Evaluation of abnormal radiological findings in children aged 2 to 36 months followed by recurrent urinary tract infection: a retrospective study

Cinar Ozen, Pelin Ertan, Feray Aras, Gul Gumuser, Mine Ozkoc and Gonul Horasan Dinc

Department of Pediatric Nephrology, Celal Bayar University, Manisa, Turkey; Department of Nuclear Medicine, Celal Bayar University, Manisa, Turkey; Department of Radiology, Celal Bayar University, Manisa, Turkey; Department of Public Health, Celal Bayar University, Manisa, Turkey

ABSTRACT
Our aim is to determine the rational usage of imaging techniques in order to prevent or minimize permanent renal damage in recurrent urinary tract infections (UTIs). This study was enrolled children aged between 2 and 36 months, following-up with the diagnosis of recurrent UTI. All children had ultrasonography (USG) and dimercaptosuccinic acid scanning, 39 of them had underwent on voiding cystourethrography. There were 133 children (87 girls, 46 boys) with the mean age of 32.82 ± 38.10 months included into the study. Forty-three kidney units were normal in ultrasonogram of which seven units had reflux whereas among 35 units with hydronephrosis 22 units had reflux. Sensitivity and specificity presence of hydronephrosis in ultrasonogram for prediction of reflux was 75.9% and 73.5%, respectively. There were 19 dilated ureters in ultrasonogram, and among them 14 had reflux. Sensitivity and specificity of presence with ureteral dilatation in ultrasonogram for prediction of reflux was found as 48.3% and 89.8%, respectively. The sensitivity of parenchymal thinning seen in ultrasonogram for the evaluation of renal parenchyma was 15.9%, whereas specificity was 98.2% . Sensitivity and specificity of dimercaptosuccinic acid for prediction of reflux was 51.6% and 72.3%, respectively. The normal ultrasonogram findings cannot rule out neither possibility of reflux presence nor development of renal scarring. Therefore, DMSA scanning has major role both in determination of parenchymal damage and prevention of scarring. Also we get an important result as ureteral dilatation seen in USG, related to presence of reflux.

ARTICLE HISTORY
Received 6 July 2016
Revised 6 September 2016
Accepted 16 September 2016

KEYWORDS
Children; radiological findings; recurrent urinary tract infection; renal imaging

Introduction
Urinary tract infection (UTI) is one of the major clinical problems in childhood. Upper UTI (pyelonephritis) can lead to renal damage, hypertension, and end stage renal disease in future. It is more difficult to differentiate cystitis or pyelonephritis clinically, particularly in cases under two years of age. Additional laboratory and imaging methods are beneficial for diagnosis. Recurrent UTI (R.UTI) is defined as; two or more pyelonephritis, once pyelonephritis with one or more cystitis (lower UTI) or three or more cystitis. Vesicoureteral reflux (VUR), is an abnormal urine flow from bladder to kidneys. The frequency of VUR is approximately 1% in the general population whereas it raises up to 30–50% in children with recurrent UTI. Therefore, presence of reflux must be investigated in especially recurrent UTIs. A number of guides have been published to demonstrate the risk factors that can lead to renal damage in UTIs. The early diagnosis and appropriate treatment of the disease is important for the renal damage risk in future. Nowadays there are various imaging modalities for diagnostic evaluation but it involves different approaches. Although diagnostic imaging method is the proposed approach in the first febrile UTI, there are debates about which is the most appropriate approach. The purpose of this study is to determine the rational use of imaging techniques in order to prevent or to minimize permanent renal damage in recurrent UTIs.

Materials and methods
After the local ethics committee approval, patients followed with the diagnosis of recurrent UTI in the Celal Bayar University Pediatric Nephrology Clinic between January 2012 and July 2015, aged 2–36 months were
Table 1. Descriptive characteristics of study population.

|                          | Boys (n = 46) | Girls (n = 87) | Total (n = 133) |
|--------------------------|--------------|---------------|----------------|
| Age, months, mean ± SD (min–max) | 12.38 ± 22.72 (2–36) | 44.87 ± 40.24 (2–36) | 32.82 ± 38.10 (2–36) |
| Labial synechia (%)       | –             | 2 (%2.3)      | –              |
| Circumcision (%)          | 6 (%13.3)     | –             | –              |
| First febrile UTI age, months, mean ± SD (min–max) | 4.70 ± 6.76 (0–25) | 16.69 ± 12.97 (0–36) | 12.54 ± 12.57 (0–36) |
| Total number of febrile UTI, mean ± SD (min–max) | 1.13 ± 1.10 (0–5) | 1.56 ± 1.10 (0–6) | 1.41 ± 1.12 (0–6) |
| Prophylaxis duration, months, mean ± SD (min–max) | 8.57 ± 6.53 (0–26) | 3.14 ± 4.79 (0–20) | 5.02 ± 6.02 (0–26) |

The study was held with 133 cases (totally 266 renal units). The mean age of the patients was 32.82 ± 38.10 months for girls and 4.70 ± 6.76 (0–25) months for boys. The number of febrile UTI episodes was higher in the first year for boys (Table 1). All cases had urinary USG and DMSA scanning. VCUG was performed for 39 cases (78 renal units).

Forty-three kidney units were normal in USG of which 7 units had VUR whereas in 35 units with abnormal USG (hydronephrosis) 22 units had VUR. In other words, among total 29 renal units with VUR, 22 of them had hydronephrosis in USG. Sensitivity and specificity of presence of hydronephrosis in USG for prediction of VUR was 75.9% and 73.5%, respectively (Table 2, kappa = 0.473, p = .001).

There were 19 dilated ureters in USG, among them 14 had VUR. Sensitivity and specificity of presence of ureteral dilatation in USG for prediction of VUR was found as 48.3% and 89.8%; respectively (Table 2, kappa = 0.410, p = .001).

There were parenchymal thinning seen in ultrasound exam of 11 renal units, among them seven had parenchymal lesion on DMSA. The sensitivity of parenchymal thinning seen in USG for the evaluation of parenchymal lesion on DMSA was 15.9%, whereas specificity was 98.2% (Table 2, kappa = 0.202, p = .001).

There were 31 renal units with parenchymal lesion on DMSA and among them 16 had reflux. On the other hand, 13 renal unit had also reflux although they were involved into the group without abnormal DMSA (n = 47). Sensitivity and specificity of DMSA for prediction of VUR was 51.6% and 72.3%, respectively (Table 2, kappa = 0.242, p = .032).

Discussion

American Academy of Pediatrics (AAP) has been updated the diagnostic and management approach for the first febrile UTI between 2 and 24 months children in 2011. USG may lead over-under diagnosis at an early stages in this age group who had first febrile UTI, so they have reported that, it would be better to do after infection. Also, they did not recommend to do routine VCUG or DMSA in children with normal USG, who had a first febrile UTI. According to data from National Institute for health and Clinical Excellence (NICE), it is
not recommended to do DMSA and/or VCUG in children under six months who had febrile UTI unless any USG findings, atypical or R.UTI. Also, it is not recommended to do USG exam in acute phase, in children after six months unless having atypical or R.UTI.2,3

Trisha et al.12 reported that the presence of reflux in 25% of patients having normal ultrasound, undergoing the first febrile UTI. It was emphasized that only USG exam would not be sufficient for determining diagnosis and follow-up due to the fact that, there may be severe degrees of reflux or need for surgery, even if the normal USG in children with recurrent pyelonephritis.

In a retrospective study evaluating diagnostic value of different imaging modalities, it has been pointed out that the normal ultrasound findings could be able to rule out high-grade reflux in children with a first febrile UTI.13 Leroy et al. evaluated 118 children with recurrent UTI, they searched for the specify of USG in the determination of VUR. The ratio of VUR had been detected as 27%, of which 7% had grade 3–5 VUR.

There had been shown to be a significant relationship (correlation) between reflux and ureteral dilatation, especially with high-grade VUR. Therefore, they reported the sensitivity and specificity of ureteral dilatation in USG for determining of high-grade VUR as 73% and 88%; respectively.14

In the present study 75.9% sensitivity and 73.5% specificity of presence of hydronephrosis have been found by ultrasound for determination of reflux, thus concluded that the normal USG findings did not exclude the diagnosis of reflux or pyelonephritis similar to the literature. However, the sensitivity of ureteral dilatation in ultrasound was found as 48.3% while specificity was 89.8% for detecting reflux (Table 2). Relatively higher agreement has been found between VUR diagnosis and ureteral dilatation (kappa = 0.410, p = .001). Also same agreement was shown between VUR diagnosis and hydronephrosis (kappa = 0.473, p = .001). Therefore, in the presence of ureteral dilatation or hydronephrosis in children with recurrent UTI, it was thought to investigate reflux at first would be more appropriate.

In the study, conducted by Nickavar et al. any significant correlation between ultrasound findings and DMSA was shown in acute pyelonephritis. Ultrasound was assessed as inadequate in the diagnosis of acute pyelonephritis (34% sensitive, 53% specific).13 Of the patients with lesions on DMSA, 30–50% may have signs of acute pyelonephritis in USG,13,15,16 therefore it was reported that normal ultrasound findings could not exclude acute pyelonephritis.13,17 Lavocat et al. investigated the importance of DMSA screening in patients with pyelonephritis, and showed the presence of USG abnormalities in 45% and parenchymal changes of DMSA in 93% of the children with febrile UTI. According to this; normal USG could not exclude the renal parenchymal lesion.18,19

In the present study, the sensitivity of renal parenchymal thinning in the ultrasound evaluation was found as 15.9%, specificity was determined as 98.2%. Although there seems to be statistically significant relation between USG and DMSA findings for the renal parenchymal evaluation, it has found low consistency due to its low kappa value (kappa = 0.202, p = .001). Therefore, we could not show significant correlation between the ultrasound findings with DMSA in our study (Table 2). These results indicated that it will not be enough just to trust ultrasonographic findings for the evaluation of renal parenchyma in patients with UTI, DMSA must be performed in the case of clinical suspicion.

It has been reported that, there was reflux in 27–70% of patients with abnormal DMSA.13,17,20 In his study of Nickavar et al. reflux was detected in 35.7% patients with DMSA lesions (sensitivity and specificity is low).13 In the study done by Bhatnagar with 89 children for the evaluation of relationship between UTI, VUR, and renal scarring; they found that 15 children among 23, had renal scarring although they did not have VUR.7 In our study there was 50% of reflux seen among the renal units having parenchymal lesion on DMSA. DMSA sensitivity and specificity for the evaluation of VUR was detected in 51.6% and 72.3%; respectively (Table 2). Although it seems to be statistically significant relation between VCUG and DMSA findings for the reflux determination, it has found low consistency due to its low kappa value (kappa = 0.242, p = .032).

Our study was discussed at DMSA, voiding cystourethrography and ultrasound triangle. Those imaging

---

### Table 2. The accuracy and reliability of diagnostic test.

| Diagnostic test | Gold standard test | +/+ a | +/− b | −/+ c | −/− d | Total (n) | Sensitivity (%) | Specificity (%) | + PV | −PV | Kappa value | p |
|-----------------|--------------------|-------|-------|-------|-------|-----------|----------------|----------------|-------|-----|-------------|---|
| USG PT          | DMSA lesion (+)    | 7     | 4     | 37    | 218   | 266       | 15.9           | 98.2           | 63.6  | 85.5| 0.202       | .001 |
| USG HN (+)      | VCUG VUR (+)       | 22    | 13    | 7     | 36    | 78        | 75.9           | 73.5           | 69.2  | 83.7| 0.473       | .001 |
| VCUG VUR (+)    | DMSA lesion (+)    | 16    | 13    | 15    | 34    | 78        | 51.6           | 72.3           | 55.2  | 69.4| 0.242       | .032 |
| USG UD (+)      | VCUG VUR (+)       | 14    | 5     | 15    | 44    | 78        | 48.3           | 89.8           | 73.7  | 74.6| 0.410       | .001 |

Other diagnostic tests are shown in Table 2.

| PV Kappa value | p |
|----------------|---|
| 0.202          | .001 |
methods are useful and easily accessible. However, one of the new imaging methods is magnetic resonance urography (MRVCUG). MRVCUG is a reliable and safe diagnostic tool to determine renal scars in VUR patients. It can substitute for Tc-DMSA scintigraphy, particularly in patients requiring follow-up scanning and, consequently, considerable radiation exposure. MRVCUG is a noninvasive and non-radiating imaging method and it is alternative to standard VCUG for diagnosing and managing patients with VUR. Therefore, this method may be preferred for the future.

Conclusions

Early diagnosis is important for renal damage in the following period. The normal findings of USG cannot exclude reflux or risk of renal scarring. Therefore DMSA scanning has major role both in determination of parenchymal damage and prevention of scarring. Also we get an important result as ureteral dilatation seen in USG, related to presence of reflux. Thus, it was thought that it is necessary to investigate the presence of vesicourethral reflux if hydronephrosis or ureteral dilatation was present in USG.

Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

1. Hoberman A, Charron M, Hickey RW, et al. Imaging studies after a first febrile urinary tract infections in young children. N Engl J Med. 2003;348:195.
2. Mori R, Lakhanpaul M, Verrier-Jones K. Diagnosis and management of urinary infection in children: summary of NICE guidance. BMJ. 2007;335:395–397.
3. National institute for health and clinical excellence. Urinary tract infection in children. London: United Kingdom; 2007. Available at: http://guidance.nice.org.uk/CG054.
4. Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management, Roberts KB. Urinary tract infection: Clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. Pediatrics. 2011;128:595–610.
5. Gökçe İ, Alpay H. Renal parenchymal scarring and reflux nephropathy. Turk Neph Dial Transpl. 2012;21:21–27.
6. Van den Abbeele AD, Treves ST, Lebowitz RL, et al. Vesicoureteral reflux in asymptomatic siblings of patients with known reflux: Radionuclide cystography. Pediatrics. 1987;79:147–153.
7. Bhatnagar D, Mitra DK, Agarwalla S, et al. The role of DMSA scans in evaluation of the correlation between urinary tract infection, vesicoureteric reflux, and renal scarring. Pediatr Surg Int. 2002;18:128–134.
8. Keren R, Carpenter MA, Hoberman A, et al. Rationale and design issue of the randomized intervention for children with vesicoureteral reflux (RIVUR) study. Pediatrics. 2008;122:240–250.
9. Mir S, Ertan P, Ozkayin N. Risk factors for renal scarring in children with primary vesicoureteral reflux disease. Saud J Kidney Dis Transpl. 2013;24:54–59.
10. International Reflux Study in Children. International system of radiographic grading of vesicoureteric reflux. Pediatr Radiol. 1985;15:105–109.
11. Hervas I, Marti JF, Gonzales A, et al. Is the depth correlation using the geometric mean really necessary in a 99mTc-DMSA scan in the paediatric population? Nucl Med Commun. 2001;22:547–552.
12. Juliano TM, Stephant HA, Clayton DB, et al. Incidence of abnormal imaging and recurrent pyelonephritis after first febrile urinary tract infection in children 2–24 months. J Urol. 2013;190:1505–1510.
13. Nickavar A, Safaeian B, Biglari Abhari M. Radiologic and clinical evaluation of children with first febrile urinary tract infection. Int J Pediatr Adolescent Med. 2015;2:24–28.
14. Leroy S, Vantalon S, Larakeb A, Duco-Le-Pointe H, Bensman A. Vesicoureteral reflux in children with urinary tract infection: Comparison and diagnostic accuracy of renal US criteria. Radiology. 2010;255:890–898.
15. Bjorgvinsson E, Majd M, Eggli KD. Diagnosis of acute pyelonephritis in children: Comparison of sonography and 99mTc-DMSA scintigraphy. Am J Roentgen. 1991;157:539–543.
16. Mackenzie JR, Fowler K, Hollman AS, Tappin D, Murphy AV, Beattie TJ. The value of ultrasound in the child with an acute urinary tract infection. Br J Urol. 1994;74:240–244.
17. Morin D, Veyrac C, Kotzki PO, et al. Comparison of ultrasound and dimercaptosuccinic acid scintigraphy changes in acute pyelonephritis. Pediatr Nephrol. 1999;13:219–222.
18. Levocat MP, Granjon D, Allard D, Gay C, Freycen MT, Dubois F. Imaging of pyelonephritis. Pediatr Radiol. 1997;27:159–165.
19. Dulczak S, Kirk J. Overview of the evaluation, diagnosis, and management of urinary tract infections in infants and children. Urol Nurs. 2005;25:185–191.
20. Sorkhi H, Nooreddini HG, Amiri M, Osia S, Farhadi-Niakae S. Prediction of vesicoureteral reflux in children with first urinary tract infection by dimercaptosuccinic acid and ultrasonography. Iran J Pediatr. 2012;22:57–62.
21. Takazakura R, Johnin K, Furukawa A, et al. Magnetic resonance voiding cystourethrography for vesicoureteral reflux. J Magn Reason Imaging. 2007;25:170–174.