Journal of Pediatric Surgery 52 (2017) 1661–1665

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

# Intraoperative ultrasound-assisted approach for endoscopic treatment of vesicoureteral reflux in children☆

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ARTICLE INFO

*Article history:*
Received 2 January 2017
Received in revised form 6 March 2017
Accepted 9 April 2017

*Key words:*
Vesicoureteral reflux
Endoscopic treatment
Endoscopic injection
Intraoperative ultrasound

ABSTRACT

*Purpose:* Despite minimal invasiveness and high success rate, guidelines still prescribe voiding Cystourethrogram (VCUG) after endoscopic treatment for vesicoureteral reflux (VUR) in children.
The aim of this paper was to analyze whether intraoperative ultrasound (IO-US) could improve surgical accuracy and perioperative counseling, thus potentially decreasing the need for postoperative VCUG.
*Methods:* We selected children treated for moderate to high grade VUR, renal scarring or repeated infections under antibiotic prophylaxis from January to December 2015. Endoscopic injection was combined with IO-US to detect optimal needle placement and to guide mound formation. IO-US findings were compared to surgeon opinion and postoperative VCUG, performed 3 months after surgery. All patients were followed-up for 1 year.
*Results:* A significant relationship was found between IO-US mound height ($p = 0.003$) or localization ($p < 0.0005$) and VCUG. Success of endoscopic treatment vs persistence of reflux groups had a mean mound height of $10.62 \pm 1.36$ mm and $8.39 \pm 1.08$ mm respectively ($p < 0.0005$).
Height maintained a significant correlation with success in simple and multivariable regression analysis. ROC curve determined ≥9.8 mm as predictor of reflux resolution (95% CI 0.825 to 0.998; $p < 0.0001$).
*Conclusions:* IO-US facilitates pediatric urologists to find an optimal location, to reach a volcano mound morphology and height, thus increasing intraoperative accuracy. IO-US also helps evaluating high-risk recurrence and guiding prognostic counseling.
*Type of study:* Treatment study.
*Level of evidence:* II.



Ultrasonography (US) represents one of the most time-efficient, cost-effective and noninvasive imaging modalities currently applied to Pediatric Urology, being the prime choice in both diagnosis and follow-up of many pathologies. Different subspecialties apply US to intraoperative surgical planning, such as Urology [1], Gynecology [2], and Cardiac Surgery [3]. Advantages in surgical and imaging technology permit the performance of combined procedures in a safe and efficient way.

Vesicoureteral Reflux (VUR) is a common urological disease, affecting approximately 1% of pediatric population and eventually leading to renal damage [4]. There are now many management options available for pediatric VUR, including watchful waiting, medical treatment with continuous antibiotic prophylaxis and various surgical alternatives, headed by the rapid growth in the use of endoscopic treatment within the last decades [5]. Endoscopic treatment is effective and well tolerated in children and long-term follow up indicates no deterioration in patients responding positively to treatment [6]. However, owing to inadequate intraoperative indicators and variable success rate, International guidelines still prescribe postoperative Voiding Cystourethrogram (VCUG) to assess reflux resolution [7]. Unfortunately, VCUG remains a distressing and uncomfortable investigation for children and their parents, graved by concern for radiation exposure, particularly in children who should undergo long term follow-up examinations. Recently some authors identified ultrasound mound appearance as a potential predictor of success of the procedure [8–10]. Moreover many technical variables could play a role in determining successful outcome, such as ureteral hydrodistention, bladder filling, and height of the obtained mound.

In this paper was analyzed whether intraoperative US mound visualization, localization and measurement could improve surgical accuracy and perioperative counseling, thus potentially decreasing the need for postoperative VCUG and personalizing follow-up.

## 1. Materials and methods

### 1.1. Indication and preoperative evaluation

Patients undergoing endoscopic subureteral injection of dextranomer/hyaluronic acid copolymer (Dx/HA) for primary VUR were prospectively

☆ Conflicts of interest: None.

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http://dx.doi.org/10.1016/j.jpedsurg.2017.04.004
0022-3468/

enrolled from our Outpatient Urological Clinic. All patients had VUR diagnosed by VCUG and graded based on the International Reflux Study by an expert radiologist. Patients with VUR less than 1 year of age were initially managed with antibiotic prophylaxis and monthly urine analysis and reevaluated at 1 year of age.

Preoperative evaluation included sex, age, VUR grade and laterality, physical examination, renal and bladder ultrasound scan (RBUS) and estimation of theoretical bladder capacity for each children.

Indications for endoscopic treatment included repeated infections on antibiotic prophylaxis, presence of scarring at renal scintigraphy and/or moderate to high grade reflux. Patients with low grade (I–II monolateral VUR), history of neurogenic bladder, overactive bladder, genitourinary anomalies or other complex syndromes were excluded from endoscopic procedure and assigned to other treatment options. Parents gave written informed consent, after being informed about the nature of the study, in accordance with the Helsinki declaration.

### 1.2. Technique

All procedures were performed under general anesthesia with the patient in supine position, by a single experienced surgeon. Using a 9 Fr cystoscope, endoscopic injections were performed with either STING or Double Hit technique as described by Puri and Kirsch [11,12] according to surgeon's preference. Bladder was kept half full, avoiding overdistention. At the same time, intraoperative ultrasound (IO-US) was performed by an expert pediatric radiologist. The equipment used included the CX50, Philips, US system with a high-resolution 8–5 MHz curved-array transducer. Ultrasonographic intraoperative bladder examination was performed with sagittal scan in order to better visualize ureteral course.

IO-US rating was based on combined variables: mound location and height. Mound location depended on both anatomy and needle placement. Needle placement at ureteral orifice was detected by sonographic identification of ureteral jet and hydrodistention during endoscopic procedure, and thus localization was classified as poor, good or optimal. Moreover, IO-US allowed mound measurement simultaneously with surgical procedure; height was measured as the maximal vertical diameter of the hyperechogenic round shaped mass visualized at ureteral orifice. Mound height was as well classified as poor, good, optimal according to reached height. Based on previous studies on mound height [13] and reabsorption rate [14], an optimal Dx/HA volcano height at US was considered for mounds higher than 11 mm, good from 11 to 9 mm, and poor less than 9 mm. Fig. 1 highlights main steps comparing surgical and IO-US views. The bladder was finally emptied and the procedure terminated. At the end of the surgical procedure, the surgeon's opinion regarding possible success was collected.

### 1.3. Postoperative protocol

An indwelling catheter was left into the bladder for 24 h after cystoscopic procedures in order to allow the stabilization of implants at the lowest pressure; patients were discharged after catheter removal, RBUS and spontaneous micturition. Postoperative follow-up protocol planned at our Institution consisted of routine RBUS and VCUG according to guidelines. Antibiotic prophylaxis was administrated until complete VUR resolution was confirmed by VCUG, performed 3 months postoperatively. The same radiologist performed preoperative and postoperative VCUG evaluation, blinded to IO-US. Postoperative US evaluation aimed to confirm presence and location of Dx/HA and was performed by the same radiologist performing IO-US. US follow-up lasted for all patients for at least 1 year following endoscopic injection. Urine analysis was usually requested on demand, if febrile urinary tract infection (UTI) was suspected.

### 1.4. Statistical analysis

Statistical analysis of quantitative and qualitative data, including descriptive statistics, was performed for all items. Continuous data are expressed as mean ± SD, unless otherwise specified. Baseline differences between groups were assessed by the chi-square test or Fisher exact test, as needed for categorical variables, and by the univariate analysis of variance (ANOVA) for parametric variables. Logistic regression analysis examined the correlation between patient characteristics (independent variables), and success of the procedure (dependent variable) in simple and multiple regression models. Multinomial logistic regression analysis was used for nominal variables as VUR grade, localization and mound height evaluation. To assess the predictive rate of different cutoff values of postoperative mound height at US scan with

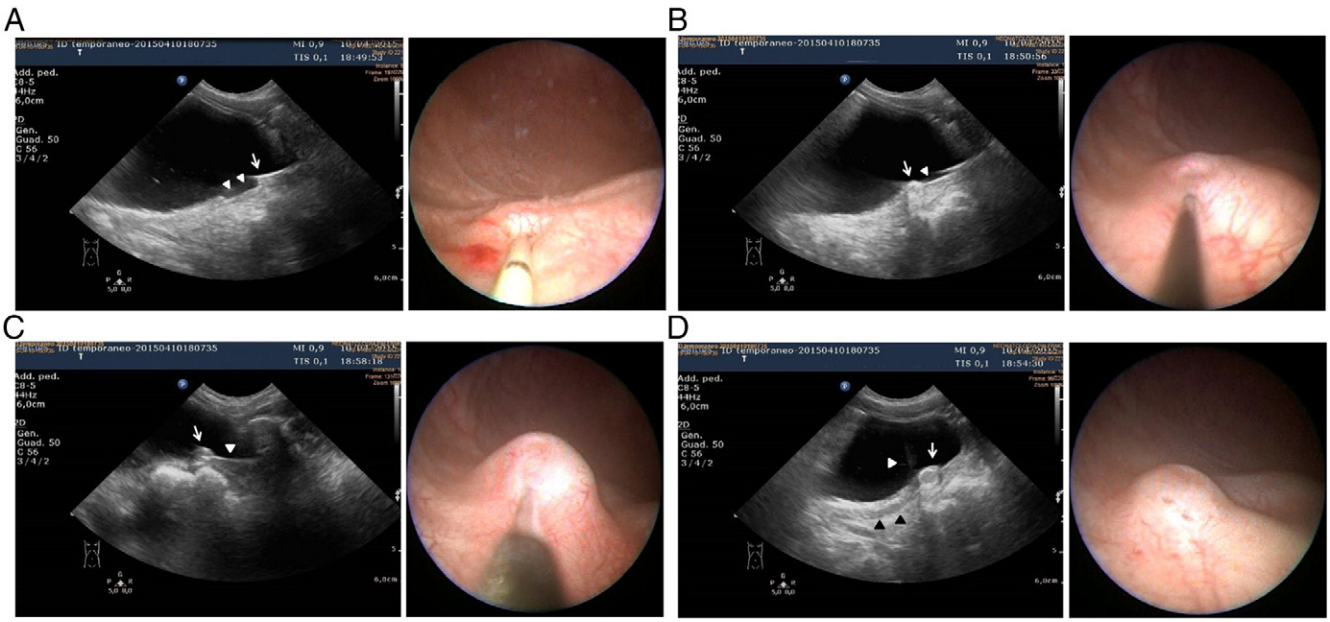


**Fig. 1.** Main steps of surgical procedure compared to IO-US: on the left IO-US views and on the right endoscopic appearance. (A) Initial catheterization (arrow cystoscope; arrowheads ureteral catheter); (B) optimal ureteral placement and initial mound formation (arrow initial mound; arrowhead needle); (C) needle injecting Dx/HA positioned (arrow mound; arrowhead needle); (D) final mound appearance (arrow mound; white arrowhead ureteral jet; black arrowheads ureteral course).