İstanbul Med J 2017; 18: 76-9
DOI: 10.5152/imj.2017.67625

Original Article

Comparison between Tc-99m DMSA and Renal Ultrasonography for the Evaluation of Renal Scarring and Function Loss in Children with Spina Bifida

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Abstract

Objective: We aimed to compare the sensitivity of ultrasonography (US) and Dimercaptosuccinic acid (DMSA) scintigraphy in evaluating renal scarring and kidney function in children with spina bifida (SB).

Methods: The study group comprised 100 patients (51 boys and 49 girls) with SB who underwent renal US and DMSA scintigraphy. The median age was 2 years (range: 6 months – 23 years). Renal US scans were performed by applying standard protocols. Subsequently, DMSA scintigraphy was performed to evaluate suspected renal damage and function loss. Sonographic criteria for renal scarring included renal contour lobulation, renal parenchymal thinning, increased renal parenchymal echo, and decreased the age of renal size. For DMSA scintigraphy, ≤44% differential function was considered abnormal, and contour irregularities and defects were accepted as indicators of renal scarring.

Results: Three patients had unilateral agenesis; thus, 197 kidneys were examined from 100 patients. DMSA scintigraphy was significantly superior to renal US in evaluating both renal scarring (p=0.016) and renal function loss (p=0.001). DMSA scintigraphy was three times more sensitive in detecting both abnormalities than US.

Conclusion: Renal US is the first imaging modality to evaluate upper and lower urinary tract infection; however, it alone is not reliable for monitoring scarring and function loss in patients with SB, who usually have rotoscoliosis, obesity, renal position anomalies, and intestinal gas distention that may corrupt the quality of the image. DMSA scintigraphy should be obtained to avoid underestimating renal scarring and function loss.

Keywords: DMSA, scintigraphy, ultrasonography, spina bifida

Introduction

Spina bifida (SB) refers to a wide range of neural tube defects, a neuro-urological disease affecting the spine and spinal cord. With a marked geographic and ethnic variation, SB has an incidence of 1–5 cases per 1000 live births. In Turkey, the incidence is 3 per 1000 live births (1), and in the eastern region of Turkey, it is 2.2 per 1000 live births (2). The basic urological problem in SB is neurogenic bladder dysfunction, resulting in urinary tract infections (UTI), incontinence, vesicoureteral reflux (VUR), hydronephrosis, chronic kidney disease (CKD), hypertension, and end-stage renal failure (3). The goal of treatment is to reduce bladder pressure and minimize urine stasis, thus preventing recurrent febrile UTI and consequent function loss. Patients should be followed up regularly against late referral because SB management is a dynamic and long-lasting process for a life time, and patient selection for aggressive treatment may prevent renal parenchymal deterioration (4).

Although renal ultrasonography (US) is used to demonstrate renal anomalies, urinary tract dilatation, signs of neurogenic bladder, renal scarring, and presumed function of the kidney, Tc-99m DMSA scintigraphy is the best for detecting renal parenchymal defects and demonstrating renal function loss with decreased differential function of the kidney. Single defects resulting in a localized deformity of renal outlines are the result of scarring and show no improvement on subsequent studies. The total renal Dimercaptosuccinic acid (DMSA) uptake is a measure of individual renal function (5). Follow-up studies with scintigraphy and US are conducted to confirm the resolution of pyelonephritic defect(s), evaluation of cortical scarring, and function loss. Patients with scarring are periodically followed up for assessment of progressive renal insufficiency. Tc-99m DMSA scintigraphy demonstrates approximately twice as many defects as renal US in the normal population (6). We hypothesized that this proportion may increase in SB patients because SB patients usually have rotoscoliosis, obesity, renal position anomalies, and intestinal gas distention that may corrupt the imaging quality of US, whereas these imaging difficulties do not affect the imaging quality of Tc-99m DMSA scintigraphy. We studied the efficiency of Tc-99m DMSA scintigraphy and renal US in the detection of renal scarring and function loss in children with SB.

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Received: 26.08.2016

Accepted: 12.12.2016

Methods

This study involved retrospective collection of clinical data from patients at the Spina Bifida Center of the İstanbul Bilim University between January 2014 and April 2015. Our study was performed in accordance with the principles of the Declaration of Helsinki. The study was approved by our local ethics committee. This study was approved by the intuitional ethics committee of our university (June 16, 2016; no: 32-284). Written consent was obtained from each participating child's parent or legal guardian. All patients were followed up at the outpatient clinic at regular intervals and underwent monitoring by several specialists. Urodynamic studies were performed at the age of 3–4 months and then every 6 months in the first year, annually until age 5, and biennially after that. SB patients were initially treated with clean intermittent catheterization, antimuscarinic agents, and antibiotic chemoprophylaxis from birth to prevent renal function loss as indicated by their bladder condition. Surgery for urinary incontinence, VUR, and recurrent infections were performed if necessary. US imaging was performed by an experienced radiologist using a Siemens Acuson S100 (Germany) device with a 4 Hz convex probe and, if necessary, a 9 Hz linear probe in younger patients. Static DMSA scintigraphy was performed using a double-headed gamma camera with a large field of view (GE Medical Systems Millennium, 2010, Israel, Model: H3000ZL, Serial no: 51679).

Patients who underwent US were investigated for horseshoe kidney anomalies, position anomalies secondary to rotoscoliosis, ectopic kidney, crossed fused ectopic kidney, renal agenesia, renal pelviectasis, hydronephrosis, difference in kidney length, renal parenchymal thinning, increased renal parenchymal echo, renal parenchymal scarring, bladder wall thickening, bladder wall trabeculation, and pseudodiverticulum of the bladder. Sonographic criteria for renal scarring included renal contour lobulation, renal parenchymal thinning, increased renal parenchymal echo, and decreased renal size (7, 8).

Bladder wall thickening, bladder wall trabeculation, and pseudodiverticulum formation of the bladder were accepted criteria for neurogenic bladder in the US. Bladder wall thickening was defined as ≥3 mm bladder wall thickness in a full bladder or ≥5 mm in an empty bladder (9).

Tc-99m DMSA scintigraphy following US was performed to evaluate suspected renal damage and function loss using a standard protocol throughout the study period. Radioactivity administered was adjusted using a body surface area correction formula or body weight with a minimum administered dose of 37 MBq. A high resolution collimator was used, and data were acquired in a 256 × 256 matrix. Images were obtained in anterior and posterior views 2–4 h after injection. Additional views with zoom magnification and pinhole collimator and prone images were obtained when necessary. Data acquisition in each projection was continued to a total of 500,000 counts per view. Differential function was quantified using geometric mean calculation and drawing regions of interest on anterior and posterior views for both kidneys.

A contribution of 45%–55% to total renal function by one kidney was considered normal, while a contribution of ≤44% was regarded as abnormal, allowing for a measurement error of up to 10%. Findings of contour irregularities and defects were accepted as indicators of renal scarring.

Statistical analysis

McNemar's test was used to compare the number of scars detected with renal US and DMSA scintigraphy. Pearson's test was used to assess the correlation between pole-to-pole length and differential renal function data gained by US and DMSA scintigraphy, respectively. Using Fisher's exact test, we studied the association between ultrasonographic renal cortical thickness loss and scintigraphy function loss. In all cases, $p<0.05$ was considered statistically significant.

Results

Patients included 100 children (51 boys and 49 girls) with a median age of 2 years (range: 6 months to 23 years). Findings on renal US are presented in Table 1. Three patients had unilateral agenesis; therefore, 197 kidneys were examined from 100 patients. Three patients had horseshoe kidneys, which were counted as separate kidneys. US demonstrated four atrophic kidney with function loss, three scarred kidneys (two on the left and one on the right), and five ectopic kidneys.

Findings on DMSA scintigraphy are presented in Table 2. Ten kidneys with scars in seven patients (seven on the left and three on the right kidney) were demonstrated with DMSA scintigraphy, whereas three kidneys with scars in three patients were demonstrated with US. During follow-up, we found that three times as many scars were seen on DMSA scintigraphy than on US. When DMSA scintigraphy was considered the gold standard test, the sensitivity of renal US for the detection of renal scarring was 30%.

Dimercaptosuccinic acid scintigraphy demonstrated 13 patients (mean age 5.4 years) with function loss (<45% differential function), whereas US demonstrated four patients with function loss according to volume and cortical thickness loss (Figure 1a, b). We

Table 1. Findings on renal US in 100 patients with 197 kidneys

US findings	n (%)
Scarring	3 (1.5)
Function loss	4 (2.0)
Neurogenic bladder	45 (22.8)
Hydronephrosis	8 (4.0)
Pelvic ectasia	31 (15.0)
Bladder diverticulosis	6 (3.0)
Position abnormality	15 (7.6)

US: ultrasonography

Table 2. Findings on renal US in 100 patients with 197 kidneys

	US n (%)	DMSA scintigraphy n (%)	p
Scarring	3 (1.5)	10 (5.0)	0,016
Function loss*	4 (0.2)	13 (6.5)	0,001

*Split function <45%; US: ultrasonography

observed that function loss was detected on DMSA scintigraphy at a rate three times higher than the renal US. When DMSA scintigraphy was considered the gold standard test for the detection of function loss, it gave a sensitivity of 30% for renal US. Among patients with function loss and renal scarring in DMSA scintigraphy, 47.3% and 57.1% of the patients had neurogenic bladder, respectively.

Ultrasonographic pole-to-pole length and cortical thickness findings correlated with split renal function on DMSA scintigraphy ($p<0.05$). Hydronephrosis demonstrated on US was also found to be correlated with split renal function loss finding on scintigraphy ($p<0.002$).

No significant relation was found between renal function loss and other risk factors such as neurogenic bladder, female sex, position abnormality, ectopy, or horseshoe kidney.

Discussion

The diagnostic strategies of children with SB differ according to the specific risks due to the dynamic nature of the disease. Pathologic innervation of the urinary bladder and urethral sphincters leads to urological complications. The lower urinary tract is primarily imaged using urodynamic studies prior to a surgical intervention. US is a noninvasive, inexpensive imaging modality with no radiation exposure, making it the first choice for children with SB. US is useful to diagnose dilatation and stones of the upper urinary tract and provide information on the lower urinary tract, such as neurogenic bladder, pelvic ectasia, diverticules. US should be performed before scintigraphy because DMSA cannot differentiate renal scarring from tumors, abscesses, or cysts, and for this reason, it needs ultrasound guidance. However, US alone may underestimate renal condition in patients with SB, who usually have rotoscoliosis, obesity, renal position anomalies, and intestinal gas distention, which may corrupt the imaging quality. Moreover, the interpretation of US is operator-dependent.

Early multidisciplinary management in newborns and good long-term follow-up of renal cortical scarring and function loss can prevent CKD and end-stage renal failure in children with SB (10). Computed tomography (CT) is expensive, reaction to contrast agents is a risk, and radiation-absorbed dose to the patient is higher (50 mSv/examination with CT and 1 mSv/examination with DMSA scintigraphy). Functional magnetic resonance imaging (MRI) is a noninvasive, developing technique with potential utility, but is expensive. MRI is not used in routine applications and must be correlated with US and DMSA scintigraphy (11).

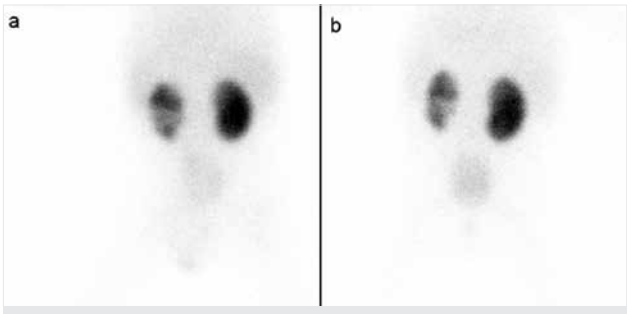

Figure 1. Operated spina bifida patient with neurogenic bladder in routine first renal ultrasonography reported normal findings. DMSA scintigraphy first performed after renal US and second after 1 year demonstrated renal function loss and scarring in posterior images below.

Filler et al. (12) observed progressive worsening of renal damage over time in SB. Mild function loss in children aged 2–5 become severe in 80% of children over time by age 10–13. They found that mild and severe unilateral renal function loss was evident in 50% patients by age 15. There was also a high prevalence of recurrent UTIs. Eighty-one percent of patients had developed at least one UTI. More than one episode was seen in 44% of patients, and more than 20 episodes were seen in 9% of patients. In their study, they emphasized using an accurate GFR to monitor renal function. Inulin clearance is the gold standard in GFR measurement but is not used in modern practice as it is impractical and difficult to use. Creatinine-based methods are insensitive because of the low muscle mass of underdeveloped musculature in the legs and the elevation of GFR by endogenous creatinine secreted from tubules. Only cystatin C-based eGFR can reliably assess global renal function in SB patients. However, if renal damage is unilateral, it cannot be diagnosed by global renal function test because of compensation by the other kidney, so nuclear medicine scans are required (12).

Dik et al. (13) reported the increasing chance of renal failure with age. Cortical damage was seen in 13.3% of children with SB under the age of 2, whereas it was in 27.3% of children with SB over the age of 10. In the follow-up of SB, they trusted the reliability of renal US without the need of scintigraphy if serum creatinine, US, and bladder pressure were all normal (13). However, in their recent study with adult SB patients, Veenboer et al. (14) compared both modalities with a focus on renal scarring and concluded that renal scars are often missed with US. In 40% of cases, US missed scars that were visualized with a DMSA scan. In the same study, the sensitivity of US in determining function loss was also mentioned low in patients with SB. However, they also mentioned that renal US had a high predictive value for split renal function and the advantage of low cost, besides being easy to perform; therefore, additional scintigraphy was needed in the case of progressive pyelocalyceal dilatation or pole-to-pole length decrease (14). In another study, Shiroyanagi et al. (15) found that positive VUR and febrile UTIs were associated with an abnormal DMSA scan. They declared that DMSA scintigraphy was useful in determining renal function loss and indicating old and new scars in children with febrile UTI and reflux.

In our study, both DMSA scintigraphy and renal US were real-time studies. Our ultrasonographist had the opportunity to evaluate the images at the same time as scintigraphy. Our main finding in this study is that the sensitivity of renal scintigraphy in the diagnosis of both renal scars and function loss was significantly higher than that of US. Scintigraphy is needed against the underestimation of pyelonephritis, function loss, and sequelae after UTI. In the need of early and prompt onset of treatment, we conclude that diagnosis is reliable with US followed by scintigraphy and recommend the evaluation of all children born with SB first at 6 months then at 2 years, unless there is febrile UTI second. If febrile UTI occurs, sequelae should be evaluated after 6 months. If there is scarring, scintigraphy should be repeated 1 year later, if not, it should be clinically evaluated.

Conclusion

In children with SB, rotoscoliosis, obesity, renal position anomalies, and intestinal gas distention may corrupt the imaging quality of US, whereas these imaging difficulties do not affect the imaging quality of Tc-99m DMSA scintigraphy. Chronic renal failure is preventable with case-specific and holistic multidisciplinary care. With a high predictive value and low cost, renal US is the first imaging modality to evaluate the upper and lower urinary tract; however, it alone is not reliable for monitoring scarring and function loss. To avoid under-detection, renal scintigraphy should also be done performed to better evaluate function loss and scarring.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of İstanbul Bilim University Clinical Research Ethics Committee (June 16, 2016; no: 32-284).

Informed Consent: Written informed consent was obtained from patients' parents who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - E.Ö., I.K.; Design - M.B.Ö.; Supervision - E.Ö., K.Ö.; Resources - E.Ö.; Materials - P.G.A.; Data Collection and/or Processing - I.K., İ.A.; Analysis and/or Interpretation - L.Ö., T.D.; Literature Search - L.Ö., T.D.; Writing Manuscript - L.Ö., E.C.G.; Critical Review - L.Ö., I.K.; Other - İ.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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