New strategy of color and power doppler sonography combined with DMSA in the assessment of acute pyelonephritis in infants

Min Guang Chen  
Wenzhou Medical University Second Affiliated Hospital

Yan Yang  
Wenzhou Medical University Second Affiliated Hospital

Qing Yang  
Wenzhou Medical University Second Affiliated Hospital

Jie Qiu Zhuang  
Wenzhou Medical University Second Affiliated Hospital

Xiao Hua Ye  
Wenzhou Medical University Second Affiliated Hospital

Wen Jie Zheng (✉️ wzwjzheng@sina.com)  
Second affiliated hospital and Yuying Children Hospital of Wenzhou Medical University  
https://orcid.org/0000-0002-1768-4432

Research article

Keywords: Color and power doppler sonography, 99mTc-dimercaptosuccinic acid scintigraphy, Acute pyelonephritis, children, Kidney

DOI: https://doi.org/10.21203/rs.2.11744/v2

License: 🐛 This work is licensed under a Creative Commons Attribution 4.0 International License.  
Read Full License
Abstract

**Background:** The purpose of this study was to evaluate the clinical value of color and power doppler sonography (CPDS) when combined with 99mTc-dimercaptosuccinic acid scintigraphy (DMSA) in assessment of acute pyelonephritis (APN) in infants.

**Methods:** A total of 79 children with APN admitted to our hospital from June 2016 to Jan 2019 were enrolled, including 52 boys and 27 girls, age range 1 month to 3 years old. All cases followed the diagnostic criteria for acute pyelonephritis and excluded anatomical abnormalities of urinary system. All 79 patients were examined by urinary ultrasonography (US), CPDS, and DMSA within 48 hours of fever and analyzed the clinical value of combining the two methods in the assessment of APN in infants.

**Results:** Among 79 children, urinary ultrasonography revealed 2 cases of renal cortical echo changes, both located in the upper pole of the kidney, 24 cases of kidney enlargement, and 1 case of left kidney shrinkage. 95 kidneys were shown to be diseased with DMSA, while 105 kidneys abnormal by CPDS. The sensitivity of CPDS was 69.4%, and the specificity was 38.1%. In children younger than 6 months, the sensitivity of CPDS was 56.9%, which was 84.2% in children between 6 months to 1 year, and 94.4% from 1 to 3 years old, respectively. The corresponding specificity of CPDS was 44.1%, 26.7%, and 35.7%. There was no significant correlation between CPDS levels and DMSA positive results. The abnormal rate of intermediate part in the kidneys was significantly lower than that in the upper and lower poles. Children with abnormal CPDS have a greater risk of renal scarring (p<0.05).

**Conclusion:** The clinical application value of CPDS is not as good as that of DMSA. But the sensitivity of CPDS is highly age-related, it can be used as a non-invasive helpful tool for early diagnosis of acute pyelonephritis in infants older than 6 months old.

**Background**

Urinary tract infection (UTI) is a common disease in children. Although most of the patients with good prognosis, acute pyelonephritis (APN), if not be treated promptly, can lead to permanent renal scar formation, which is an important cause of chronic renal failure in young people. Therefore, it's important to identify APN early and give it positive treatment [1]. However, the accurate diagnosis of APN in children still quite difficult on the basis of clinical and laboratory findings alone [2,3].

Since 1972, The technetium 99m dimercaptosuccinic acid (DMSA) has been considered to be a gold standard for diagnosing APN at present [4]. However, there are still many disadvantages. Quite a few hospitals do not have this inspection equipment which is radiation and expensive. Therefore, a simple, inexpensive and non-radiative alternative method is required to help early identification and follow-up of children with APN.

Previous studies have shown that color and power doppler sonography (CPDS) can be used to evaluate renal cortical blood flow and contribute to the diagnosis of APN [5,6], and compared the diagnostic
difference between CPDS and DMSA in children with APN[7-12]. Some studies believe that doppler ultrasonography can be used as a predictive tool for permanent kidney damage following acute pyelonephritis[13], while others disagree[14,15].

Most of the above studies focused on whether the CPDS could instead of DMSA for the diagnosis and follow-up of APN. But in our opinion, it maybe better to make full use of the respective advantages of the two inspection instead of replacing it. Thus, the purpose of this study was to assess the new role of CPDS in the application of APN in infants by prospective combined use of DMSA.

**Methods**

**Study population**

From June 2016 to Jan 2019, 79 children diagnosed with acute pyelonephritis were enrolled (52 boys and 27 girls), who were admitted to the Yuying Children's Hospital affiliated to Wenzhou Medical University. The inclusion criteria were as follows: (1) age between 1 month to 3 years old; (2) clinical diagnosis of APN including (i) high-grade fever (≥38.5°C), (ii) pyuria (>10 white blood cells per cubic millimeter) or a positive urine culture (bacteriuria to the extent of 10^4 colony-forming units per milliliter), (iii) elevated blood leukocytes or C-reactive protein (CRP) [16]. Exclusion criteria included congenital structural anomalies of the urinary system.

**Data collection**

All 79 patients underwent both CPDS and DMSA within 48 hours of hospitalization. The CPDS was operated by a senior ultrasound physician and was unaware of the results of the 99mTc-DMSA test. CPDS was performed using the Siemens Sequoia 512 scanner, with a 8-14 MHz (for children less than 3 months) and 2.5-4 MHz (for children more than 3 months) curved-array transducer. To standardize the inspection, an empiric 9-point semiquantitative analysis that evaluated the parenchymal perfusion size of each kidney was performed. The kidneys were divided into three zones which are the upper pole, midzone, and lower pole. Then the parenchymal perfusion of each zone was scored from 0 (no perfusion) to 3 (normal perfusion). The sum of each zone score was considered the total score of each kidney. An 8-9 score was considered CPDS negative (normal), a score less than eight was considered CPDS positive (abnormal).

The 99mTc-DMSA examination was performed by a senior doctor of ECT in our hospital and was unaware of the results of CPDS. Tc-99m DMSA renal scintigraphy was performed by SPECT vertex v60 ADAC (USA). 3.7 MBq/kg (0.1 mCi/kg) Tc-99m DMSA was intravenously injected, and 2–4 h later, images were obtained in the planar anterior, posterior, and right and left posterior oblique using an Orbiter Siemens gamma camera with a low-energy high-resolution parallel-hole collimator. Images were obtained for 300,000–500,000 counts on a 256×256 matrix format. To standardize the interpretation, a same 9-point semiquantitative analysis that assessed the lesion size and radioactivity of each kidney was performed. The kidneys were divided into three zones, and the radioactive uptake of each zone was
scored from 0 (no uptake) to 3 (normal uptake). A normal negative DMSA was determined by a total score of 8-9 in each kidney. A abnormal positive DMSA was considered by a total score less than eight.

**Statistical analysis**

Comparisons between CPDS or DMSA findings were performed using Mann-Whitney nonparametric tests. The diagnostic values (sensitivity, specificity, predictive values, and accuracy) of CPDS and DMSA were assessed with contingency tables. A P value ≤0.05 was considered significant.

**Results**

**Comparison of US, CPDS, and DMSA results in children**

All 79 patients met the APN diagnostic criteria. Urinary ultrasonography revealed 2 cases of renal cortical echo changes which both located in the upper pole of the kidney, 24 cases (48 kidneys) of kidney enlargement, and 1 case of left kidney shrinkage. Among 79 children (158 kidneys), 95 kidneys had abnormal DMSA and 105 had abnormal CPDS. The gross US changes were more apparent in the DMSA+ group ($x^2=19.397$, $P<0.01$) (See Table 1). The sensitivity of CPDS was 69.4% and the specificity was 38.1%. The positive predictive value of CPDS was 62.8%, and the negative predictive value was 45.3%. (See Table 2).

| Group  | US + | US - | Total |
|--------|------|------|-------|
| DMSA + | 42   | 53   | 95    |
| DMSA - | 7    | 56   | 63    |
| Total  | 49   | 109  | 158   |

+, Positive; -, negative.

| Group  | DMSA + | DMSA - | Total |
|--------|--------|--------|-------|
| CPDS + | 66     | 39     | 105   |
| CPDS - | 29     | 24     | 53    |
| Total  | 95     | 63     | 158   |

+, Positive; -, negative.

**Comparison of CPDS and DMSA results in children with different age**

The sensitivity of CPDS detection was lower in children younger than 6 months of age, and the sensitivity increased with age. The sensitivity of CPDS was 56.9%(group 1), 84.2%(group 2) and 94.4%(group 3). The specificity of CPDS was 44.1%(group 1), 26.7%(group 2) and 35.7%(group 3). (See Table 3).
Comparison of abnormal results of different kidney zones

There was no significant correlation between CPDS levels and DMSA positive results ($P > 0.05$). No matter CPDS or DMSA, the abnormal rate in midzone of kidney was significantly lower than that in the upper and lower poles (See Table 4).

| Group | Group 1 ($<5M$) | Group 2 ($6M - <1Y$) | Group 3 ($1Y - <3Y$) |
|-------|-----------------|-----------------------|---------------------|
| CPDS + | 33 | 16 | 17 |
| CPDS - | 25 | 3 | 1 |
| Total | 58 | 19 | 18 |

+, Positive; -, negative.

Discussion

APN is considered to be one of the most common and serious illnesses in infants. It may lead to permanent renal scar formation if it does not be recognized and be used by effective antibiotic treatment at the first 48 hours after onset of the disease. Studies have shown that the incidence of renal scar can reach 64% and a considerable number of cases therefore progress to ESRD. The biggest challenge is not treatment, but early diagnosis and identification. Therefore, it is important to assess APN and treat it effectively as early as possible.

Imaging plays an essential role in the diagnosis of APN. Our data showed that a few children had normal white blood cells or normal CRP, but they had fever and abnormal urine tests. Therefore, it is crucial to identify APN by combining with imaging tests.

Tc-99m DMSA renal scintigraphy has been used for the detection and localization of APN inflammation with high sensitivity and specificity. And it is considered the gold standard for the diagnosis of APN. The invasiveness procedure, radiation exposure, and cost limit its clinical application. Meanwhile, negative DMSA results cannot completely rule out APN\textsuperscript{7}. In this study, 7 patients had typical clinical manifestations of APN whose urine cultures were positive, peripheral blood leukocytes and CRP were significantly increased but had negative DMSA. Interestingly, 6 of these 7 cases showed positive CDPS. Early diagnosis of APN is still difficulty in clinical practice.
Various types of renal vascular and renal parenchymal lesions are closely related to changes in intrarenal arterial hemodynamics \([17]\). CPDS is developed on color Doppler technology and is superior to color doppler flow imaging in showing sensitivity and continuity of blood flow. Because this test is more sensitive to low-speed blood flow, it reflects the integrated power from the reflected echo of the renal parenchyma \([9]\). Bude et al \([18]\) first reported the imaging ability of PDS on renal cortical blood perfusion. Since then, many studies have used PDS to study the effects of various kidney diseases on renal blood flow \([15,19-21]\). Previous studies have shown that CPDS can contributes to the diagnosis of APN, Anne Hitzel \([7]\) has shown that although the predictive value of CPDS for renal scar is not high, the results of CPDS and DMSA are consistent in 81% of APN kidneys, suggesting that it has certain clinical application value. In view of the fact that the study did not cover all children and did not involve the exploration of specific parts of the infection, it is necessary to further explore.

Our study showed that the positive rate of DMSA is only 6% in patients older than 6 months with negative CPDS. Two double-blind controlled studies have also suggested that the specificity of CPDS for the diagnosis of APN is 85% to 95%, and the sensitivity is 55% to 75%, which is highly consistent with DMSA examination \([5,8]\). The data showed that the sensitive of CPDS is highly age-related. With the increase of age, the sensitivity of CPDS gradually increased. It may be related to a change in kidney blood flow caused by infant crying in an unsedated situation. In order to avoid deviations in the test results, infants should be tested in a quiet state.

Our study also found that there was no significant correlation between CPDS abnormal level and DMSA positive results, which was inconsistent with our pre-expected results. We also observed that the location of renal abnormalities found by CPDS and DMSA is not the same. The pathophysiologic mechanism responsible for CPDS imaging abnormalities are focal ischemia due to vascular compression induced by interstitial edema \([22]\). While the uptake of 99mTc-DMSA by the renal parenchyma is dependent on the glomerular perfusion and the transport function of the proximal tubule cell membrane. Since the detection mechanism of CPDS and DMSA is different when which be used to detect APN. DMSA abnormalities can not be judged from blood supply abnormalities or renal tubular epithelial cell damage, while CPDS can determine the blood supply of the kidneys, so these two methods have good complementarity.

**Conclusion**

It is not necessary to focus on replacing DMSA with CPDS in clinical practice, but to synergistically utilize their respective advantages to improve the clinical APN assessment level. The clinical application value of CPDS is not as good as that of DMSA but it can be used as a non-invasive helpful tool for early diagnosis of acute pyelonephritis in infants older than 6 months old especially when some families refuse DMSA inspection due to radiation exposure.

**Declarations**
Acknowledgements

The authors wish to thank the staff of the department of Nephrology Rheumatology Ultrasonics for their important contributions. The results presented in this paper have not been published previously in whole or part.

Consent for publication

Not applicable

Funding

No funding was received for this work.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author's contributions

MGC participated in research design, data collection, data analysis and writing of the article. YY participated in data collection and operating ultrasound examination of all patients. QY participated in research design and writing of the article. JQZ participated in data collection and writing of the article. WJZ participated in research design, data collection, data analysis and writing of the article. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This retrospective study was reviewed and approved by the Institutional Ethics Committee from the The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, China. As this was a retrospective study, written consent to participate from the study subjects was not required.

Competing interests

The authors declare no conflicts of interest or competing interests.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details
References

1. Jacobson SH, Eklof O, Lins LE, Wikstad I, Winberg J. Long-term prognosis of post-infectious renal scarring in relation to radiological findings in childhood-a 27-year follow-up. Pediatr Nephrol. 1992;6:19-24.

2. Hoberman A, Chao HP, Keller DM, Hickey R, Davis HW, Ellis D.. Prevalence of urinary tract infection in febrile infants. J Pediatr. 1993;123:17–23.

3. Cornu C, Cochat P, Collet J-P, Delair S, Haugh MC, Rolland C. Survey of the attitudes to management of acute pyelonephritis in children. Pediatr Nephrol. 1994;8:275-7.

4. Jakobsson B, Nolstedt L, Svensson L, Söderlundh S, Berg U. Tc-99m DMSA scan in the diagnosis of acute pyelonephritis in children: relation to clinical and radiological findings. Pediatr Nephrol. 1992;6:328-34.

5. Halevy R, Smolkin V, Bykov S, Chervinsky L, Sakran W, Koren A. Power Doppler ultrasonography in the diagnosis of acute childhood pyelonephritis. Pediatr Nephrol. 2004;19(9):987-91.

6. Basiratnia M, Noohi AH, Lot M, Alavi MS. Power Doppler sonographic evaluation of acute childhood pyelonephritis. Pediatr Nephrol. 2006;21(12):1854-7.

7. Hitzel A, Liard A, Véra P, Manrique A, Ménard JF, Dacher JN. Color and power Doppler sonography versus DMSA scintigraphy in acute pyelonephritis and in prediction of renal scarring. J Nucl Med. 2002;43(1):27-32.

8. Stogianni A, Nikolopoulos P, Oikonomou I, Gatzola M, Balaris V, Farmakiotis D, et al. Childhood acute pyelonephritis: comparison of power Doppler sonography and Tc-DMSA scintigraphy. Pediatr Radiol. 2007;37(7):685-90.

9. Bykov S, Chervinsky L, Smolkin V, Halevi R, Garty I. Power Doppler sonography versus Tc-99m DMSA scintigraphy for diagnosing acute pyelonephritis in children: are these two methods comparable? Clin Nucl Med. 2003;28(3):198-203.

10. Yoo JM, Koh JS, Han CH, Lee SL, Ha US, Kang SH, et al. Diagnosing Acute Pyelonephritis with CT, Tc-DMSA SPECT, and Doppler Ultrasound: A Comparative Study. Korean J Urol. 2010;51(4):260-5.

11. Mohkam M, Maham S, Rahmani A, Naghi I, Otokesh B, Raiiati H, et al. Technetium Tc 99m dimercaptosuccinic acid renal scintigraphy in children with acute pyelonephritis: correlation with other imaging tests. Iran J Kidney Dis. 2010;4(4):297-301.
12. Ayazi P, Mahyar A, Noroozian E, Esmailzadehha N, Barikani A. Comparison of renal ultrasonography and dimercaptosuccinic acid renal scintigraphy in febrile urinary tract infection. Infez Med. 2015;23(4):323-9.

13. Mohammadjafari H, Aalaee A, Salehifar E, Shiri A, Khademloo M, Shahmohammadi S. Doppler ultrasonography as a predictive tool for permanent kidney damage following acute pyelonephritis: comparison with dimercaptosuccinic acid scintigraphy. Iran J Kidney Dis. 2011;5(6):386-91.

14. Narchi H, Donovan R. Renal power Doppler ultrasound does not predict renal scarring after urinary tract infection. Scott Med J. 2008;53(4):7-10.

15. Shajari A, Nafisi-Moghadam R, Malek M, Smaili A, Fallah M, Pahlusi A. Renal power Doppler ultrasonographic evaluation of children with acute pyelonephritis. Acta Med Iran. 2011;49(10):659-62.

16. Stunel H, Buckley O, Feeney J, Geoghegan T, Browne RF, Torreggiani WC. Imaging of acute pyelonephritis in the adult. Eur Radiol. 2007;17:1820-8.

17. Wang SM, Lai MK, Chueh SC, Chen J. The utility of resistance index of distal interlobular arteries in evaluating renal graft function. Transplant Proc, 2004;36(7): 2184-85.

18. Bude RO, Rubin JM, Adler RS. Power versus conventional color Doppler stenography: comparison in the depiction of normal intrarenal vasculature. Radiology, 1994;192: 777-780.

19. Bernardes LS, Francisco RP, Saada J, Salomon R, Ruano R, Lortad-Jacob S, et al. Quantitative analysis of renal vascularization in fetuses with urinary tract obstruction by three-dimensional power-Doppler. Am J Obstet Gynecol, 2011;205: 572.

20. Vreju F1, Ciurea M, Roşu A, Muşetescu A, Grecu D, Ciurea P. Power Doppler sonography, a non-invasive method of assessment of the synovial inflammation in patients with early rheumatoid arthritis. Rom J Morphol Embry. 2011;52:637-643.

21. Miyajima T, Yokoyama H, Taira H, Tsuji Y. Quantitative estimation of renal blood flow by power Doppler ultrasonography in renovascular hypertensive dogs. Kidney Int, 2005;68: 2781-2786.

22. Majd M, Nussbaum Blask AR, Markle BM, Shalaby-Rana E, Pohl HG, Park JS, et al. Acute pyelonephritis: comparison of diagnosis with 99mTc-DMSA, SPECT, spiral CT, MR imaging, and power Doppler US in an experimental pig model. Radiology. 2001;218(1):101-8.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- renamed119e1.jpeg