The Utility of Ureteral Jet Angle Sonography as Initial Screening Tool for Assessing Vesico-Ureteral Reflux in the Philippines: A Prospective, Cross-sectional Trial

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Introduction: One of the common risk factors in urinary tract infection is vesico-ureteral reflux. According to some studies, it is seen in 30%-50% of children and 40%-50% present with febrile urinary tract infection. The presence of moderate to severe reflux is an important risk factor in terms of acute pyelonephritis and reflux nephropathy. Investigation of children with urinary tract infection has undergone change so as to detect those who will benefit from diagnosis and treatment at the same time avoid over investigation.[1]

Objective: The present study aimed to determine the role of ureteral jet angle (UJA) in detecting vesicoureteral reflux (VUR) as compared to the gold standard of voiding cystourethrography (VCUG).

Methods: A total number of 152 kidneys from 76 patients (37 female and 39 males) ages from 2 months up to 11 years old were included in this study. These patients presented with recurrent urinary tract infection as confirmed via routine urinalysis and/or urine culture and sensitivity and assessed to have vesico-ureteral reflux disease as confirmed by voiding cystourethrogram (VCUG). They were included regardless of the grade of reflux (grade I-V). Patients with urinary tract infection but negative VCUG were also included. Excluded from the study were parents with no consent, patients with neurogenic bladder disorder as cause of recurrent urinary tract infection, patients who had postoperative correction of vesico-ureteral reflux prior to ureteral jet angle sonography, patients currently taking medication for urinary tract infection and patients currenlty symptomatic for recurrent urinary tract infection i.e. fever, chills, dysuria. All of the participants underwent kidney, urinary bladder ultrasound with ureteral jet angle sonography and all data were collected.

Results: Out of 152 kidneys, vesicoureteral reflux was seen in 91 of them (60%). Low grade reflux defined as grade I or grade II reflux was present in 32 kidneys (21%) and high grade reflux defined as grade III-V reflux was seen in 59 kidneys (39%). In both right and left kidneys, no significant difference was observed in bladder volume and expected bladder capacity (EBC) by VUR status. On the other hand, there was a significant difference observed in volume to reach reflux by VUR status of both right and left kidneys.No significant difference was observed in UJA volume, EBC, EBC% and UJA degrees by VUR status in the right kidneys. On the other hand, UJA volume, EBC and EBC % was significantly different by VUR status in the left kidneys.All AUCs were less than 0.7 even if EBC was considered. Therefore, UJA may have poor ability to classify patients correctly according to their VUR status.

Conclusion: Doppler flow ultrasound measurement of ureteral jet angle may be a simple and real non invasive test in children of any age but it only showed poor correlation compared to voiding cystourethrography in detecting vesicoureteral reflux. The ureteral jet angle sonography may not be a good initial diagnostic test in assessing vesicoureteral reflux due to its low sensitivity and specificity in detecting the said disease.

Key words: vesico-ureteral reflex, ureteral jet angle sonography

Introduction

Vesicoureteral reflux (VUR) represents the retrograde flow of urine from the bladder to the upper urinary tract. It is an anatomical and/or functional disorder with potentially serious consequences, such as renal scarring, hypertension, and renal failure.[2] The probability of VUR in children assessed to have UTI is said to range from 29%-50%. VUR provides a mechanical hydrodynamic mechanism which facilitates ascension of micro-organisms from the bladder to the kidneys. This may be an accelerant for renal tissue infection that comes after bacterial colonization.[3]

Currently, there are five grades of reflux used to describe the appearance of the ureter, renal pelvis, and calyces as seen on radiographic contrast images generated by voiding cystourethrogram (VCUG).[4] However, there is the presence of parental concern over the invasiveness and radiation exposure of the cystogram.[5]

It is hypothesized that higher grade of reflux is related to the ureteral orifice being more laterally placed and has a shorter intramural tunnel length causing a bolus of urine to be ejected more perpendicularly to the bladder base.[6] This study, aimed to perform VCUG in patients only with significant ureteral jet angle measurements and avoid unnecessary VCUG in patients without reflux while determining the minimum bladder volume to have a highly sensitive and highly specific result.

Currently, the standard imaging tests for assessing VUR include renal and bladder ultrasonography, VCUG and nuclear renal scans.[7]

The standard criterion in the diagnosis of VUR is VCUG, especially at the initial work-up. This test remains the gold standard because it allows better determination of the grade of VUR and assessment of the bladder and urethral configuration but due to its invasive nature, some parents are hesitant to proceed with VCUG.[8] Ureteral jet angle (UJA) sonography is non invasive and provides minimal traumatic and adverse effects. UJA sonography may be a reliable initial screening tool in assessing vesico-ureteral reflux. The ureteral jet angle may vary as contour of the bladder changes as bladder volume increases thus affecting the accuracy of the said procedure.

The known effects of VUR on the upper tracts are largely what direct the need for diagnosis and correction of reflux. Currently, the American Academy of Pediatrics guidelines recommend VCUG if hydronephrosis, sonographic indication of possible renal scarring and dysmorphism, or other findings that suggest high-grade VUR are present.[9] This newer recommendation would seem to balance the attendant invasiveness, radiation exposure, and patient and family trepidation surrounding VCUG. Although clinically significant VUR diagnosis may still be delayed or missed because renal abnormalities may exist even in the presence of normal renal ultrasonography, the addition of ureteral jet angle sonography may aid in the screening of patients with VUR.

Materials and Methods

A total of 152 kidneys from 76 patients, 37 females (49%) and 39 males (51%) with ages of 2 months up to 11 years old were included in this study. These patients presented with recurrent urinary tract infection as confirmed via routine urinalysis and/or urine culture and sensitivity. Patients with recurrent urinary tract infection but negative VCUG were also included. Excluded from the study were parents with no consent, patients with neurogenic bladder disorder as cause of recurrent urinary tract infection, patients who had postoperative correction of vesico-ureteral reflux prior to ureteral jet angle sonography patients currently taking medication for urinary tract infection and patients currenlty symptomatic for recurrent urinary tract infection i.e. fever, chills, dysuria.

Baseline characteristics measured included age, sex, estimated bladder capacity, grade of reflux, ureteral jet angle measurement.

Patients involved in this study underwent voiding cystourethrogram, the current gold standard in diagnosing vesico-ureteral reflux, to confirm presence or absence of the disease. Ureteral jet angle sonography was also performed on the participants prior to VCUG.

All voiding cystourethrogram was done by one urologist and all ureteral jet angle sonography was done by only one radiologist at the UST Hospital using only one model of ultrasound machine. The radiologist was blinded through out the whole duration of the research. Kidney, urinary bladder with ureteral jet angle sonography was requested prior to performing VCUG.

The ultrasound probe was placed on top of the hypogastric area visualizing the interureteral ridge. Using Doppler color flow, the authors measured the angle between the direction of the ureteral flow and the interureteral ridge. The estimated bladder capacity was also measured for each patient as well as the bladder volume upon measurement of the ureteral angle.

Patients were still managed accordingly based on the result of the voiding cystourethrogram. The course of management was not influenced by the result of the ureteral jet angle sonography. Once reflux was confirmed by voiding cysto-urethrogram and watchful waiting was the treatment option of choice, the patient underwent another ureteral jet angle sonography together with the voiding cysto-urethrogam upon follow-up. If surgical correction was indicated, the parents of the patient was appraised with the surgical plan and the patient had the operative procedure once consent was obtained.

The following variable were obtained: For VCUG- expected bladder capacity (<2 years old: month x 2.5 + 38; > 2 years old: age +1 x 30)[10], bladder volume when reflux was reached, maximum bladder volume. For UJA- expected bladder capacity (<2 years old: month x 2.5 + 38; > 2 years old: age +1 x 30)[10], ureteral jet angle in degrees, bladder volume when ureteral jet angle was measured and maximum bladder volume.

Data were encoded in MS Excel by the researcher. Data processing and analysis were performed using Stata SE version 12 SE. Chi square test was used for categorical variables while ANOVA was used for continuous variables. Significant ANOVA results were further analyzed by using Scheffe for pairwise comparison of means. In order to determine the deterministic capability of UJA in classifying patients with high-grade VUR, the Area Under the Curve (AUC) was determined through the Receiver Operating Characteristic (ROC) curve. P values less than 0.05 were considered significant.

Results

All subjects underwent ureteral jet angle sonography measurements without any complication. Out of 152 kidneys, vesicoureteral reflux was seen in 91 kidneys (60%) (Table 1). Low grade reflux defined as grade I or grade II reflux was present in 32 kidneys (21%) and high grade reflux defined as grade III-V reflux was seen in 59 kidneys (39%).

A higher proportion of males were found to have high grade VUR in both right and left kidneys compared to females (46% vs. 35%; 46% vs. 27%, respectively). Similar results were found in low grade VUR. However, there was no significant difference observed in the proportion of patients with VUR according to sex ($p>0.05$).

In terms of age, a higher proportion of patients <1 year old had high grade VUR for both right and left kidneys compared to other age groups. On the other hand, low grade VUR was mostly found among patients who were between the ages of 3 and 5. However, there was no statistically significant difference observed in the proportion of patients having VUR by age group ($p>0.05$)

VCUG

In both right and left kidneys, no significant difference was observed in bladder volume and EBC by VUR status (Table 2). On the other hand, there was a significant difference observed in volume to reach reflux by VUR status of both right and left kidneys.

On the other hand, mean volume to reach reflux in left kidney was significantly higher in patients with low grade VUR compared to patients with high grade VUR ($p=0.050$) and no VUR ($p<0.0001$).

UJA

No significant difference was observed in UJA volume, EBC, EBC% and UJA degrees by VUR status in the right kidneys. On the other

Table 1. Demographic profile of study subjects.

Variables		Right Kidney				Left Kidney			
	Total (N=76) N%	High Grade VUR (N=31) N%	Low Grade VUR (N=15) N%	Normal (N=30) N%	P Value	High Grade VUR (N=28) N%	Low Grade VUR (N=17) N%	Normal (N=31) N%	P Value
Sex									
Male	39 (49)	18 (46)	8 (21)	13 (33)	0.508	18 (46)	9 (23)	12 (31)	0.144
Female	39 (51)	13 (35)	7 (19)	17 (46)		10 (27)	8 (22)	19 (51)	
Age first seen									
<1 year old	30 (40)	16 (52)	3 (10)	11 (27)	0.294	15 (50)	6 (20)	9 (30)	0.109
1-3 years old	20 (26)	7 (35)	5 (25)	8 (40)		7 (35)	4 (20)	9 (45)	
3-5 years old	14 (18)	5 (36)	5 (36)	4 (28)		5 (36)	5 (36)	4 (28)	
>5 years old	12 (16)	3 (25)	2 (17)	7 (58)		1 (8)	2 (17)	9 (75)	

Table 2.

Variables	Right Kidney				Left Kidney			
	High Grade VUR (N=31) Mean ± SD	Low Grade VUR Mean ± SD	Normal (N=30) Mean ± SD	P Value	High Grade VUR (N=31) Mean ± SD	Low Grade VUR Mean ± SD	Normal (N=30) Mean ± SD	P Value
VCUG								
EBC	94.1 ± 56.9	107.9 ± 52.6	108.3 ± 59.8	0.5781	88.2 ± 45.2	100.3 ± 52.7	116.5 ± 66.3	0.1601
cc to reach reflux	43.4 ± 34.4	60.3 ± 53.3	0	<0.00001*	37.2 ± 26.2	65.9 ± 72.2	0	<0.00001*
Bladder volume	82.9 ± 52.7	88.7 ± 65.8	90.3 ± 54.7	0.8682	69.6 ± 31.4	101.2 ± 72.6	94.8 ± 59.7	0.1070
UJA								
Volume	84.1 ± 88.2	75.1 ± 64.2	99.9 ± 167.8	0.7902	61.8 ± 44.2	119.5 ± 122.7	72.8 ± 63.0	0.0421*
EBC	88.3 ± 88.0	105.1 ± 62.4	101.7 ± 73.9	0.7206	67.9 ± 51.7	97.6 ± 66.6	122.7 ±93.5	0.0229*
EBC%	1.3 ± 1.0	0.9 ± 0.8	1.2 ± 2.6	0.7392	1.2 ± 0.8	1.2 ± 1.1	0.7 ± 0.5	0.0330*
Degrees	51.4 ± 18.8	51.6 ± 26.0	49.95 ± 18.6	0.9487	55.5 ± 16.2	54.2 ± 16.4	54.5 ± 20.6	0.9643

hand, UJA volume, EBC and EBC % were significantly different by VUR status in the left kidneys.

Further analysis showed that mean UJA volume of the left kidneys was significantly higher in patients with high grade VUR compared to those with low grade VUR (p=0.05). No significant difference was observed between high grade and low grade VUR compared to no VUR (p>0.05). No significant difference was observed between high grade vs. low grade VUR, and low grade vs. no VUR (p>0.05).

Discriminatory Ability of UJA in Classifying Patients with High Grade VUR

For the purpose of analysis, the UJA readings of the right and left kidneys were combined.

Table 3.

VUR Classification	Other Conditions	AUC
High grade vs. low grade/normal	-	0.5359
High grade vs. low grade	-	0.5334
High grade vs. low grade/normal	EBC≥80	0.6034
High grade vs. low grade/normal	EBC≥60	0.5766
High grade vs. low grade	EBC≥60	0.5624
High grade vs. low grade/normal	EBC<60	0.4033
High grade vs. low grade	EBC<60	0.4112
High/Low grade vs. normal	EBC≥80	0.5570

Several analyses were performed in order to determine the capability of UJA to predict patients with high grade VUR versus those with low grade and/or normal patients. All AUCs were less than 0.7 even if EBC was considered. Therefore, UJA may have poor ability to classify patients correctly according to their VUR status.

Present data show that among 53 kidneys with a UJA of at least 52 degrees and reached at least 80% of the expected bladder capacity, 56% had vesicoureteral reflux as confirmed by voiding cystourethrography. Upon further analysis, this showed sensitivity of 60.53% and specificity of 58%.

Discussion

The incidence of vesicoureteral reflux in this study is 60%. Diagnostic modality for investigating vesico-ureteral reflux (VUR) in pediatric patients encompasses both radiologic and sonographic modalities. Vesico-ureteral reflux is a common problem among pediatric patients. The possibility of renal damage due to vesico-ureteral reflux, consequently renal function impairment and hypertension gives the necessary impetus for the diagnosis or exclusion of this problem. Voiding cystourethrography remains the primary diagnostic procedure of choice for diagnosing vesico-ureteral reflux.[4] Effort is being made to eliminate unnecessary exposure to this procedure.

Voiding cystourethrography provides images with fine anatomic details. It should always be used with fluoroscopy with the lowest pulse setting. Catheterization is done under sterile setting. Contrast medium is administered via the catheter. The bladder is filled and voiding studies are documented. Grading of reflux severity is based on the international reflux grading system comprised of 5 grades. Grade 1 denotes that the reflux is limited to the ureter and grade 5 denotes reflux in a massive dilated ureter and pelvocalyceal system.[4]

Ureteral jet angle sonography uses color Doppler ultrasonography. It measures the angle between the direction of the ureteral jet and the ureteral ridge. It is a non-invasive out patient procedure. According to a paper by Asanuma, et al. UJA value significantly increases with higher grades of vesicoureteral reflux. They also noted a cut off angle of 55 degrees or greater to detect grade III to V and grade IV/V reflux with a sensitivity of 85.5% and 94.7%, respectively. A cutoff angle of 70 degrees or greater diagnosed grade IV/V reflux with a sensitivity of 81.6% and a specificity of 82.7%.[11]

Currently, the American Academy of Pediatrics guidelines recommend VCUG if hydronephrosis, sonographic indication of possible renal scarring and dysmorphism , recurrent febrile urinary tract infection or other findings which suggest that high-grade VUR is present.[9] According to Asanuma et al the use of ureteral jet angle sonography is proposed to diagnose high-grade vesicoureteral reflux selectively and avoid unnecessary voiding cytourethrogram without missing severe scarred kidneys in pediatric patients with urinary tract infection.[11]

In this study, the sensitivity and specificity of this method in detecting reflux is low however this may provide a simple and time saving method that only requires a few minutes if the patient is well-hydrated. Sedation is no longer necessary. Vesicoureteral reflux is still one of the main underlying diseases in children specially in those with recurrent urinary tract infection.

This study showed the poor correlation between ureteral jet angle sonography and vesicoureteral reflux however other functional abnormalities may have affected the result such as voiding dysfunction because urodynamic studies were not routinely performed in this study.

The normal ureteral jet angle is yet to be determined in any literature and normal values may help improve the specificity and sensitivity of this study with regards to diagnosing vesicoureteral reflux disease.

Conclusion

Doppler flow ultrasound measurement of ureteral jet angle may be a simple and real non invasive test in children of any age but it only showed poor correlation compared to voiding cystourethrography in detecting vesicoureteral reflux. The ureteral jet angle sonography may not be a good initial diagnostic test in assessing vesicoureteral reflux due to its low sensitivity and specificity in detecting the said disease.

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