Research paper

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Diagnostic role of contrast-enhanced voiding urosonography (ceVUS) in pediatric duplex kidneys – a comparison with voiding cystourethrography (VCUG)

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duplex kidney; vesicoureteral reflux (VUR); contrast-enhanced voiding urosonography (ceVUS); voiding cystourethrography (VCUG); ureterocele

Abstract

Aim: The present study aimed to assess the diagnostic efficacy of contrast-enhanced voiding urosonography (ceVUS) using SonoVue for evaluating duplex kidneys, and to compare it with fluoroscopic voiding cystourethrography (VCUG). **Material and methods:** Forty-six children with duplex kidneys confirmed by surgical intervention or cystoscopy were included in the study, resulting in a total of 46 duplex kidneys and 46 normal kidneys (138 pyeloureteral units). **Results:** The overall sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of RBUS for diagnosing duplex kidney disease were 73.91%, 80.43%, 79.07%, and 75.51%, respectively. The diagnostic performance of RBUS and ceVUS in detecting duplex kidney yielded an overall sensitivity, specificity, PPV, and NPV of 89.13%, 84.78%, 85.42%, and 88.64%, respectively. The sensitivity, specificity, PPV, and NPV of VCUG in diagnosing duplex kidney disease were 17.31%, 86.96%, 57.14%, and 51.23%, respectively. For the 42 pyeloureteral units with VUR, Cohen's weighted kappa value for the agreement between ceVUS and VCUG in grading VUR was 0.702 (95% CI, 0.551 ~ 0.854; p <0.05). **Conclusions:** RBUS effectively diagnoses duplex kidneys with renal pelvic dilation, while ceVUS can further elucidate whether reflux occurs in the upper or lower moiety in cases of duplex kidneys with VUR. Compared to VCUG, both RBUS and ceVUS provide more intuitive diagnoses for duplex kidneys with VUR and ureterocele. Additionally, there is good consistency between ceVUS and VCUG in grading VUR. CeVUS is recommended as an initial evaluation method for patients suspected of having duplex kidneys associated with urinary tract infections.

Introduction

A duplex kidney is a frequently encountered anatomical variation characterized by the presence of two separate collecting systems, with reported incidence and prevalence ranging from 0.7% to 4% in the general population. Approximately 50% of cases may have asymptomatic presentation, but the distinguishing feature lies in the elongated structure of duplex kidneys compared to those with a single collecting system. Nevertheless, aberrant duplex kidneys can be linked to vesicoureteral reflux (VUR), incontinence, ureterocele, or obstructive uropathy[1]. In patients with high-grade VUR, duplex kidney disease is the main anomaly associated with urological conditions[2]. Various imaging modalities, such as ultrasonography and certain radioactive techniques, can be employed for the diagnosis and evaluation of VUR in individuals with duplex kidney. With the increasing utilization of ultrasonic contrast agents (UCAs) in pediatric patients, multiple studies have demonstrated that ceVUS represents a valid alternative for evaluating VUR[3,4]. However, to the best of our knowledge, no study has been conducted specifically focusing on the assessment of the duplex kidney using ceVUS and VCUG.

In this study, we aimed to further elucidate the diagnostic role of ceVUS in the detection of duplex kidneys, while comparing its efficacy with that of VCUG.

Materials and methods

Compliance with ethical standards

This retrospective study was approved by the Medical Ethics Committee at our hospital (2022-IRB-065), and the necessity for written informed consent was waived.

Study population

Forty-six children with duplex kidneys confirmed by either surgery or cystoscopy between October 2019 and January 2024 at our hospital were included in the study, resulting in a total of 46 duplex kidneys and 46 normal kidneys (138 pyeloureteral units, PUUs). These patients underwent ceVUS for UTIs, followed by VCUG within one year. Two independent pediatric radiologists performed ceVUS and VCUG, reviewed the images, and reported the presence of duplex kidney and ureterocele, as well as the grading of VUR (grades I–V).

Instruments and technique

An EPIQ5 ultrasound system (Philips) equipped with a C5-1 transducer, which offers CEUS mode at a low mechanical index range of 0.06–0.10, was utilized in our study. Dual images (i.e. contrast image and grayscale image) of the organs could be observed simultaneously on the same screen. For contrast-enhanced ultrasound imaging, one milliliter of SonoVue (Bracco, Milan, Italy) was diluted in 250 ml of saline solution. The SonoVue-infused saline solution was suspended 1 meter above the examination table. Prior to ceVUS, all patients underwent RBUS examinations with a full bladder. Aseptic transurethral catheterization using a 5–8 Fr feeding tube was then performed, and the bladder was emptied. Subsequently, the saline solution was connected to the catheter via a venous infusion tube. The contrast material was slowly infused into the bladder by force of gravity. The bladder and kidneys were examined alternately with longitudinal and transverse images during the filling and voiding phases. Bladder capacity was calculated using a simplified formula based on age (age in years+2) ×30 mL for children over one year old or weight (in kilograms) ×7 mL for infants[5].

The Collimator Type R-50 (Shimadzu, Japan) was utilized for VCUG in the study. Pulsed fluoroscopy was conducted at a frame rate of 3 frames/s. Due to the necessity of visualizing the bladder and urethra, it was not feasible to implement gonadal radiation protection during VCUG.

Reflex grading and image analysis

The reflux grade of VCUG was based on the International Classification of VUR, while the ceVUS reflux grade was assessed using the system proposed by Darge and Troeger[5].

Pediatric ultrasonography was performed by Dr. Yang, who has 10 years of experience in this field. Prior to ceVUS, RBUS was conducted, followed by the administration of CeVUS. Subsequently, the images stored in the archiving system were reviewed, and a report was generated indicating the presence of duplex kidney and ureterocele, as well as grading VUR from grades I–V. Dr. Chen, a pediatric radiologist with a decade of experience, performed VCUG, meticulously reviewed the acquired images, and subsequently generated comprehensive reports.

Statistical analysis was conducted using IBM Corp's SPSS software version 22.0 for Windows. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated for RBUS, RBUS/ceVUS, and VCUG. Cohen's kappa coefficient of agreement was calculated to assess the concordance in grading VUR between ceVUS and VCUG.

Strengths and limitations of the study

This study focused on the diagnostic role of ceVUS in cases of duplex kidneys with VUR. We obtained high-quality ceVUS images depicting duplex kidneys with VUR; however, there were instances where the time interval between ceVUS and VCUG was relatively long.

Results

1. Our study included a total of 46 patients with duplex kidneys, comprising 20 males and 26 females, ranging in age from three to 151 months. The mean age was 36 months. Among these patients, the left side had 26, while the right side had 20 duplex kidneys.

2. RBUS identified pelvic dilation in 34 out of 46 duplex kidneys involving either the upper or lower moiety (34/46). The remaining 12 duplex kidneys without pelvic dilation were not detected (12/46). The overall sensitivity, specificity, PPV and NPV of RBUS for the diagnosis of duplex kidney disease were 73.91%, 80.43%, 79.07%, and 75.51%, respectively. CeVUS identified a total of 32 patients with VUR in duplex kidneys, 25 of whom exhibited pelvic dilation and seven of whom did not exhibit pelvic dilation on RBUS. Furthermore, ceVUS clearly visualized the upper or lower moiety of VUR in these patients (32/46). Among them, four patients presented incomplete duplications with a split ureter (Fig. 1). The occurrence of six VUR was observed in nonduplicated kidneys. Among the 12 patients without pelvic dilation, lower moiety VUR was detected in seven patients, confirming the presence of duplex kidneys by ceVUS. The overall sensitivity, specificity, PPV, and NPV of RBUS and ceVUS for the diagnosis of duplex kidney disease were 89.13%, 84.78%, 85.42%, and 88.64%, respectively.

3. VCUG was able to accurately diagnose four patients with duplex kidneys with lower moiety VUR and four patients with incomplete duplications with a split ureter. The sensitivity, specificity, PPV, and NPV of VCUG in the diagnosis of duplex kidney disease were 17.31%, 86.96%, 57.14%, and 51.23%, respectively (Tab. 1).

4. The accuracy rate of RBUS for detecting ureterocele reached 100%, regardless of whether an incision was made. CeVUS successfully identified all nonincised ureteroceles (Fig. 2), but it missed three incised ureteroceles. On the other hand, VCUG identified only one out of 13 ureteroceles.

5. The consistency of grading VUR between ceVUS and VCUG in 42 patients with VUR yielded a weighted kappa value of 0.702 (95% CI, 0.551–0.854; p <0.05), as shown in Tab. 2.

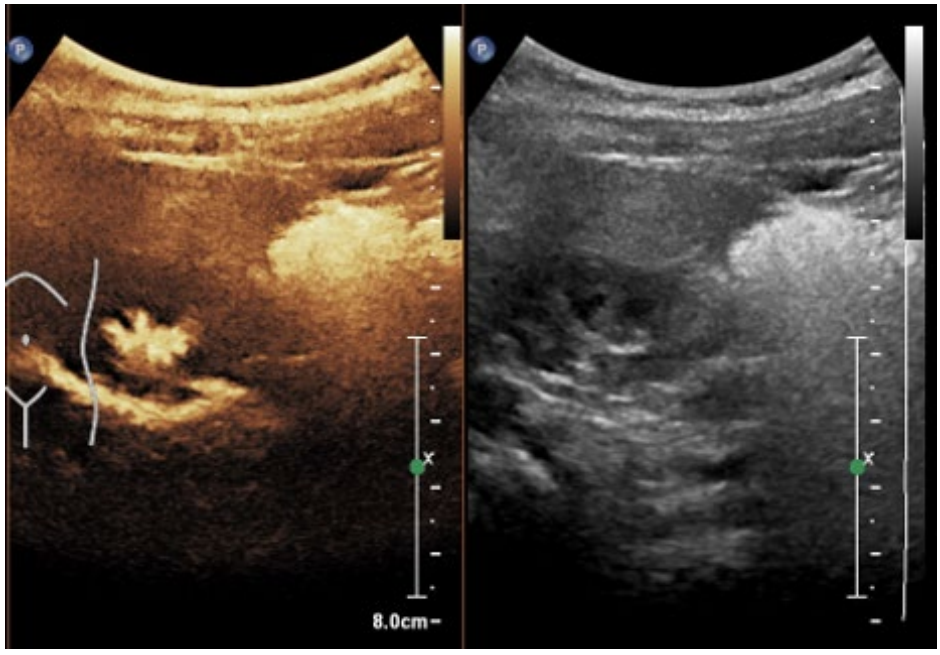

Fig. 1. *Incomplete duplication with a split ureter through ceVUS*

Tab. 1. Sensitivity, specificity, and positive and negative predictive values of RBUS, ceVUS, and VCUG

	Sensitivity, %	Specificity, %	Positive predictive value, %	Negative predictive value, %
RBUS	73.91	80.43	79.07	75.51
ceVUS + RBUS	89.13	84.78	85.42	88.64
VCUG	17.31	86.96	57.14	51.23

RBUS – renal and bladder ultrasound; ceVUS – contrast-enhanced voiding urosonography; VCUG – voiding cystourethrography

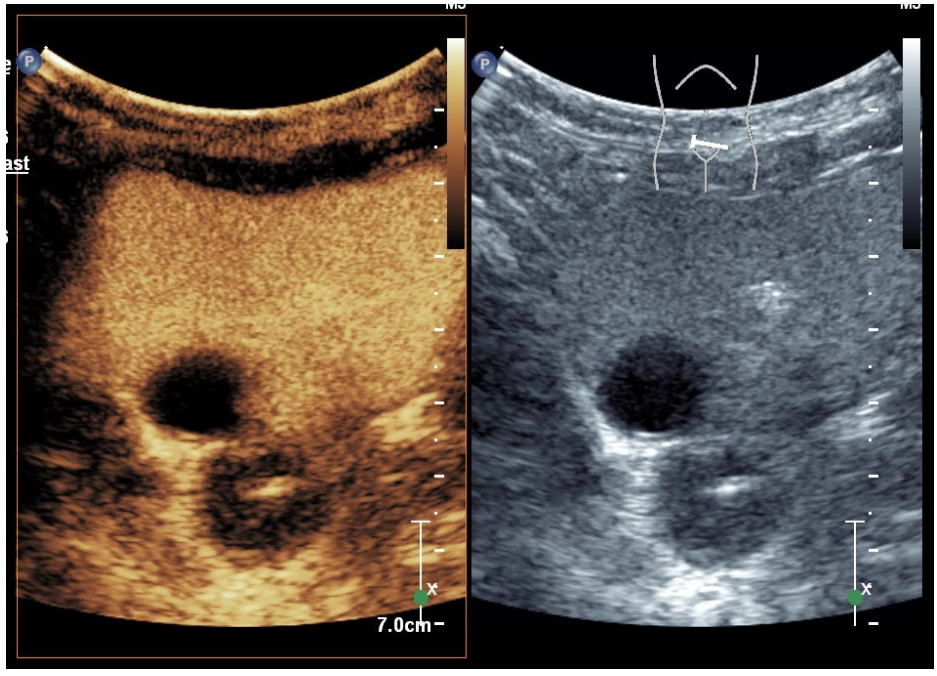

Fig. 2. *Revealing ureterocele through ceVUS*

Tab. 2. Consistency of VCUG and ceVUS in grading VUR

	Grade	I	II	III	IV	V	Total
CeVUS	I	0	0	0	0	0	0
	II	0	2	1	0	0	3
	III	0	1	8	2	0	11
	IV	0	0	3	12	3	18
	V	0	0	0	2	8	10
	Total	0	3	12	16	11	42

Weighted kappa value, 0.702; 95% CI, 0.551 ~ 0.854; p <0.05
ceVUS – contrast-enhanced voiding urosonography; VCUG – voiding cystourethrography; VUR – vesicoureteral reflux

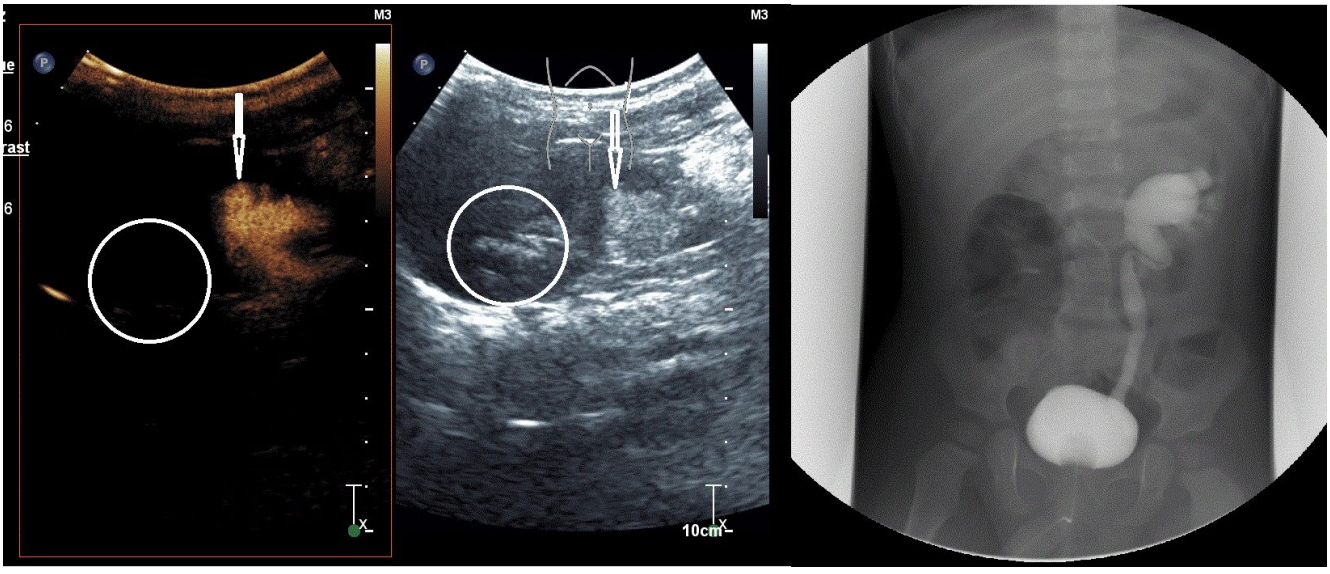

Fig. 3. *Comparison of CeVUS and VCUG in the context of lower moiety VUR (the arrow indicates the presence of VUR in the lower moiety, while the circle represents the absence of VUR in the upper moiety)*

Representative images comparing ceVUS and VCUG are presented in Fig. 3 and Fig. 4.

Discussion

Duplex kidney, a common anatomical anomaly characterized by two collecting systems, has an incidence and prevalence ranging from 0.7% to 4% in the population. Pathological involvement is observed in approximately 50% of patients. In the lower moiety, VUR is frequently encountered, while ureteropelvic junction obstruction and ureterovesical junction obstruction occur less frequently. Conversely, the upper moiety often presents with obstructed ureters accompanied by renal pelvic and ureter dilation or ureterocele; however, VUR is less commonly observed. Our study revealed that among the 46 duplex kidneys examined, 13 exhibited renal pelvic and ureter dilation as well as ureterocele in the upper moiety. VUR was found in four patients with lesions affecting the upper moiety, 24 patients with lesions involving the lower moiety, and four patients with incomplete duplications with a split ureter affecting both the upper and lower moieties. Additionally, six occurrences of VUR were identified in nonduplex kidneys.

As an easily accessible, noninvasive and radiation-free imaging technique, RBUS serves as an initial screening alternative for evaluating structural abnormalities in the urinary system[6]. Longer kidney length, abnormal parenchymal contour, and asymmetrical upper and lower moieties may indicate the existence of a duplex kidney. However, in children, some normal kidneys may exhibit irregular contours, which can pose challenges for radiologists when diagnosing duplex kidneys. Nevertheless, if both the upper and lower moieties of the duplex kidney appear normal, it is considered a normal variant within the normal range. Therefore, whether a duplex kidney is diagnosed in such patients does not significantly impact clinical outcomes. RBUS can reliably confirm the presence of duplex kidneys when dilation is observed in one or both renal pelvises. However, it becomes difficult to diagnose duplex kidney using RBUS alone when unequal kidney lengths are present without any pelvic or ureteral dilation associated with vesicoureteral reflux (VUR). In this study, 34 out of the 46 patients were diagnosed with duplex kidney based on RBUS due to coexisting upper or lower moiety pelvic dilation along with ureteral dilation with/without ureterocele, whereas the remaining 12 patients without any renal pelvic or ureteral dilation were not confirmed by RBUS. The presence of a duplex kidney was confirmed in seven out of the 12 patients by ceVUS. Among the nine patients who showed signs of duplex kidney based on RBUS findings, including unequal kidney lengths and abnormal parenchymal contours, two patients were ruled out as having duplex kidney after undergoing ceVUS due to one single-collecting system VUR.

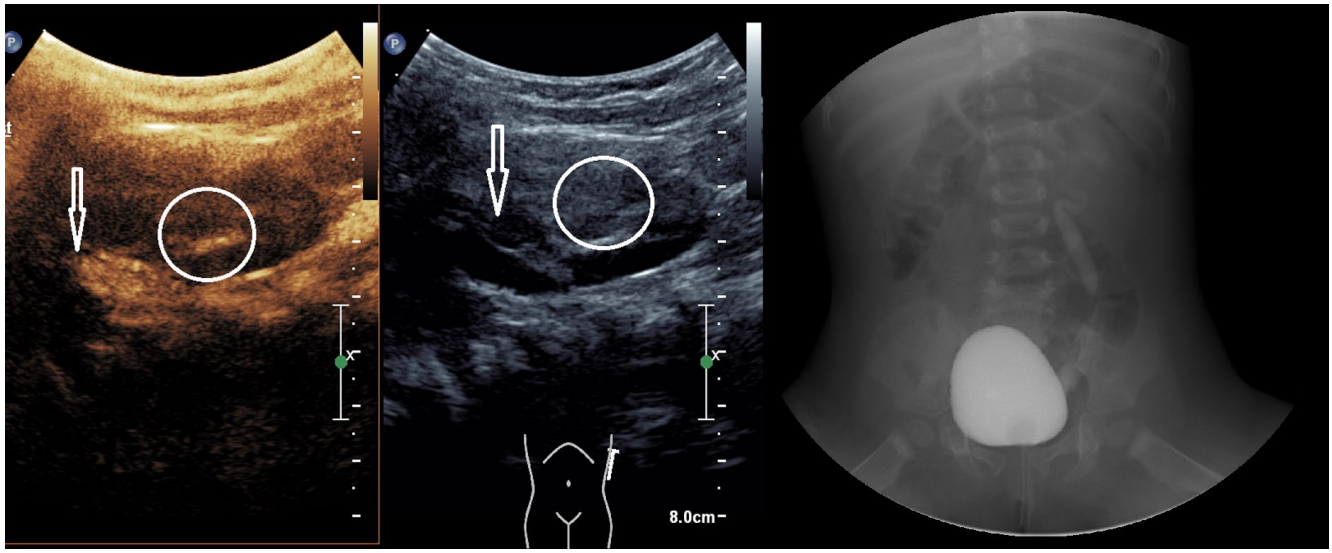

Fig. 4. *Comparison of CeVUS and VCUG in the context of upper moiety VUR (the arrow indicates the presence of VUR in the upper moiety, while the circle represents the absence of VUR in the lower moiety)*

With the implementation of UCAs in pediatric patients, ceVUS is now recommended as a viable alternative for assessing VUR in children. In comparison to VCUG, the primary advantage of ceVUS lies in its utilization of a radiation-free technique. Several studies have demonstrated that ceVUS exhibits comparable efficacy to VCUG in both detecting and grading VUR[5,7]. RBUS, preceding ceVUS, facilitates the comprehension of renal anatomy by radiologists, thereby significantly aiding in the implementation of ceVUS. Through dual imaging techniques, simultaneous display of grayscale and contrast views enables the provision of anatomical information on duplex kidneys as well as detecting and grading of VUR. Moreover, it offers a clear and definitive visualization method to determine whether VUR occurs in the upper or lower moiety. This is particularly advantageous for patients experiencing UTIs following ureterocele incision, facilitating identification of the kidney with VUR. In our study, 32 kidneys were diagnosed as duplex kidneys with VUR by ceVUS. Among them, seven kidneys exhibited no pelvic dilation and were identified as duplex kidneys with the lower moiety VUR by ceVUS. Nevertheless, for 14 of the duplex kidneys without VUR, ceVUS did not contribute to the diagnosis of duplex kidneys. However, VCUG detected only four cases of duplex kidney with lower-moiety VUR and four instances of incomplete duplications with a split ureter.

VCUG is a conventional method for assessing VUR in high-risk patients. When an abnormal duplex kidney is suspected, VCUG is often performed to further evaluate the presence of VUR[8]. VCUG can be used to diagnose complete urinary tract duplication (VUR into only one moiety) by examining the axis of the renal collecting system[9]. However, unlike ceVUS, it does not provide detailed anatomical information about the kidneys. Therefore, accurately diagnosing whether VUR occurs in a duplex kidney or a single collecting system using VCUG poses a challenge.

In our study, RBUS revealed 13 cases of ureterocele, regardless of surgical intervention, which is consistent with the findings in the literature that RBUS enables a more comprehensive assessment of ureterocele by effectively evaluating the wall layers and thickness, surpassing the capabilities of VCUG and ceVUS[4]. However, in diagnosing preincision occluded ureteroceles, ceVUS outperforms VCUG. Ureteroceles can be dynamic; during early filling, they appear as filling defects within the bladder on VCUG. Conversely, during the later filling stage, ureteroceles become effaced and may become invisible on VCUG. In some instances, they can even evert during voiding and mimic a bladder diverticulum[10,11]. Therefore, radiologists face increased challenges in achieving precise diagnoses. However, the dual technique enables clear and definitive visualization of ureteroceles through simultaneous comparison of grayscale and contrast views.

Siomou *et al.* reported that Cohen's weighted k value was 0.53 for the diagnosis of VUR of any degree using ceVUS and VCUG, while it was 0.64 for the diagnosis of VUR grades III and IV[12]. In our study, we obtained a Cohen's weighted k value of 0.702, which may be attributed to the majority of cases being grade III–V.

However, despite one of the main advantages of ceVUS being its ability to simultaneously display contrast and grayscale images, a limitation of ceVUS lies in its lack of panoramic view. Furthermore, when there is no VUR, ceVUS does not contribute to the evaluation of duplex kidney.

In conclusion, the diagnosis of duplex kidney without pelvic dilation poses challenges when using RBUS; however, ceVUS can provide confirmation in cases of VUR. CeVUS offers a more intuitive approach than VCUG for diagnosing duplex kidney with VUR and ureterocele, enabling clearer identification of reflux occurrence in either the upper or lower moiety. As a radiation-free technique, it can serve as an initial modality for evaluating duplex kidneys with UTIs.

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Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

Ethics approval

This study was performed in accordance with the principles of the Declaration of Helsinki Compliance with Ethical Standards. This retrospective study was approved by the Medical Ethics Committee of Children's Hospital, Zhejiang University School of Medicine, National Clinical Research Center for Child Health (2022-IRB-065).

Consent to participate

Written informed consent was obtained from the parents.

Consent to publish

The authors affirm that the human research participants provided informed consent for publication of the images in the figures.

Author contributions

Original concept of study: XY, ZX, JY, JF. Writing of manuscript: XY. Analysis and interpretation of data: XY, ZX, ZC, GC, DT. Final acceptation of manuscript: XY, ZX, GC, DT, JY, JF. Collection, recording and/or compilation of data: XY. Critical review of manuscript: XY, JY, JF.

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