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Original Research Article

Comparison of Colour Doppler Flow Imaging with Voiding Cystourethrography in the Detection of Vesicoureteric Reflux in Children

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ABSTRACT

Introduction: *Early detection and management of Vesicoureteric reflux (VUR) prevents the adverse renal effects. Voiding cystourethrography (VCUG) is considered the gold standard for diagnosis of VUR. Colour Doppler flow imaging (CDFI) is an attractive alternate imaging modality as it does not involve urethral catheterisation, contrast agent and ionising radiation.*

Aim of the study: *To assess the sensitivity, specificity, positive and negative predictive value of CDFI as compared to VCUG in the detection of VUR.*

Materials and Methods: *Seventy children between the ages of 1 to 12 years who were clinically suspected to have VUR were evaluated with VCUG and detection and grading of VUR was done. Then the sonologist who was unaware of the findings of VCUG performed CDFI. The sensitivity, specificity, positive and negative predictive values were calculated.*

Results & Discussion: *VUR was detected in 94 ureters in 56 patients by VCUG and in 78 ureters in 45 cases by CDFI. The sensitivity, specificity, positive and negative predictive values of CDFI were 77.7%, 91.3%, 94.8% and 66.7%. Accuracy was 82.1%. Sensitivity for low grade reflux was 27.78%, grade III reflux was 91.67%, grade IV and grade V reflux was 100%. There were 4 false positive results in CDFI. Identical grades were seen in 68 of the 74 ureters with reflux in both tests. There was significant coefficient of agreement (kappa) between grading by both tests (0.718).*

Conclusion: *The sensitivity of CDFI is low for low grade reflux which may be a physiological condition and excellent for grade IV and V reflux. The low negative predictive value means that a negative result on CDFI does not rule out VUR. There is good specificity and positive predictive value. The false positive rate of 2.9 % may indicate that CDFI may detect intermittent reflux missed on VCUG. Whenever CDFI detected reflux, there was good correlation between grades with a significant coefficient of agreement. The results indicate that CDFI may be used for follow up of children with VUR with VCUG being done only when CDFI is negative, hence reducing radiation exposure.*

Keywords: *Vesico-Ureteral Reflux; Ultrasonography, Colour Doppler; Urinary Tract Infections; Voiding Cystourethrography.*

Introduction

Vesicoureteric reflux (VUR) is the abnormal retrograde flow of urine from the urinary bladder into the ureter across the vesicoureteric junction.[1] The prevalence of VUR in normal children has been estimated at 0.4–1.8%.[2] However, up to 50% of infants and children with urinary tract infection (UTI) are known to have VUR.[3] Untreated VUR predisposes to urinary tract infections that may progress to reflux nephropathy and end in renal failure. It adversely affects the growth and development of the kidney and also the general somatic growth of the child. Most children with VUR fall in the lower weight percentile group. Early detection and management prevents the adverse renal effects and hence early diagnosis of VUR is of paramount importance.

Voiding cystourethrography (VCUG) is considered the gold standard for diagnosis of vesicoureteric reflux.[4] It delineates the anatomy of the urinary tract, aids in the diagnosis of associated structural anomalies like posterior urethral valves and also helps in grading of vesicoureteric reflux. The main disadvantages are exposure to radiation at a young age, use of catheterization and introduction of contrast agent.

Other investigations used in VUR are conventional gray scale ultrasound (US), voiding urosonography with ultrasound contrast agents (VUS), radionuclide cystography (RNC) and colour Doppler flow imaging (CDFI). Colour Doppler flow imaging is an attractive imaging modality as it eliminates the need for urethral catheterisation and contrast agent and is free from harmful ionising radiation.[5] Doppler study in conjunction with conventional US can evaluate the kidneys for echo texture, parenchymal thickness and scars while dilatation of the pelvicalyceal system helps in the grading of VUR. The direction of the ureteric jet and the changes in the pelvicalyceal system are assessed for the diagnosis and grading of VUR.

Objectives

The present study aims to assess the sensitivity, specificity, positive and negative predictive value of colour Doppler flow imaging as compared to voiding cystourethrography as the gold standard in the detection of vesicoureteric reflux.

Materials and Methods

A diagnostic test evaluation study was conducted in the Department of Radiodiagnosis, Government Medical College, Thrissur from January 2015 to July 2016 with the approval of the Institutional Ethics Committee involving children in the age group of 1-12 years who were clinically suspected to have VUR and were referred to the Department of Radiodiagnosis, Government Medical College Thrissur from the Department of Paediatric Surgery, Government Medical College Thrissur for performing VCUG within the study period.

Sample size was calculated using the formula N = (TP + FN) /P where N= Sample size, TP=True Positives, FN=False Negatives, P= Prevalence (50%)[3]

$$TP+FN= \frac{(Z\alpha/2)2 \times SN \times(1-SN)}{d2}$$

SN = Least sensitivity in previous studies (85%) 6, d = permissible error (0.08)

N is calculated to be 153.

However a sample size of only 70 cases could be obtained in the study period considering the inclusion and exclusion criteria.

The Inclusion criteria were children with clinical suspicion of VUR, children who are outpatients or inpatients of the Department of Paediatric Surgery, Government Medical College, Thrissur, children who are referred to the Department of Radiodiagnosis for performing VCUG, age of children between 1 to 12 years, a sterile urine culture at the time of the tests, both tests done on the same day within 24 hours of each other. The Exclusion criteria were children whose guardians are not willing to participate in the study and uncooperative children.

Patients referred to the department of Radiodiagnosis for performing voiding cystourethrography were selected based on the inclusion and exclusion criteria stated above. Informed consent was obtained from the legal guardians of the children

regarding willingness to participate in the study. A brief history was taken and clinical examination done. First VCUG was performed using fluoros-copy technique in Allengers RF Angiotab 9090.

A parent or relative was allowed to be present with the child during the study. The child was placed on the X ray table and a preliminary plain radiograph AP view of the KUB area was taken. The child's bladder was catheterized under aseptic precautions using local anaesthetic gel with an age appropriate catheter. Then diluted contrast (sodium diatrizoate) was introduced into the bladder via the catheter till bladder capacity is reached. Bladder capacity was calculated using the formula: volume= (years of age + 2) × 30 ml and a full bladder film was taken. Then the catheter was removed and a voiding radiograph taken (oblique projection in case of boys and AP projection in case of girls). Detection and grading of VUR will be done by the International Reflux Study Committee Classification System.[7] Post void radiograph is also taken.

Then the sonologist who is unaware of the findings of VCUG performs the colour Doppler ultrasound using Mindray DC[8] ultrasound machine. Colour Doppler examination is carried out using 4 MHz convex sector probes. Colour gain settings and filters are optimized for slow flow sensitivity. The colour map was red toward the probe and blue away from it. Hence reflux was seen as a blue coloured jet and normal ureteric jet was red. All patients were examined by conventional US before fluid intake to record pelvicalyceal system dimensions and to provide baseline information about the kidneys (size, shape, parenchymal thickness and scars). The child was then asked to drink water or tea until he/she had a full-bladder sensation. The lower ends of the ureters were scanned in the transverse and longitudinal planes, and bladder jets from the ureter to bladder, and any reversal of flow from bladder to ureter were noted. In cases of doubt these colour jets were differentiated from nearby vascular structures by combining pulsed Doppler and colour Doppler. At the end of the filling period there was a second conventional US of the kidney to detect possible pelvicalyceal dilatation. The child was then asked to void or strain and again the lower end of the ureter was continuously monitored for reflux. The changes in the pelvicalyceal system were also evaluated. High-grade VUR was diagnosed based on collecting system dilatation including both scans at baseline and during the study. High-grade VUR was confirmed by the presence of collecting system dilatation in the ipsilateral kidney and ureter only during the study. If there was a collecting system dilatation on baseline scans, high- grade reflux was inferred by the presence of increased collecting system dilatation during the study compared with baseline findings.

The data was managed in Microsoft Office Excel 2007 and statistical analysis was done using IBM SPSS Statistics 19. The sensitivity, specificity, positive and negative predictive values were calculated and expressed in percentage.

Results

In this study, VUR was detected in 94 ureters in 56 patients by VCUG and in 78 ureters in 45 patients by CDFI. The overall sensitivity, specificity, positive and negative predictive values of CDFI were 78.7%, 91.3 %, 94.9% and 67.7%. Accuracy was 82.9%.

Table 1: Contingency table

		VCUG	
		+	-
CDFI	+	74	4
	-	20	42

CDFI did not detect VUR in 20 ureters which were seen to be refluxing on VCUG (false negative). Of these 15 cases were grade I, 3 were grade II and 2 were grade III on VCUG. No grade IV or grade V cases were missed by CDFI. Sensitivity for low grade reflux was 21.74%, grade III reflux was 91.67 %, grade IV and grade V reflux was 100 %.

Table 2: Cases missed on CDFI and their VCUG grade

VCUG Grade	Number of cases
Grade I	15
Grade II	3
Grade III	2
Grade IV	0
Grade V	0

There were 4 false positive results in CDFI, probably because these patients had intermittent reflux which was not detected by VCUG.

Table 3: Grid with distribution of grades in both tests

		Voiding cystourethrography				
		No reflux	Low grade	Grade III	Grade IV	Grade V
CDFI	No reflux	42	18	2	0	0
	Low grade	4	5	1	0	0
	Grade III	0	0	19	1	0
	Grade IV	0	0	2	19	2
	Grade V	0	0	0	0	25

The figures in bold across the diagonal are the number of ureters where the tests are in total agreement and the figures farther from this axis show increasing degrees of disagreement between the two tests. Of the 74 ureters which showed reflux in both tests, identical grades were seen in 68 ureters. If Grade 0 is also considered, identical grades are seen in 110 (42 + 68) ureters. There were 6 ureters with differing grades on CDFI and VCUG. In all these cases there was a difference of one grade. VCUG showed a higher grade in all ureters except two.

Coefficient of agreement Kappa = 0.718 with a p value = 0.000

Figure 1: VCUG image of a 4 year old girl showing Grade V reflux on right and Grade IV reflux on left

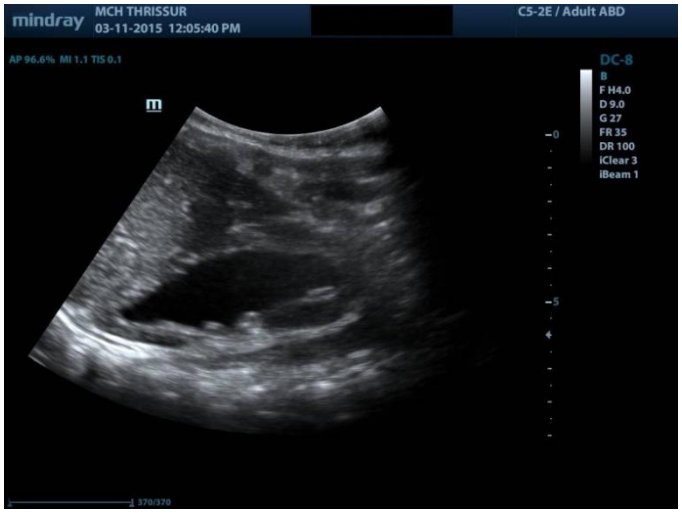

Figure 2: Ultrasound image of the right kidney of the same girl showing gross hydronephrosis

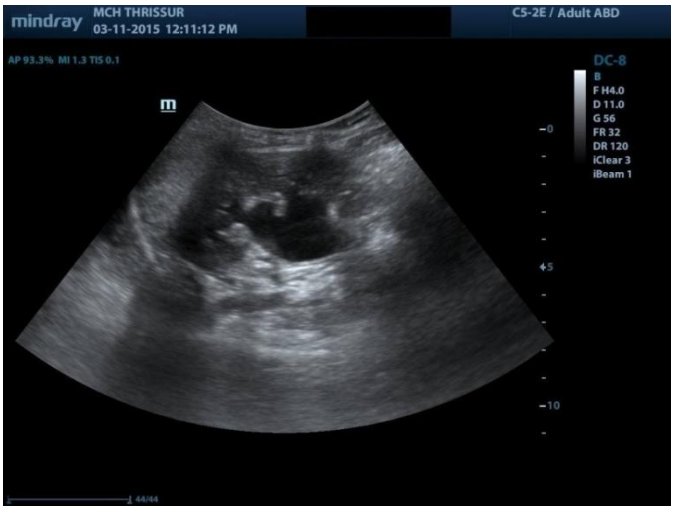

Figure 3: Ultrasound image of the left kidney of the same girl showing moderate hydronephrosis

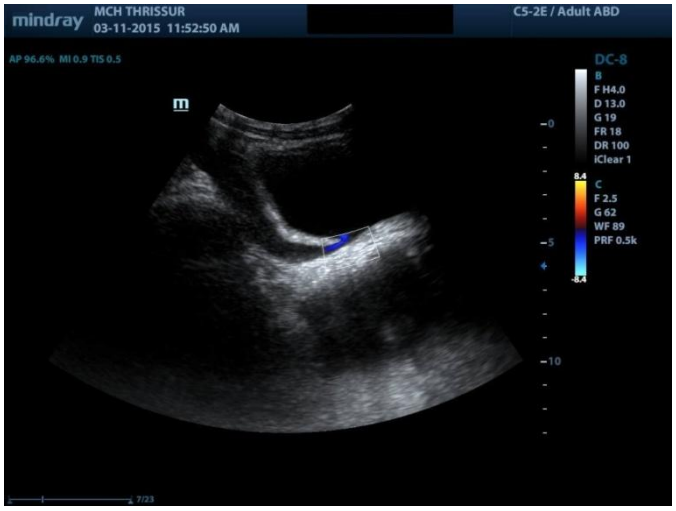

Figure 4: CDFI showing right ureteric jet in blue in the same girl

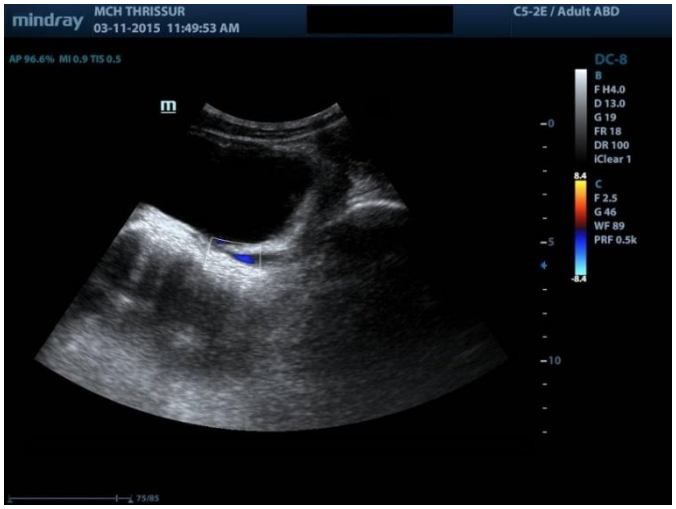

Figure 5 : CDFI showing left ureteric jet in blue in the same girl

Discussion

In our study, the overall sensitivity, specificity, positive and negative predictive values of CDFI were 78.7%, 91.3 %, 94.9% and 67.7%. Accuracy was 82.9%. In the study by Kosar et al8 sensitivity and specificity were 90 % and 93 % respectively. In the study by Salih et al[9] sensitivity, specificity, positive and negative predictive values were 96.3%, 80%, 89.7% and 92.3%. The study by Yousefi et al[6] had sensitivity, specificity, positive and negative predictive values of 85%, 90%, 92% and 81% respectively

CDFI did not detect VUR in 20 ureters which were seen to be refluxing on VCUG (false negative). Of these, 15 cases were grade I, 3 were grade II and 2 were grade III on VCUG. No grade IV or grade V cases were missed by CDFI. Sensitivity for low grade reflux was 21.74%, grade III reflux was 91.67 %, grade IV and grade V reflux was 100 %. Salih et al9 showed correlation of 90%, 100% and 75% between VCUG and CDFI in low grade, grade III and grade IV reflux. Haberlik10 also reported CDFI to be less sensitive in the detection of VUR grade I and II. To prove this, they studied 38 asymptomatic children with normal urological status and negative urine culture aged 3 to 15 years. 4 children were found to have unilateral reflux. This indicated that asymptomatic grade I and II reflux might be a physiological condition.

There were 4 false positive results in CDFI, probably because these patients had intermittent reflux. There is evidence from radionuclide cystography to suggest that reflux occurs even in children with a negative result on VCUG.[11] Kosar et al, Oak et al, Salih et al, Yousefi et al, Haberlik also reported false positive cases (2/70, 2/72, 3/42, 1/48, 10/154 respectively) in their studies comparing CDFI and VCUG.[8,12,9,6,10]

Grading in both tests

Of the 74 ureters which showed reflux in both tests, identical grades were seen in 68 ureters. If grade 0 is also considered, identical grades are seen in 110 ureters. In the 6 ureters where grades differed it was by a difference of 1 grade. VCUG had a higher grade in all ureters except 2. The coefficient of agreement between grading by both tests Kappa = 0.718, p=0.000 which is significant. In the study by Yousefi et al,6 contingency coefficient was r = 0.798, p<0.001.

Conclusion

The sensitivity is low for lower grades of reflux and excellent for grade IV and V reflux. However as the study by Haberlik10 shows, grade I and II reflux might be a normal physiological condition seen in healthy children and hence missing them may not have any therapeutic implication. The low negative predictive value of 67.7 % means that a negative result on CDFI does not rule out VUR. Hence if there is a negative result on CDFI, VCUG should be used for confirmation. The specificity and positive predictive value of CDFI are good (91.3% and 94.9% respectively). The false positive rate of 2.9 % may indicate that CDFI is able to detect cases of intermittent reflux that may be missed on VCUG. Whenever CDFI detected reflux, there was good correlation between grades on CDFI and VCUG with a significant coefficient of agreement. There was only a one grade difference in the differing cases with a tendency to downgrade on CDFI. There was good agreement of results between CDFI and VCUG in the postsurgical cases. CDFI may therefore be used for follow up of children with

previously detected VUR thus obviating the need for frequent VCUG and radiation exposure. Only if the result is negative on CDFI, should VCUG be done to confirm resolution of reflux. A limitation of the study is that the calculated sample size could not be attained in the study period. Moreover, testing in children below the age of one year when VUR is highly prevalent could not be done by CDFI because of the patient compliance required.

Conflict of Interest: conflict of interest

Acknowledgement

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