

Review Article

Imaging Study of Vesicoureteral Reflux



Parisa Honarpisheh¹ , Azar Nickavar^{2*}

1. Pediatric Respiratory Diseases Research Center, National Research Institute of Tuberculosis and Lung Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

2. Department of Pediatric Nephrology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.



Citation Honarpisheh P, Nickavar A. Imaging Study of Vesicoureteral Reflux. *Journal of Pediatric Nephrology*. 2022; 10(2):55-58. <https://doi.org/10.22037/jpn.v10i2.38245>

doi <https://doi.org/10.22037/jpn.v10i2.38245>



Article info:

Received: 20 Apr 2022

Accepted: 14 Jul 2022

Publish: 01 Apr 2022

Corresponding Author:

Azar Nickavar,
Address: Department of
Pediatric Nephrology,
School of Medicine, Iran
University of Medical
Sciences, Tehran, Iran.
E-mail: anickavar@yahoo.com

ABSTRACT

Different radiologic and radionuclide cystography studies have been suggested to detect and follow up vesicoureteral reflux (VUR) in children, with conflicting results. Conventional voiding cystourethrography seems the preferred method to evaluate urinary tract abnormality, voiding dysfunction, and accurate grading of VUR. However, radioisotopic cystography is a preferred method to evaluate VUR in women, patients without voiding dysfunction, and re-evaluate VUR.

Keywords: Vesicoureteral reflux, Cystography, Radionuclide imaging, Urinary tract infection, Child

Introduction

Vesicoureteral Reflux (VUR) is the most common congenital urinary tract abnormality in children and the most common risk factor for Urinary Tract Infection (UTI) in the pediatric age group accounting for 30%-50% of these patients. About 8.5%-18% of children with chronic kidney disease have underlying reflux nephropathy. Therefore, early diagnosis and appropriate management of VUR may prevent its long-term complications, such as hypertension, proteinuria, and decreased renal function [1].

Conventional radiologic and Radioisotopic Cystography (RNC) are common diagnostic procedures for VUR with benefits and limitations. This review was conducted to evaluate the different aspects of these diagnostic procedures to introduce an appropriate method for diagnosing VUR.

Evidence Acquisition

This review study was conducted by reviewing the literature of medical databases, including PubMed, Google Scholar, ISI, Web of Science, and Scopus using the keywords “VUR”, “voiding cystourethrography”, “RNC”, and “UTI”.

Results and Discussion

Investigating VUR has been suggested by different guidelines, such as the American Academy of Pediatrics (AAP) or the National Institute for Health and Care Excellence (NICE) guideline in patients with renal ultrasound findings, including high-grade VUR, obstructive uropathy, renal scarring, in addition to the complex clinical circumstances, such as atypical UTI, and recurrent febrile UTI.

Different imaging methods have been suggested to detect VUR in children, and fluoroscopic Voiding CystoUrethrography (VCUG) and Direct Radionuclide Cystography (DRNC) is commonly used.

VCUG has been the traditional gold standard method for diagnosing VUR [2, 3]. However, the introduction of DRNC provided multiple challenges and controversies in choosing the appropriate and safe imaging method for diagnosing VUR [4], and the benefits of VCUG were questioned in many conditions. However, VCUG and DRNC require urinary catheterization unpleasant for patients and parents [3].

Some of the limitations of RNC included a low-resolution rate and a lack of accurate diagnosis of bladder anatomy, male urethra, mild VUR, and intra-renal reflux [5]. In addition, it is not a precise method to grade VUR [6] accurately. The International Reflux Study Committee has classified VUR into 5 grades by VCUG, with grade I and grade II corresponding to mild VUR, grade III to moderate, and grades IV-V to severe VUR, respectively, according to DRNC grading [7].

Meanwhile, displaying the anatomic details of the urinary tract system, especially the male urethra or calyceal anatomy, in addition to post voiding urine residue and accurate grading of VUR, are the major advantages of VCUG [8]. Goldman et al. detected urinary tract abnormality in 22 of 45 male neonates. Of them, 21 neonates had VUR. They suggested routine ultrasound and VCUG after the first UTI in male neonates less than 8 weeks [9]. In addition, the proper grading of VUR is a major predictor of further spontaneous resolution and avoidance of unnecessary antibiotic prophylaxis in low-grade VUR [3].

Intermittent monitoring of urine backflow increases the possibility of undetected VUR by VCUG, higher than DRNC [8]. However, continuous monitoring of DRNC increases the detection rate of VUR [4, 10] and misses only 6% of patients [10, 11], mostly grade I

[8]. DRNC has been advocated as the essential complementary method for diagnosing VUR [6]. Kogan et al. reported failure of conventional VCUG in 10 cases with VUR, in whom isotope cystogram indicated significant degrees of VUR [12]. Several studies showed the priority of RNC to detect VUR in children with normal VCUG findings, especially in those with hydronephrosis, abnormal Dimercaptosuccinic Acid (DMSA) scan, and recurrent febrile UTI [6, 12, 13]. In addition, some studies showed a higher sensitivity of RNC in younger children compared to a higher sensitivity of VCUG in older patients [14, 15]. However, several studies reported similar sensitivity and good correlation to detect VUR by these two methods [6, 15]. About 85% agreement between these two procedures was reported and VCUG was recommended if it was adequately justified against alternative procedures [16, 17]. However, it is essential to emphasize that VUR is an intermittent condition and cannot be completely excluded by negative imaging results [18].

The main advantage of DRNC is less radiologic irradiation of gonads and bladder (10-20 μ Gy), which is approximately 100-fold less than the conventional VCUG technique [15, 19]. However, during the last decade, a technical evolution occurred in fluoroscopy VCUG by shifting from analog to digital imaging systems, resulting in a considerable decrease (89%) in radiation burden from VCUG [1, 20]. In addition, the researchers have proved that low-dose fluoroscopic VCUG is a practical alternative approach with less radiation than the radionuclide technique in girls with VUR [21].

According to the guidelines proposed by the European Association of Nuclear Medicine (EANM), clinical indications of DRNC consisted of “follow-up of previously diagnosed VUR, re-evaluation of endoscopic/surgical anti-reflux surgery, screening of sibling or parents of the involved patient, serial evaluation of VUR in the neurogenic bladder, and detection of VUR in kidney transplant recipients” [18].

In a study conducted by Medina et al., RNC instead of VCUG was more costly and affordable than VCUG ($P < 0.001$) if clinically appropriate [22]. However, in a recently published study by Pauchard et al., cystography was not recommended in infants younger than 3 months with the first febrile UTI, *E. coli* infection, and normal renal ultrasound for the very low possibility of undiagnosed high-grade VUR ($P < 1\%$) [23]. Therefore, there are controversies about the preferred diagnostic method of VUR in different studies. Accordingly, the proper imaging study depends on individual

risks and benefits of the diagnostic procedure, such as age, gender, suspected structural or functional urinary tract abnormalities, and cost, with no absolute indication for any diagnostic modality. It is reasonable that the imaging procedure should be minimally invasive and toxic, with high sensitivity and specificity. The VCUG seems to be the preferred radiologic study in men, patients with voiding dysfunction and suspected anatomical or functional abnormalities of the urinary tract. Meanwhile, the researchers have proved that DRNC is a preferred diagnostic procedure in women and re-evaluation of VUR.

Ethical Considerations

Compliance with ethical guidelines

This is a review article with no human or animal samples.

Funding

This research did not receive any funding.

Authors' contributions

All authors equally contributed to the preparation of this article.

Conflict of interest

The authors declared no conflict of interest.

References

- [1] Nickavar A, Valavi E, Safaeian B, Moosavian M. Validity of urine neutrophile gelatinase-associated lipocalin in children with primary vesicoureteral reflux. *Int Urol Nephrol*. 2020; 52(4):599-602. [DOI:10.1007/s11255-019-02355-3] [PMID]
- [2] Darge K, Riedmiller H. Current status of vesicoureteral reflux diagnosis. *World J Urol*. 2004; 22(2):88-95. [DOI:10.1007/s00345-004-0404-1] [PMID]
- [3] Lee LC, Lorenzo AJ, Koyle MA. The role of voiding cystourethrography in the investigation of children with urinary tract infections. *Can Urol Assoc J*. 2016; 10(5-6):210-4. [DOI:10.5489/cuaj.3610] [PMID] [PMCID]
- [4] Zorc JJ, Kiddoo DA, Shaw KN. Diagnosis and management of pediatric urinary tract infections. *Clin Microbiol Rev*. 2005; 18(2):417-22. [DOI:10.1128/CMR.18.2.417-422.2005] [PMID] [PMCID]
- [5] Kleinman PK, Diamond DA, Karellas A, Spevak MR, Nimkin K, Belanger P. Tailored low-dose fluoroscopic voiding cystourethrography for the reevaluation of vesicoureteral reflux in girls. *AJR Am J Roentgenol*. 1994; 162(5):1151-4. [DOI:10.2214/ajr.162.5.8166001] [PMID]
- [6] Saraga M, Staničić A, Marković V. The role of direct radionuclide cystography in evaluation of vesicoureteral reflux. *Scand J Urol Nephrol*. 1996; 30(5):367-71. [DOI:10.3109/00365599609181312] [PMID]
- [7] Unver T, Alpay H, Biyikli NK, Ones T. Comparison of direct radionuclide cystography and voiding cystourethrography in detecting vesicoureteral reflux. *Pediatr Int*. 2006; 48(3):287-91. [DOI:10.1111/j.1442-200X.2006.02206.x] [PMID]
- [8] Lim R. Vesicoureteral reflux and urinary tract infection: Evolving practices and current controversies in pediatric imaging. *Am J Roentgenol*. 2009; 192(5):1197-208. [DOI:10.2214/AJR.08.2187] [PMID]
- [9] Goldman M, Lahat E, Strauss S, Reisler G, Livne A, Gordin L, et al. Imaging after urinary tract infection in male neonates. *Pediatrics*. 2000; 105(6):1232-5. [DOI:10.1542/peds.105.6.1232] [PMID]
- [10] Fettich J, Colarinho P, Fischer S, Frökier J, Gordon I, Hahn K, et al. Guidelines for direct radionuclide cystography. *Eur J Nucl Med Mol Imaging*. 2002; 25(2):106-11. [DOI:10.1007/s00259-003-1137-x] [PMID]
- [11] De Sadeleer C, De Boe V, Keuppens F, Desprechins B, Verboven M, Piepsz A. How good is technetium-99m mercaptoacetyl triglycine indirect cystography? *Eur J Nucl Med*. 1994; 21(3):223-7. [DOI:10.1007/BF00188670] [PMID]
- [12] Kogan SJ, Sigler L, Levitt SB, Reda EF, Weiss R, Greifer I. Elusive vesicoureteral reflux in children with normal contrast cystograms. *J Urol*. 1986; 136(1):325-8. [DOI:10.1016/S0022-5347(17)44855-5]
- [13] Dalirani R, Mahyar A, Sharifian M, Mohkam M, Esfandiari N, Ghehsareh Ardestani A. The value of direct radionuclide cystography in the detection of vesicoureteral reflux in children with normal voiding cystourethrography. *Pediatr Nephrol*. 2014; 29(12):2341-5. [DOI:10.1007/s00467-014-2871-y] [PMID]
- [14] Poli-Merol M-L, Francois S, Pfliger F, Lefebvre F, Roussel B, Liehn J, et al. Interest of direct radionuclide cystography in repeated urinary tract infection exploration in childhood. *Eur J Pediatr Surg*. 1999; 8(6):339-42. [DOI:10.1055/s-2008-1071228] [PMID]
- [15] Sükan A, Bayazit AK, Kibar M, Noyan A, Soyupak S, Yapar Z, et al. Comparison of direct radionuclide cystography and voiding direct cystography in the detection of vesicoureteral reflux. *Ann Nucl Med*. 2003; 17(7):549-53. [DOI:10.1007/BF03006667] [PMID]
- [16] Piscitelli A, Galiano R, Serrao F, Concolino D, Vitale R, D'Ambrosio G, et al. Which cystography in the diagnosis and grading of vesicoureteral reflux? *Pediatr Nephrol*. 2008; 23(1):107-10. [DOI:10.1007/s00467-007-0651-7] [PMID]
- [17] Perisinakis K, Raissaki M, Damilakis J, Stratakis J, Neratzoulakis J, Gourtosyiannis N. Fluoroscopy-controlled voiding cystourethrography in infants and children: Are the radiation risks trivial? *Eur Radiol*. 2006; 16(4): 846-51. [DOI:10.1007/s00330-005-0072-6] [PMID]

- [18] Fettich J, Colarinha P, Fischer S, Frökier J, Gordon I, Hahn K, et al. Guidelines for direct radionuclide cystography in children. *Eur J Nucl Med Mol Imaging*. 2003; 30(5):B39-44. [DOI:10.1007/s00259-003-1137-x] [PMID]
- [19] Dave S, Khoury AE. Diagnostic approach to reflux in 2007. *Adv Urol*. 2008; 2008:367320. [DOI:10.1155/2008/367320] [PMID] [PMCID]
- [20] Tzanis E, Raissaki M, Konstantinos A, Damilakis J, Perisnakis K. Radiation exposure to infants undergoing voiding cystourethrography: The importance of the digital imaging technology. *Phys Med*. 2021; 85:123-8. [DOI:10.1016/j.ejomp.2021.05.006] [PMID]
- [21] Haid B, Becker T, Koen M, Berger C, Langsteger W, Gruy B, et al. Lower radiation burden in state of the art fluoroscopic cystography compared to direct isotope cystography in children. *J Pediatr Urol*. 2015; 11(1):35.e1-6. [DOI:10.1016/j.jpuro.2014.08.015] [PMID]
- [22] Medina LS, Aguirre E, Altman NR. Vesicoureteral reflux imaging in children: Comparative 60. cost analysis. *Acad Radiol*. 2003; 10(2):139-44. [DOI:10.1016/s1076-6332(03)80037-5] [PMID]
- [23] Pauchard J-Y, Chehade H, Kies CZ, Girardin E, Cachat F, Gehri M. Avoidance of voiding cystourethrography in infants younger than 3 months with *Escherichia coli* urinary tract infection and normal renal ultrasound. *Arch Dis Child*. 2017; 102(9):804-8. [DOI:10.1136/archdischild-2016-311587] [PMID]