Original article

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Comparison of shear wave elastography and dimercaptosuccinic acid renal cortical scintigraphy in pediatric patients

Ahmet Salan[a], Mehmet Sait Menzilcioglu[b], Ahmet Gokhan Guler[c] and Kamil Dogan[d]

Background Although it causes low-dose radiation exposure, dimercaptosuccinic acid (DMSA) renal cortical scintigraphy is the gold standard examination method in the noninvasive diagnosis of renal scar tissue (RST). Shear wave elastography (SWE) has recently come to the fore as a technique for measuring kidney stiffness in the examination of RST. The present study aims to compare DMSA and SWE tests to evaluate whether SWE can be used instead of DMSA as a test that does not cause radiation exposure in pediatric patients.

Methods In this prospective study, sonographic elastography was performed on pediatric patients with DMSA images. In the SWE examination, measurements were made from each kidney's upper, middle and lower parts. DMSA and elastography data were compared for the diagnosis of RST.

Results A total of 64 patients were included in the present study. There were 68.8% female ($n=44$) and 31.2% ($n=20$) male patients. There were 45 pediatric patients [Female 30 (66.7%), male 15 (33.3%)] in group 1 (pathological group) and 19 pediatric patients [Female 14 (73.7%), male 5 (26.3%)] in the control group. When DMSA data and SWE values were compared, it was found that elastography did not show a statistically significant performance in predicting renal scarring

Conclusion In the existing literature, various studies reported different values for the diagnosis of renal stiffness using SWE. Similar to some previous studies, the present study observed no significant correlations between DMSA and SWE. Thus, DMSA preserves its major role and effectiveness as an important predictor of RST in pediatric patients. *Nucl Med Commun* 44: 691–696 Copyright © 2023 Wolters Kluwer Health, Inc. All rights reserved.

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[a]Department of Nuclear Medicine, Faculty of Medicine, Sutcu Imam University, Kahramanmaras, [b]Department of Radiology, Faculty of Medicine, Gaziantep University, Gaziantep, [c]Department of Pediatric Surgery, Faculty of Medicine, Sutcu Imam University and [d]Department of Radiology, Faculty of Medicine, Kahramanmaras Sutcu Imam University, Kahramanmaras, Turkey

Correspondence to Ahmet Salan, Department of Nuclear Medicine, Faculty of Medicine, Sutcu Imam University, Kahramanmaras, Turkey
Tel: +90 543400043, fax: +90 3443003409; e-mail: asalan@hotmail.com

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Introduction

Dimercaptosuccinic acid static (DMSA) renal cortical scintigraphy is a sensitive and widely acknowledged method, particularly compared with renal ultrasonography (US), for the detection of cortical lesions, such as renal scars, without any contraindications [1,2]. In addition, the combination of DMSA scan and US contributes remarkably to the differentiation ability of lesions [1]. However, this method causes exposure to low-dose radiation exposure [2]. In contrast, shear wave elastography (SWE) helps quantitatively evaluate the stiffness of renal sequelae without radiation exposure [3,4]. SWE has been used to measure renal stiffness in numerous studies because of its superior performance in quantifying tissue stiffness, but different results have been reported [5]. The present study, measured lesion stiffness on DMSA scan and SWE to compare the performances of both methods in pediatric patients. This study aimed to assess the feasibility of elastography as a screening test that does not lead to any radiation exposure and to explore its potential as an alternative modality to DMSA scans. The findings will inform future studies on the same topic.

Methods

Ethics statements

The present study was approved by the local ethics committee in the August 2019 session (with decision number: 08 on 30 April 2019) and performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and all subsequent revisions. Written informed consent was obtained from the parents of all patients.

Study design and population

Pediatric patients who were referred for DMSA scan from the Pediatric Surgery Department of a tertiary hospital between 1 May 2019 and 15 February 2021, and whose DMSA scans were obtained were included in this prospective study. SWE was also performed in the following week. In a female patient, no scar tissue was observed in either kidney on DMSA scan. The right

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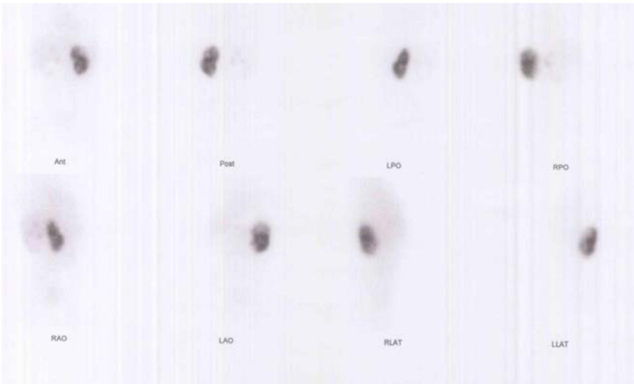
Fig. 1



Pathological DMSA scan of a 2-year-old female patient. DMSA, dimercaptosuccinic acid static.

kidney of this patient was smaller than normal, and the split renal function was 39%. Therefore, the patient was excluded from the study. Another male patient was diagnosed with hydronephrosis and atrophy based on DMSA scan. Split renal function values were 4% on the left side and, 96% on the right side. In this patient, SWE measurements could not be performed because of the markedly thinned parenchyma due to advanced hydronephrosis on US. Therefore, the patient was excluded. In other words, patients with intermediate findings like these two patients were excluded because they were considered as the intermediate group. Patients whose kidneys could not be visualized using DMSA scan because of possible renal agenesis were included. Patients with severely atrophic kidneys were also included if SWE values could be measured. On DMSA images, the left kidney was not visualized in two patients, probably due to agenesis. Statistical evaluation was performed based on the right kidneys of these two patients.

Imaging and data collection

Scintigraphic images were obtained using a dual-headed e.cam gamma camera (Siemens, Erlangen, Germany) equipped with a low-energy, all-purpose parallel-hole collimator. The patients were examined with the device within 2 and 3 h after the injection for DMSA scan. The dosages were adjusted in compliance with the EANM Dosimetry guidelines [6]. Only planar images were obtained in the anterior, posterior, bilateral lateral, and oblique positions when the patients were lying in the supine position.

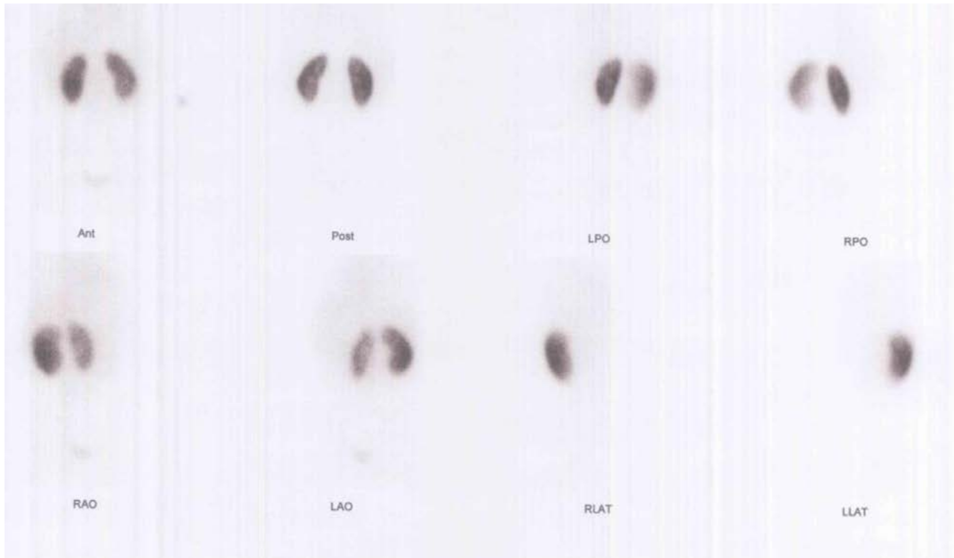
Patients with contour loss or decreased radiotracer uptake on DMSA scan images were included in the pathological group (group 1). An example of a DMSA scan evaluated as pathological is given in Fig. 1. Patients with normal radiotracer distribution in DMSA scan were included in the control group. An example of a normal DMSA scan is given in Fig. 2. Patients in the intermediate group were excluded. A follow-up DMSA scan was not requested by the pediatric surgeon who followed up with the patients. Additionally, radiation exposure needed to be limited. Therefore, a follow-up DMSA scan could not be performed. Evaluations were based on the initial scans only. The age of pediatric patients at the time of DMSA scan was considered. In group 1 and control group, the renal regions on the DMSA scans were classified based on the presence of lesions on the renal poles and the middle zone of the renal cortex. Split renal function was recorded in both kidneys. Patients with renal agenesis or severely atrophic, if any, were recorded. All elastographic examinations were performed by an experienced radiologist blinded to the DMSA scan reports and, the laboratory and clinical data of the patients. The kidney dimensions and parenchymal thickness were measured using a grayscale US device (Logiq E9 ultrasound system with an XDclear platform (General Electric, Boston, Massachusetts, USA).

SWE values in kilopascals (kPa) were also obtained for the renal poles and central regions using a special software installed on the same device. SWE was performed using a curved 2–5-MHz broadband transducer. As for the patient position, the position in which the kidney images were best obtained (decubitus or supine) was preferred. The body position of each patient was not recorded separately. First, the kidneys were visualized using grayscale US. In the long axis of each kidney, long-dimension measurements were made by connecting the extreme points. In addition, the parenchymal thickness was measured by including the cortex and medulla from the deep side in the mid-section short-axis image. The renal pyramids were specifically avoided when SWE was measured. The SWE measurements were performed only in the cortex, excluding the medulla. The measured diameter was standardized for each patient. For this purpose, the diameter was set to 6 mm. Measurements were obtained from both kidneys of each patient. Measurements were taken from three parts of each kidney (both poles and the mid-section), and the average value was used.

Statistical analysis

Continuous data are summarized as mean values and standard deviations, whereas categorical data are summarized as numbers and percentages. The chi-square (χ^2) test was used to evaluate two independent categorical groups, whereas the Student *t*-test was used to compare two independent non-categorical groups. A receiver operating characteristic (ROC) curve was used to measure the accuracy of US in the diagnosis of renal scar tissue (RST). According to this method, the main criteria for sensitivity, false positive (1-specificity = 0) value, and area under the curve (AUC) were set to 100%, 0, and 1, respectively. Additionally, the diagnostic value of the AUC was accepted at $P < 0.05$. The level of statistical significance was also set at $P < 0.05$. SPSS, version 25 (IBM

Fig. 2



Normal DMSA scintigraphy of a 7-year-old female patient. DMSA, dimercaptosuccinic acid static.

Corp., Armonk, New York, USA) was used to perform statistical analysis.

Results

In total, 64 pediatric patients who underwent DMSA scan were included. Patients were aged 1 - 18 years (mean age, 6.31 ± 3.7 years). There were 44 (68.8%) female patients and 20 (31.2%) male patients. In group 1, 30 (66.7%) of the 45 pediatric patients were female and 15 (33.3%) were male. Of 19 pediatric patients in the control group, 14 (73.7%) were female and 5 (26.3%) were male. The mean ages were 6.9 ± 3.8 and 5.4 ± 3.4 years in group 1 and the control group, respectively. The sex and age distributions were similar in both groups (P = 0.306 and P = 0.318, respectively).

When the DMSA images were examined, 70.3% (n = 45) of patients' kidneys were found to be pathological, whereas 19 (29.7%) were considered normal. When evaluated in terms of the left upper scar on the DMSA scan, 37 kidneys (57.8%) were normal, 25 (39.1%) had a scar, and 2 (3.1%) were not visualized. In the left middle region, 44 (68.9%) kidneys were normal, 18 (28.1%) had scars, and 2 (3.1%) kidneys were not visualized. When evaluated in terms of the left lower scar, 40 (62.5%) kidneys were normal, 22 (34.4%) had scars, and 2 (3.1%) were not visualized. When evaluated in terms of the presence of a right upper scar, 46 kidneys (71.9%) were evaluated as normal and 18 (28.1%) had a right upper scar. In the right middle region, 50 (78.1%) kidneys were normal and 14 (21.9%) had scarring. The right lower scar was normal in 50 (78.1%) and 14 (21.9%) kidneys, respectively. When the results of SWE measurements of the six regions of the kidneys, which were evaluated as pathological and normal according to DMSA scan, were compared, no statistically significant difference was found between group 1 and the control group (Table 1). The AUC, P values, and cutoff values for the predictive performance of the six different renal regions of elastography in diagnosing RST in both kidneys are shown in Table 2. The ROC curves of the predictive power of SWE for the RST are presented in Fig. 3. SWE measurements could not differentiate between pathological and normal patients (Fig. 4).

Discussion

DMSA scan remains the gold standard test for the non-invasive diagnosis of scar tissue in adults and children. It also facilitates the monitoring of renal contours at different positions and the calculation of differential renal functions [1]. Ultrasound elastography is used to detect tissue elasticity using various techniques including SWE [5]. SWE is a cost-effective, noninvasive, and rapid modality that enables the acquisition of two- or three-dimensional images. It measures the propagation velocity of sound waves sent to the tissue in meters per second in real-time. Then, the stiffness is quantified in kPa based on the calculated Young modulus values [4,7,8]. Similar to these studies, the present study measured the stiffness in kPa. However, the presence of RST was based on different criteria used in various comparative elastography studies. This makes it difficult to standardize interpretation and comparison. To overcome these difficulties, in the present study, the presence of RST (regardless of the cause) was based on DMSA scan findings.

Table 1 Comparison of patients' dimercaptosuccinic acid static results and shear wave elastography data

	DMSA	N	SWE Mean	SWE SD	*P*-value
Left kidney upper pole					0.633
	Pathological	39	21.33	10.62	
	Control group	18	22.74	10.56	
Left kidney central region	Pathological	39	20.11	10.19	0.671
	Control group	18	18.10	8.58	
Left kidney lower pole	Pathological	39	19.10	9.52	0.508
	Control group	18	21.10	13.18	
Right kidney upper pole	Pathological	39	17.67	7.91	0.144
	Control group	18	20.92	8.23	
Right kidney central region	Pathological	39	17.96	8.94	0.075
	Control group	18	21.33	10.63	
Right kidney lower pole	Pathological	39	22.74	10.56	0.474
	Control Group	18	20.11	10.19	

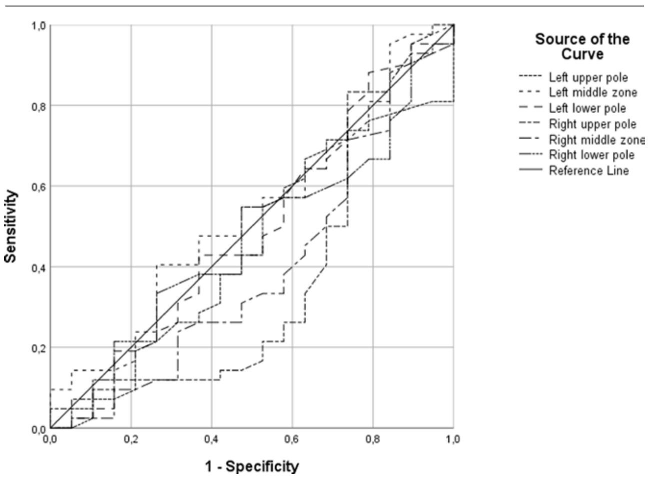
$P < 0.05$ is the level of statistical significance.
DMSA, dimercaptosuccinic acid static; SWE, shear wave elastography.

Table 2 The predictive performance of elastography in the diagnosis of renal scars

Test result variable(s)	Cut-off	Sens.	Spes.	AUC	95% CI	*P*-value
Left upper pole SWE	18.7	52.4	47.4	0.446	29.0–60.2	0.503
Left middle zone SWE	16.8	57.1	47.4	0.529	37.2–68.6	0.720
Left lower pole SWE	15.7	54.8	42.1	0.487	32.4–65.0	0.870
Right upper pole SWE	16.0	50.0	31.6	0.367	19.8–53.7	0.099
Right middle zone SWE	15.3	52.4	31.6	0.392	23.1–55.2	0.178
Right lower pole SWE	17.2	54.8	47.4	0.467	31.2–62.1	0.680

$P < 0.05$ is the level of statistical significance.
AUC, area under the curve; CI, confidence interval; DMSA, dimercaptosuccinic acid static; Sens., sensitivity; Spes., specificity; SWE, shear wave elastography.

Fig. 3



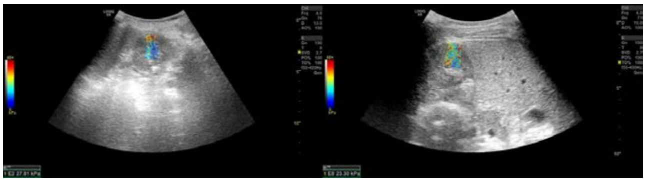
ROC curve of SWE values of right and left kidneys. ROC, receiver operating characteristic; SWE, shear wave elastography.

SWE has also been used in pediatric patients. However, in an SWE study, the diagnosis of RST in adult patients with chronic renal failure (CRF) was based on the estimated glomerular filtration rate (GFR) criterion [9]. In another study, not related to SWE but related to strain wave elastography, the presence of RST was indirectly based on the clinical diagnosis of CRF using certain criteria [5]. Similarly, a study comparing resistivity and strain indice in adult patients with CRF indirectly diagnosed the presence of scar tissue using GFR values [10]. In other words, the aforementioned studies did not directly diagnose the presence of scar tissue using DMSA scintigraphy. This indicates the novelty of the present study.

In addition, in another meta-analysis of the existing literature, the presence of scar tissue was not diagnosed using the gold standard test, the DMSA scan. Instead, a diagnosis was made in patients with CRF based on the clinical picture and laboratory results, and SWE was performed. The presence of RST was not confirmed by DMSA scan, and it has been reported that SWE alone is successful in the diagnosis of RST [4]. However, our findings did not support this result.

Leong *et al.* [11]. correlated serum urea, creatinine, and estimated GFR levels with SWE. Although they proposed a cutoff value with a higher accuracy rate for the differentiation of normal and pathological kidneys, the presence of scar tissue was not compared using DMSA scans. Similarly, another study on the evaluation of renal stiffness (and scar tissue) using two-dimensional SWE did not correlate with DMSA scans. In the present study, the renal medulla was excluded from the measurements to prevent renal anisotropy. SWE can also be used to monitor CRF [12]. Anisotropy is defined as the presence of different anatomical structures in the renal cortex and medulla [8]. A meta-analysis reported that a threshold value may provide higher accuracy in the diagnosis of RST [4]. However, although a threshold value was determined for

Fig. 4



SWE measurement obtained from the right kidney middle section of the patient whose DMSA image is shown in Fig. 1 on the left (from the pathological group) and SWE measurement obtained from the right kidney middle section of the patient whose DMSA image is shown in the right Fig. 2 (from the control group). DMSA, dimercaptosuccinic acid static; SWE, shear wave elastography.

SWE in our study, no statistically significant relationship was found. In a patient with severely reduced split renal function, SWE measurement could not be performed due to the thinness of the parenchyma. Therefore, it was excluded from the study and not included in the statistical evaluation (left kidney, 4%; right kidney, 96%). Since the left kidney had < 10% function and was paper-thin on US, it was considered non-functional [13]. Therefore, another important advantage of DMSA scan is that it provides quantitative data even in patients whose SWE cannot be performed.

A study comparing acoustic radiation force impulse (ARFI) elastography and DMSA scans found that the quantitative shear wave velocity (SWV) values were significantly higher in undamaged kidneys (with negative DMSA scan findings) than indamaged kidneys. It was also suggested that it could be helpful in the evaluation of scar tissue [14]. Another study observed a correlation between SWV values obtained using ARFI elastography in pediatric patients with CRF and estimated GFR values from DMSA scans. However, the estimated GFR values calculated for each kidney were determined using differential renal function obtained from a DMSA scan [15]. This highlights the critical role of DMSA scan used in our study. In addition, we evaluate that these two studies [14,15] comparing DMSA scintigraphy and elastography were designed, similar to our study, because of the harmful effects of radiation exposure in pediatric patients and the inability of conventional US to evaluate renal scarring. Another study demonstrated that the Young modulus values for the renal cortex obtained using real-time SWE following conventional US was higher in pediatric patients diagnosed with biopsy-verified CRF than in controls, and the cutoff values were calculated for each kidney [7]. The present study offers the possibility of evaluation without the costs and difficulties associated with a biopsy. Herein, SWE measurements were obtained by excluding the renal medulla and collecting system by considering anisotropy. Recently, a study was conducted on pediatric patients who developed unilateral vesicoureteral reflux and excluded the renal medulla in SWE measurements [3]. Additionally similar to the present study, SWE measurements in the renal upper and lower poles and the central region were compared with the relevant regions on DMSA scan, and, no follow-up scintigraphy was performed. Although the authors did not neglect anisotropy, they reported that SWE could not be integrated into current diagnostic algorithms. However, DMSA scan still occupies an important position in current diagnostic algorithms. Thus more comprehensive studies on DMSA scans should be conducted in the future, especially including follow-up scintigraphy, to provide further details on this topic. Another recent meta-analysis study on patients with CRF reported that renal SWV was generally lower in different elastography studies and that the results of various studies differed significantly [16]. Similar to a previous meta-analysis [4], it was suggested that renal elastography could not be considered a solid element of routine monitoring because it required technical improvements. We interpreted this claim to favor DMSA scan as being preferable to SWE. Although DMSA scintigraphy is the gold standard for differentiating scars from pyelonephritis, especially when combined with follow-up scintigraphy, we could not find any studies involving follow-up scintigraphy. Therefore, more comprehensive studies on DMSA scans should be conducted in the future, especially including follow-up scintigraphy, to provide further details on this topic.

The number of pediatric patients was low owing to the pandemic, the accuracy of the SWE data was not confirmed by biopsy, and follow-up scintigraphy could not be performed, which limits the study. On DMSA scans, renal contours are clear and interobserver differences are minimal. Compared with SWE, DMSA scans can be to locate scar tissue in the kidney and calculate split kidney function. As in the evaluation of children diagnosed with vesicoureteral reflux, the indication area for DMSA scanning is gradually expanding [17]. It is an inexpensive and easily applicable test for people of all ages, including newborns. In the detection of renal scar, it can give equivalent results to tests such as MRI, which are expensive and cannot be applied to claustrophobic patients [18].

In conclusion, although SWE, which has been used in many studies in the current literature, quantifies renal stiffness to some extent, a DMSA scan is more beneficial for detecting renal damage. Despite claims to the contrary, the present study statistically proved that DMSA scintigraphy is more effective than SWE for diagnosing RST. However, future studies involving follow-up scintigraphy may provide further information. In addition, DMSA scintigraphy has the power to expand its indications in the future.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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