HUMAN BIOLOGY
2025, VOL. 95, ISSUE 2
ORIGINAL ARTICLE

OPEN ACCESS

Risk Factors for Recurrent Urinary Tract Infections after Endoscopic Incision of Ureterocele in Infant

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ABSTRACT

Objectives: Much dispute encompasses the treatment of ureterocele. Generally, in patients with ureterocele, endoscopic incision (EI) is recommended to prevent urinary tract infections (UTIs) or progressive hydronephrotic complications and preserve renal function. To clarify the impact of EI for ureterocele as an initial procedure, focusing on end points of postoperative recurrent febrile UTIs and need for second surgery.

Methods: Between December 2006 and December 2019 primary EI was performed in 80 consecutive patients with ureterocele. We retrospectively investigated patient preoperative radiological and clinical data and postoperative radiological and clinical outcomes.

Results: All 80 patients who underwent EI were identified and included in our study, and EI was conducted at an average of 4.6 (IQR 2.5 to 8.5) months. Twenty-nine patients with ureterocele had postoperative recurrent febrile UTIs during the follow-up of 36 months, and 22 out of 29 patients were recommended secondary intervention. Initial recurrent febrile UTIs in most child occurred <12 months after EI, the recurrent febrile UTIs-free rate after EI was 63.75%. The risk factor for recurrent febrile UTIs was VUR on postoperative VCUG, antibiotic prophylaxis treatment might be beneficial in preventing recurrent febrile UTIs after EI.

Conclusion: EI is optimal for instant ureterocele decompression, and it avoids a complete reconstruction in most patients. However, it is not a definitive approach in cases with postoperative VUR. Our study determined the critical period and risk factor for recurrent febrile UTIs after EI for the treatment of ureterocele.

INTRODUCTION

Duplex system ureterocele (DSU) accounts for the majority of ureterocele diagnoses in infants. In contrast to simplex system ureterocele (SSU), DSU can negatively affect urodynamics and renal function as well as cause recurrent UTIs Wang et al. (2023), incontinence, and critically compromised function Gomes et al. (2002), Chertin et al. (2001) and often presents with dysplasia or obstructive nephropathy of the corresponding ureter, and vesicoureteral reflux (VUR) to the ipsilateral inferior moiety or contralateral renal unit Chertin et al. (2003), Merlini et al. (2004).

With the advancement of endoscopic invasive surgery, early intervention is preferable to maintain moiety function and decrease UTIs Castagnetti et al. (2009), Pfister et al. (1998). Moreover, recent reports suggest that EI may effectively treat ureterocele Hagg et al. (2000). Hence, more invasive secondary procedures can be reserved for symptomatic individuals, regardless of VUR status and upper-pole function Di Renzo et al. (2010), Castagnetti et al. (2013). However, little is known about long-term effect after ureterocele decompression, and management of ureterocele in infants is controversial Gomes et al. (2002). This work evaluated the incidence of and risk factors for recurrent febrile UTIs after EI for ureterocele.

MATERIALS AND METHODS

Study population and selection process

We received ethical approval from our institutional review board before the initiation of the study. For this retrospective study, we reviewed 184 children with ureterocele diagnosed at the Xin Hua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine. Those patients who were managed conservatively without any surgical intervention, with length of follow-up less three years, with a history of previous ureterocele surgery and lack of preoperative data were excluded from the

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Keywords: endoscopic incision, ureterocele, new onset reflux, secondary surgery, split renal function

study, and we included 80 patients with ureterocele who received EI in the study.

Data Collection and Outcome of interest

Among the analyzed patient demographics were gender, age at diagnosis, history of prenatal diagnosis, clinical presentation, type of ureterocele (DSU or SSU and intravesical or extravesical) and preoperative and postoperative results of ultrasonography, 99mtechnetium ethylene dicysteine nuclear scan and VCUG. We also gathered details regarding the side of the ureterocele and degree of ureteral dilatation. The fraction of renal activity was calculated for each kidney after background correction. Of note, the male patients with ureterocele were uncircumcised. Diagnosis was based on a kidney–bladder ultrasonography (US) in all patients. US evaluation was performed in patients after emptying bladder to assess the exact severity of hydronephrosis dilatation. It was recommended that the same position of the patient should be used for each to make accurate comparison. All but two patients received pre-operative 99mtechnetium ethylene dicysteine renal scan, while two patients received urgent ureterocele puncture. Based on the classification by the Urology Section of the American Academy of Pediatrics, ureterocele is classified as orthotopic--located on the trigone with the ureteral meatus in the normal position and draining a single collecting system, and ectopic--located distal to the normal ureteral position, thus, extending towards and occasionally into the urethra, and associated with a duplicated system Glassberg et al. (1987).

EI is recommended for ureterocele as minimally invasive surgery in young infant. Surgery is indicated in the breakthrough febrile UTIs, progressive renal parenchymal change or loss of function, bladder outlet obstruction Aikins et al. (2019). The ureterocele was incised through a neonatal or pediatric cystoscope with a miniature electrocautery hook, holmium laser according to patient anatomy and surgeon preference. A single ureterocele incision was made through the intravesical portion of the ureterocele until stable adequate decompression was visualized.

Patients underwent an US scan and renal scintigraphy immediately after the operation and subsequent follow-up US at 2, 6, and 12 months. Low-dose antibiotic prophylaxis was given to children with febrile UTIs and was maintained until toilet training was achieved. In addition, the patients underwent VCUG and renal nuclear scan, and were reviewed for requiring an additional operation. The status of UTI and urinary continence was reviewed and documented at each follow up. Additional micturating cystourethrogram and dynamic renal scintigraphy studies were only done if necessary. Our primary study outcomes were the recurrent febrile UTIs after EI and need for additional intervention during follow up period. Additional intervention was recommended only under the following conditions: symptomatic postoperative VUR, breakthrough febrile UTIs, reduction in renal function or evidence of bladder outlet obstruction. Each child defined as recurrent febrile UTIs had one or two febrile UTIs after EI up to the time of second surgery. F-UTI represented body temperature≥38 °C and UTI. UTI was defined as significant pyuria (> 10 white blood cells/high power field) and bacteriuria (> 100,000 colony-forming units/mL of midstream clean-catch collection) on urine analysis. Recurrent F-UTIs was defined these children had experienced more than two febrile urinary tract infections during study period.

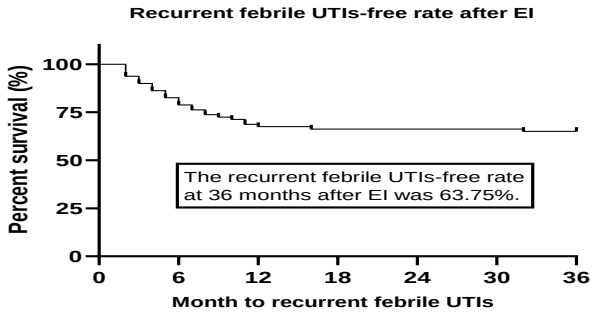
Statistical analysis

Significance was identified using two-tailed paired t-tests at $p < 0.05$. Categorical variables were presented as frequencies (percentages) and continuous data as means ± standard deviation or medians ± range. Continuous variables were compared with Mann–Whitney test and categorical variables with Fisher's exact test. Cumulative event curves were generated with the use of the Kaplan–Meier method, and the risk of recurrent febrile UTIs was estimated as a risk ratio with a 95% confidence interval (CI), which was derived with the use of a Cox proportional-hazards model.

RESULTS

A total of 80 patients treated by EI met our study criteria were identified during this study (Fig.1).

Figure 1: Recurrent febrile UTIs-free rate after endoscopic incision



Patient characteristics are shown in Table 1. Among the 80 patients with ureterocele, 49 (61.3%) were females, 56 (70%) were antenatally diagnosed, and the ureterocele was on the bilateral side in 10 (12.5%). There were 15 patients with a single system intravesical ureterocele and 65 cases with a duplex system including 56 intravesical and 9 ectopic ureterocele. The clinical manifestations of all patients were breakthrough UTIs in 41 (51.3%), followed by progressive hydronephrosis and voiding dysfunction. VUR was detected prior to surgery in twelve cases, in the ipsilateral upper-pole moiety in six cases, ipsilateral lower-pole moiety in four cases, and in the contralateral moiety in two cases. Twenty-three patients performed preoperative and postoperative nuclear renal scans, and three patients had poor-functioning upper moieties.

Table 1: Characteristics of patients with ureterocele

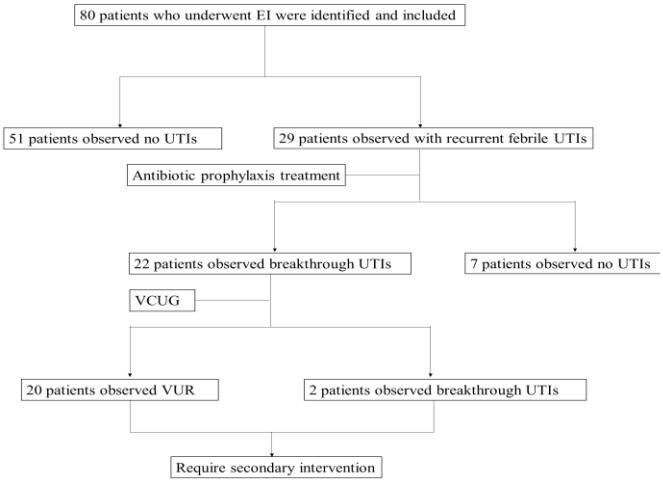
Patient characteristics	Total (n=80)
Gender	
Female—no. (%)	49 (61.3)
Male—no. (%)	31 (38.7)
Diagnosis	
Antenatal—no. (%)	56 (70)
Postnatal—no. (%)	24 (28)
Affected units	
Bilateral units—no. (%)	10 (12.5)
Unilateral unit—no. (%)	70 (87.5)
Type of ureterocele	
Intravesical—no. (%)	71 (88.8)
Ectopic—no. (%)	9 (11.2)
Ureterocele unit	
Single system—no. (%)	15 (18.7)
Duplex system—no. (%)	65 (81.3)
VUR on preoperative VCUG	
Upper moiety unit—no. (%)	6 (7.5)
Lower moiety unit—no. (%)	4 (5)
Contralateral unit—no. (%)	2 (2.5)
No—no. (%)	60 (75)
N/A—no. (%)	8 (10)
VUR on postoperative VCUG	
Ureterocele unit—no. (%)	23 (28.7)
No—no. (%)	40 (50)
N/A—no. (%)	17 (21.3)
Clinical manifestations	
Breakthrough UTIs	41 (51.3)
Progressive hydronephrosis	30 (37.5)
Voiding dysfunction	9 (11.2)
Median preoperative APD (IQR) (mm)	22 (15.2-28.7)
Median postoperative APD (IQR) (mm)	8 (0-13)
Median preoperative UD (IQR) (mm)	11 (9-13)
Median postoperative UD (IQR) (mm)	0 (0-7)
Median preoperative DRF (IQR) (%)	42.5 (35.6-46.7)
Median postoperative DRF (IQR) (%)	44.1 (38.8-46.8)
Median age at surgery (IQR)(months)	4.6 (2.5-8.5)
Postoperative recurrent febrile UTIs	29 (36.3)
Secondary surgery	22 (27.5)

APD, anteroposterior pelvic diameter; UD, ureteral diameter; DRF, differential renal function; N/A, not available.

Most of the poorly functioning segments exhibited any improvement in function during postoperative renal scintigraphy. Overall postoperative differential renal function showed a slight increase (preoperative, 40.08 vs postoperative, 44.37; p = 0.005) at the end of follow up as observed via nuclear scan.

Among 29 children with recurrent febrile UTIs during follow-up, no additional surgery was indicated in seven. Recurrent febrile UTIs in most children occurred in 29 children <12 months after EI, and the recurrent febrile UTIs-free rate after EI was 63.75% (Fig. 2).

Figure 2: Flow chart showing patient outcomes



The characteristics of the children with recurrent febrile UTIs are shown in Table 2. At last follow-up, successful ureterocele decompression was seen in 78 of 80 patients (97.5%) on postoperative US, 26 of those successful cases after EI showed some degree of upper urinary tract dilatation. Among 80 patients in this study, 58 cases did not require additional intervention during the duration of the study. However, 22 out of 80 were recommended secondary intervention, due to postoperative VUR or inadequate decompression. The secondary intervention of these 22 patients included ureteric reimplantation in 4 cases, ureteric reimplantation and DSU resection in 3 patients, ureteric reimplantation and partial nephrectomy in 2 patient, ureteroureterostomy or ureteric reimplantation in 2 patient, secondary partial nephrectomy and DSU resection in 4 patients, and secondary partial nephrectomy in 7 patients. 23 patients exhibited VUR on postoperative VCUG, including the ipsilateral upper-pole moiety in 11 case, ipsilateral lower-pole moiety in 6 cases, ipsilateral moiety in 2 cases, contralateral moiety in 2 case, bilateral side in 2 cases (Fig.3). The recurrent febrile UTIs-free rates after EI were:57.1% in girls and 90.3% in boys; 66.2% in children with a duplex system and 93.3% in children with a single system; 26% in children with VUR on postoperative VCUG and 83% in children without

Table 2: The characteristics of the children with recurrent febrile UTIs.

Variable	Non-recurrent febrile UTIs (n=51)	Recurrent febrile UTIs (n=29)
Gender		
Female	27 (52.9)	22 (75.9)
Male	24 (47.1)	7 (24.1)
Diagnosis		
Antenatal	35 (68.6)	21 (72.4)
Postnatal	16 (31.4)	8 (27.6)
Affected units		
Bilateral units	44 (86.3)	26 (89.7)
Unilateral unit	7 (13.7)	3 (10.3)
Type of ureterocele		
Intravesical	46 (90.2)	25 (86.2)
Ectopic	5 (9.8)	4 (13.8)
Ureterocele unit		
Duplex system	37 (72.5)	28 (96.6)
Single system	14 (27.5)	1 (3.4)
Preoperative VUR		
Yes	6 (11.8)	6 (20.7)
No	39 (76.4)	21 (72.4)
N/A	6 (11.8)	2 (6.9)
Preoperative UTIs		
Yes	22 (44)	19 (65.5)
No	28 (56)	10 (34.5)
Postoperative VUR		
Yes	3 (5.9)	20 (68.9)
No	44 (86.2)	9 (31.1)
N/A	4 (7.9)	0 (0)

VUR, Vesicoureteral reflux; N/A, not available; UTIs, urinary tract infections

VUR on postoperative VCUG; and 80% in children with bilateral units and 68.8% in children with unilateral unit;66.7% in children with postnatal diagnosis and 71.4% in children with antenatal diagnosis;66.7% in children with ectopic ureterocele and 71.8% in children with intravesical ureterocele (Fig. 4). The Cox proportional hazard model showed that duplex system and VUR on postoperative VCUG were associated with significantly higher risks of recurrent febrile UTIs in Table 3.

Figure 3: Representative pictures of pre- and postoperative VCUG in a patient with ureterocele in a duplex collecting system. (A) No VUR appears after endoscopic incision; B) VUR appears in the ipsilateral upper-pole moiety unit after endoscopic incision; (C) VUR appears in the (ipsilateral lower-pole moiety unit after endoscopic incision; (D) VUR appears in the ipsilateral moiety unit after endoscopic incision

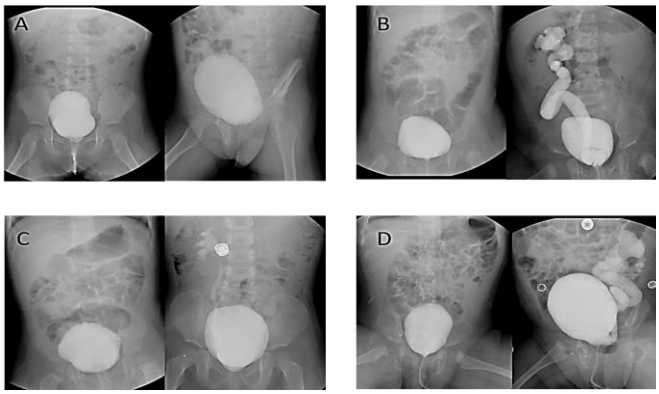
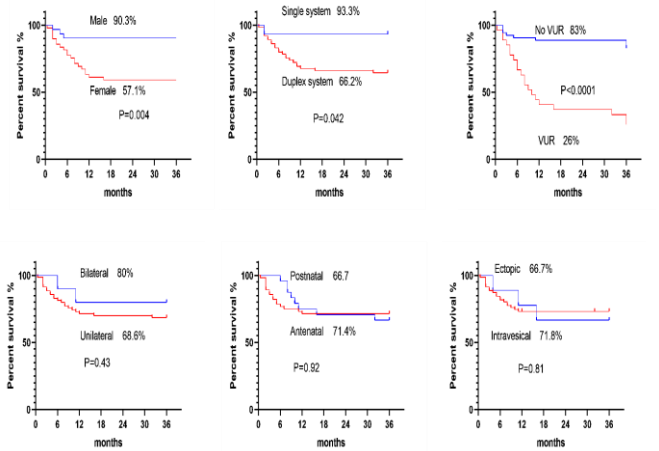


Table 3: Risk factors for recurrent febrile UTIs

Variable	Risk ratio (95% CI)	P value
Female	1.383(0.542-3.525)	0.497
Antenatal	0.807(0.344-1.892)	0.621
Bilateral	1.590(0.431-5.865)	0.486
Ectopic ureterocele	1.183(0.394-3.555)	0.765
Duplex system	12.858(1.640-100.808)	0.015
VUR on postoperative VCUG	1.885(1.273-2.791)	0.002

VUR, Vesicoureteral reflux; VCUG, voiding cystourethrogram

Figure 4: Recurrent febrile UTIs-free rate after endoscopic incision based on each risk factors.



(A) 57.1% girls and 90.3% in boys; (B) 66.2% in children with a duplex system and 93.3% in children with a single system; (C) 26% in children with VUR on postoperative VCUG and 83% in children without VUR on postoperative VCUG; (D) 80% in children with bilateral units and 68.8% in children with unilateral unit;(E) 66.7% in children with postnatal diagnosis and 71.4% in children with antenatal diagnosis;(F) 66.7% in children with ectopic ureterocele and 71.8% in children with intravesical ureterocoele.

DISCUSSION

In the present study, we found that the recurrent febrile UTIs-free rate after EI was 63.75% and that risk factors for recurrent febrile UTIs were duplex system and VUR on postoperative VCUG. In 29 children with recurrent febrile UTIs after EI, this occurred <12 months in most children.

The management protocol for children with ureterocele is a controversial subject without a clear consensus on the therapeutic choices for pediatric urologists. Among the surgical interventions for the ureterocele treatment are endoscopic decompression, nephroureterectomy and complete reconstruction. However, advocates of heminephrectomy raise concerns about the possibility of secondary interventions, especially in DSU, along with higher iatrogenic injury risk to the lower pole vessels Cohen et al. (2015). Theoretically, a complete reconstruction would be ideal in this situation, concerns regarding surgical complications have restricted its usage, despite no evidence that a complete reconstruction would increase urodynamic morbidity Gander et al. (2016). Hence, in the past few decades, EI of ureterocele was a well-established optimal treatment; however, it was not a definitive intervention in DSU for relieving obstruction without preserving the ureterovesical valve mechanism Jayanthi et al. (1999).

There are a few studies reported long-term effectiveness of EI in both SSU and DSU. EI treatment provides definitive treatment in most patients with SSU. In our series 94% of patients with SSU were not documented to have recurrent febrile UTIs after EI, comparable to the rate reported8,16. In multiple studies it has been noted that the recurrent febrile UTIs rate is higher in patients with DSU comparing SSU Chertin et al. (2001), Investigators et al. (2014). Furthermore, there was statistically significant difference in recurrent febrile UTIs after EI between DSU to SSU in our study. More recently most investigators did find a higher proportion of DSU presenting with recurrent UTIs postoperatively, and a higher proportion of these required secondary procedures compared with SSU Aikins et al. (2019), Jawdat et al. (2018). This is consistent with our results, which showed a significantly greater risk of postoperative recurrent febrile UTIs in patients with DSU compared to cases with SSU.

There have always been several studies reported that EI offers the great advantage for definitive means of intravesical ureteroceles and EI would likely result in subsequent surgery for ectopic ureteroceles Investigators et al. (2014), Andrioli et al. (2018). Although the role of endoscopic treatment has been established in the management of intravesical ureteroceles, there is no consensus on its effectiveness for treating ectopic ureteroceles Sander et al. (2015). It is noteworthy that series of studies have demonstrated that the location of the ureterocele does not affect the recurrent UTIs and reoperation rate in children with ectopic ureterocele Hagg et al. (2000), Cohen et al. (2015). We analyzed the value of EI in intravesical and ectopic ureteroceles cases and found no significant difference in in the efficacy of primary EI for ectopic and intravesical cases.

There has always been general acceptance that the primary concern of EI is the possibility of new onset VUR, which may require further intervention Gomes et al. (2002), Sander et al. (2015). However, it is noteworthy that VUR after endoscopic puncture of ureterocele can resolve spontaneously in a subset of patients Jesus et al. (2011). Recently, Hodhod et al detected new VUR in 23.3% of DSU patients Hodhod et al. (2017). Indeed, endoscopic decompression combined with endoscopic correction of symptomatic VUR to ureterocele moiety or either to ipsilateral or contralateral kidney and associated moieties appear to be long-term effective and safe approach Pani et al. (2022). According to our current study, 20 patients developed VUR and underwent additional surgery. Nevertheless, several studies have shown that antibiotic prophylaxis reduces the incidence of recurrent UTIs in patients with primary VUR Investigators et al. (2014), Kjell et al. (2020), however, there is no convincing evidence that antibiotic prophylaxis treatment can reduce the incidence of recurrent febrile UTIs in cases of ureterocele after EI Hodhod et al. (2017). Further studies are necessary to clarify the effectiveness of antibiotic prophylaxis in this situation, but it might be beneficial in preventing recurrent UTIs and renal scarring during the critical period for symptomatic UTIs identified after EI. In 7 of these 29 patients (24.1%), of whom all had a DSU, the patient did well with antibiotic prophylaxis.

Early decompression may potentially preserve some renal function, even though the possibility of a functioning renal parenchyma is low. An affected upper pole does not drastically alter the entire renal function. In fact, the quantifiable loss of function after upper pole partial nephrectomy was 1.25%, whereas the gain in function after EI was 2.25% on average Vates et al. (1996). Gomes and Mendes, for instance, do not recommend EI for enhancing renal function in renal segments with reduced function, unless the renal reserve is depleted, as in majority of the cases the affected renal segment tends to be hypodysplastic Gomes et al. (2002). Nevertheless, we retrieved data on ipsilateral function from most of the analyzed patients. Based on our analysis, one of patients experienced loss of renal function after surgery. Several studies have shown there was no discernible enhancement of renal function after DSU decompression Chertin et al. (2001), Connolly et al. (2002). Alternately, we showed a small enhancement of renal function after EI. Given that the upper pole moiety is frequently dysplastic or exhibits post-obstructive or infectious scarring, preservation of the renal moiety may markedly elevate hypertension risk. Unfortunately, currently, there are limited data on the long-term morbidity of a non-eliminated dysplastic upper moiety. We speculate that ureterocele decompression leads to satisfactory drainage of the previously obstructed

System. Based on Chertin's survey, a decompressed upper pole segment, that shows poor function and no VUR, is not in need of further intervention and does not have increased morbidity Chertin et al. (2005).

CONCLUSION

EI offers a minimally invasive procedure with relatively low morbidity. It facilitates quick and effective ureterocele decompression. We found that risk factors for postoperative recurrent febrile UTIs were duplex system and VUR. In 29 children with recurrent febrile UTIs after EI, this occurred <12 months in most children.

DECLARATIONS

Data availability

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Funding

This research was funded by the Natural Science Foundation of Shandong Province (Grant No. ZR2023MH279) and Qingdao Natural Science Foundation (Grant No. 23-2-1-205-zyyd-jch).

Competing interests

The authors declare no competing interests.

Authors' contributions

Jinbin Wang and Hongquan Geng and Hongting Lu contributed to the conception and design of the manuscript. Zhoutong Chen, Qi Liu and Jiaxiang Tang collected data and management, Qiang Gao, Nianfeng Sun, Jiabin Yu and Xiaoliang Fang edited the manuscript. Yining Zhao and Binyi Yang performed statistical analysis. All the authors contributed to the literature search, revised the article and approved its final version.

Ethical approval

All procedures performed in studies were in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards, and with the ethical standards of the institutional and national research committee. This study was approved by the institutional ethical committee, and it complies with the ethical consent policy of the journal.

Consent to participate

Informed consent regarding the surgical procedure was obtained from the parents of all individual participants included in the study.

Consent for publication

Yes, we consent for publication.

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