



Transurethral incision as initial option in treatment guidelines for ectopic ureterocele associated with duplex systems

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Received: 7 June 2018 / Accepted: 13 December 2018 / Published online: 2 January 2019
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Abstract

Purpose Treatment strategies for children with ectopic ureterocele (EUs) and duplex collecting systems or vesicoureteral reflux are controversial. Transurethral incision (TUI) of EUs associated with duplex systems has been considered only as a temporizing technique. This study aimed to evaluate whether primary TUIs could be considered as an initial treatment option in EUs with duplex systems.

Materials and methods Forty-seven children with EUs associated with duplex systems underwent primary TUIs at our institution between November 2007 and October 2017. We retrospectively analyzed patient characteristics such as age, sex, upper tract status, ureterocele location, differential renal function, and preoperative vesicoureteral reflux with regard to postoperative complications requiring additional surgery, postoperative incontinence, and renal function.

Results The mean age at operation was 4.8 ± 4.7 months. Of the 47 patients, 26 (55.3%) underwent primary TUIs only, 3 (6.4%) underwent secondary TUIs, and 18 (38.3%) underwent other secondary procedures such as common-sheath reimplantation (CSR) and ureterocelelectomy. Secondary surgeries in 21/47 (44.7%) patients occurred during a mean follow-up of 47.7 ± 23.3 months, and the most common type of secondary surgery was CSR. The most common reason for secondary surgery was febrile urinary tract infection (14/21 patients [66.7%]). There were three cases (3/26 [11.5%]) of voiding problems after primary TUI and two cases (2/15 [13.4%]) after secondary CSR.

Conclusions Primary TUIs should be considered as initial treatment options for EUs in duplex systems and not just a temporizing technique.

Keywords Ectopic ureterocele · Transurethral incision · Duplex system

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Introduction

The management of ectopic ureteroceles (EUs) with duplex systems, which seeks to prevent infection and damage to the kidneys, remains a great challenge in pediatric urology, and various treatment modalities have been developed to overcome the complexity of these combined lesions [1–4]. Although transurethral incisions (TUIs) are widely used for intravesical ureteroceles, they remain a temporizing technique before open surgery for the management of EUs [1] via either an upper tract approach (UTA), including ureteroureterostomy or heminephrectomy, or a bladder-level approach (BLA), including common-sheath reimplantation (CSR) with ureterocelelectomy or total reconstruction of the upper and lower urinary tracts with ureterocelelectomy, ureteral reimplantation, and heminephrectomy [5, 6]. Although the UTA is effective and does not involve the bladder during surgery, it is not indicated for cases, where high-grade vesicoureteral reflux (VUR) is present [6]. In such a situation, a BLA should be performed. However, these approaches have limitations, including the technical difficulty involved with small bladder volumes in infants and the concerns for high morbidity and postoperative incontinence due to disturbances of the trigones in immature bladders [2].

The use of primary TUIs for the treatment of EUs has been widely reported. Adorisio et al. [3] found that this approach is effective, though they did not evaluate postoperative complications. Furthermore, many studies have reported high rates of secondary surgery during long-term follow-ups [7, 8]. Of note, the only comprehensive meta-analysis to date found that an increased risk of secondary operations is associated with EUs with duplex systems [9]. However, we hypothesize that primary TUIs in EUs with duplex systems should be considered as initial treatment options. This study was performed to evaluate whether primary TUIs are effective in treating EUs with duplex systems by reporting our experience with endoscopic treatments and describing success rates and postoperative complications.

Materials and methods

Patients

A total of 47 patients under 10 years age who were treated for EUs associated with duplex systems between November 2007 and October 2017 in our institution that were followed up for more than 6 months postoperatively were retrospectively studied. Three patients were lost to follow-up

before undergoing postoperative dimercaptosuccinic acid (DMSA) scans and were excluded from the postoperative differential renal function (DRF) decrease analysis. The study design and protocols were approved by the Institutional Review Board.

Inclusion criteria and indications for surgery

All patients with EUs associated with duplex systems were considered for surgery, particularly (1) those with symptoms, such as febrile urinary tract infections, and (2) those with aggravated dilatation measured by ultrasonography. Patients were initially administered antibiotics, and UTA was considered first for cases without ipsilateral high-grade VUR or severely dilated upper pole ureters. However, if the upper tract approach was not indicated, we initially performed primary TUI to provide a delay that was sufficient to allow for the preferred BLA at a later date. Whether to perform secondary TUI or other BLA approaches was decided according to the surgeon's preferences. The success of TUI was defined as no indication for surgery of EUs associated with duplex systems after the primary TUI.

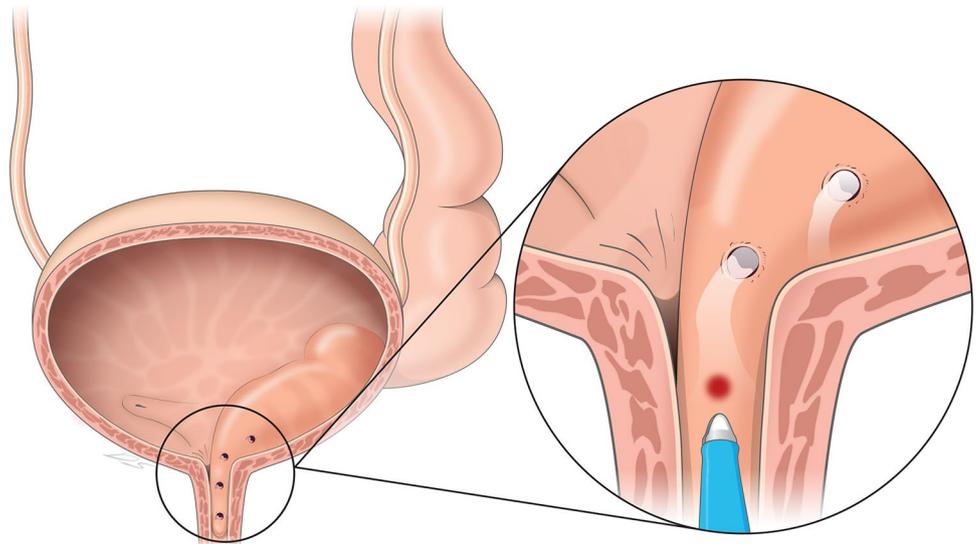
Operation technique

All surgeries were performed by three operators (S.W.H., Y.S.L., and S.W.K.); all the three have great amounts of surgical experience in pediatric urology. TUI was performed using an 8F cystoscope. An adequate puncture was made in the ureterocele using a 1000- μ m holmium–yttrium–aluminum garnet laser. The pulse energy and rate were set to the lowest possible settings and titrated upward as needed. Dependent positions of the ureteroceles were punctured to ensure good drainage and prevent VUR. The incision size was tried to be minimized to the diameter of the laser. Only the small hole with the size of the laser was made that only laser could be introduced. Multiple punctures were made longitudinally if necessary (Fig. 1). CSR was performed by making an approximately 2.5-cm Pfannenstiel incision along the inguinal crease followed by Paquin method reimplantation or intravesical detrusorrhaphy, as previously described [2, 10].

Outcome measures

We recorded patient characteristics, including age, sex, imaging results, operation factors, and postoperative results. All patients were evaluated regularly throughout their follow-up, assessing blood pressure, biochemistry assays, and urine analysis. The pre- and postoperative evaluations included renal and bladder ultrasonographies, DMSA scans, and voiding cystourethrographies (VCUG). Follow-up ultrasonographies were performed approximately 6 weeks

Fig. 1 Incision made in the dependent position of an ectopic ureterocele (EU) with a duplex system using a holmium–yttrium–aluminum–garnet laser



after surgery and repeated later depending on the results. DMSA scans were initially performed before the surgery and approximately 6–18 months after surgery and repeated if necessary. Postvoid residual urine was measured during the follow-up period using a three-dimensional handheld scanner. The presence of continuous incontinence at any age or daytime incontinence after an age of 5 years was also assessed [2, 11]. Incontinence was defined as uncontrollable leakage of urine, while continuous incontinence was defined as constant urine leakage. Daytime incontinence was defined as incontinence during the day [11].

Statistical analysis

Data are reported as means and standard deviations for continuous variables and as percentages for categorical variables. For univariate analyses, a *t* test was used to compare continuous variables. Risk factors that were significantly associated in the univariate analysis were included in the multivariate analysis with multivariate models of logistic regression. SPSS software version 23.0 (IBM Corp., Armonk, NY) was used for statistical analyses, and all the statistical tests were two-tailed. A *P* value of < 0.05 was considered statistically significant.

Results

Characteristics of the study population

The characteristics of the patients included in the study are shown in Table 1. Among the 47 patients, the mean age at operation was 4.8 ± 4.7 months (median 3.4 months). EUs were detected by antenatal

Table 1 Characteristics of the patients with ectopic ureterocele associated with duplex system

	Study population (<i>n</i> =47)
Age (months)	4.8 (4.7)
Follow-up period (months)	47.7 (23.3)
Presentation (%)	
Prenatal	38 (80.9%)
Postnatal	9 (19.1%)
Gender (%)	
Male	4 (8.5%)
Female	43 (91.5%)
Ureterocele site (%)	
Right	15 (31.9%)
Left	29 (61.7%)
Bilateral	3 (6.4%)
Preoperative DRF (%)	46.1 (10.7)
VUR at presentation (%)	
Yes	25 (53.2%)
No	22 (46.8%)
Primary outcome (%)	
Only single TUI	26 (55.3%)
Secondary surgery	21 (44.7%)

Data are shown as mean (SD) and weighted percentages for categorical variables

DRF differential renal function, TUI transurethral incision, VUR vesicoureteral reflux

ultrasonography in 38 patients (80.9% [38/47]) and were diagnosed in the other 9 patients (19.1% [9/47]) after birth because of febrile urinary tract infections and all patients showed ureterohydronephrosis. Among 9 patients who had febrile urinary tract infections, all

of them had VUR at the lower moiety ipsilateral kidney. EUs were in the right excretory system in 31.9% (15/47) of the patients, in the left ureterocele in 61.7% (29/47), and were bilateral in 6.4% (3/47). Primary TUIs only were performed in 55.3% (26/47) of the patients, 6.4% (3/47) underwent secondary TUIs, and 38.3% (18/47) underwent procedures other than TUIs (Table 2 and Fig. 2). Preoperative VUR was present in 53.2% (25/47) of patients: in the lower and upper moieties of the ipsilateral kidneys in 64.0% (16/25) and 24.0% (6/25), respectively, and in the contralateral kidney in 12.0% (3/25). VUR resolved in 10 patients as determined by postoperative VCUG. De novo VUR, which was defined as VUR that developed after surgery when there was no VUR previously, developed in five patients after primary TUIs were completed with no need for further intervention and in two patients after CSR, for a total of 22 patients with postoperative VUR. Postoperative ultrasonography demonstrated that hydronephroureterosis in all patients who underwent primary and secondary surgeries decreased to normal or mild degrees thereof.

Postoperative complications requiring additional surgery

Secondary surgery was necessary for 21/47 (44.7%) patients during a mean follow-up of 47.7 ± 23.3 months, most commonly for febrile urinary tract infections (14/21 [66.7%]) (Table 2). Among 14 patients with febrile urinary tract infections, 3 patients underwent secondary TUIs, and 11 patients underwent CSR. Among 14 patients, four had VUR in the upper moiety ipsilateral kidney, and six had VUR in the lower moiety ipsilateral kidney. Three patients underwent secondary surgery due to aggravation of hydronephrosis. Three patients initially had hydronephrosis grade 4 at the upper moiety of the ipsilateral kidney, and hydronephrosis was aggravated after the primary TUIs. The most common type of secondary surgery was CSR (Table 3), which was performed a median 336 days (mean 455.3 days) after primary TUIs. Secondary TUIs were performed a median of 72 days (mean 99.3 days) after primary TUIs.

Postoperative incontinence

Voiding problems occurred in 3/26 (11.5%) patients who underwent primary TUIs only, two of whom had continuous

Table 2 Reasons for secondary surgery

Febrile UTI	14 (66.7%)
Aggravation of HN	3 (14.3%)
Ipsilateral high-grade VUR	4 (19.0%)
Decreased DRF	0 (0%)

Data are weighted percentages for categorical variables

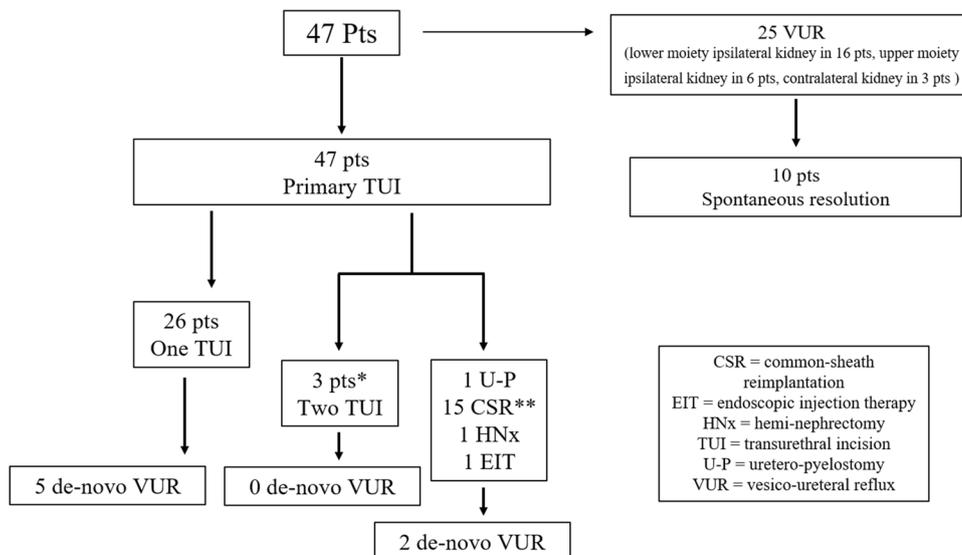
DRF differential renal function, HN hydronephrosis, UTI urinary tract infection, VUR vesicoureteral reflux

Table 3 Types of secondary surgery

Secondary TUI	3 (14.3%)
Uretero-pyelostomy	1 (4.8%)
Common-sheath reimplantation	15 (71.4%)
Heminephrectomy	1 (4.8%)
Endoscopic injection therapy	1 (4.8%)

TUI transurethral incision

Fig. 2 Flow chart showing patient outcomes. Asterisk: All three patients had febrile urinary tract infection events. Double asterisk: 11 patients (78.6%) had febrile urinary tract infection events



CSR = common-sheath reimplantation
 EIT = endoscopic injection therapy
 HN = hemi-nephrectomy
 TUI = transurethral incision
 U-P = uretero-pyelostomy
 VUR = vesico-ureteral reflux

Table 4 Voiding problems after primary TUI (26 patients) and CSR (15 patients)

	Primary TUI	CSR
More than 20-mL postvoid residual urine	0 (0.0%)	1 (6.7%)
Continuous incontinence at any age	2 (7.7%)	0 (0.0%)
Daytime incontinence after 5 years	1 (3.8%)	1 (6.7%)
Total	3 (11.5%)	2 (13.4%)

CSR common-sheath reimplantation, TUI transurethral incision

incontinence and one who had daytime incontinence after an age of 5 years (Table 4), whereas 2/15 (13.4%) patients exhibited voiding problems after secondary CSR (Table 4), which was not significantly different from that in the group that underwent primary TUI only ($P=0.866$). One patient had more than 20 mL of postvoid residual urine repeatedly, and one patient had daytime incontinence after an age of 5 years.

Postoperative renal function

Postoperative DMSA scan analyses were available for 44 patients. DRF decreased by $>5\%$ in 7/44 (15.9%) patients, including six patients who required secondary surgery. Five of these patients underwent CSR and one patient underwent a secondary TUI. DRF increased by $>5\%$ in 2/44 (4.3%) patients, including one who underwent CSR and one who underwent a secondary TUI. Among those successfully treated with TUI and for whom DMSA scans were available, DRF decreased by $>5\%$ in 1/25 (4.0%) patients. There was no difference between mean postoperative and preoperative DRF values (47.7 ± 7.6 versus 48.0 ± 8.0 ; $P=0.877$). During the follow-up period, no patient exhibited hypertension or proteinuria.

Discussion

The management of EUs with duplex systems remains a great challenge, and various treatment modalities exist, such as TUI; UTA, including ureteroureterostomy or heminephrectomy; or a BLA, including CSR with ureterocelectomy or total reconstruction of the upper and lower urinary tracts with ureterocelectomy, ureteral reimplantation, and heminephrectomy. UTA is effective and does not involve the bladder during surgery; however, several contraindications exist, such as the presence of high-grade VUR. While BLA could be performed, where UTA is contraindicated, it has several limitations.

At our institution, a UTA is preferred for the management of patients with EUs. However, in patients with ipsilateral high-grade VUR for whom UTA is not indicated, CSR is

typically performed. CSR results in effective decompression in 92.3% of cases, with 17.9% requiring an additional operation [2]. Beganovic et al. [12] reported that 31.5% of patients required secondary surgery for VUR and obstructive voiding. We found that TUIs resulted in successful decompression in 61.7% of patients with duplex systems, though 44.7% required second surgical procedures. However, direct comparisons among these studies are difficult, as different surgical modalities were applied.

Several studies found that TUI alone is rarely safe and effective, with success rates ranging from 29 to 40% [13–17]. Moreover, Decter et al. [1] reported that all patients treated with TUIs required open surgery because of persistent ureterocele. Therefore, TUIs have been considered as temporary until open reconstructive surgery can be performed. However, primary TUIs were successful in 55.3% of the patients included in our study, similar to the success rate of 56% reported by Adorisio et al. [3]. The differences between these success rates would be dependent on the methods of TUI. Among the studies that reported the success rates of the TUI, Wang et al. [13] reported the success rate of 6% and they have performed TUI using a Buggbee electrode and no specific description of methods has been described. Jayanthi and Koff [16] punctured at the junction of the ureterocele and bladder floor using a cold knife urethrotome or 3F electrode which showed success rates of 20%. Adorisio et al. [3] made a longitudinal incision from the distal extent of the ureterocele through the bladder neck using the stylet of a 3F urethral catheter. However, we used 1000- μm holmium–yttrium–aluminum–garnet laser which have been reported to allow precise incision and decompression [18, 19] and made puncture at the dependent position of the ureterocele to ensure proper drainage which leads to adequate decompression (Fig. 1).

Our success rate after secondary TUI was 61.7%, whereas Adorisio et al. reported a secondary success rate of 93% [3], a difference that may be attributed to the selection of second surgery procedures according to the surgeons' preferences. Whereas secondary TUIs were performed in the study reported by Adorisio et al. [3], these were only performed in patients in our study that were too young for a BLA. However, in many of our cases, the primary TUI procedure provided a delay that was sufficient to later enable the preferred BLA. Nevertheless, further study is needed to determine whether a secondary TUI or BLA should be performed after the failure of a primary TUI.

The median age at operation for patients in our study (3.4 months) is similar to that for patients who underwent proximal ureteroureterostomy (75 days) in our previous study [20]. Thus, the TUI can be considered as the first option in BLA, compared to initial option of proximal ureteroureterostomy in UTA. By contrast, the median age of

patients who underwent CSR in our previous study was 16.5 months [20], for which TUI was considered a temporizing technique. In accordance with our data in this study, we find that the success rate of primary TUIs warrants their use as an initial option in BLAs.

DRF decreased by > 5% in seven patients, and among them, six required secondary surgery. Decreased renal function would primarily be due to the febrile urinary tract infection events, since most of the patients who experienced decreases in renal function were those who required secondary surgery due to the febrile urinary tract infection events. However, renal scarring could have also decreased renal function.

There are some concerns regarding the potential voiding problems such as incontinence after a BLA for the treatment of EUs [21]. Previous studies have found incontinence rates ranging from 0 to 13% [10, 22, 23]. In our previous study, we found an incontinence rate of 7.9%, with 18.4% of patients exhibited voiding problems after CSR. In the present study, the rates of voiding problems after TUI were slightly lower, but the difference was not significant. However, it is difficult to determine whether voiding problems result from the bladder surgery or from the underlying disease. It has long been believed that operations involving the BLA induce voiding problems via disruptions to the anatomy of the bladder, for example, by altering the bladder neck configuration or harming the vascularization and innervation of the bladder [22]. In addition, there is a possibility for iatrogenic injury to the bladder neck or external urethral sphincter during surgery [23], though supporting evidence is lacking [11]. For example, Abrahamsson et al. [21] reported that there was no incontinence in the groups that underwent operations involving a BLA, and Vereecken and Proesmans [22] found that voiding problems in patients with EUs were associated with the disease rather than surgical complications. Accordingly, our previous study showed that preoperative DRF was the only risk factor for incontinence after CSR [2]. The results presented here also indicate that the surgical procedure does not promote voiding problems, as there were no significant factors for incontinence after primary TUI and there was no significant difference between primary TUI and CSR.

For the management of EU, we previously suggested a treatment algorithm that initially involves a UTA (Fig. 3), which requires a smaller incision and fewer technical challenges than a BLA and thus a reduced risk of morbidity. However, BLA, especially CSR with ureterocoelectomy, is suggested as the next option in cases with ipsilateral high-grade VUR or severely dilated upper pole ureters [24]. Total reconstruction, which requires an additional operation, and heminephrectomy, which has risks of developing lower pole loss and postoperative hypertension and proteinuria, were excluded as treatment options [2, 20]. CSR requires the reimplantation of the bulky common-sheath ureter,

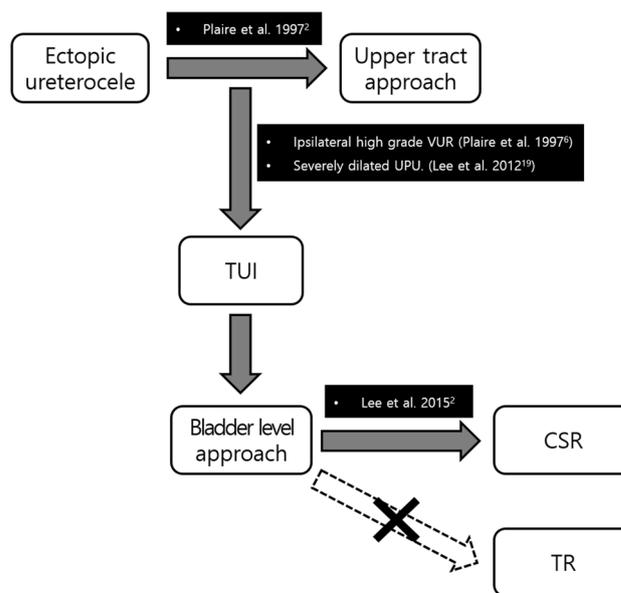


Fig. 3 Treatment algorithm for the management of ectopic ureterocele (EUs) with a duplex system

often with plication. Although this technique does not disturb bladder anatomy, it involves some technical difficulty. By contrast, TUI is a simpler procedure and is primarily performed before CSR. TUIs for EUs reduce urinary stasis and the risk of infection, with minimal morbidity [25], enabling BLA to be adapted appropriately in 30–50% of cases [4, 25–29]. It is also reported to facilitate lower urinary tract reconstruction in infant bladders with decompressed and less dilated ureters [4, 25]. Nevertheless, TUIs are used only for initial temporary management in many institutions, and the success rate for TUIs has been low [30]. The data presented here provide further evidence that TUIs can effectively decompress EUs, with a relatively high success rate, and should be considered as a first option when a UTA is not appropriate.

In our treatment algorithm, we considered that the advent of symptoms such as febrile urinary tract infections or diagnosis of ureterohydronephrosis by ultrasonography occurs mostly in infants. For older patients in whom there are no concerns for technical difficulty due to a small bladder and no concerns for high morbidity and postoperative incontinence due to immature bladders, BLA would be considered as a primary treatment approach.

Regarding indications for secondary surgery after primary TUI, Castagnetti et al. [31] suggested that decompression is the key to the success of this treatment and that once decompression is achieved, recurrent febrile urinary tract infections would be rare. Our study is consistent with this study in that secondary surgery was mostly performed due to febrile urinary tract infections in individuals who had not fully achieved decompressed hydronephroureterosis.

Moreover, three patients underwent secondary surgery due to aggravation of hydronephrosis. Although we should consider ultrasonography as the most important postoperative diagnostic tool, we should not disregard upper pole function and VUR status, since four patients required secondary surgery due to VUR.

There are several limitations of this study. First, due to the retrospective study design, some of the data from examinations is missing, and there is a potential for selection bias. Moreover, the surgical indication for secondary TUIs was not clear, since it was based on surgeon's surgical preferences. The success rates of TUIs would have increased if there was clear indication of secondary TUIs, since most of the patients underwent open surgery. Second, DRF, in our study, reflects a combination of upper and lower pole kidney functions. A separate analysis of upper and lower pole kidneys would provide more information. Using the three-dimensional DMSA scan, we could accurately assess upper and lower pole kidney functions. Future prospective studies should include three-dimensional DMSA scan. Furthermore, there were no DMSA scan data for patients with febrile urinary tract infections. Third, the number of patients with postoperative incontinence after primary TUIs was small, resulting in low statistical power. Fourth, there were no VCUG data after primary TUIs. Fifth, toilet-training status has not been reported due to the ambiguity in its terminology and limitation of the retrospective study. Finally, circumcision status was reported due to the limitation of the retrospective analysis. However, low numbers of circumcisions are performed in our country, and the number of male participants in our study was small, such that it would not have greatly affected our results. Although data on the exact locations of the puncture site have not been reported in this study, future research to establish TUIs as the treatment option of EUs with duplex system should correlate with the puncture site and continence after TUI.

Conclusion

The results presented here show that TUIs can effectively decompress EUs with a high rate of success. In addition, postoperative incontinence was not associated with the surgical procedures. Therefore, when a UTA is not appropriate, TUI should be considered as an effective treatment modality and not just a temporizing technique.

Acknowledgements The authors would like to thank Dong-Su Jang, MFA, (Medical Illustrator) for his help with the illustrations.

Author contributions JSP: project development, data analysis, and manuscript writing/editing. YSL: project development, data analysis, and manuscript editing. CNL: data collection. SHK: data collection.

SWK: project development and data analysis. HL: data collection. SWH: project development, data analysis, and manuscript editing.

Compliance with ethical standards

Conflict of interest All of the authors declare that they have no conflicts of interest.

Ethical approval All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was not required for the purposes of this study, as it was based upon retrospective anonymous patient data and did not involve patient intervention or the use of human tissue samples.

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