10.5152/turkjnephrol.2020.3803

Original Article

Turkish Journal of Nephrology

Comparison of GFR Values Measured with Different Methods and the Relative Renal Functions in Patients with Proven or Suspected Obstructive Uropathy

Fadime Demir[1], Tansel Ansal Balcı[2], Fikri Selçuk Şimşek[2], Mustafa Demir[3]

[1]Department of Nuclear Medicine, Tokat Gaziosmanpaşa University School of Medicine, Tokat, Turkey
[2]Department of Nuclear Medicine, Fırat University School of Medicine, Elazığ, Turkey
[3]Department of Nephrology, Fırat University School of Medicine, Elazığ, Turkey

Abstract

Objective: We compared the glomerular filtration rate (GFR) values as measured by the gamma camera and eGFR methods, calculated by the Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula in patients who underwent diethylenetriamine penta-acetic acid (DTPA) dynamic renal scintigraphy for suspected obstructive uropathy.
Materials and Methods: A total of 59 patients were included in this retrospective study. On the basis of the eGFR results, patients were divided into three groups; eGFR >90 mL min-1 (Group 1), 60-90 mL min-1 (Group 2), and <60 mL min-1 (Group 3). The groups were compared in terms of GFR measuring methods, percentage of reduction in relative renal function, and pathologic findings detected in radiological imaging methods.
Results: We found that eGFR values calculated by CKD-EPI formula were slightly more compatible with GFR values measured by the camera method compared with eGFR values calculated by MDRD formula (mean difference of -17 and -21 respectively, at Bland-Altman plot). We also showed that although there was no decrease in eGFR values, we could show relative function in any kidney under 30% by the scintigraphic method (in 14 patients).
Conclusion: The camera method can be used as an alternative for GFR measurement, but it should be noted that it may be slightly higher than the values calculated by the formula. In addition, it should be kept in mind that there may be a decrease in relative renal function values of the kidneys even if GFR values are normal in patients with obstructive uropathy.
Keywords: Dynamic renal scintigraphy, glomerular filtration rate, obstructive uropathy

Corresponding Author: Fadime Demir ✉ drfadimedemir@hotmail.com
Received: 18.02.2019 **Accepted:** 21.08.2019

Presented in: This study was presented at the 14th Congress of the Balkan Cities Association of Nephrology, Dialysis, Transplantation and Artificial Organs, September 20-23, 2018, Budva, Montenegro.

Cite this article as: Demir F, Balcı TA, Şimşek FS, Demir M. Comparison of GFR Values Measured with Different Methods and the Relative Renal Functions in Patients with Proven or Suspected Obstructive Uropathy. Turk J Nephrol 2020; 29(3): 190-5.

INTRODUCTION

Obstructive uropathy (OU) develops from a blockage in the urine drainage system. Obstruction can occur anywhere in the urinary tract, such as the kidney, ureter, and the bladder. As a result, urine is collected and flushed back into the kidneys, which may lead to damage to the renal calyces, renal pelvis, and ureter. Imaging modalities play an important role in the diagnosis of urinary tract diseases. The methods used often in renal imaging include ultrasound (USG), urography, dynamic renal scintigraphy (DRS), static scintigraphy, and computed tomography. DRS is a reliable test for functional assessment and determination of relative renal functions (RRFs) of each kidney in OU (1). RRF, expressed as a percent of total renal function, is important in the assessment and treatment of patients suffering from renal diseases (2). DRS can also determine the presence of obstruction and may differentiate between complete, severe, or partial obstruction (3).

Glomerular filtration rate (GFR) refers to the amount of filtrate generated by a kidney per unit of time; it is an important index used to evaluate renal function in clinical routines. Urinary clearance of inulin is considered the gold standard in the measurement of GFR, but it is a difficult substance to measure and is not reproducible for clinical practice. Other exogenous filtration markers are ethylenediaminetetraacetic acid (EDTA) or diethylenetriaminepentaacetic acid (DTPA). Determination of the plasma concentration of the injected radiotracer requires analysis of 99mTc DTPA levels in multiple blood samples; this is considered a reference method. The camera-based method, introduced by Gates, measures renal uptake of 99mTc DTPA without blood sampling and is a widely used method (4). In clinical practice, GFR is most often estimated from serum levels of endogenous filtration markers instead of being measured directly (eGFR). The most commonly used equations are the Modification of Diet in Renal Disease (MDRD) formula (5). In addition, there are equations for the estimation of creatinine, cystatin C, β2-microglobulin, and β-trace protein (6).

Our goal was to compare the GFR values, measured by the camera-based method, and the eGFR values, calculated by the MDRD formula, in patients who underwent DTPA DRS for suspected OU. We also aimed to compare the RRF with eGFR values to investigate whether assessment of patients with only GFR measurements is reliable.

MATERIALS AND METHODS

We retrospectively analyzed a total of 59 patients with proven or suspected OU, who were referred to the Nuclear Medicine Department of Fırat University hospital between January 2016 and March 2018 and underwent dynamic renal imaging.

The patients' serum creatinine, age, gender, and race information were used in the MDRD and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula to calculate the GFR value.

Based on the eGFR (calculated with MDRD and CKD-EPI formula) results, patients were divided into three groups: Group 1 eGFR >90 mL min^{-1}, group 2 60-90 mL min^{-1}, and group 3 <60 mL min^{-1}.

Main Points

- Evaluation of kidney functions with GFR is an indicator of the total function of both kidneys.
- GFR, measured by the camera-based method, gives higher GFR values compared to the eGFR methods obtained with the formulas of MDRD and CKD-EPI, and the difference is less visible with the eGFR values obtained with the CKD-EPI formula.
- Relative renal function is an indicator of the participation of each kidney in the total function of the kidney individually, especially in patients with obstructive pathologies, there may be a significant decrease in the function of the affected kidney compared to the other kidney, even without a significant decrease in the GFR value.
- RRF values calculated by scintigraphy in evaluation and follow-up continue to be an important parameter in patients with or suspected of obstructive uropathy.

A renal dynamic study with 99mTc DTPA was performed on all patients. All patients were instructed to drink 500-1000 mL of water for hydration approximately 30 minutes before the examination. After urination, a 5 mCi 99mTc DTPA intravenous injection was administered under a gamma camera (General Electric infinia 2, Israel). Dynamic kidney scintigraphy was initiated with the injection. The syringe was imaged before and after injection to determine the total injected dose. After entering the height and weight of the patient, the GFR was automatically calculated by Xeleris Software according to Gate's algorithm (7). RRF values were made using a hand-drawn bean-shaped renal region of interest (ROI) and a perirenal (for background extraction) ROI on the kidney (Figure 1). A value of 30% was used as a cut-off, which was assessed a significant hypofunction in the kidneys. The patients were evaluated in two categories: RRF >30% and ≤30% of any of their kidneys.

Statistical Analysis

Continuous variables are reported as median values and ranges, whereas categorical variables are reported as frequencies and percentages. Differences between the groups were assessed with Kruskal-Wallis test (continuous variables), chi-square test, and Fisher exact test (categorical variables). Bland-Altman analysis was used with R software to assess the degree of agreement between measurements. A value <0.05 was considered significant. All analyses were performed with the IBM Statistical Package for the Social Sciences 20.0 version (IBM SPSS Corp.; Armonk, NY, USA).

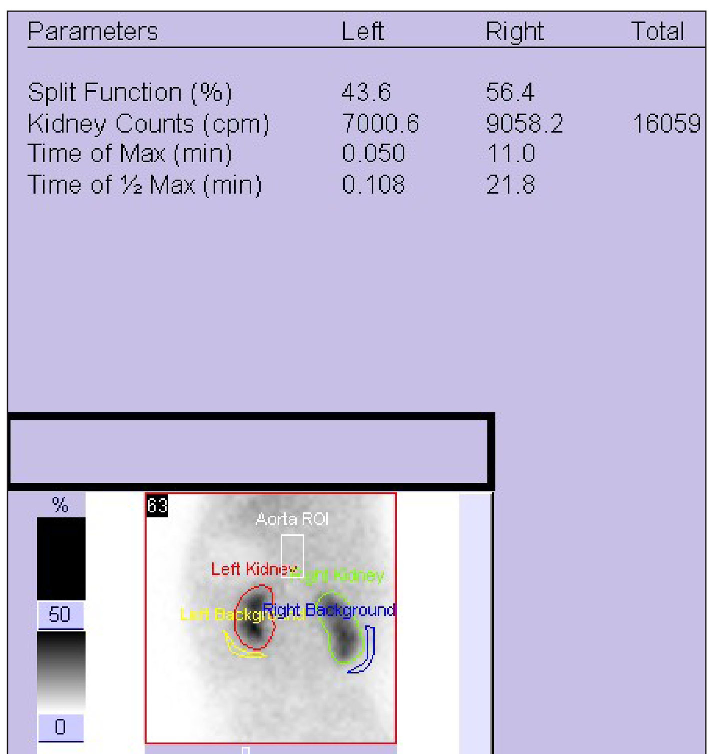

Figure 1. Regions of interest drawn in DTPA scintigraphy.

Turk J Nephrol 2020; 29(3): 190-5

RESULTS

Of the 59 patients included in the study, 26 were female, and 33 were male, with an average age of 48±13 years. There were 33 patients in Group 1, 18 in Group 2, and 8 in Group 3 for eGFR calculated by the MDRD formula. There were 36 patients in Group 1, 15 in Group 2, and 8 in Group 3 for eGFR calculated by the CKD-EPI formula. There was no significant difference between the groups in terms of gender and age (p>0.05). The general information and subgroup data of the study participants are summarized in Tables 1 and 2.

Bland-Altman plot for camera-based GFR and eGFR (calculated with MDRD formula) in all the patients showed a mean difference of -21.00 (95% confidence interval [CI]=[-13.10; -28.90]). The limit of agreement ranged from 38.42 to -80.42 (Figure 2).

Bland-Altman plot for camera-based GFR and eGFR (calculated with CKD-EPI formula) in all the patients showed a mean difference of -17.00 (95% confidence interval [CI]=[-11.52; -24.26]). The limit of agreement ranged from 30.0 to -65.77 (Figure 3).

The relative function of the kidneys was >30% in 35 (59%) patients, whereas the relative function of one of the kidneys was ≤30% in 24 (41%) patients.

Fourteen patients in Group 1, five in Group 2, and five in Group 3 had RRF values ≤30% for eGFR calculated by the MDRD formula. Furthermore, 14 patients in group 1, 6 patients in group 2, and 4 patients in group 3 had RRF values ≤30% for eGFR calculated by the CKD-EPI formula.

Renal radiological evaluations of patients are summarized in Table 3. Among the 24 patients who were evaluated as normal radiologically, the RRF was ≤30% (24% and 29%) in two patients, and eGFR was <60% (35%, 39%, and 54%) in three patients.

DISCUSSION

In our study, we found that eGFR values calculated by CKD-EPI formula were slightly more compatible with GFR values measured by the camera method than were eGFR values calculat-

Table 1. General information and subgroup data (calculated by MDRD)

	Total (n=59)	Group 1 (>90 mL min^{-1}) (n=33)	Group 2 (90-60 mL min^{-1}) (n=18)	Group 3 (<60 mL min^{-1}) (n=8)	p
Sex, n (%)	F=26 (44%) M=33 (66%)	F=16 (48%) M=17 (52%)	F=5 (28%) M=13 (72%)	F=5 (62.5%) M=3 (37.5%)	0.192
Age, years	48.27±13.31	46.21±11.44	48.44±13.44	56.37±18.43	0.149
BUN, mg dL^{-1}	30.92±0.37	28.96±9.6	36.72±9.35	60.12±34.18	<0.001**
Creatinine, mg dL^{-1}	0.92±0.37	0.7±0.14	1.05±0.16	1.5±0.52	<0.001**
Camera-based GFR, mL min^{-1}	72.80±28.31	80.97±24.19	73.80±26.62	36.86±21,75	0.001*
RRF of kidneys <30%	35 (59%)	19 (57.6%)	13 (72.2%)	3 (37.5%)	0.239
RRF of kidneys ≤30%	24 (41%)	14 (42.4%)	5 (27.8%)	5 (62.5%)	

*p<0.05
**p<0.001
F: female; M: male; BUN: blood urea nitrogen; GFR: glomerular filtration rate; RRF: relative renal function

Table 2. General information and subgroup (calculated by CKD-EPI)

	Total (n=59)	Group 1 (>90 mL min^{-1}) (n=36)	Group 2 (90-60 mL min^{-1}) (n=15)	Group 3 (<60 mL min^{-1}) (n=8)	p
Sex, n (%)	F=26 (44%) M=33 (66%)	F=16 (44%) M=20 (56%)	F=6 (40%) M=9 (60%)	F=4 (50%) M=4 (50%)	0.897
Age, years	48.27±13.31	44.52±11.22	52.20±11.93	57.75±18.63	0.012*
BUN, mg dL^{-1}	30.92±0.37	28.75±9.23	37.46±6.86	62.62±33.04	<0.001**
Creatinine, mg dL^{-1}	0.92±0.37	0.73±0.17	1.03±1.17	1.58±0.49	<0.001**
Camera-based GFR, mL min^{-1}	72.80±28.31	83.11±23.07	68.36±25.55	34.74±24.76	<0.001**
eGFR (calculated with CKD-EPI formula)	90.69±24.56	107.02±8.90	75.60±10.36	45.50±13.87	<0.001**
RRF of kidneys <30%	35 (59%)	22 (61%)	9 (60%)	4 (50%)	0.844
RRF of kidneys ≤30%	24 (41%)	14 (39%)	6 (40%)	4 (50%)	

*p<0.05
**p<0.001
F: female; M: male; BUN: blood urea nitrogen; GFR: glomerular filtration rate; RRF: relative renal function

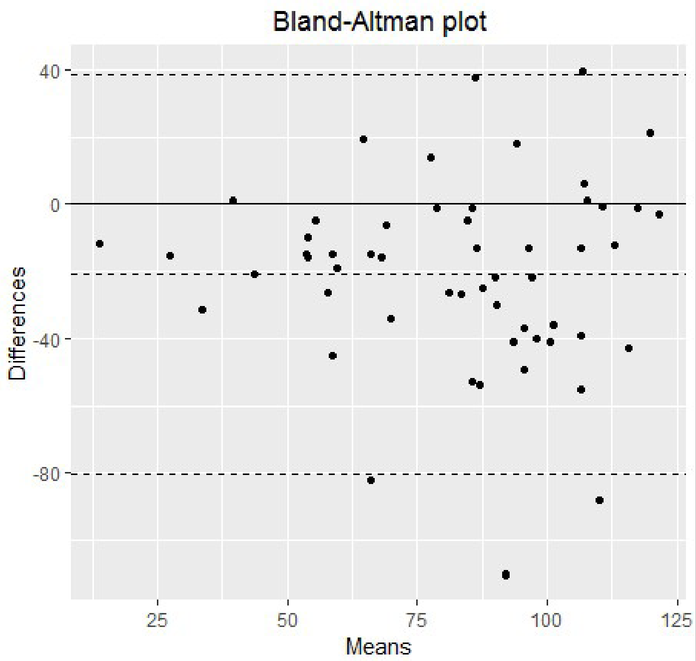

Figure 2. Comparisons of glomerular filtration rate estimated with camera-based GFR and eGFR (with MDRD) (Bland-Altman test).

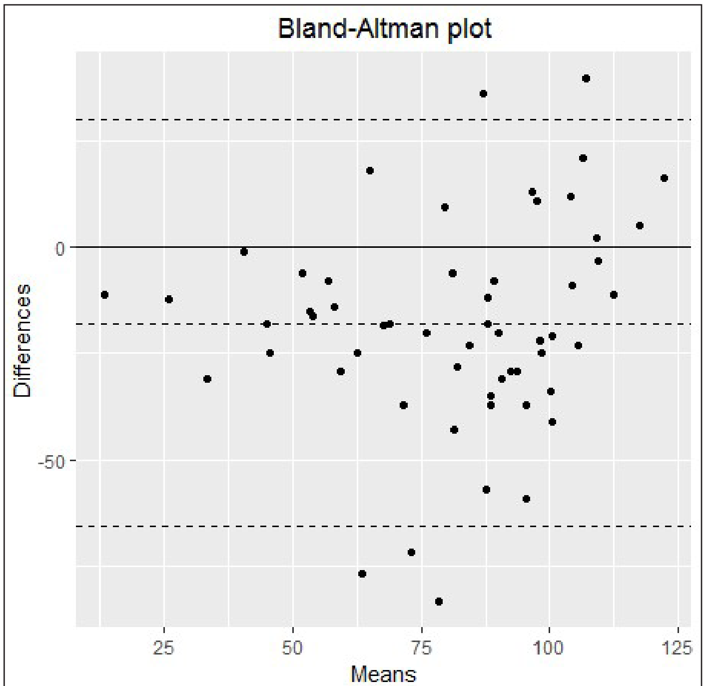

Figure 3. Comparisons of glomerular filtration rate estimated with camera-based GFR and eGFR (with CKD-EPI) (Bland-Altman test).

ed by the MDRD formula. We also demonstrated that although there was no decrease in eGFR values, we could show relative function in any kidney under 30% by the scintigraphic method.

In studies comparing the methods used in GFR measurement in the literature, there were various conclusions on the advantages and disadvantages of the tests (8-11).

Table 3. Radiological evaluation of 118 kidneys in 59 patients

	Right kidney	Left kidney
Normal	26 (44.1%)	22 (37.3%)
Stone	12 (20.3%)	10 (16.9%)
Hydronephrosis+stone	5 (8.5%)	3 (5.1%)
Hydronephrosis	5 (8.5%)	7 (11.9%)
Ureteropelvic junction obstruction	2 (3.4%)	3 (5.1%)
Pelviectasis	1 (1.7%)	5 (8.5%)
Atrophy	2 (3.4%)	3 (5.1%)
Without radiological assessment	6 (10.2%)	6 (10.2%)

Aydın et al. (8) made comparisons between single plasma sample method (SPSM) and double plasma sample method (DPSM), gamma camera method, creatinine clearance, prediction equation, and GFR measurements in the case of potential kidney donors with normal renal function. They reported that SPSM correlates well with DPSM. However, the Gates' 24-hour endogenous creatinine clearance method and the prediction equations (Cockcroft-Gault, MDRD) could not calculate GFR accurately. All these techniques tend to overestimate GFR and may result in errors in the management of potential kidney donors.

In a similar study, Hephzibah et al. (9) made a comparison of the GFR measured by the plasma sample technique, Cockroft-Gault method, and Gates' method in voluntary kidney donors and renal transplant recipients. The mean GFR (standard deviation) using the SPSM DPSM, camera method, and Cockroft-Gault method was 134.6 (25.9), 137.5 (42.4), 98.6 (15.9), and 83.5 (21.1), respectively. They reported that the SPSM correlates moderately well with the DPSM, but neither Gates' method nor Cockroft-Gault prediction equation could calculate GFR accurately.

In a study about the effect of Gates' 99mTc DTPA GFR, serum creatinine, and urea in the diagnosis of chronic renal failure conducted by Miftari et al. (10), 99mTc DTPA scintigraphy is a very sensitive method for the early detection of patients with chronic renal failure in cooperation with biochemical tests. The sensitivity of uremia and creatinemia for detection of renal failure was 83.33%, whereas the sensitivity of 99mTc DTPA GFR was 100%. The specificity of uremia and creatinemia was 63%, whereas the specificity of 99mTc DTPA GFR was 47.5%.

One of the studies in the literature that contributes to the understanding of our results is that by Huang et al. (11). In this study, reference value was accepted, and the GFR measured by double serum-sampled DTPA. They then compared it with the camera-based method, MDRD, and eGFR methods. They reported that in the group of patients with GFR values between 30 and 60 mL min^{-1}, the camera-based method was superior to the other methods. They concluded that it was a helpful method during follow-up of patients with stages 3a and 3b chronic renal failure.

The 99mTc Dimercaptosuccinic acid (^{99m}DMSA) is considered the most reliable method to measure RRF. Some of the studies in the literature have reported that DTPA scintigraphy gives results with a similar accuracy to that with DMSA in calculating RRF. Yalçın et al. (12) compared the results of 144 adult patients with DMSA and DTPA with different renal pathologies. They found a positive correlation between 99mTc DTPA and 99mTc DMSA results in calculating relative kidney function. Although the 99mTc DMSA is considered the most reliable method of calculating relative kidney function, the 99mTc DTPA is a good method in terms of evaluating GFR, renogram graphs, and relative renal function in the adult patients group. A similar result has been published in a study by Momin et al. (13) where they found that DTPA scintigraphy is preferred in cases in which both renogram and GFR measurements were necessary because of the significant positive correlation between the two methods.

In recent years, RRF measurements with conventional imaging methods have been evaluated in the literature. In one of these, Artunc et al. (14), GFR and RRF measurements using MRI in donor candidates showed similar results with DTPA measurements. Thus, they suggested that anatomical and functional evaluation could be performed together in MR imaging. In another study, Genseke et al. (15) compared MRI and DRS in children with OU and reported that DRS better identified situations requiring early intervention and therefore, should be the first preference.

In our study, we found a kidney with RRF values <30% in patients with GFR >90. This result suggested that the decrease in GFR values, which are indicative of total renal function, may not develop even though functional loss in any of the kidneys begins. This may be due to compensatory mechanisms.

The most significant disadvantage of this study was that the number of patients in some groups was low because of its being a retrospective study. We propose that future studies be conducted in larger groups for a more substantial contribution to the literature.

CONCLUSION

DTPA scintigraphy is one of the first methods that can be used to calculate RRF of the kidneys in patients with OU. DTPA scintigraphy for GFR measurement can be used as an alternative method. In addition, it should be kept in mind that even if the GFR values are normal in patients with OU, there may be a decrease in RRF values in the kidneys and only GFR should not be used to evaluate kidney function.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Fırat University (Approval Date: September 20, 2018; Approval Number: 15/12).

Informed Consent: Informed consent is not necessary due to the retrospective nature of this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - F.D.; Design - F.D.; Supervision - F.D.; Resource - F.D., F.S.Ş., T.A.B.; Materials - M.D.; Data Collection and/or Processing - F.D., T.A.B., F.S.Ş.; Analysis and/or Interpretation - F.D.; Literature Search - F.D., M.D.; Writing - F.D.; Critical Reviews - F.D.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Genseke P, Rogasch JMM, Steffen IG, Neumann G, Apostolova I, Ruf J, et al. Detection of obstructive uropathy and assessment of differential renal function using two functional magnetic resonance urography tools. Nuklearmedizin 2017; 1: 39-46. [Crossref]
2. Momin MA, Abdullah MNA, Reza MS. Comparison of relative renal functions calculated with 99mTc-DTPA and 99mTc-DMSA for kidney patients of wide age ranges. Phys Med 2018; 45: 99-105. [Crossref]
3. Hadzhiyska V, Kostadinova I, Demirev A. Is there an advantage in performing a combined examination: Diuretic renal scintigraphy and low dose computed tomography compared to the separate use of these methods in urolithiasis. Hell J Nucl Med 2015; 18: 90-92.
4. Assadi M, Eftekhari M, Hozhabrosadati M, Saghari M, Ebrahimi A, Nabipour I, et al. Comparison of methods for determination of glomerular filtration rate: Low and high-dose Tc-99m-DTPArenography, predicted creatinine clearance method, and plasma sample method. Int Urol Nephrol 2008; 40: 1059-65. [Crossref]
5. Garcia-Covarrubiasa L, Barragana J, Castroa I, Hernandeza K, Redingb A, Hinojosaa H, et al. Correlation of the glomerular filtration rate measured with the use of DTPA-Tc99m in live kidney donors with equations based on creatinine and cystatin C. Transplant Proc 2018; 50: 423-7. [Crossref]
6. Vart P, Grams ME. Measuring and assessing kidney function. Semin Nephrol 2016; 36: 262-72. [Crossref]
7. Gates GF. Split renal function testing using Tc-99m DTPA. A rapid technique for determining differential glomerular filtration. Clin Nucl Med 1983; 8: 400-7. [Crossref]
8. Aydın F, Güngör F, Cengiz AK, Tuncer M, Mahsereci E, Özdem S, et al. Comparison of glomerular filtration rate measurements with the two plasma sample and single plasma sample, gamma camera Gates, creatinine clearance, and prediction equation methods in potential kidney donors with normal renal function. Nucl Med Commun 2008; 29: 157-65. [Crossref]
9. Hephzibah J, Shanthly N, Oommen R. Comparison of glomerular filtration rate measured by plasma sample technique, Cockroft Gault method and Gates' method in voluntary kidney donors and renal transplant recipients. Indian J Nucl Med 2013; 28: 144-52. [Crossref]
10. Miftari R, Nura A, Topçiu-Shufta V, Miftari V, Murseli A, Haxhibeqiri V. Impact of Gate 99mTc DTPA GFR, serum creatinine and urea in diagnosis of patients with chronic kidney failure. Acta Inform Med 2017; 25: 99-102. [Crossref]
11. Huang Q, Chen Y, Zhang M, Wang S, Zhang W, Cai G, et al. Comparative evaluation of technetium-99m-diethylenetriaminepentaacetic acid renal dynamic imaging versus the Modification of Diet

in Renal Disease equation and the Chronic Kidney Disease Epidemiology Collaboration equation for the estimation of GFR. Int Urol Nephrol 2018; 50: 733-43. [Crossref]
12. Yalçın H, Özen A, Günay EC, Özaslan A, Özer C. Can Tc 99m DTPA be used in adult patients in evaluation of relative renal function measurement as the reference Tc 99m DMSA method. Mol Imaging Radionucl Ther 2011; 20: 14-8. [Crossref]
13. Momin MA, Abdullah MNA, Reza MS. Comparison of relative renal functions calculated with 99mTc-DTPA and 99mTc-DMSA for kidney patients of wide age ranges. Phys Med 2018; 45: 99-105. [Crossref]
14. Artunc F, Yildiz S, Rossi C, Boss A, Dittmann H, Schlemmer HP, et al. Simultaneous evaluation of renal morphology and function in live kidney donors using dynamic magnetic resonance imaging. Nephrol Dial Transplant 2010; 25: 1986-91. [Crossref]
15. Genseke P, Rogasch JM, Steffen IG, Neumann G, Apostolova I, Ruf J, et al. Detection of obstructive uropathy and assessment of differential renal function using two functional magnetic resonance urography tools. A comparison with diuretic renal scintigraphy in infants and children. Nuklearmedizin 2017; 56: 39-46. [Crossref]