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# Diagnostic accuracy of ultrasonography versus Tc-99m DMSA for detecting renal parenchymal damage in children with recurrent urinary tract infections and vesicoureteral reflux: Patient-level and regression-based analyses

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## ABSTRACT

**Objective:** We aimed to assess the diagnostic performance of renal ultrasonography (USG) compared with technetium-99m dimercaptosuccinic acid renal cortical scintigraphy (DMSA scintigraphy) in detecting renal parenchymal damage in paediatric patients with vesicoureteral reflux (VUR) and/or recurrent urinary tract infection (rUTI).

**Materials and Methods:** We retrospectively analysed 181 paediatric patients who underwent both renal USG and DMSA scintigraphy. Kidneys coded as absent were excluded. Diagnostic accuracy indices (sensitivity, specificity, PPV, NPV, accuracy, and AUC with 95% confidence intervals) were calculated at kidney and patient levels. Logistic regression was performed to evaluate the impact of age, gender, and renal uptake.

**Results:** In comparison to DMSA scintigraphy as the reference standard, USG identified parenchymal damage with a sensitivity of 50.9% for the left kidney and 44.7% for the right kidney, while demonstrating exceptional specificity (>99%). At the patient level (n=162), USG achieved a sensitivity of 49.4%, specificity of 100%, accuracy of 76%, and AUC of 0.75. DMSA scintigraphy identified significantly more kidneys with parenchymal injury than USG in all age cohorts. Logistic regression further indicated that advancing age and diminished renal uptake on DMSA scintigraphy were independent predictors of parenchymal damage, while sex was not significant.

**Conclusion:** Ultrasonography demonstrated excellent specificity but limited sensitivity compared with DMSA scintigraphy. These findings indicate that USG alone is inadequate for the early detection of renal parenchymal damage in children with VUR and/or rUTI. DMSA scintigraphy remains essential in this high-risk population.

**Keywords:** Pyelonephritis, Tc-99m DMSA, urinary tract infections, ultrasonography, vesicoureteral reflux

## Introduction

Urinary tract infection (UTI) is among the most common bacterial infections of childhood, while VUR predisposes to recurrent UTIs and renal damage (1,2). Both conditions can lead to long-term complications such as hypertension, renal scarring, and chronic kidney disease (3–7). The prompt identification and prevention of recurrent infections are crucial.

The incidence of UTIs varies by sex, age, and circumcision status, and is higher in females than in males (8,9). VUR has been reported in 16–23% of pediatric populations and is more prevalent in females (10). The risk of renal impairment increases with reflux grade and may approach 50% in children with grade IV–V VUR (10,11). Recurrent urinary tract infections (rUTIs) occur in 10–30% of children after an initial febrile episode, particularly in those with VUR or bladder-bowel dysfunction (12).

Imaging modalities are crucial for the evaluation and surveillance of children with rUTI and VUR. Ultrasonography is radiation-free, widely available, and recommended as an initial modality for assessing renal morphology and urinary tract obstruction (13). However, previous studies have shown that its sensitivity for renal scars and subtle parenchymal changes is limited (14,15). DMSA scintigraphy is a reference method for evaluating cortical integrity and differential renal function and can identify both acute pyelonephritis and chronic scarring (13,16).

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Prior research has shown that USG may miss a substantial proportion of parenchymal lesions compared with DMSA scintigraphy (14,15). Similar findings have been reported in children with febrile UTI despite normal renal USG results (17). Missed early lesions may progress to scarring (4,7), increasing the risk of hypertension and renal insufficiency in later life (3,5,6,16). Accordingly, guidelines emphasise complementary use of USG and DMSA scintigraphy, particularly in children with VUR and rUTI (2,12,13).

Therefore, the primary aim of this study was to compare the diagnostic performance of USG against Tc-99m DMSA scintigraphy for detecting renal parenchymal damage in children with VUR and/or recurrent UTI at both kidney and patient levels. The secondary aim was to evaluate whether age, sex, and differential renal uptake were independently associated with DMSA-defined parenchymal damage. We hypothesized that USG would show high specificity but limited sensitivity relative to DMSA scintigraphy, and that older age and lower renal uptake would be associated with parenchymal damage.

## Materials and Methods

### Study population

We retrospectively reviewed the records of 400 pediatricpatients who underwent DMSA scintigraphy at Goztepe Prof. Dr. Suleyman Yalcin City Hospital between May 2020 and January 2022. Patients under the age of 18 years with a diagnosis of VUR and/or rUTI who had both renal USG and DMSA scintigraphy performed within a 90-day interval were eligible. Patients who underwent DMSA scintigraphy for other indications were omitted. A total of 181 patients (117 girls, 64 boys; 174 left kidneys and 169 right kidneys) met the inclusion criteria and were analysed. Kidneys classified as “absent” (code=2) were excluded from the comparative analyses. The interval between USG and DMSA scintigraphy was up to 90 days, which may have allowed progression from acute pyelonephritis to chronic scarring. Thus, our analyses reflect overall parenchymal damage rather than acute versus chronic differentiation.

### USG evaluation

USG examinations were performed and reported by pediatricradiologists according to institutional protocols. For the purposes of this study, USG reports were retrospectively categorised as either normal (code=0) or abnormal (code =1) based on predefined parenchymal features: loss of corticomedullary differentiation, diffuse increased parenchymal echogenicity, cortical thinning or irregularity, renal asymmetry in size, and compensatory hypertrophy of the contralateral kidney. Simple, uncomplicated cysts were not considered abnormal findings.

### DMSA scintigraphy protocol

Tc-99m DMSA scintigraphy was performed in accordance with the European Association of Nuclear Medicine (EANM) guidelines (13). Administered activity was weight-adjusted (15–185 MBq). Planar anterior, posterior, and oblique views were obtained 2–3 hours post-injection using a Mediso Anyscan gamma camera (128×128 matrix, 500K counts). Single-photon emission computed tomography (SPECT) acquisition was performed after planar imaging. Patients were hydrated prior to imaging, and no sedation was required.

### Image interpretation

The DMSA scintigraphy results were independently evaluated by two experienced nuclear medicine physicians. The geometric mean of anterior and posterior counts was used to calculate differential renal function. Hypoactive cortical areas, contour irregularities, and focal defects were defined as parenchymal damage/scarring. For statistical comparisons, DMSA scintigraphy was used as the reference standard.

### Statistical analysis

All statistical analyses were performed using STATA version 18.0 (StataCorp LLC, College Station, TX, USA), IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA), and Python version 3.10. Diagnostic accuracy indices (sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, and area under the ROC curve (AUC) with 95% confidence intervals) were calculated separately for left and right kidneys and also at the patient level (defined as abnormal if either kidney was abnormal). For AUC analyses, p-values were computed assuming a null AUC of 0.5 (reflecting no discrimination). Logistic regression analysis was used to evaluate independent predictors of parenchymal damage on DMSA scintigraphy, including age, gender, and renal uptake. Odds ratios (OR) with 95% confidence intervals were reported. A two-sided $p < 0.05$ was considered statistically significant. Model assumptions were assessed with standard tests (Breusch–Pagan, White). A formal a priori power analysis was not performed due to the retrospective design. However, logistic regression models had adequate events per variable (EPV ≈ 26 at the patient level), exceeding the commonly recommended threshold of 10 for stable estimates. In addition to regression outputs (ESM1; Tables S1–S3), raw contingency tables are provided for kidney- and patient-level diagnostic accuracy (ESM1; Tables S4–S6).

## Results

### Study population

A total of 181 pediatricpatients (117 girls, 64 boys) with VUR and/or rUTI were included. After excluding kidneys coded as absent, 174 left kidneys and 169 right kidneys were analysed. At the patient level, paired USG and DMSA scintigraphy data were available for 162 children. Baseline demographics and functional characteristics are summarised in Table I.

### Diagnostic performance of USG (kidney-based analysis)

For the left kidney, USG identified parenchymal damage with a sensitivity of 50.9%, a specificity of 100%, accuracy of 85%, and an AUC of 0.76 (95% CI: 0.69–0.83; p<0.001). For the right kidney, sensitivity was 44.7%, specificity 99.2%, accuracy 84%, and AUC 0.72 (95% CI: 0.64–0.80; p<0.001). The reported p-values for ROC analyses reflect testing against a null hypothesis of AUC=0.5.

**Table I: Demographic and functional characteristics of the study population**

| Characteristic | Value |
|---|---|
| Total patients | 181 |
| Girls* | 117 (64.6) |
| Boys* | 64 (35.4) |
| Left kidneys analysed | 174 |
| Right kidneys analysed | 169 |
| Patient-level analyses | 162 |
| Age (years) | 8.8 (5.2–13.2)†<br>9.1±5.0‡ |
| Differential renal uptake (%) | |
| Left† | 51.0 (45.0–59.0) |
| Right† | 49.0 (41.0–55.0) |

**: n(%), †: median (IQR), ‡: mean ± SD*

**Table II: Diagnostic performance of USG compared with DMSA scintigraphy**

| Metric | Left kidney- Value | Right kidney - Value |
|---|---|---|
| Sensitivity* | 50.9 | 44.7 |
| Specificity* | 100.0 | 99.2 |
| Accuracy* | 85.0 | 84.0 |
| PPV* | 100.0 | 95.5 |
| NPV* | 82.3 | 82.3 |
| AUC | 0.76 | 0.72 |
| 95% CI | 0.69–0.83 | 0.64–0.80 |

**: %, **PPV:** Positive predictive value, **NPV:** Negative predictive value, **AUC:** Area under the ROC curve*

**Table III: Diagnostic performance of USG compared with DMSA scintigraphy at the patient level**

| Metric | Value |
|---|---|
| Sensitivity* | 49.4 |
| Specificity* | 100 |
| Accuracy* | 76 |
| PPV* | 100.0 |
| NPV* | 68.6 |
| AUC | 0.75 |
| 95% CI | 0.67–0.82 |

**: %, **PPV:** Positive predictive value, **NPV:** Negative predictive value, **AUC:** Area under the ROC curve*

These kidney-based results are presented in Table II, with ROC curves illustrated in Figure 1.

### Representative cases

Figure S1-3 in ESM 1 provide representative DMSA scintigraphy from three patients in whom USG failed to detect parenchymal defects that were clearly visible on scintigraphy, which emphasises the clinical value of DMSA scintigraphy in this population.

### Diagnostic performance at the patient level

When parenchymal damage was defined as abnormality in either kidney on DMSA scintigraphy, USG showed a sensitivity of 49.4%, a specificity of 100%, an accuracy of 76%, and an AUC of 0.75 (95% CI: 0.67–0.82; p<0.001) (Table III).

### Age-related distribution

The age distribution of normal and abnormal kidneys differed between modalities. Compared with USG, DMSA scintigraphy identified more kidneys with parenchymal damage across nearly all age groups, as illustrated in Figure S4 and Figure S5.

**Table IV: Logistic regression analysis for predictors of parenchymal damage**

| Variable | Left kidney | | | Right kidney | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | p | OR | 95% CI | p |
| Age (per year) | 1.12 | 1.03–1.22 | 0.005 | 1.10 | 1.01–1.21 | 0.020 |
| Gender | 1.50 | 0.66–3.39 | 0.330 | 1.10 | 0.49–2.44 | 0.820 |
| Renal uptake (%) | 0.93 | 0.89–0.96 | <0.001 | 0.94 | 0.90–0.97 | <0.001 |

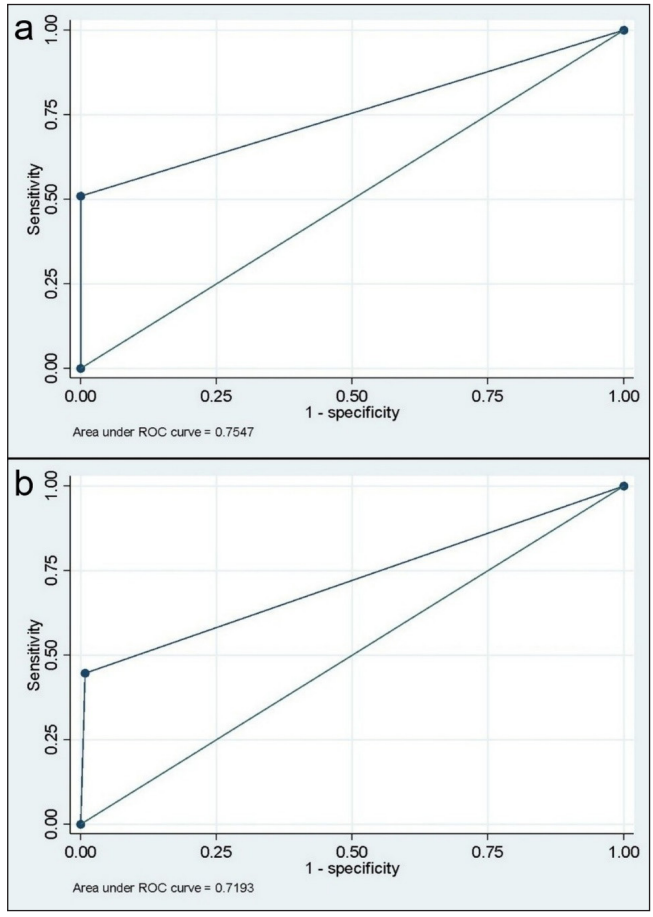



**Figure 1:** Receiver operating characteristic (ROC) curve of ultrasonography for detecting parenchymal damage in the (a) left and (b) right kidneys

### Predictors of parenchymal damage (logistic regression)

Multivariable logistic regression identified increasing age (OR 1.12 per year, 95% CI 1.05–1.23; p=0.005 for the left kidney; OR 1.10, 95% CI 1.04–1.20; p=0.02 for the right kidney) and decreasing renal uptake (OR 0.93 per 1% decrease, 95% CI 0.90–0.97; p<0.001 for the left kidney; OR 0.94, 95% CI 0.90–0.97; p<0.001 for the right kidney) as independent predictors of parenchymal damage on DMSA scintigraphy. Gender was not associated with damage (female vs male: OR 1.50, 95% CI 0.66–3.39; p=0.33 for the left kidney; OR 1.10, 95% CI 0.49–2.44; p=0.82 for the right kidney) (Table IV, Table S1 and Table S2). Re-estimation with heteroskedasticity-robust (HC3) standard errors did not materially change the effect estimates or statistical significance (Figure 2, Table S3, Figure S6).

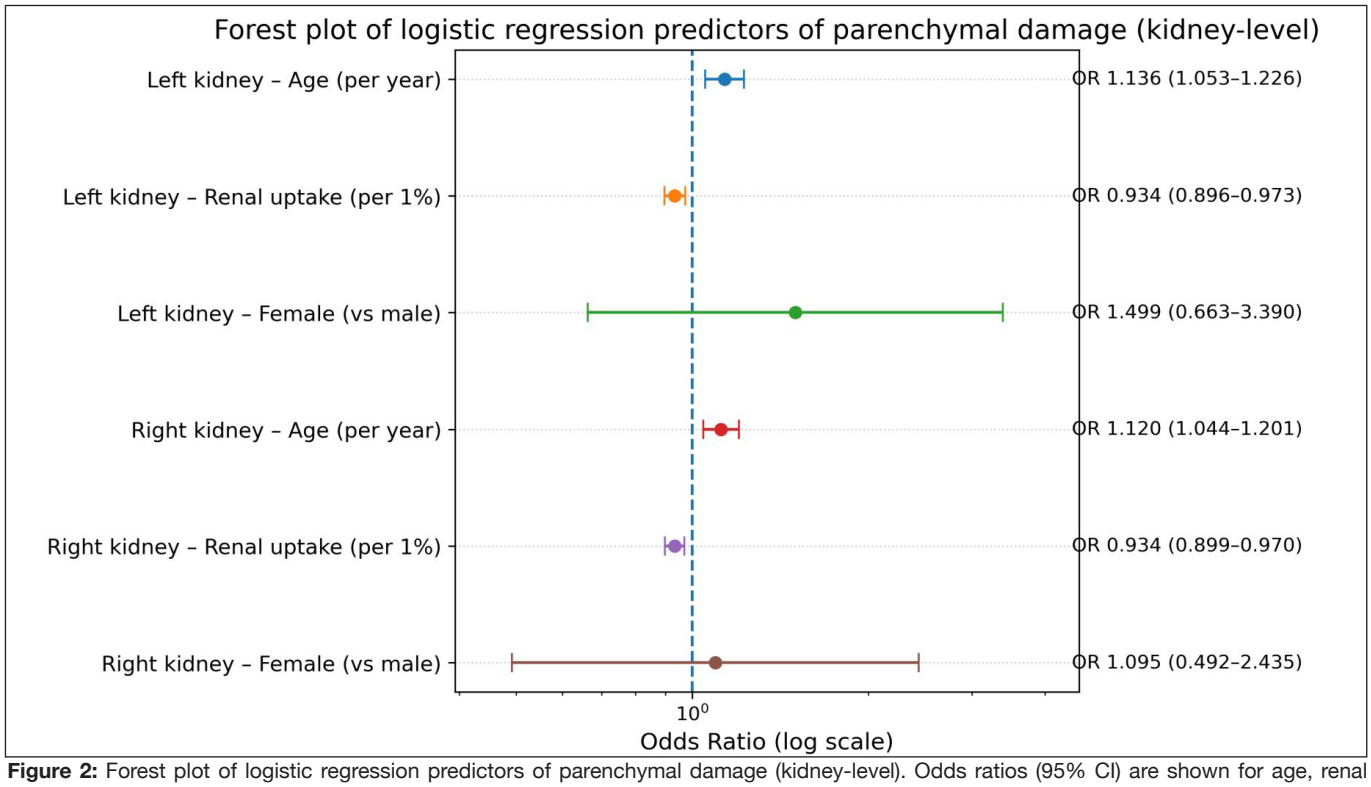



**Figure 2:** Forest plot of logistic regression predictors of parenchymal damage (kidney-level). Odds ratios (95% CI) are shown for age, renal uptake, and gender (female vs male). The dashed line represents the null value (OR = 1.0).

When stratified by age categories, DMSA scintigraphy positivity increased from 28.6% (<5 years) to 40.9% (5–10 years) and 57.5% (>10 years). The trend was statistically significant ($\chi^2 = 9.67$, p=0.008).

## Discussion

The present study reaffirms that renal USG, despite its excellent specificity (>99%), has limited sensitivity (≈45–51% at the kidney level and 49% at the patient level) compared with DMSA scintigraphy. Our incremental contribution is twofold: first, we quantify these performance gaps at the patient level, which better reflects clinical decision-making; and second, we identify age and lower differential renal uptake as independent predictors of parenchymal damage in multivariable models. Together, these findings provide confirmatory yet clinically useful evidence to guide imaging pathways in high-risk rUTI/VUR cohorts.

While DMSA should remain the reference test for confirming cortical damage in high-risk children, magnetic resonance imaging (MRI) can be considered in selected circumstances such as contraindications to radiopharmaceuticals, the need for multiparametric assessment, or equivocal DMSA scintigraphy. In clinical practice, a stepwise strategy can be applied: ultrasound serves as the initial screening tool, while DMSA scintigraphy or MRI can be performed when necessary for patients at high clinical risk or to confirm the renal scar, guiding treatment and follow-up decisions.

Cost and availability vary widely across settings; DMSA scintigraphy is generally accessible and relatively low-dose. Yet parental concerns about radiation are legitimate and should be addressed through shared decision-making and clear communication of benefits and risks. Our patient-level results caution against USG-only strategies in high-risk children, given the substantial false-negative rate.

Our logistic regression model confirmed that increasing age and decreasing renal uptake were independent predictors of parenchymal damage consistent with the progressive nature of scarring in children with VUR and rUTI.

Re-estimation with heteroskedasticity-robust standard errors did not materially change effect estimates or statistical significance.

The age effect was also supported by categorical analyses showing progressively increasing rates of DMSA scintigraphy positivity from early childhood to adolescence. The trend across age groups (<5, 5–10, >10 years) was statistically significant, strengthening the interpretation that parenchymal damage increases with age.

Our findings are consistent with previous literature. Hoberman et al. (14) reported that USG frequently misses acute pyelonephritis and renal scars, but DMSA scintigraphy clearly identifies them. Lavocat et al. (15) similarly showed the limited sensitivity of USG in early parenchymal damage (17). Research indicates that around 20% of children with febrile UTI exhibit kidney damage identified by DMSA scintigraphy, despite normal USG results. These data underscore the risk of relying on USG alone in high-risk children.

Unnoticed parenchymal defects can progress to scarring, and are associated with long-term outcomes such as hypertension and reduced kidney function (3-7,16). Guidelines recommend combining USG and DMSA scintigraphy for comprehensive evaluation (2,12,13).

While USG is useful for assessing renal size, asymmetry, hydronephrosis, and bladder abnormalities, it lacks sufficient sensitivity for the reliable detection of cortical scars (14,15,17); DMSA scintigraphy, particularly with SPECT acquisition, remains the gold standard (13,18–20).

Although treated as the reference standard here, DMSA scintigraphy is not infallible; timing relative to acute infection and inter-observer variability may affect interpretation. These caveats underscore the value of standardized acquisition/reading and, where feasible, correlation with clinical course.

This single-centre, retrospective study relied on existing USG reports, introducing potential operator variability and selection bias (21, 22). The USG–DMSA scintigraphy interval (≤90 days) may have allowed lesion evolution, and the lack of standardized timing for infections and imaging limited the ability to distinguish acute pyelonephritis from chronic scarring. Blinded re-review of USG images and a narrower imaging window were not feasible retrospectively. We also did not perform separate analyses of SPECT versus planar acquisitions or lesion counts (18–20). A priori power analysis was not conducted; however, the number of events per variable at the patient level (~26) exceeded conventional thresholds, supporting model stability. Finally, although radiation exposure remains a concern, the effective dose of DMSA scintigraphy is relatively low (~1 mSv), and recent studies suggest transient DNA effects without long-term oxidative stress (23,24). Generalisability to other settings warrants prospective validation.

## Limitations

Despite these limitations, our research confirms and expands upon previous findings. Using a large single-center cohort and rigorous statistical analyses, we present compelling evidence that, despite being highly specific, USG guidance fails to detect nearly half of children with kidney parenchymal damage. This highlights that DMSA scintigraphy serves an essential role in the evaluation and follow-up of pediatricpatients with VUR and recurrent urinary tract infections.

Our inclusion of patient-level diagnostic accuracy is clinically meaningful since management decisions are made for patients rather than individual kidneys. This analysis shows the practical limitations of USG as an independent test.

In conclusion, USG alone is insufficient for detecting renal parenchymal damage in pediatricpatients with VUR and/or rUTIs. DMSA scintigraphy is essential for accurate diagnosis, risk evaluation, and management guidance in this high-risk group of patients.

## Conclusion

In children with rUTI and/or VUR, renal USG demonstrated excellent specificity but insufficient sensitivity, with nearly half of affected patients missed if used as the sole imaging modality. Increasing age and low renal uptake emerged as independent predictors of parenchymal damage. DMSA scintigraphy is essential for definitive diagnosis, risk assessment, and long-term follow-up in children at risk of renal scarring.

### Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Medeniyet University Göztepe Training and Research Hospital (24/11/2021, reference number: 0597).

### Contribution of the authors

Study conception and design: MTT, Eİ, data collection: MTT, analysis and interpretation of results: MTT, Eİ. draft manuscript preparation: MTT, and All authors reviewed the results and approved the final version of the article.

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The authors declare the study received no funding.

### Conflict of interest

The authors declare that there is no conflict of interest.

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