Bland-Altman plots of GFR determined by $SPSM_{120}$, $SPSM_{180}$, $SPSM_{240}$, Gates'$_{ROI1,}$ and Gates'$_{RO2}$, against that by the plasma sample method, respectively in a group of patients with eGFR < 60 mL/min/1.73 m^2

Table 3. Bias and 95% limits of agreement (bias –1.96 SD; bias +1.96 SD) values in a group of patients with eGFR < 60 mL/min/1.73 m²

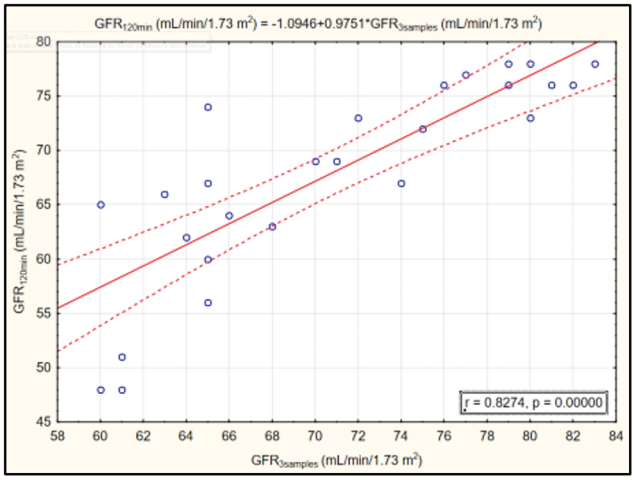
Bias and 95% limits of agreement (bias −1.96 SD; bias +1.96 SD) values			
Method	Bias (SD)	Bias −1.96 SD	Bias +1.96 SD
$SPSM_{120}$	−4.29 (9.10)	−22.13	13.55
$SPSM_{180}$	−1.74 (5.45)	−12.43	8.95
$SPSM_{240}$	0.26 (4.28)	−8.13	8.65
$Gates_{ROI1}$	−19.90 (10.67)	−40.81	1.01
$Gates_{ROI2}$	−3.48 (11.38)	−25.78	18.82

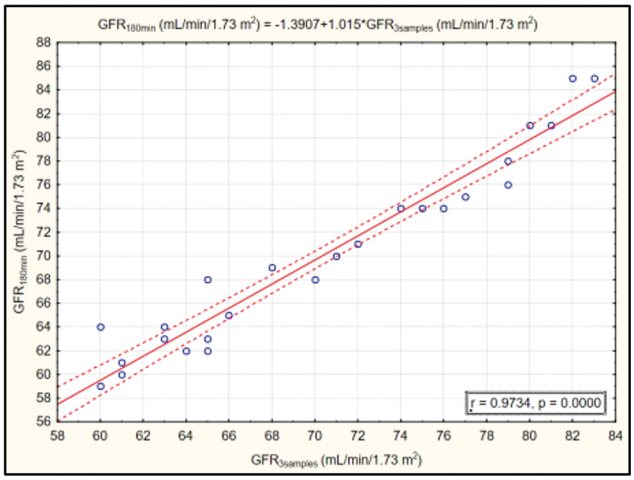
Gates — Gates' protocol; SD — standard deviation; SPSM — single plasma sample method

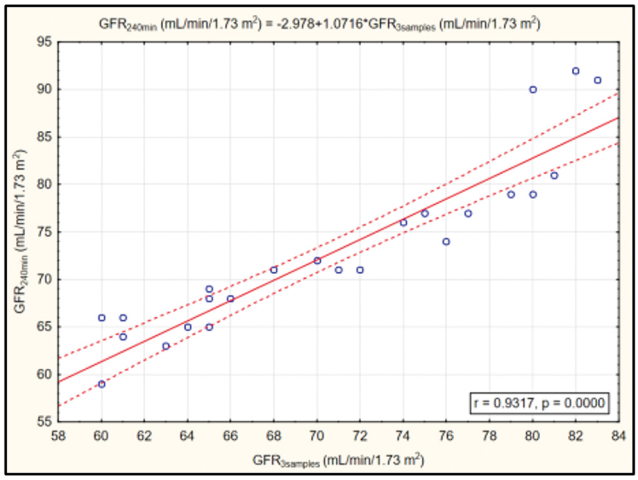
Table 4. Bias and 95% limits of agreement (bias –1.96 SD; bias +1.96 SD) values in a group of patients with eGFR 60–84 mL/min/1.73 m²

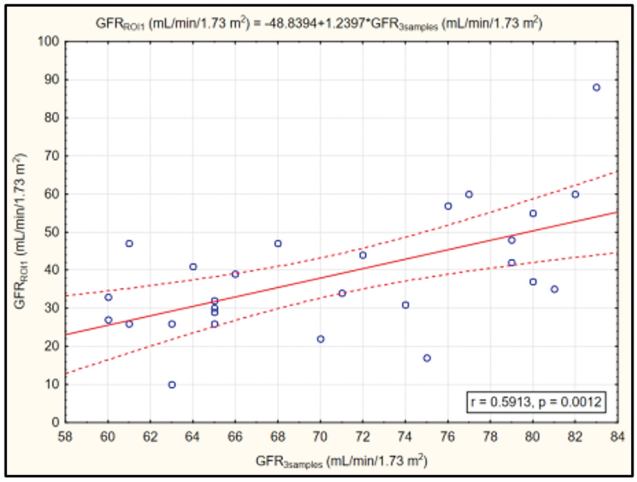
Bias and 95% limits of agreement (bias −1.96 SD; bias +1.96 SD) values			
Method	Bias (SD)	Bias −1.96 SD	Bias +1.96 SD
$SPSM_{120}$	−2.85 (5.09)	−12.82	7.12
$SPSM_{180}$	−0.33 (1.84)	−3.94	3.28
$SPSM_{240}$	2.07 (3.26)	−4.32	8.46
$Gates_{ROI1}$	−31.93 (13.12)	−57.65	−6.21
$Gates_{ROI2}$	−10 (17.93)	−45.15	25.15

Gates — Gates' protocol; SD — standard deviation; SPSM — single plasma sample method









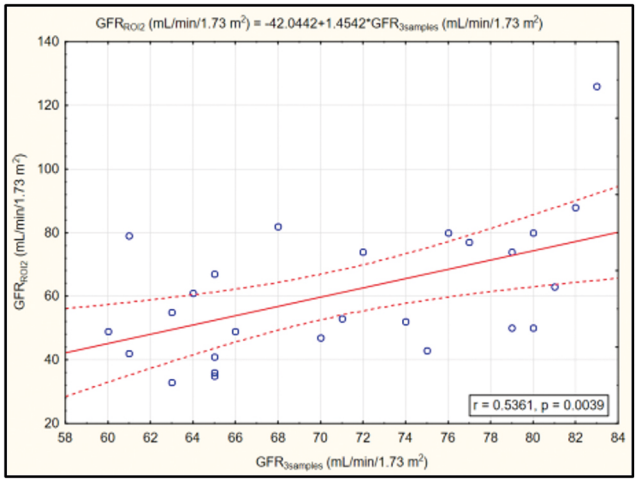


Figure 4. Scatter plots of GFR determined by $SPSM_{120}$, $SPSM_{180}$, $SPSM_{240}$, $Gates'_{ROI1}$, and $Gates'_{RO2}$, against that by the plasma sample method, respectively in a group of patients with eGFR 60–84 mL/min/1.73 m²

Table 5. Bias and 95% limits of agreement (bias –1.96 SD; bias +1.96 SD) values in a group of patients with eGFR ≥ 85 mL/min/1.73 m²

Bias and 95% limits of agreement (bias −1.96 SD; bias +1.96 SD) values			
Method	Bias (SD)	Bias −1.96 SD	Bias +1.96 SD
$SPSM_{120}$	−3.54 (1.29)	−6.07	−1.01
$SPSM_{180}$	−3.08 (2.48)	−7.94	1.78
$SPSM_{240}$	−0.83 (4.10)	−8.87	7.21
$Gates_{ROI1}$	−42.19 (9.75)	−61.30	−23.08
$Gates_{ROI2}$	−18.95 (14.27)	−46.92	9.02

Gates — Gates' protocol; SD — standard deviation; SPSM — single plasma sample method

standard" [9, 10]. This method that takes into account the distribution phase requires multiple blood samples and is time-consuming, which is the reason why we choose the slope-intercept method as a reference in our study. The literature reports a significant correlation between the slope-intercept method with the bi-exponential fitting method even for low GFR values < 10 mL/min/1.73 m² [11, 12].

A large number of studies have shown that the SPSM can be used as an appropriate and clinically easier applicable alternative for GFR estimation. This is in agreement with the results obtained in our study. Our analysis revealed a very strong positive significant correlation between each of the three SPSMs with the TPSM in a wide range of GFR values in our population. In the group of patients with GFR values less than 60 mL/min/1.73 m², the agreement between the methods was lower than in the other groups. The highest correlation was observed between the $SPSM_{240}$ with the reference method with a correlation coefficient $r = 0.9782$. From the Bland-Altman plot (Fig. 2) for $SPSM_{240}$ with TPSM it can be seen that the reason for the wide limits of agreement between the methods is GFR values less than 30 mL/min/1.73 m². For higher GFR values (31–60 mL/min/1.73 m²), an agreement between the methods around the line of equality can be seen. However, because of the small number of patients, additional research should be implemented in which this group of patients would be divided into two groups with GFR values from 0–30 mL/min/1.73 m² and 31–60 mL/min/1.73 m². For the latter group, the same protocol would be retained where the accuracy of the $SPSM_{240}$ with TPSM would be examined. In the former (0–30 mL/min/1.73 m²) group, the accuracy of the single sample method at 24 hours post-injection would be examined, and this method is recommended in the literature for GFR values lower than 30 mL/min/1.73 m² [13, 14].

In the group of patients with GFR values from 61 to 84 mL/min/1.73 m², a very strong positive significant correlation between each of the three SPSMs with the TPSM was found with the highest correlation coefficient observed in the case of $SPSM_{180}$. Also, the narrowest limits of agreement were observed in the case of $SPSM_{180}$ where the bias ± 1.96 SD was −0.33 ± 3.61.

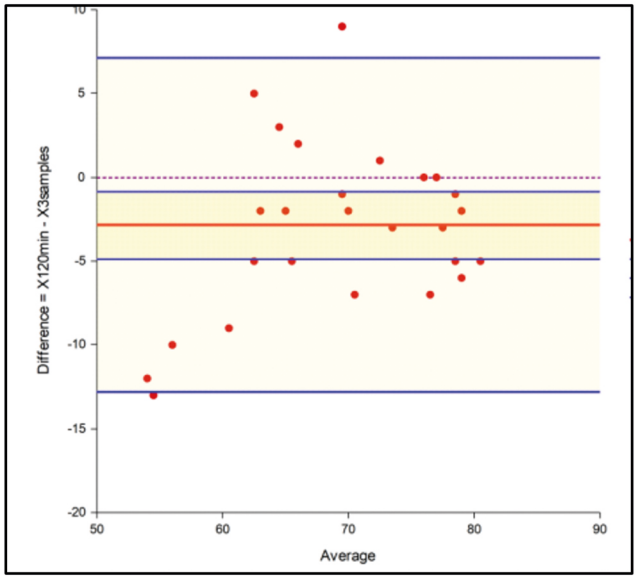
In the third group of patients with mGFR ≥ 85 mL/min/1.73 m², we found a very strong positive significant correlation between SPSM at 120 min, 180 min, 240 min with the reference method, but the highest correlation coefficient (r = 0.9894) and narrowest limits of agreement (−3.54 ± 2.53) were found in the case of $SPSM_{120}$.

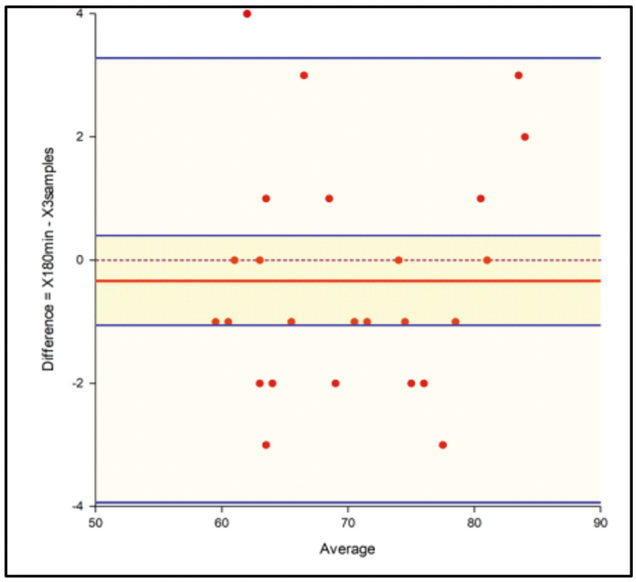
The results obtained in our study correlate with the findings of other authors. Osman and Elmadani found a correlation coefficient r = 0.96 between Fleming's single sample method and the slope-intercept method as the reference one [15]. These authors concluded that the SPSM significantly correlated with the reference method, especially in the interval of GFR values from 40 to 90 mL/min/1.73 m² and reported slight underestimation for both, very low and very high values of GFR. This is also in agreement with our results, especially in the case of patients with high GFR values. Osman and Elmadani concluded that Fleming's SPSM could be the method of choice for the calculation of GFR, particularly when the serum creatinine level is normal and the sample is obtained at 3 h after the injection of the radiotracer. Fleming et al. [16] concluded that one-sample equations gave reliable estimates of GFR, which may be used for quality control of slope-intercept GFR assessment, especially in the case of two plasma-sample methods where one cannot be sure if these two points fit the true curve. They also found that using the single sample the errors on GFR varied with GFR, timing of sample, and patient size. Variation in the differences between one-sample and slope-intercept methods with GFR has also been shown in other studies [17].

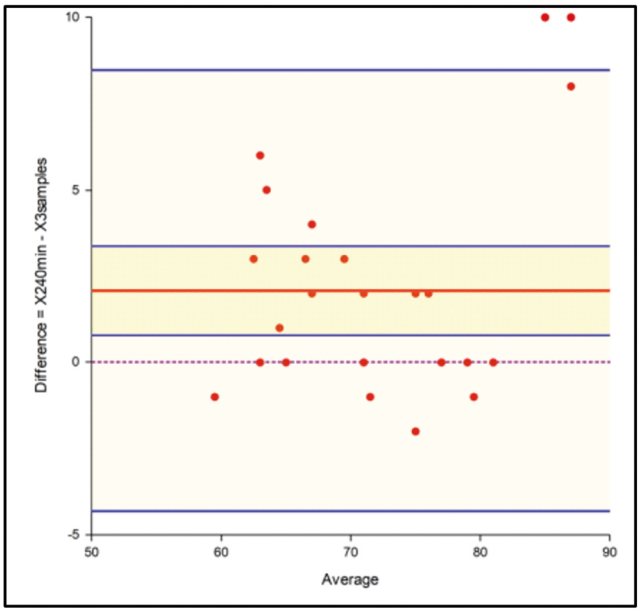
Delanaye et al. [18] also found that the performance of the single-sample plasma clearance method was similar to the more complex multiple-sample plasma clearance. Discrepancies were observed in some specific clinical settings, especially in patients with very high BMI (40 kg/m²) and in the low GFR range. In their study, they found that when mGFR was > 30 mL/min, the SPSM at 240 min time point was the strategy of choice and that in all patients SPSM at 120 min was the least accurate. Like Gaspari et al. [19], we also that the best concordance was at 240 min best for GFR ≥ 40 mL and at 180 min for the highest GFR levels. However, the concordance within 5% was better in our study and, more importantly, we found no significant regression intercept between the two methods with a very high concordance correlation coefficient.

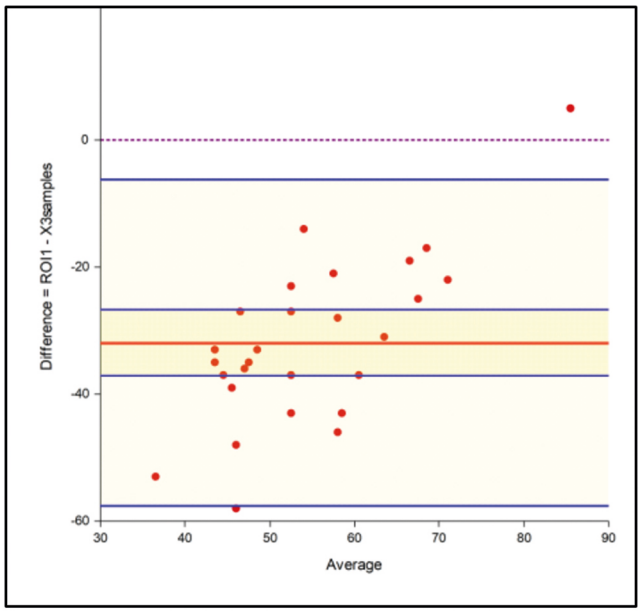
Gates' method is a simple and non-invasive method that excludes the complex calculations performed in the plasma sample method. Because of this, the interest in its routine application is considerable but its relevance is debatable and there are controversial results in the literature regarding this method. In our study, the highest bias and mean percentage error were found in the $Gates'_{ROI1}$ method. Gates' method tended to underestimate GFR in all three groups of patients, especially when using infrarenal background ROIs (ROI1). Also, underestimation was higher in patients with higher GFR values. Our results according to the unsatisfactory accuracy of the Gates' method are in agreement with the results reported by other authors. Mulligan et al. [20] correlated Gates' method with the plasma sample method as the reference one. They observed significant differences and poor correlation between the methods for all GFR values [20]. De Santo et al. [21] in their study examined the correlation between the Gates' method (ROI2) and the inulin clearance as a reference method. They observed a significant overestimation of GFR values in patients with low GFR values and an overestimation in patients with high GFR. They also concluded that Gates' method is less precise even from the creatinine method for GFR estimation. They obtained a correlation coefficient of r = 0.758 that indicated an average-expressed correlation between the methods [21]. This is similar to our results.

For Gates' methods, in both cases of the extrarenal region of interest, we obtained an underestimation of GFR for all GFR values. The deviation was especially expressed when ROI1 was used as an extrarenal region of interest. Underestimation of GFR values when Gates' method is used has been found by other authors. Galli et al. [22] discovered that Gates' method constantly









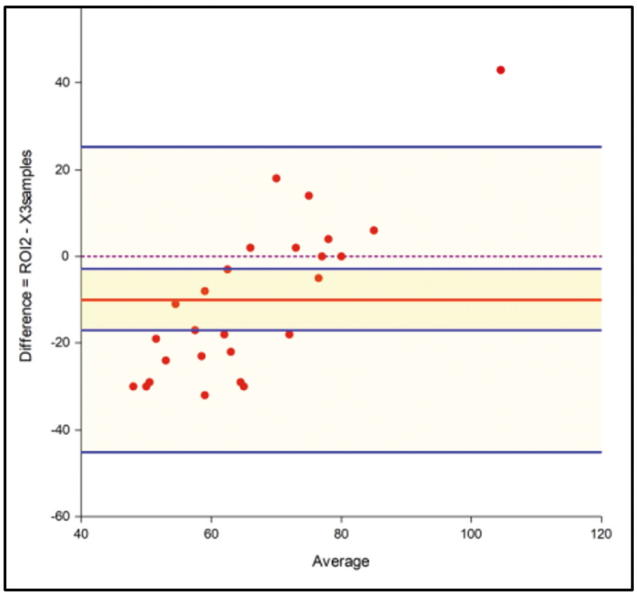
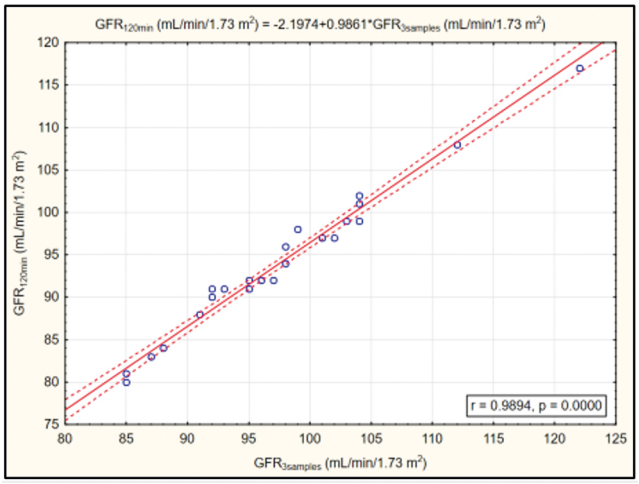
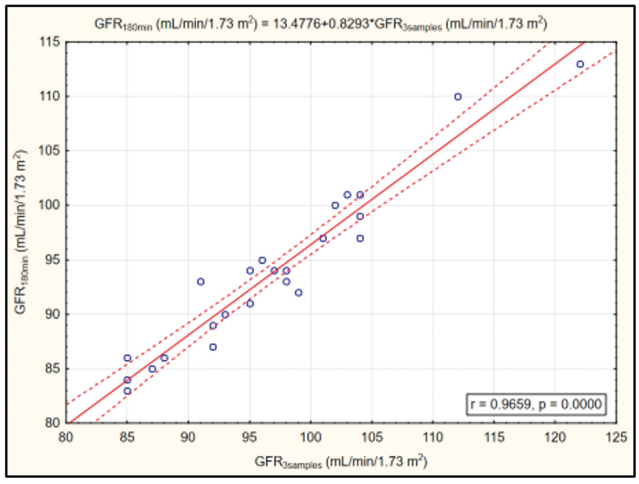
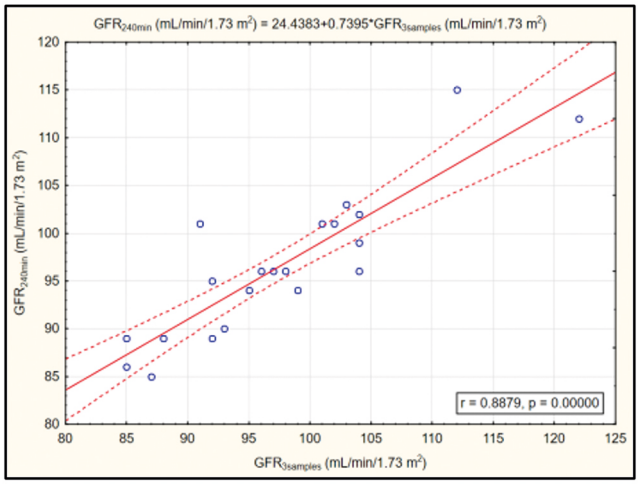
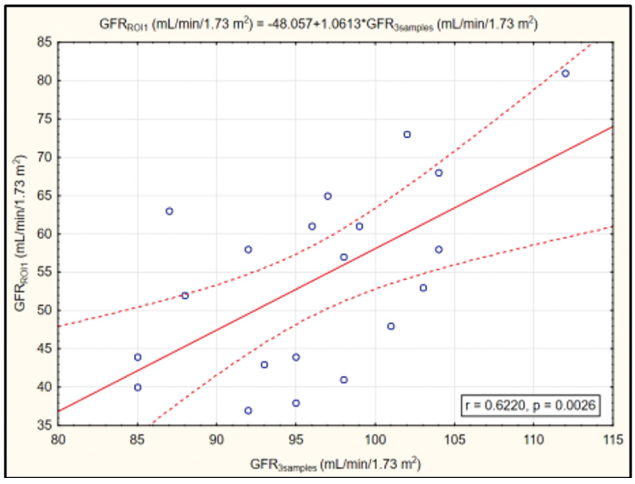


Figure 5. Bland-Altman plots of GFR determined by $SPSM_{120}$, $SPSM_{180}$, $SPSM_{240}$, Gates'$_{ROI1,}$ and Gates'$_{RO2}$, against that by the plasma sample method, respectively in a group of patients with eGFR 60–84 mL/min/1.73 m^2









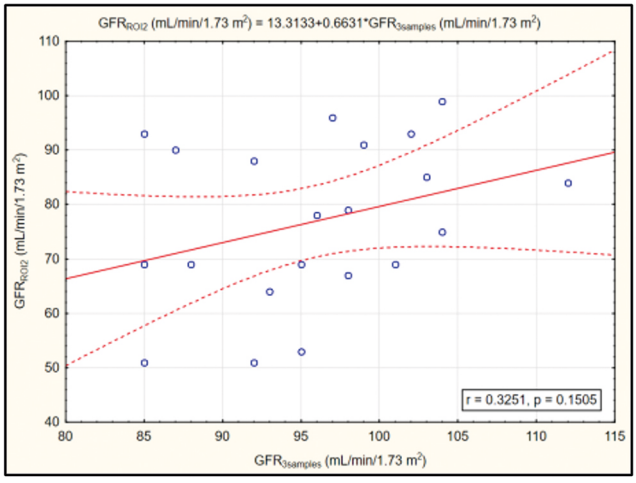
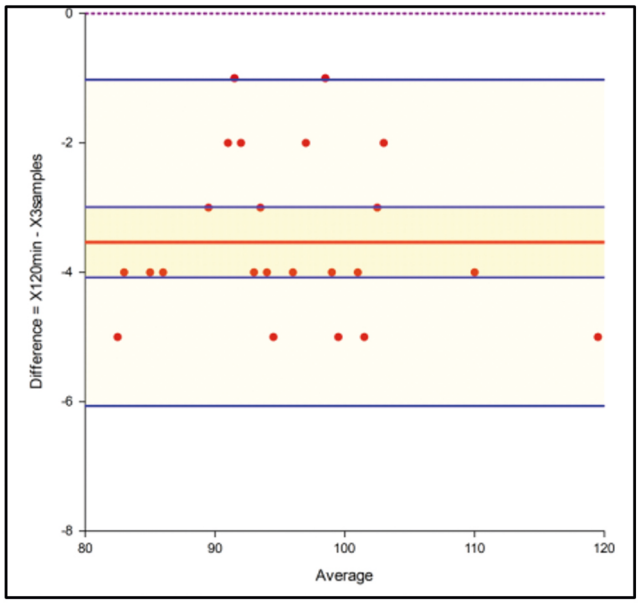
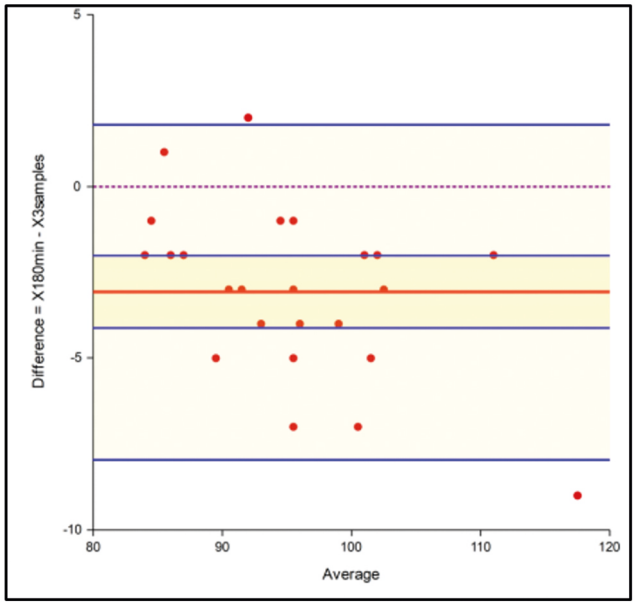


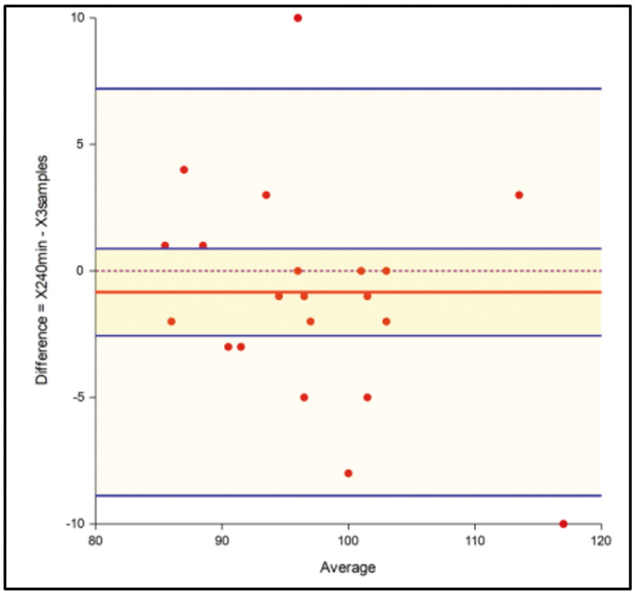
Figure 6. Scatter plots of GFR determined by $SPSM_{120}$, $SPSM_{180}$, $SPSM_{240}$, Gates'$_{ROI1,}$ and Gates'$_{RO2}$, against that by the plasma sample method, respectively in a group of patients with eGFR ≥ 85 mL/min/1.73 m²

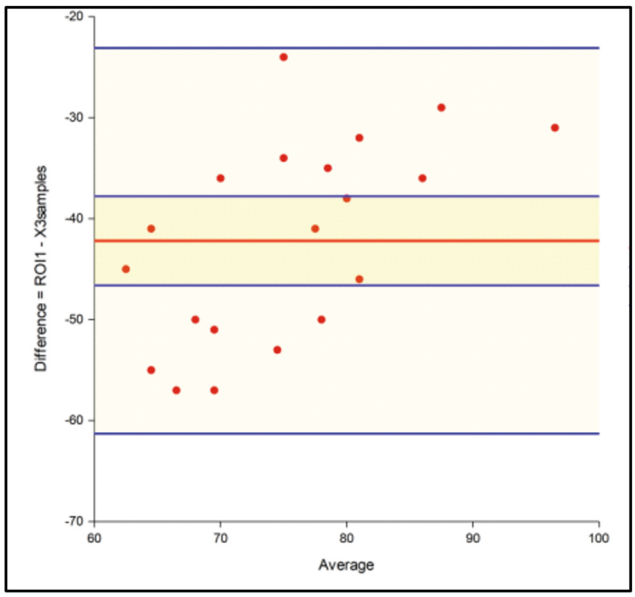
underestimated GFR in patients with GFR values between 25 and 150 mL/min. In their study, they included 40 patients and correlated Gates' method with the Rassels two-plasma sample method using [^{51}Cr]Cr-EDTA [21, 22]. As the main reason for these results, Andre et al., using the Rassels method as a reference, pointed out the attenuation correction for soft tissues. In their study, the highest deviations were observed in patients with high BSA values [23, 24].

Although between the method of Gates' (ROI 1 and ROI 2) and TPSM, we found a statistically significant correlation, it was moderately expressed. Additionally, in both cases with the Bland-Altman plot, we obtained confidence intervals that were significantly wider than those we defined as acceptable. Therefore, we can conclude that the Gates' method should not be the method of choice when accurate determination of GFR is necessary.









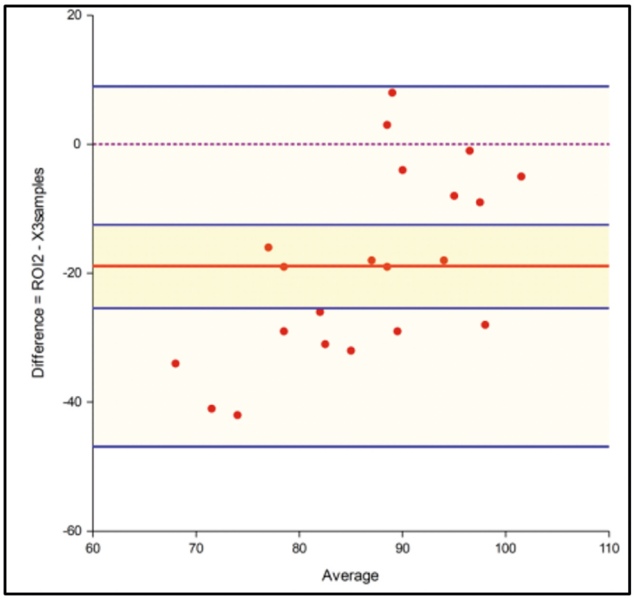


Figure 7. Bland-Altman plots of GFR determined by $SPSM_{120}$, $SPSM_{180}$, $SPSM_{240}$, $Gates'_{ROI1}$, and $Gates'_{RO2}$, against that by the plasma sample method, respectively in a group of patients with eGFR ≥ 85 mL/min/1.73 m^2

Conclusions

Our analyses revealed that Gates' method showed high bias and moderate to strong correlation, and hence it should not be used for routine GFR estimation. On the contrary, the SPSM method showed a very strong correlation with the reference one and a low bias in all three groups of patients. In patients with expected GFR values of 30–60 mL/min/1.73 m^2, the SPSM at 240 min should be used. Having in mind the highest correlation coefficient, and the lowest mean difference (bias and the most acceptable limits of agreement), we can conclude that in patients with expected GFR 60–84 mL/min/1.73 m^2, the SPSM at 180 min should be used and in patients with expected GFR ≥ 85 mL/min/1.73 m^2, the SPSM at 120 min should be used. Our results demonstrated the necessity of further investigation in the group of patients with eGFR < 60 mL/min/1.73 m^2, especially in patients with eGFR < 30 mL/min/1.73 m^2 since a higher bias was observed in this interval of GFR values.

Conflict of interest

The authors have no conflict of interest to disclose.

References

1. O'Malley J, Ziessman H. Nuclear medicine and molecular imaging: the requisites 5th ed. Elsevier Health Sciences 2020.
2. Blaufox MD, De Palma D, Taylor A, et al. The SNMMI and EANM practice guideline for renal scintigraphy in adults. Eur J Nucl Med Mol Imaging. 2018; 45(12): 2218–2228, doi: 10.1007/s00259-018-4129-6, indexed in Pubmed: 30167801.
3. Murray AW, Barnfield MC, Waller ML, et al. Assessment of glomerular filtration rate measurement with plasma sampling: a technical review. J Nucl Med Technol. 2013; 41(2): 67–75, doi: 10.2967/jnmt.113.121004, indexed in Pubmed: 23658207.
4. Chapter 1: Definition and classification of CKD. Kidney Int Suppl (2011). 2013; 3(1): 19–62, doi: 10.1038/kisup.2012.64, indexed in Pubmed: 25018975.
5. Vidal-Petiot E, Courbebaisse M, Livrozet M, et al. Comparison of Cr-EDTA and Tc-DTPA for glomerular filtration rate measurement. J Nephrol. 2021; 34(3): 729–737, doi: 10.1007/s40620-020-00932-9, indexed in Pubmed: 33661505.
6. Hsu CY, Bansal N. Measured GFR as "gold standard"— all that glitters is not gold? Clin J Am Soc Nephrol. 2011; 6(8): 1813–1814, doi: 10.2215/CJN.06040611, indexed in Pubmed: 21784836.
7. Fleming JS, Zivanovic MA, Blake GM, et al. British Nuclear Medicine Society. Guidelines for the measurement of glomerular filtration rate using plasma sampling. Nucl Med Commun. 2004; 25(8): 759–769, doi: 10.1097/01.mnm.0000136715.71820.4a, indexed in Pubmed: 15266169.
8. Kumar M, Arora G, Damle NA, et al. Comparison between Two-sample Method with Tc-diethylenetriaminepentaacetic acid, Gates' Method and Estimated Glomerular Filtration Rate Values by Formula Based Methods in Healthy Kidney Donor Population. Indian J Nucl Med. 2017; 32(3): 188–193, doi: 10.4103/ijnm.IJNM_17_17, indexed in Pubmed: 28680201.
9. Rehling M, Møller ML, Thamdrup B, et al. Simultaneous measurement of renal clearance and plasma clearance of 99mTc-labelled diethylenetriaminepenta-acetate, 51Cr-labelled ethylenediaminetetra-acetate and inulin in man. Clin Sci (Lond). 1984; 66(5): 613–619, doi: 10.1042/cs0660613, indexed in Pubmed: 6423339.
10. Speeckaert MM, Seegmiller J, Glorieux G, et al. Measured glomerular filtration rate: the query for a workable golden standard technique. J Pers Med. 2021; 11(10), doi: 10.3390/jpm11100949, indexed in Pubmed: 34683089.
11. Waller DG, Keast CM, Fleming JS, et al. Measurement of glomerular filtration rate with technetium-99m DTPA: comparison of plasma clearance techniques. J Nucl Med. 1987; 28(3): 372–377, indexed in Pubmed: 3546626.
12. Brøchner-Mortensen J. Current status on assessment and measurement of glomerular filtration rate. Clin Physiol. 1985; 5(1): 1–17, doi: 10.1111/j.1475-097x.1985.tb00742.x, indexed in Pubmed: 3882316.
13. Gref MC, Karp KH. Single-sample 99mTc-diethylenetriamine penta-acetate plasma clearance in advanced renal failure by the mean sojourn time approach. Nucl Med Commun. 2009; 30(3): 202–205, doi: 10.1097/MNM.0b013e328315e0c6, indexed in Pubmed: 19262281.
14. Burniston M. Clinical Guideline for the measurment of glomerular filtration rate (GFR) using plasma sampling. Approved by the British Nuclear Medicine Society Professional Standards Committee. 2018. https://cdn.ymaws.com/www.bnms.org.uk/resource/resmgr/guidelines/bnms_gfr_guidelines_in_bnms_.pdf (19.02.2023).
15. Osman AO, Elmadani AE. Comparison of slope-intercept with single plasma sample methods in estimating glomerular filtration rate using radionuclides. Saudi J Kidney Dis Transpl. 2014; 25(2): 321–325, doi: 10.4103/1319-2442.128521, indexed in Pubmed: 24625998.
16. Fleming JS, Persaud L, Ralls K, et al. Quality control of two-sample GFR measurements using single-sample estimates. Nucl Med Commun. 2002; 23(4): 389, doi: 10.1097/00006231-200204000-00037.
17. Fleming JS, Persaud L, Zivanovic MA. A general equation for estimating glomerular filtration rate from a single plasma sample. Nucl Med Commun. 2005; 26(8): 743–748, doi: 10.1097/01.mnm.0000171783.18650.80, indexed in Pubmed: 16000995.
18. Delanaye P, Flamant M, Dubourg L, et al. Single- versus multiple-sample method to measure glomerular filtration rate. Nephrol Dial Transplant. 2018; 33(10): 1778–1785, doi: 10.1093/ndt/gfx345, indexed in Pubmed: 29319814.
19. Gaspari F, Guerini E, Perico N, et al. Glomerular filtration rate determined from a single plasma sample after intravenous iohexol injection: is it reliable? J Am Soc Nephrol. 1996; 7(12): 2689–2693, doi: 10.1681/ASN.V7122689, indexed in Pubmed: 8989750.
20. Mulligan JS, Blue PW, Hasbargen JA. Methods for measuring GFR with technetium-99m-DTPA: an analysis of several common methods. J Nucl Med. 1990; 31(7): 1211–1219, indexed in Pubmed: 2194005.
21. De Santo NG, Anastasio P, Cirillo M, et al. Measurement of glomerular filtration rate by the 99mTc-DTPA renogram is less precise than measured and predicted creatinine clearance. Nephron. 1999; 81(2): 136–140, doi: 10.1159/000045268, indexed in Pubmed: 9933747.
22. Galli G, Rufini V, Vellante C, et al. Estimation of glomerular filtration rate with 99Tc(m)-DTPA: a comparative assessment of simplified methods. Nucl Med Commun. 1997; 18(7): 634–641, doi: 10.1097/00006231-199707000-00007, indexed in Pubmed: 9342101.
23. Russell CD, Dubovsky EV, Russell CD, et al. Measurement of glomerular filtration rate: single injection plasma clearance method without urine collection. J Nucl Med. 1985; 26(11): 1243–1247, indexed in Pubmed: 3903074.
24. Dias AH, Pintão S, Almeida P, et al. Comparison of GFR calculation methods: MDRD and CKD-EPI vs. (99m)Tc-DTPA tracer clearance rates. Scand J Clin Lab Invest. 2013; 73(4): 334–338, doi: 10.3109/00365513.2013.780663, indexed in Pubmed: 23586782.