Ultrasound Detection of Vesicoureteral Reflux in Children

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Purpose: We present different ultrasound techniques to detect vesicoureteral reflux in children with special emphasis on voiding urosonography.

Materials and Methods: Urinary tract infection is a common problem in children that may be related to vesicoureteral reflux. Currently there is no consensus on investigations in children after the first urinary tract infection. The least invasive imaging with the smallest radiation burden should be used in children. Ultrasound to detect reflux meets several of these criteria. The development of echo enhancing agents has markedly improved reflux visualization by ultrasound.

Results: We discuss the clinical relevance of voiding urosonography. We reviewed the currently available literature and the results of our studies of this issue. We also describe our endeavors to avoid catheterization and detect vesicoureteral reflux based on various sonomorphological features, ie indirect voiding urosonography and ureteral jet Doppler waveform analysis, to avoid applying any substance into the bladder.

Conclusions: Voiding urosonography is safe and reliable to detect vesicoureteral reflux. When indicated, considerably decreased radiation exposure can be achieved by voiding urosonography instead of established cystography methods. Indirect voiding urosonography and ureteral jet Doppler waveform analysis could be an alternative to invasive voiding cystography, at least in children older than 3 years.

Key Words: ureter, vesico-ureteral reflux, ultrasonography, urinary tract infections, contrast media

Abbreviations and Acronyms

DRVC = direct radionuclide voiding cystography

IVUS = indirect VUS

PUU = pelviureteral unit

UJDW = ureteral jet Doppler wave form

UTI = urinary tract infection

VCUG = voiding cystourethrography

VUR = vesicoureteral reflux

VUS = voiding urosonography

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We present different techniques of ultrasound detection of VUR in children with special emphasis on VUS. We reviewed the current literature and the results of our studies. We discuss VUS advantages and limitations, and criteria to select the imaging modality to detect VUR. The ultimate goal would be a reliable, inexpensive, radiation-free, catheter-free examination to detect VUR.

VESICOURETERAL REFLUX

VUR is a common problem in children. The most serious consequences of reflux nephropathy are hypertension and impaired renal function. Although childhood UTI is common, chronic kidney disease and the likelihood that acute pyelonephritis will cause renal damage progressing to chronic kidney disease are rare.[1] Until recently it was generally accepted that the urinary tract should be imaged in all children after the first UTI. However, current scientific information does not justify imaging in all of these children. The most appropriate choice, extent and timing of investigation must still be defined. The focus of investigation should be based

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on what is happening to the kidney in regard to scarring and less invasive techniques with less radiation should be used.[2,3] A select group of children can be identified clinically according to defined risk factors to decrease the number who undergo imaging.[1] The top-down approach involving ^{99m}Tc-dimercapto-succinic acid renal scan as close as possible to the acute UTI episode may be used to identify children most at risk.[4]

IMAGING TECHNIQUES

Until recently 2 methods have been routinely used to detect VUR in children, namely x-ray VCUG and DRVC. Unfortunately these techniques involve exposure to ionizing radiation. Modern equipment has considerably decreased radiation exposure in examined children. However, radiation induced adverse effects in children examined by VCUG are causing growing concern, especially given the high VCUG incidence, direct exposure of the gonadal area and the long life expectancy of children. Perisinakis et al reported that the radiation risk associated with fluoroscopically controlled VCUG may not be considered trivial.[5] Thus, VCUG should be efficiently justified since several alternatives to detect VUR are available with less or no radiation exposure. Absent gonadal radiation even when observation time is extended is the main advantage of VUR sonographic detection. Considering the recent emergence of stabilized echo contrast agents, and the widespread availability and constant technical improvement of ultrasound equipment, using ultrasound to detect VUR seems even more reasonable.

VUS IN CHILDREN

Each voiding cystogram basically entails certain steps, including urinary tract imaging before contrast agent application, catheterization, intravesical administration of a suitable contrast agent according to the chosen method, and urinary tract evaluation during and after voiding. Thus, VUS is similar to VCUG or DRVC and unfortunately bladder catheterization is unavoidable.[6,7] However, the main difference is the complete absence of radiation.

Stabilized Echo Enhancing Agents

The development of commercially available, stabilized echo enhancing agents has markedly improved ultrasound detection of fluid movement in the urinary tract and, thus, VUR visualization by ultrasound (VUS). The most commonly used contrast agent is Levovist®, which consists of 99.9% microcrystalline galactose microparticles and 0.1% palmitinic acid. By adding water and agitating a milky suspension containing air filled microbubbles is obtained. The microbubbles are adsorbed onto the surface of galactose microparticles and covered with a thin film of palmitinic acid to render them more stable. Due to their acoustic properties air filled microbubbles are basically an effective echo enhancing agent that renders urine echogenic and makes it suitable for ultrasound visualization. The detection of hyperechogenic microbubbles in the ureter or renal pelvis is consistent with VUR.

In 2001 a second generation echo contrast agent was approved for intravenous use in adults, namely SonoVue®.[8] It is composed of phospholipid stabilized microbubbles of sulfur-hexafluoride. Gathered preliminary results suggest that low mechanical index imaging is the most favorable ultrasound modality for VUS when SonoVue is applied. For VUS the echo contrast agent is added intravesically through the same catheter after the bladder is filled to capacity with saline solution. In clinical studies the necessary SonoVue volume was less than 1% of predicted bladder volume compared to 5% to 10% when Levovist was used. Thus, in vivo SonoVue use is expected to yield a significant dose decrease so that 1 vial can be used for more than 1 examination. A measurable cost decrease can consequently be achieved.[7]

Imaging Modalities to Detect VUR

Several studies have been published in the last decade showing the reliability of VUS to detect VUR in children.[6,9–15] Comparisons among VUS, VCUG and DRVC show high concordance regarding VUR diagnosis. However, in some studies VUS was more sensitive than VCUG.[16] Moreover, VUR missed by VCUG was predominately of higher grade and, thus, clinically more important than VUR missed by VUS.[2,17] Most recently Darge reported a wide-ranging review and a critical analysis of studies comparing VUS with VCUG and DRVC.[8] Most studies compared VUS with VCUG. Using VCUG as the reference method, the accuracy for VUR detection was 90% and greater. VUR was detected only by VUS in 19% of PUUs and only by VCUG in 10%. Thus, in 9% of PUUs more VUR was detected by VUS. In about 20% of PUUs VUS detected higher grade VUR than VCUG. Of VUR episodes missed on VCUG and detected only on VUS 70% were grade II–V. In contrast, 68% of episodes detected only by VCUG were grade I.

Almost simultaneously with the first reports of Levovist enhanced VUS[9,15] we examined VUS reliability to detect VUR in children.[6] Our approach was original for 2 reasons. 1) VUS results were compared exclusively to DRVC. 2) The 2 investigations were performed simultaneously without causing additional discomfort to the patient. Thus, exactly the same conditions applied to the 2 modalities. There were sev-