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# Comparison of 99mTc-DMSA Renal Scan and Power Doppler Ultrasonography for the Detection of Acute Pyelonephritis and Vesicoureteral Reflux

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**Purpose:** Urinary tract infection (UTI) is one of the common infectious diseases in children. Several imaging modalities can be used to confirm the presence of acute pyelonephritis (APN). Among them the 99mTcdimercaptosuccinic acid renal scan (DMSA scan) is used as a gold standard for diagnosis. Ultrasonography technology is evolving. Therefore, in this study, we investigated the sensitivity and specificity of Power Doppler ultrasonography (PDU) compared to the results from the previous study.

**Methods:** There were 260 patients included in this study, aged between 1 and 12 months old. The patients were admitted to the Yeungnam University Medical Center between January 2008 and December 2015. All patients underwent both DMSA scan and PDU within 5days of admission. Voiding cystourethrography (VCUG) was performed in 195 patients with abnormal DMSA scan or PDU.

**Results:** The diagnostic sensitivity of APN using PDU was 45.5% and specificity was 85.5% in 260 patients following detection of a defect on DMSA scan that was defined as APN. The diagnostic sensitivity and specificity of PDU for VUR were 65.5 % and 60.1%, respectively. The diagnostic sensitivity and specificity of DMSA scan for VUR were 95.7% and 14.1%, respectively.

**Conclusion:** PDU has a high specificity but low sensitivity, so there are limitations in using it to replace a DMSA scan for the diagnosis of APN in children. DMSA scan and PDU have different sensitivity and specificity in diagnosis of VUR, respectively. Therefore, we suggest that the sensitivity and specificity of each test can be helpful in diagnosing APN and VUR when used in conjunction.

**Key words:** 99mTc-DMSA, Power Doppler Ultrasonography, Pyelonephritis, Vesicoureteral Reflux

## Introduction

Urinary tract infection (UTI) is one of the common bacterial infectious diseases in childhood. There are inherent difficulties in diagnosing infants because they frequently have nonspecific symptoms[1)]. Upper UTI in some infants can cause hypertension and chronic renal damage[2)]. Therefore, rapid diagnosis and treatment are critical.

Using a 99mTc-dimercaptosuccinic acid renal scan (DMSA scan), acute pyelonephritis (APN) can be diagnosed at the acute phase, and renal scarring can be diagnosed at 3-6 months following infection[3,4)]. However, DMSA scans

involve exposure to radiation as well as requiring intravenous drug administration and sedation. The use of computed tomography (CT) has a high sensitivity for APN diagnosis; however, it involves a high dose of radiation and requires administration of a contrast agent[5]. Therefore, a DMSA scan is preferred in clinical practice. Magnetic resonance imaging (MRI) can also be used to diagnose APN, but it is not suitable for practical clinical applications because of time consuming and high cost[6,7]. Power Doppler ultrasonography (PDU) is a noninvasive technique that can be used to monitor the size and shape of the kidney[8-10]. The presently used technique of color doppler ultrasonography can provide an image in color only when the speed of the blood flow is higher than a specific speed and does not expose a vessel adequately if the angle between the insonation beam and vessel is sharp or if the vessel is in a region at a distance from the transducer. PDU was developed to overcome these disadvantages. This technique displays color on the basis of the total strength of the Doppler signal, thus, making it easy to examine weak blood flow. In addition, interference from the angle is relatively small; therefore, PDU is more sensitive than color doppler ultrasonography[11].

About a decade ago, the author's hospital reported the sensitivity and specificity of PDU in the diagnosis of APN [12]. Ultrasonography technology is evolving. Therefore, in this study, we investigated the sensitivity and specificity of PDU compared to the results from the previous study and the patients with VUR.

## Material and methods

A total of 260 patients were included in this study, aged between 1 and 12 months old. The patients were admitted to the Yeungnam University Medical Center between January 2008 and December 2015 and diagnosed with a UTI for the first time. All colony-forming counts were higher than $5\times10^4$ in urine culture with suprapubic aspiration or catheterization. Blood samples were performed for all the patients before administration of antibiotics, including leukocyte counts, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and blood culture. Children with an underlying disease, including known congenital urogenital anomalies (e.g. renal agenesis, renal hypoplasia, renal dysplasia, polycystic kidneys, multicystic dysplastic kidneys and duplex ureters) were excluded from this study. All patients underwent both a DMSA scan and PDU after the fever subsided. The tests were performed within 5 days of admission.

DMSA scan images were obtained by intravenous injection of 111 MBq Tc-99mTc-DMSA and the kidneys were scanned with continuous rotation images after 3 hours. After correcting the background, left and right activity fractions were calculated for each kidney and an uptake of 45-55% of the total kidney activity was presumed normal. When the labeled DMSA showed one or more local or diffuse intake reductions in the kidney or an overall decrease in the enlarged kidney, it was judged to be abnormal. PDU images were obtained on both sides, in prone and supine positions using variable-frequency curved transducers on a LOGIQ7 ultrasound imaging system (General Electric Company). Gray-scale sonography was also performed, and PDU was judged to be abnormal when there was no or decreased flow in the kidney parenchyma compared with other areas of the same depth in the same kidney. VCUG was performed in 195 patients with suspected VUR following abnormal findings on the DMSA scan or PDU. Statistical analysis was performed using the Mann-Whitney test and the Fisher's exact test using SPSS version 22.0 (IBM).

## Results

Of the 260 patients included in the study, 191 were diagnosed with a cortical defect in their DMSA scan and were diagnosed with APN. Of the 191 APNs diagnosed, the majority, 137 (72%) were boys and 54 (28%) were girls ($P<0.05$). *Escherichia coli* (*E. coli*) was cultured in most of the patients (173, 91%). When we compared the patients with positive findings and those with negative findings in the DMSA scan, leukocyte counts, ESR, and CRP were significantly higher in the positive group (Table 1).

Of the 191 patients with a defect on their DMSA renal scan, there were 87 patients with PDU defects, and among 69 patients with a normal DMSA scan, 59 also showed normal findings in PDU. When the DMSA scan was used as the reference for APN, the diagnostic sensitivity of PDU was 45.5%, specificity was 85.5%, positive predictive value

was 89.6%, and negative predictive value was 36.2%. The diagnostic sensitivity of PDU for 520 left and right kidneys was 42.1%, specificity was 96.5%, positive predictive values were 90.6% and negative predictive values were 67.8%. (Table 2).

Among the 260 patients included in the study, 195 children underwent VCUG. VUR was found in 47 (24.1%) children and was found in 61 (15.6%) kidneys. Of the 47 patients with VUR, there were 45 patients with abnormal finding in DMSA scan, and 31 patients with a defect in PDU. There were 31 patients with abnormalities in both tests. Of the 61 kidneys, international VUR grade 1 was found in 3 (0.8%), grade 2 in 9 (2.3%), grade 3 in 17 (4.4%), grade 4 in 24 (6.2 %), and grade 5 in 8 (2.0%). The diagnostic sensitivity and specificity of the DMSA scan for VUR were 95.7% and 14.1 %, respectively. The diagnostic sensitivities and specificities of PDU for VUR were 65.5% and 60.1%, respectively (Tables 3).

The 191 patients with abnormal findings in their DMSA scan were followed up for 6 months. Except for 82 patients who were lost to follow up at 6 months, 109 patients performed DMSA scan. The cortical defect was improved in 73 (67%) of the patients, however, a cortical defect was still observed in 36 (33%). At 6 months of follow-up, abnormalities were detected in the initial PDU in 38 (52.1%) of 73 patients in whom the cortical defect disappeared and in 20 (55.5%) of 36 patients in whom a cortical defect was still present. Patients with cortical defect had slightly more initial PDU abnormalities but, there were no significant differences. The 36 patients with a persistent cortical defect at 1 year performed a follow-up DMSA scan. Except for 22 patients who were lost to follow up at 1 year, 14 patients performed DMSA scan. Two patients (14.3%) out of 14 patients were improved and a cortical defect was still observed in 12 (85.7%) children. Of the 12 patients in whom a cortical defect was still present at 1 year, the kidney size decreased in 1 patient and renal uptake was reduced in 3 patients. At 2 years of follow-up, two patients still had cortical defect and renal scarring, but there were no clinical symptoms in the patients with renal scarring.

## Discussion

In children, UTI is one of the common infectious diseases and is known to have a prevalence of 3% in girls and 1% in boys[13]. However, it is difficult to diagnose, as symptoms are often nonspecific[14]. Renal scarring, one of the major complications of APN, has been reported to occur in appro-

Table 2. Diagnostic and Predictive Values of PDU Comparison with DMSA

| | In 260 patients | In 520 Kidneys |
|---|---|---|
| Sensitivity | 45.5% | 42.1% |
| Specificity | 85.5% | 96.5% |
| Positive predictive value | 89.6% | 90.6% |
| Negative predictive value | 36.2% | 67.8% |

Abbreviations: PDU, power doppler ultrasonography; DMSA, 99mTc-dimercaptosuccinic acid.

Table 3. Diagnostic Values of DMSA and PDU for VUR

| | DMSA scan | PDU |
|---|---|---|
| Sensitivity | 95.7% | 65.5% |
| Specificity | 14.1% | 60.1% |

Abbreviations: DMSA, Tc-99m dimercaptosuccinic acid; PDU, power doppler ultrasonography; VUR, vesicoureteral reflux.

Table 1. Demographics and Laboratory Data of the Patients

| | DMSA scan | | Total |
|---|---|---|---|
| | Normal | Abnormal (APN) | |
| Number of patients | 69 | 191 | 260 |
| Mean age(month) | 4.8±2.5 | 5.3±2.3 | 5.2±2.4 |
| Sex (M:F) | 4.8:1 | 2.5:1 | 2.9:1 |
| WBC(/μL) | 13,698.4±5,136.9 | 16,877.5±6,429.7* | 15,593.0±6,209.4 |
| ESR (mm/h) | 21.4±18.9 | 41.4±29.6* | 36.1±28.5 |
| CRP (mg/L) | 2.37±2.20 | 6.58±5.89* | 5.46±5.48 |
| Abnormal finding in PDU | 10 | 87 | 97 |

Abbreviations: DMSA, 99mTc-dimercaptosuccinic acid; WBC, white blood cell count; CRP, c-reactive protein; ESR, erythrocyte sedimentation rate; PDU, power doppler ultrasonography.
*$P$<0.05.

ximately 64% of children, and this renal damage can lead to end-stage renal disease[15,16]. Therefore, early diagnosis and treatment is especially important to prevent complications. Many imaging studies have been used to diagnose pediatric APN, and several studies have been conducted to evaluate usefulness of specific techniques[9]. Pathophysiologically, the blood flow of renal parenchyma is reduced by vasoconstriction of peripheral arterioles in the vascular phase of APN and the damaged segment can be detected by DMSA scan, CT, or PDU[15,17,18].

According to the Clinical Practice Guideline for the Diagnosis and Management of Initial UTI in Febrile Infants and Children 2 to 24 Months proposed by the American Academy of Pediatrics in 2011, noninvasive conventional renal ultrasonography is recommended as a primary imaging test for pediatric patients with urinary tract infection to detect anatomical abnormalities. Renal ultrasonography is typically used to diagnose hydronephrosis, renal abscess, and anomalies in the urinary system[19]. In addition, the sensitivity of PDU for detecting ischemic injuries in blood vessels in the kidney, including the interlobar and arcuate arteries, is high. However, its sensitivity for detecting renal parenchymal invasion to diagnose pyelonephritis is low[20].

In 2007, we reported sensitivity and specificity values for the use of PDU for the diagnosis of APN. The age of the patients ranged from 1 month to 7 years old and the total number of patients was limited to 25. Compared with the previous study, we selected patients aged between 1 and 12 months, and the total number of patients was recruited 260. In 2007, the sensitivity and specificity for the use of PDU for diagnosis of APN were 38.1% and 50%, respectively. In this study, the diagnostic sensitivity was 42.1%, the specificity was 96.5%, demonstrating that the sensitivity was similar but the specificity was increased compared with the results of 2007. The reasons for the between-study differences may be: First, the sample size was larger, and the patient age range was limited in the present study. Second, the test quality might have improved because the examiner had performed the procedure many times since the previous study and PDU equipment might be improved.

The sensitivity and specificity of the DMSA scan for VUR were 95.7% and 14.1%, respectively, and the sensitivity of PDU was 65.5%, which was lower than DMSA scan, but the specificity of PDU was 60.1% which was higher the DMSA scan. In addition, of the 195 patients who underwent VCUG, 88 patients had abnormal findings with only a DMSA scan, and among them 14 patients (15.9%) had VUR, whereas among 84 patients with abnormal findings on both DMSA scan and PDU, 31 patients (36.9%) had VUR, and VUR was significantly higher in patients with abnormal findings in both tests ($P$<0.05).

Considering VUR grades 1-3 as low-grade reflux and VUR grades 4 and 5 as high-grade reflux, 20 of 47 pediatric patients had low-grade reflux and 27 had high-grade reflux. For the diagnosis of low-grade VUR, the sensitivity and specificity of DMSA scan were 85.1% and 5%, respectively and the sensitivity and specificity of PDU were 39.9% and 35.0%, respectively. For diagnosing high-grade VUR, DMSA scan showed a sensitivity and specificity of 86.9% and 3.7%, respectively, and PDU had a sensitivity and specificity of 42.9% and 33.3%, respectively. Thus, there was no significant difference of the sensitivity or specificity in diagnosing low- and high-grade VUR. In diagnosing VUR, the DMSA scan showed high sensitivity but low sensitivity. In addition, both the DMSA scan and PDU test showed a significantly higher rate of VUR diagnosis than using a DMSA scan alone.

The limitation of the present study was that a comparison couldn't be made with pediatric patients showing abnormalities on PDU, because only those who showed abnormalities on the DMSA scan were followed up. Moreover, it was difficult to consider the exact values of DMSA and PDU because patients with urogenital anomaly were excluded. PDUs have many advantages, including no requirement for sedation, no exposure to radiation and no need for IV drugs. According to Jack S. Elder, about 50% of febrile UTI patients were positive on DMSA scan[21], however, in this study, 193 of 260 patients (73.5%) were considered positive. In addition, the inflammatory markers such as leukocyte counts, ESR, and CRP were significantly higher in the positive group in DMSA scan. Moreover, in our study and our results of 2007, it seems that it is difficult to replace the DMSA scan with PDU because of its low sensitivity in the diagnosis of APN. But, PDU and DMSA scan show different sensitivities and specificities in the diagnosis of APN and VUR, respectively. Therefore, we suggest that the sensitivity and specificity of each test can be helpful in diagnosing APN and VUR when they are used in parallel.

## Ethics statement

This present study was reviewed and approved by the Institutional Review Board of Yeungnam University Hospital (IRB number YUMC 2018-07-042).

## Conflicts of interest

No potential conflict of interest relevant to this article was reported.

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