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Is there a correlation between kidney size in ultrasonography and split renal function in ^{99m}tc-dmsa renal scintigraphy

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Abstract
Objective: The purpose of this study was to determine the correlation between kidney sizes in ultrasonography (USG) and split renal function in ^{99m}Technetium Dimercapto Succinic Acid (^{99m}Tc-DMSA) renal scintigraphy (RS) in adults, and find out cut off values of many kidney sizes to detect decreased renal function.
Material and Methods: A total of 133 patients who had ultrasonography of kidney and decreased split renal function in ^{99m}Tc--DMSA were enrolled in this retrospective study. Patients were divided into two groups: Group 1 (G1) had no previous urologic operations, or no information about the kidney size, previously. Group 2 (G2) had a urologic operation at related kidney. The correlation between longitudinal size, transvers size, axial size, and split renal function of related kidney in ^{99m}Tc--DMSA was applied. Kidney size cut-off values were calculated to detect <30%, <20%, and <10% split renal functions, respectively.
Results: There was a linear correlation between longitudinal kidney size in USG and split renal function in ^{99m}Tc--DMSA in G1 (p=0.001), but there wasn't in G2 (p=0.125). The longitudinal kidney size cut-off value to detect <30%, <20%, and <10% split renal functions in ^{99m}Tc--DMSA were calculated as 71 mm (with 80% sensitivity), 66 mm (with 90% sensitivity), and 56 mm (with 90% sensitivity) for G1, and 95mm(with 80% sensitivity), 82mm(with 90% sensitivity), and 52mm(with 90% sensitivity) for G2, respectively.
Conclusions: There is a correlation between kidney size and split renal function in ^{99m}Tc-DMSA-RS, and detected cut-off values will help to decide about split renal function without need for ^{99m}Tc-DMSA-RS.

Keywords: kidney, ultrasonography, ^{99m}technetium Dimercapto succinic acid renal scintigraphy

1. Introduction

In many reports, the gold standard method of renal cortical imaging is reported to be ^{99m}Technetium Dimercapto Succinic Acid Renal Scintigraphy (^{99m}Tc-DMSA-RS). This method is highly used at initial diagnoses and follows up of many urologic conditions like detection of decreased split renal function, diagnoses of acute pyelonephritis, identification of renal scarring, ectopic kidney, solitary kidney, renal infarction, and horseshoe kidney [1, 2]. However, it has some disadvantages: radiation exposure is the main concern about the protocol, lengthy procedure time is another drawback, and need for sedation especially in children is a major limitation [3]. The initiation of the ALARA (as low as reasonable and available) principle in urologic radiology practice has been making us think about the minimal use of radiation based techniques. Dynamic magnetic resonance imaging (MRI) could be a choice for examining both renal anatomy and renal function without the use of radiation. Rohrschneider *et al*. reported a significant correlation between MRI and diuretic renal scintigraphy for morphology, excretion and split renal function [4]. Despite having no radiation, being a long lasting procedure, being an expensive method, and having need for sedation, MRI has many disadvantages as described for ^{99m}Tc-DMSA-RS.

The most used, easy reached, and cheaper technique without radiation seems to be ultrasonography (USG) of kidney for the evaluation of renal anatomy. Comparing USG and ^{99m}Tc-DMSA-RS, Grimart *et al*. reported 34 and 87 scarred renal unit detection in USG and ^{99m}Tc-DMSA-RS in children [3], respectively; Roebuck *et al*. reported low sensitivity of USG [5] for detection of renal scars; Hains *et al*. reported similar detection rates of scars with contrast enhanced USG (CEUSG) [6] in children.

In a routine USG of kidney, renal lengths are the main measurements. Especially in adults, kidney size may be an indicator of renal function. In the literature, there is no study comparing the kidney size and renal function in adults. In this study, we have two hypotheses: the first one is "there is a correlation between kidney size in USG and split renal function in ^{99m}Tc-DMSA-RS in adults", and the second one is "there is a cut off value for kidney size to detect decreased renal function".

2. Materials and Methods

The ethical acceptance of this study was approved by our Institute's Ethical Committee, and the study is followed by ethical standards described in Helsinky Declaration Statement.

Between January 2010 and December 2017, a total of 180 men who had ultrasonography of kidney (USG) and decreased split renal function in ^{99m}Technetium Dimercapto

Succinic Acid Renal Scintigraphy (^{99m}Tc--DMSA) enrolled in this retrospective study (prospectively collected data reviewed retrospectively). The indications for USG were pain at related side, and previous urologic operations. The indications for ^{99m}Tc--DMSA were smaller kidney size in USG and previous urologic operations. There was no exclusion criterion for USG or ^{99m}Tc--DMSA.

Forty-seven patients were excluded from study due to excessive incomplete information examined for the formation of this study. Patients were divided into two groups: Group 1 (G1) had no previous urologic operations, or no information about the kidney size, previously. Group 2 (G2) had a urologic operation at related kidney. Additionally, patients in G2 were divided into 8 groups: G2a had neprolithotomy (NL), G2b had ureterolithotomy (UL), G2c had partial nephrectomy, G2d had percutaneous nephrolithtotomy (PNL), G2e had pyeloplasty, G2f had ureteroneocycostomy, G2g had kidney repair after trauma, G2h had pyelolithotomy.

The correlation between longitudinal size, transvers size, axial size, and split renal function of related kidney in ^{99m}Tc--DMSA was applied. Longitudinal, transvers, and axial kidney size cut-off values were calculated to detect <30%, <20%, and <10% split renal functions, respectively.

2.1. USG Imaging Protocol

All the examinations were performed with a 2-to 5-MHz convex transducer connected to US systems with the same brand (General Electric, LOGIQ 9, GE Healthcare, Milwaukee, WI). Renal measurements were made for each kidney in the supine position and, if possible, during deep inspiration. For all the cases, maximal values on transverse image for transverse size (transvers size) and on longitudinal image for craniocaudal (longitudinal size) and anteroposterior (axial size) sizes were noted.

2.2. ^{99m}Tc--DMSA Imaging Protocol

All ^{99m}Tc--DMSA scans were performed in a standardized protocol. Each scintigraphy was interpreted by one nuclear medicine specialist, who was unaware of the US results. All patients were injected with 37-111 MBq of the radiopharmaceutical and static images were acquired using a dual detector gamma camera (NM/CT670; GE Healthcare, Pittsburgh, PA) with a high-resolution, 256 × 256 matrix, low-energy collimator after 4 h in the anterior, posterior, left and right posterior oblique projections (250 kcounts/view or 5 min/view). Relative renal function was calculated using the geometric mean counts of the anterior and posterior images with background correction made by drawing a perirenal background around each kidney by a nuclear medicine physician.

2.3. Statistical Analysis

Statistical analysis was done using Statistical Package for Social Sciences 20.0 Software (SPSS 20.0 for MAC). Descriptive statistics of nominal samples were expressed with numbers and percentiles. Descriptive statistics of scale samples were expressed as mean±standard deviation (minimum-maximum). Shapiro-Wilk, Kurtosis, and Skewness Tests were used to assess the variables' normalization. Pearson Correlation Test was used to correlate two scale samples. ROC curve was used to detect kidney size cut-off values. Probability of p<0.05 was accepted as statistically significant.

3. Results

Finally, a total of 133 patients were included in this study. G1 and 2 included 90 and 43 patients. There were 23, 3, 2, 3, 7, 3, 1, and 1 patients in G2a, b, c, d, e, f, g, and h, respectively. The mean patient age was 21.16±5.20 (ranging 19-43), and 23.55±5.44 (19-40) years in G1 and 2, respectively. The effected renal unit was right kidney in 44(48.9%) and left kidney in 46(51.1%) patients in G1. For G2, the effected unit was right kidney in 20(46.5%) and left kidney in 23(53.5%) patients. The mean kidney size was 76.38±18.76 (20-110) millimeter (mm) in longitudinal axis, 34.25±10.31 (19-52) mm in transvers axis, and 30.6±5.81 (22-38) mm in axial axis in G1, respectively. The mean kidney size was 99.25±31.01 (11-150) mm in longitudinal axis, 46.35±15.22 (6-100) mm in transvers axis, and 25.0±15.03 (3-45) mm in axial axis in G2, respectively. In detail, the mean kidney size in longitudinal axis was 96.9±23.92(49-140)mm, 55.66±39.14(11-84)mm, 58.5±4.28(55-62)mm, 124.66±10.78(117-137)mm, 129.0±16.05(112-150)mm, 105.33±25.73(89-135)mm, 80mm (only 1 patient), and 40mm (only 1 patient) in G2a,b,c,d,e, f, g, and h, respectively. There was no hydronephrosis in 79(87.9%) and 15(34.9%) patients in G1 and G2, respectively. There was no parenchymal thinning in 73(81.1%) and 21(48.8%) patients in G1 and G2, respectively (Table 1).

The mean split renal function in ^{99m}Tc--DMSA was 22%±10.97% (0%-39%) and 27.11%±11.0% (0%-54%) for G1 and G2, respectively. In detail, the mean split renal function was 23.04%±10.51% (0%-43%), 25.06%±8.5% (16%-32%), 27%±11.31% (19%-35%), 33.66%±3.21% (30%-36%), 34.42%±10.19% (19%-51%), 36.33%±17.03% (20%-54%), 25% (only 1 patient), and 29% (only 1 patient) in G2a,b,c,d,e, f, g, and h, respectively.

There was a linear correlation between longitudinal kidney size in USG and split renal function in ^{99m}Tc--DMSA in G1 (p=0.001) (Fig. 1). For G2, there was no significant correlation between longitudinal kidney size in USG and split renal function in ^{99m}Tc--DMSA (p=0.125). In detail, there was no significant correlation between longitudinal kidney size in USG and split renal function in ^{99m}Tc--DMSA for G2a, and G2e (p=0.192 and 0.253, respectively) (Fig. 1). However, for G2b, c, d, f, g, and h, we couldn't calculated a correlation p value due to small sample size.

Looking for transvers axis kidney size, there was a linear correlation between transvers kidney size in USG and split renal function in ^{99m}Tc--DMSA in G1 (p=0.001) (Fig. 1). For G2, there was no significant correlation between transvers kidney size in USG and split renal function in ^{99m}Tc--DMSA (p=0.125). In detail, there was a significant correlation between transvers kidney size in USG and split renal function in ^{99m}Tc--DMSA in G2a (p=0.001), but there was no significant correlation in G2e (p=0.686) (Fig. 1). However, for G2b, c, d, f, g, and h, we couldn't calculated a correlation p value due to small sample size.

Looking for axial axis kidney size, there was no correlation between axial kidney size in USG and split renal function in ^{99m}Tc--DMSA in G1 (p=0.747) (Fig. 1). For G2, we couldn't calculate a correlation p value due to small sample size.

The ROC curves were created for G1 and 2 (Fig. 2). Using the ROC curves, the longitudinal kidney size cut-off value to detect <30%, <20%, and <10% split renal functions in ^{99m}Tc--DMSA were calculated as 71 mm (with 80%

sensitivity), 66 mm (with 90% sensitivity), and 56 mm (with 90% sensitivity) for G1, and 95mm(with 80% sensitivity), 82mm (with 90% sensitivity), and 52 mm (with 90% sensitivity) for G2, respectively (Table 2).

The transvers kidney size cut-off value to detect <30%, <20%, and <10% split renal functions in ^{99m}Tc--DMSA were calculated as 31 mm (with 80% sensitivity), 30 mm (with 90% sensitivity), and 23 mm (with 90% sensitivity) for G1, respectively. For G2, the transvers kidney size cut-off value to detect <30%, <20% split renal functions were 41 mm (with 80% sensitivity), and 29 mm (with 80% sensitivity), respectively. However, we couldn't calculated a transvers kidney size cut off value for <10% split renal function due to missing information about size and function in G2 (Table 2).

The axial kidney size cut-off value to detect <30%, <20% split renal functions in ^{99m}Tc--DMSA were calculated as 26 mm (with 100% sensitivity), and 25 mm (with 100% sensitivity) for G1, respectively. We couldn't calculated an axial kidney size cut off value for <10% split renal function due to missing information about size and function in G1. For G2, the axial kidney size cut-off value to detect <30% split renal function was 16 mm (with 80% sensitivity). We couldn't calculated an axial kidney size cut off value for <20% and <10% split renal functions due to missing information about size and function in G2 (Table 2).

4. Discussion

We couldn't find any report including both the renal function in ^{99m}Tc-DMSA-RS and the kidney size in USG in the literature. Therefore, we think that our study will reveal useful results for clinical practice.

Deciding a simple nephrectomy in periphery hospitals may be difficult due to lack of some detailed laboratory tests. Indication for a simple nephrectomy is the inability to solve the related pathology using reconstructive methods in a nonfunctioning or poor functioning kidney. A poor or non-functioning kidney is mainly due to causes like calculi in kidney, congenital dysplasia, infection, vesicoureteral reflux, nephrosclerosis, or unknown causes. On the other side, simple nephrectomy of a functioning kidney may be applied to relieve severe and intractable pain, bleeding, hypertension, and persistent infection. Therefore, a simple and reachable laboratory test is essential for examining the renal function in periphery hospitals [7].

^{99m}Tc-DMSA-RS is the most sensitive diagnostic tool to detect renal parenchymal defects in urology practice from 1990s [8, 9]. According to European and North America guidelines, it provides the most reliable information about the renal parenchyma and split renal function [10]. Arnold *et al.* reported that that sensitivity of ^{99m}Tc-DMSA-RS scintigraphy in demonstrating renal scars was 85% and its specificity was 97% [11]. It is almost necessary to identify many urologic abnormalities. Focal scarring; acute pyelonephritis; renal shrinking after infection; renal congenitally abnormalities like horseshoe kidney, crossed fused renal ectopia, duplex kidney; confirmation of a non-functioning kidney as seen in multicystic dysplastic kidney are the some disorders for which the diagnoses are dependent to ^{99m}Tc-DMSA-RS [12, 13]. The high sensitivity of ^{99m}Tc-DMSA-RS for renal parenchyma is related to its metabolism. The radionuclide tracer ^{99m}Tc-DMSA conjoins to the plasma proteins, sail in blood, is cleared from plasma by tubular absorption, and retained by renal cortex. The uptake of renal parenchyma is also highly dependent of renal blood flow, glomerular filtration, and endocytosis in proximal tubules [10]. The ideal image acquisition is taken at 2-3 hours after the radionuclide tracer injection. Later images more than 4 hours are more accurate for calculation of split renal function [14]. Patient is positioned in supine as close as possible to the collimator. Anterior, posterior, oblique, and some additional images are taken to identify better kidney localization and split renal function. The small movements of the patient may cause motion artifacts [14]. So it is a difficult, long lasting, but a necessary technique for kidney disorders. The main drawback of this test is the radiation exposure, and this laboratory test is located in tertiary hospitals.

MRI is another technique to evaluate the renal and ureteral anatomy together with functioning. Rohrschneider *et al.* reported the most elaborate examination of MRI for kidney function in 2002 [4]. They compared the results of USG, dynamic MRI, and diuretic renal scintigraphy (DRS) using MAG3 in patients with congenitally urinary tract dilatation in children. They reported the superiority of MRI in morphological examination compared to USG. In dynamic analyze for differential renal function and urinary excretion, they reported that MRI yielded detailed information with strong agreement compared to DRS. However, the interpretation of the dynamic MRI needs a great professionalism, the procedure was difficult to apply, and it is a contrast medium dependent test. Cerwinka *et al.* compared the ^{99m}Tc-DMSA-RS and MRI for the identification of renal parenchymal defects and reported similar detection rates of scars after vesicoureteral reflux or acute pyelonephritis (APN). They also mentioned that MRI detected mild and moderate sized multiple defects, whereas ^{99m}Tc-DMSA-RS detected large and single defects [15]. Another reported point was the correlation between the split renal functions in MRI and ^{99m}Tc-DMSA-RS. The main drawbacks of the MRI were being a long lasting, difficult to interpret, sedation needed, expensive technique. It is also mainly used in children for renal pathologies. All these features make MRI to be located in tertiary hospitals as ^{99m}Tc-DMSA-RS. On the other side, the studies did not correlate the kidney size in MRI and the renal function in ^{99m}Tc-DMSA-RS.

Because of being cheap, radiation free, and easy available, USG is the commonly used technique in urology practice. The positive predictive value (PPV) of USG for detecting parenchymal scars was reported to be 64%-88% in literature [3]. Levart *et al.* reported that USG detected 100%, 79.2%, and 31.8% of severe, moderate, and mild renal parenchymal defects in DMSA, respectively [16]. Most of the studies in literature mentioned that the USG had lower sensitivity for detecting renal scars than ^{99m}Tc-DMSA-RS. Grimard *et al.* reported the negative predictive value (NPV) of USG was to be 77%, and mentioned that this value was lower than the ^{99m}Tc-DMSA-RS, either [3]. Bush *et al.* reported that USG had 41% sensitivity, 81% specificity, 81% NPV, and 19% false negative ratio for detecting scars in ^{99m}Tc-DMSA-RS [17]. However, these studies were designed for children diagnosed as VUR or febrile urinary tract infection.

In our study, we used the major and easy USG features for evaluation of our adult patients: kidney diameters in three dimensions. We compared the longitudinal, transvers, and axial kidney sizes to ^{99m}Tc-DMSA-RS split renal function results. We think our results will help the urologists in deciding the renal function in many hospitals especially in primary ones. In our study, we detected a strong correlation with kidney size and ^{99m}Tc-DMSA-RS split renal function especially when the patient had no previous urologic operation. On the other side, we found that some kidney size cut off values for detecting <30%, <20%, and <10% split renal functions. For example, longitudinal kidney size cut-off values for detecting <30%, <20%, and <10% split renal functions as 71 mm (with 80% sensitivity), 66 mm (with 90% sensitivity), and 56 mm (with 90% sensitivity) in primary patients, respectively. So, if the longitudinal kidney size was 56mm, you could easily say that the function was <10%, and decide an operation. We also detected cut-off values for transvers and axial kidney sizes, too.

5. Limitations

The major limitation of our study is the operator or observer dependent nature of two tests: USG and ^{99m}Tc-DMSA-RS. The second limitation was the patient sample size and retrospective nature of the study. Randomized controlled studies with more patients will reveal better results.

6. Tables and Figures

Table 1: Analysis of kidney size and split renal function of each group.

	Longitudinal Kidney Size (mm)	Transvers Kidney Size (mm)	Axial Kidney Size (mm)	Split Renal Function (%)
Group 1	76.38±18.76 (20-110)	34.25±10.31 (19-52)	30.6±5.81 (22-38)	22%±10.97% (0%-39%)
Group 2	99.25±31.01 (11-150)	46.35±15.22 (6-100)	25.0±15.03 (3-45)	27.11%±11.0% (0%-54%)
Group 2a	96.9±23.92 (49-140)			23.04%±10.51% (0%-43%)
Group 2b	55.66±39.14 (11-84)			25.06%±8.5% (16%-32%)
Group 2c	58.5±4.28 (55-62)			27%±11.31% (19%-35%)
Group 2d	124.66±10.78 (117-137)			33.66%±3.21% (30%-36%)
Group 2e	129.0±16.05 (112-150)			34.42%±10.19% (19%-51%)
Group 2f	105.33±25.73 (89-135)			36.33%±17.03% (20%-54%)
Group 2g	80 (only 1 patient)			25% (only 1 patient)
Group 2h	40 (only 1 patient)			29% (only 1 patient)

Table 2: Statistical evaluation of renal size in each group to detect <30%, <20%, and <10% split renal function in ^{99m}Tc--DMSA.

		Longitudinal Kidney Size Cut-Off (mm)	Transvers Kidney Size Cut-Off (mm)	Axial Kidney Size Cut-Off (mm)
To detect <30% split renal function	Group 1	71mm(with 80% sensitivity)	31mm(with 80% sensitivity)	26mm(with 100% sensitivity)
	Group 2	95mm(with 80% sensitivity)	41mm(with 80% sensitivity)	16mm(with 80% sensitivity)
To detect <20% split renal function	Group 1	66mm(with 90% sensitivity)	30mm(with 90% sensitivity)	26mm(with 100% sensitivity)
	Group 2	82mm(with 90% sensitivity)	29mm(with 80% sensitivity)	Couldn't calculated
To detect <10% split renal function	Group 1	56mm(with 90% sensitivity)	23mm(with 90% sensitivity)	Couldn't calculated
	Group 2	52mm(with 90% sensitivity)	Couldn't calculated	Couldn't calculated

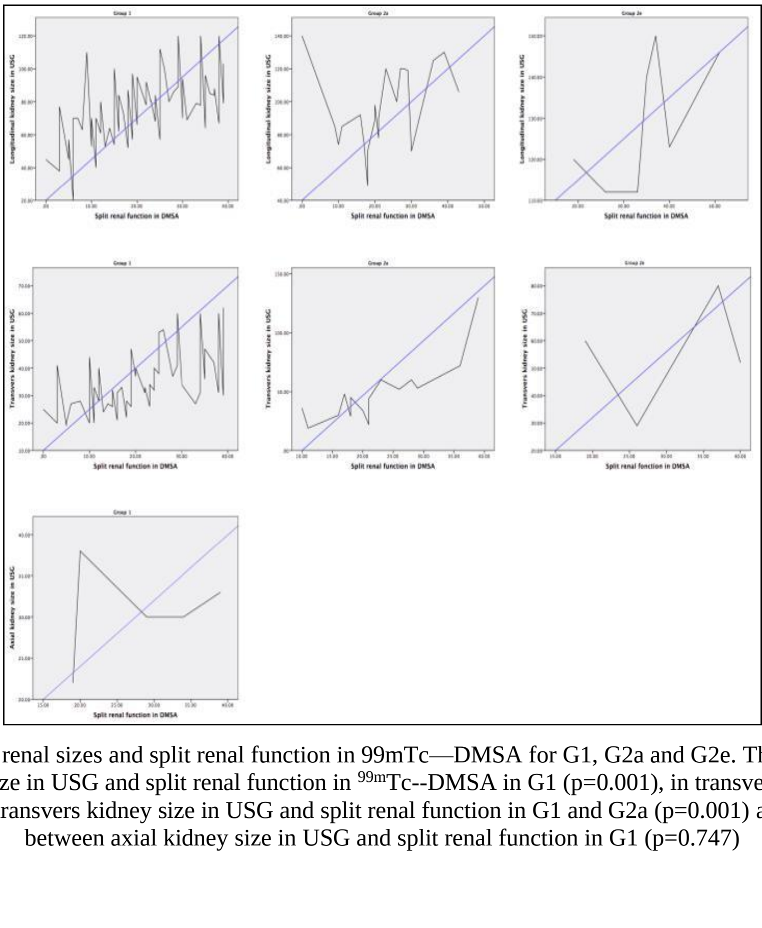

Fig 1: Correlation between renal sizes and split renal function in 99mTc—DMSA for G1, G2a and G2e. There was a linear correlation between longitudinal kidney size in USG and split renal function in ^{99m}Tc--DMSA in G1 (p=0.001), in transvers axis kidney size, there was a linear correlation between transvers kidney size in USG and split renal function in G1 and G2a (p=0.001) and there was no correlation between axial kidney size in USG and split renal function in G1 (p=0.747)

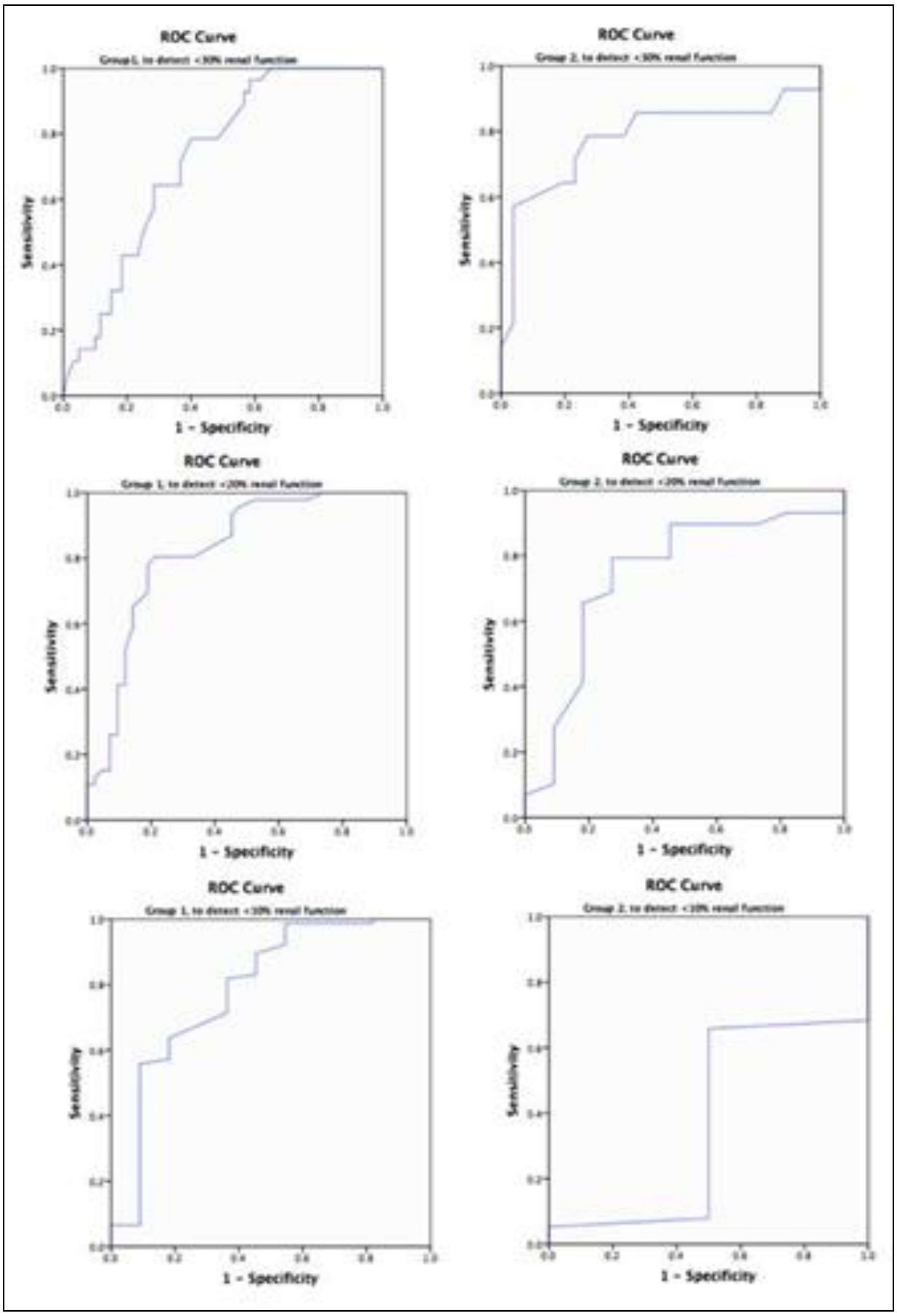

Fig 2: Comparison of ROC curves in G1 and G2.

7. Conclusion

There is a strong correlation between kidney size and split renal function in ^{99m}Tc-DMSA-RS, and detected cut-off values will help to decide about split renal function without need for ^{99m}Tc-DMSA-RS.

8. Conflict of Interests

None of the contributing authors have any conflicts of interest, including specific financial interests, relationships, and affiliations relevant to the subject matter or materials discussed in the manuscript.

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