The value of ultrasonography in the detection of renal scarring after urinary tract infection in children: preliminary results

Farid Niafar[1], Abolhassan Seyedzadeh[2], Sedighe A. Hamedani[3], Sepehr Hamidi[4]

[1]Department of Radiology, Imam-Reza Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran
[2]Department of Pediatrics, Imam-Reza Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran
[3]Resident, Department of Radiology, Imam-Reza Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran
[4]School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Corresponding author:
Dr. Farid Niafar
Department of Radiology, Imam-Reza Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran
E-mail: fniafar@kums.ac.ir

Submitted: 14 May 2007
Accepted: 02 July 2007

Arch Med Sci 2007; 3, 3: 245-248

Abstract

Introduction: There is controversy whether ultrasonography (US) can be reliably used to diagnose renal scars in children following pyelonephritis. This study aimed to assess the value of US in detecting renal scars using ^{99m}Tc-dimercaptosuccinic acid (DMSA) scintigraphy as the reference diagnostic test.
Material and methods: In a prospective setting, 62 children who had been diagnosed as having pyelonephritis were studied. All children were evaluated with DMSA scintigraphy and US, each performed by one examiner. The interval between DMSA scanning and US was at most 2 days. A radiologist recorded his findings for each kidney as scarred or unscarred based on established criteria. The sensitivity of US relative to DMSA scintigraphy in the detection of renal scarring was calculated.
Results: The study subjects were 20 boys and 42 girls, with a median age of 15 months (range, 2 months-6 years). Twenty-nine children were reported to have renal scarring on DMSA scintigraphy, of whom 12 (41.4%) were correctly diagnosed as having renal scars on US. The sensitivity of US in detecting scarred kidneys was 36.8%, and its specificity 97.7%. The sensitivity of US in detecting kidneys with multiple scars was higher than kidneys with a single scar (p=0.007). The development of renal scarring was not related to gender (p=0.3). Increasing age was associated with developing renal scars with an odds ratio of 1.53 for each year increase in age after adjustment for sex.
Conclusions: The results of this preliminary study show that US cannot be used reliably as the sole imaging method for detecting pediatric renal scarring.

Key words: DMSA, ultrasonography, renal scarring, urinary tract infection.

Introduction

Urinary tract infection (UTI) is one of the most commonly encountered infections during childhood [1]. Renal scarring, defined as permanent damage of the renal parenchyma, has been strongly associated with vesicoureteric reflux (VUR) and UTI [2]. There is indisputable evidence that renal scarring is an important cause of renal failure and hypertension in children during later life [1, 3].

Intravenous urography (IVU) used to be the preferred method of imaging for the detection of renal scars. With the advent of dimercaptosuccinic acid (DMSA) scintigraphy the DMSA scan has become the golden standard for diagnosing renal scars [4]. Ultrasonography (US), being an available and safe technique, is usually the primary diagnostic imaging in the evaluation of children with UTI. Added to the mentioned benefits of US, is its ability to detect major malformations and dilatation of the urinary tract [5].

To date, several authors have tried to compare the sensitivity of US and DMSA scanning in assessing renal scars [6]. However, findings have been inconsistent and the question whether US can be used as an alternative to DMSA scintigraphy is still a subject of interest. This preliminary study aimed to investigate the value of US relative to DMSA scan in diagnosing pediatric renal scars after UTI.

Material and methods

From February to November 2006, a total of 62 children referred from the department of pediatrics to the department of nuclear medicine to undergo DMSA scintigraphy for the evaluation of a recent pyelonephritis were prospectively enrolled. The diagnosis of pyelonephritis was based on clinical symptoms and a positive urine culture. Positive urine culture was defined as growth of any number of colonies of bacteria from suprapubic aspirate in less than 1 year old infants; and in children older than 1 year, it was defined as growth of bacteria over 10^3 colony-forming units/ml from a urine sample collected by a vesical catheter or over 10^5 colony--forming units/ml from clean-voided midstream urine.

The interval between the diagnosis of UTI and DMSA scan was at least 3 months in all subjects except in two 2-month old infants in whom the interval was more than one month. Within two days after performing DMSA scan, each child was referred to the department of radiology for ultrasonographic evaluation by one single radiologist with experience in pediatric renal sonography. The radiologist was blinded to the results of DMSA scan or any previous radiological examinations in patients. Parental consent was obtained for each child and the study was approved by the ethics committee of Kermanshah University of Medical Sciences.

Renal scans were obtained 2–3 hours after intravenous administration of ^{99m}Tc DMSA (120 MBq/1.73 m^2). Images were recorded with the child lying over the γ-camera, equipped with a high resolution collimator. Posterior, anterior, left and right posterior oblique planar views were recorded. All images were reviewed and reported by one nuclear medicine specialist unaware of the patients' medical history or previous examinations. Renal scarring on DMSA scans was defined by the presence of decreased uptake of labeled DMSA with loss of the contours of the kidney or by the presence of cortical thinning with decreased volume.

All ultrasonographic evaluations were performed with real-time B-mode US using a low frequency (3.5 MHz) convex and a high frequency (7.5MHz) linear transducer on a GE Logiq Alpha 200 system. Renal images were obtained in the supine and prone positions. The criteria of Barry et al. 1998, were used in the diagnosis of renal scarring with US i.e. (1) proximity of sinus echoes to cortical surface, (2) loss of pyramids, (3) irregularity of outline, (4) loss of definition of capsular echo, or (5) calyceal dilatation [7]. For each patient, a checklist was completed by the radiologist and the presence or absence of renal scarring was recorded.

SPSS version 13.0 for Windows was used for statistical analyses. Using DMSA scan as the reference imaging method, the sensitivity and specificity of US were determined and reported as percentages with approximate 95% confidence intervals (CI). Chi-squared and Fisher's exact tests were employed to compare the proportion of categorical variables between patients as appropriate. Logistic regression models were used to calculate the odds of developing renal scar for each year of increasing age and male sex. To compare means of continuous variables between patients, an independent t-test was applied. Statistical significance was set at $p<0.05$.

Results

Twenty (32%) boys and 42 (68%) girls were enrolled in the study. Median age of children was 15 months (range, 2 months-6 years) at the time of DMSA scintigraphy. There was no significant difference between the mean age of boys and girls, 21.1±18.5 months vs. 22.4±20.6 months, respectively ($p=0.8$).

Twenty-nine (46.8%) children had renal scarring (20 unilateral and 9 bilateral) on DMSA scan and 12 (22.6%) of them were correctly diagnosed to have scarring on US. Gender was not related to the development of renal scarring, 43% (18 of 42) in girls vs. 55% (11 of 20) in boys ($p=0.3$). Children with renal scarring were significantly older than children without renal scarring, 27.8±21.7 months vs. 16.8±16.7 months, respectively ($p=0.03$). Increasing age was associated with an unadjusted odds ratio (OR) of 1.51 (95% CI, 1.04–2.21) for the development of scarring, and an OR of 1.53 (95% CI, 1.05–2.24) after adjustment for sex.

Table I displays the characteristics of studied kidneys. The sensitivity of US in the detection of scarred kidneys was 36.8% (95% CI, 21.5-52.2%), and its specificity was 97.7% (95% CI, 94.5-99.9%). US had a higher sensitivity in the detection of kidneys with multiple scars than kidneys with a single scar, 64.3% (9 of 14) vs. 20.8% (5 of 24), respectively ($p=0.007$).

Discussion

This study shows that US does not have sufficient sensitivity to be used as a reliable imaging modality for the detection of renal scarring in children following UTI. However, considering the high specificity of US, normal ultrasonographic results should reassure us that there is a low likelihood of renal scarring.

We tried to idealize the study conditions to achieve an accurate assessment of power of US to detect renal scarring We deliberately timed the scan to be at least three months after the diagnosis of the UTI. This was due to evidence that transient changes might cause false positive results in DMSA scan interpretations, even up to two months after infection [8, 9]. Although the interval was at least one month in two infants, their kidneys were subsequently found to be normal on scintigraphy. Contrary to some previous studies which reviewed US reports or hard copies [10, 11], we did a live and contemporary recording of ultrasonographic findings. In order to enhance the preciseness of the results, we employed single experienced examiners for interpreting DMSA and US investigations.

The frequency of renal scarring in this study (46.8%) was comparable to rates previously reported in medical literature [12-15], although somewhat high compared with other studies [16-18]. This variability of the incidence of renal scarring may be partly explained by the method of imaging used, as DMSA scan detects more scars than IVU [19]. In addition, the presence of VUR or UTI recurrence increase the risk of renal scarring. Of 58 children whose previous imaging records were available in our study, 42 (72.4%) had VUR which was bilateral in 25 subjects.

Unsurprisingly, we noted that US performed much better in finding kidneys with multiple scars and most of the scarred kidneys missed by US had a single scar. Also, we observed that more than half (63.2%) of the kidneys reported to be scarred on DMSA scintigraphy had a single scar. Obviously, the sensitivity of US will increase if we only consider kidneys with multiple scars. The incapacity of US in detecting renal single scar is a known issue and has been shown previously [20-22]. From clinical point of view, the significance of these unifocal areas of renal scarring is, as yet, unknown. Several follow-up studies have shown that many of children with single scarred kidneys do not develop scarring in later life [5]. However, most clinicians would agree that positive findings on DMSA scans, even a single scar, would warrant long term follow up with antibiotic prophylaxis together with rapid treatment of any UTI.

While there is great variation between studies regarding the sensitivity of US, many authors have pointed to the relatively high specificity of this method in diagnosing renal scars [10-12, 17, 21]. It is of note that DMSA scintigraphy per se is not an ideal modality in detecting renal scars as was shown by Arnold et al. [23]. This imaging can lead to false positive results following pyelonephritis [5]. However, considering the importance of renal scarring, it would be very risky to refrain from performing DMSA scanning in children with proven pyelonephritis.

Table I. Findings of DMSA scintigraphy and ultrasound (US) in examined kidneys

Renal status	DMSA	US
Total number	124	123*
No scarring (%)	86 (69.4)	107 (87)
Scarred (%)	38 (30.6)	16 (13)**
Cortical inflammation	47	–
Nephrolithiasis	–	6
Horseshoe kidney	3	3

**One kidney was not appreciated by US (due to its shrinkage by multiple scars) and it was found to be ectopic on DMSA scan*
***Two kidneys were falsely diagnosed as scarred on US*

Given the safety, availability and cost-effectiveness of US, it would be optimal if DMSA scintigraphy – which requires intravenous injection and irradiation – could be replaced by US. However, US is restricted by the fact that it is an operator-dependent technique and highly reliant on the radiologist's skills. It has been shown that the agreement and inter-observer reliability on diagnosing renal scarring are very low even between experienced radiologists [12]. This might be due to the fact that the criteria for the detection of renal scarring on US are not well-defined and established. In the current study, we applied the proposed system by Barry et al. [7], but we could not achieve satisfactory results. We therefore think the practicality of their criteria needs to be tested by further studies.

This preliminary study did not identify a significant difference in the occurrence of renal scarring between boys and girls. It is known that girls older than six are more susceptible to urinary infections and the rate of recurrent UTI is higher among girls [24]. However, data regarding the occurrence of renal scars in male and female children is contradictory. Some authors point to the higher incidence of renal scarring in girls [13, 25], whilst others have stated that gender has no influence [26].

Increasing age was associated with a higher incidence of renal scars. This was independent of sex. Some studies have not shown any association between age and renal scarring others have reported a higher incidence of renal scarring in younger children [27], whilst some have demonstrated a greater incidence in older children [13]. Overall, it is believed that in older children, the renal parenchyma is more resistant to infection and thus the formation of scars is less common [28]. Vernon et al. 1997 reported that the risk of new renal scars developing in children aged 4 and older was very low.

It is possible that many of the older children included in our study were suffering from recurrent UTI and had developed renal scars at a younger age. As we did not have access to the data regarding the state of renal scarring in most of our patients prior to this study, it is difficult to comment on this issue.

Conclusions

According to the results of this study, US should not be used as the sole imaging modality to find renal scars in children due to its insufficient sensitivity. Future studies are needed to develop a well defined sets of criteria for ultrasonic detection of pediatric renal scarring.

Acknowledgments

Our special thanks go to Dr. Mehrshad Abbasi – from the Department of Endocrinology at Vali-Asr Hospital – for his invaluable assistance in performing the statistical analyses.

References

1. Jakobsson B, Esbjörner E, Hansson S. Minimum incidence and diagnostic rate of first urinary tract infection. Pediatrics 1999; 104: 222-6.
2. Bailey RR. The relationship of vesico-ureteric reflux to urinary tract infection and chronic pyelonephritis-reflux nephropathy. Clin Nephrol 1973; 1: 132-41.
3. Mannhardt W, Schofer O, Schulte-Wissermann H. Pathogenic factors in recurrent urinary tract infections and renal scar formation in children. Eur J Pediatr 1986; 145: 330-6.
4. Piepsz A, Blaufox MD, Gordon I, et al. Consensus on renal cortical scintigraphy in children with urinary tract infection. Scientific Committee of Radionuclides in Nephrourology. Semin Nucl Med 1999; 29: 160-74.
5. Practice parameter: the diagnosis, treatment, and evaluation of the initial urinary tract infection in febrile infants and young children. American Academy of Pediatrics. Committee on Quality Improvement. Subcommittee on Urinary Tract Infection. Pediatrics 1999; 103: 843-52.
6. Roebuck DJ, Howard RG, Metreweli C. How sensitive is ultrasound in the detection of renal scars? Br J Radiol 1999; 72: 345-8.
7. Barry BP, Hall N, Cornford E, Broderick NJ, Somers JM, Rose DH. Improved ultrasound detection of renal scarring in children following urinary tract infection. Clin Radiol 1998; 53: 747-51.
8. Rushton HG, Majd M. Dimercaptosuccinic acid renal scintigraphy for the evaluation of pyelonephritis and scarring: a review of experimental and clinical studies. J Urol 1992; 148: 1726-32.
9. Jakobsson B, Berg U, Svensson L. Renal scarring after acute pyelonephritis. Arch Dis Child 1994; 70: 111-5.
10. Shanon A, Feldman W, McDonald P, et al. Evaluation of renal scars by technetium-labeled dimercaptosuccinic acid scan, intravenous urography, and ultrasonography: a comparative study. J Pediatr 1992; 120: 399-403.
11. Smellie JM, Rigden SP, Prescod NP. Urinary tract infection: a comparison of four methods of investigation. Arch Dis Child 1995; 72: 247-50.
12. Stokland E, Hellström M, Hansson S, Jodal U, Odén A, Jacobsson B. Reliability of ultrasonography in identification of reflux nephropathy in children. BMJ 1994; 309: 235-9.
13. Macedo CS, Riyuzo MC, Bastos HD. Renal scars in children with primary vesicoureteral reflux [Portuguese]. J Pediatr (Rio J) 2003; 79: 355-62.
14. Stokland E, Hellstrom M, Jacobsson B, Jodal U, Sixt R. Renal damage one year after first urinary tract infection: role of dimercaptosuccinic acid scintigraphy. J Pediatr 1996; 129: 815-20.
15. Benador D, Benador N, Slosman DO, Nussle D, Mermillod B, Girardin E. Cortical scintigraphy in the evaluation of renal parenchymal changes in children with pyelonephritis. J Pediatr 1994; 124: 17-20.
16. Merrick MV, Notghi A, Chalmers N, Wilkinson AG, Uttley WS. Long-term follow up to determine the prognostic value of imaging after urinary tract infections. Part 2: Scarring. Arch Dis Child 1995; 72: 393-6.
17. Christian MT, McColl JH, MacKenzie JR, Beattie TJ. Risk assessment of renal cortical scarring with urinary tract infection by clinical features and ultrasonography. Arch Dis Child 2000; 82: 376-80.
18. Hoberman A, Charron M, Hickey RW, Baskin M, Kearney DH, Wald ER. Imaging studies after a first febrile urinary tract infection in young children. N Engl J Med 2003; 348: 195-202.
19. De Sadeleer C, Tondeur M, Melis K, Van Espen MB, Verelst J, Ham H, et al. A multicenter trial on interobserver reproducibility in reporting on 99mTc-DMSA planar scintigraphy: a Belgian survey. J Nucl Med 2000; 41: 23-6.
20. Tasker AD, Lindsell DR, Moncrieff M. Can ultrasound reliably detect renal scarring in children with urinary tract infection? Clin Radiol 1993; 47: 177-9.
21. Levart TK, Kenig A, Fettich JJ, Kljucevsek D, Novljan G, Kenda RB. Sensitivity of ultrasonography in detecting renal parenchymal defects in children. Pediatr Nephrol 2002; 17: 1059-62.
22. Moorthy I, Wheat D, Gordon I. Ultrasonography in the evaluation of renal scarring using DMSA scan as the gold standard. Pediatr Nephrol 2004; 19: 153-6.
23. Arnold AJ, Brownless SM, Carty HM, Rickwood AM. Detection of renal scarring by DMSA scanning – an experimental study. J Pediatr Surg 1990; 25: 391-3.
24. Hansson S, Jodal U. Urinary tract infection. In: Barratt TM, Avner ED, Harmon WE, editors. Pediatrics Nephrology. 4th ed. Baltimore: Lippincott, Williams & Wilkins; 1999: 835-50.
25. Zaki M, Badawi M, Al Mutari G, Ramadan D, Adul Rahman M. Acute pyelonephritis and renal scarring in Kuwaiti children: a follow-up study using 99mTc DMSA renal scintigraphy. Pediatr Nephrol 2005; 20: 1116-9.
26. Goldraich NP, Goldraich IH. Followup of conservatively treated children with high and low grade vesicoureteral reflux: a prospective study. J Urol 1992; 148: 1688-92.
27. Polito C, La Manna A, Rambaldi PF, Nappi B, Mansi L, Di Toro R. High incidence of a generally small kidney and primary vesicoureteral reflux. J Urol 2000; 164: 479-82.
28. Benador D, Benador N, Slosman D, Mermillod B, Girardin E. Are younger children at highest risk of renal sequelae after pyelonephritis? Lancet 1997; 349: 17-9.
29. Vernon SJ, Coulthard MG, Lambert HJ, Keir MJ, Matthews JN. New renal scarring in children who at age 3 and 4 years had had normal scans with dimercaptosuccinic acid: follow up study. BMJ 1997; 315: 905-8.