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Understanding Ectopic Kidneys: Insights from a Single-Center Study

Ektopik Böbreklerin İncelenmesi: Tek Merkezli Bir Çalışmadan İzlenimler

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Abstract

Introduction: The failure of the normal ascent of the kidney can result in ectopic kidneys (EK) and fusion anomalies. EKs are often accompanied by urological and extrarenal abnormalities. This study aims to provide a comprehensive overview of EKs, associated renal and extrarenal anomalies, and kidney functions among patients with simple and cross ectopic kidneys.

Materials and Methods: Clinical records of patients diagnosed with EK admitted to the pediatric nephrology unit between June 2017 and June 2022 were retrospectively evaluated.

Results: In this study, 41.20% (n: 61) of patients had crossed ectopic (CE) kidneys. The most common type of crossed ectopia was inferior CE (n:33 56.9%). The most frequent presenting features were an empty renal fossa (7.40%, n: 11). During the first evaluation, 18.91% (n:28) of patients had hydronephrosis, most of which were mild (SFU 1-2). Vesicoureteric reflux (VUR) was evident in 7.4% of patients. The mean DMSA (dimercaptosuccinic acid) uptake was lower in EK (40.37±7.31) compared to orthotopic kidneys. Comparison of simple and CE kidneys showed similar results regarding the presence of hydronephrosis, vesicoureteral reflux (VUR), and differential function of EKs. In both groups, serum creatinine levels and estimated glomerular filtration rate (eGFR) were preserved.

Conclusion: Patients with ectopic kidneys often present with renal and extrarenal anomalies. Although hydronephrosis is a common occurrence, it is usually mild and transient, and incidence of vesicoureteral reflux is low. Considering the preservation of renal function in mid-term period, it may be more appropriate to evaluate each patient's need for a complete urological examination on a case-by-case basis.

Keywords
Ectopic kidney, fusion anomalies, VUR, DMSA

Anahtar kelimeler
Ektopik böbrek, füzyon anomalileri, VUR, DMSA

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Öz

Giriş: Böbreğin normal yerleşimindeki başarısızlığı, ektopik böbreklerin (EB) ve füzyon anomalilerinin ortaya çıkmasına neden olabilir. EB'ler genellikle ürolojik ve ekstrarenal anomalilerle birlikte görülür. Bu çalışmanın amacı, basit ve çapraz ektopik böbrekleri olan hastalardaki EB'leri, ilişkili renal ve ekstrarenal anomalileri ve böbrek fonksiyonlarını kapsamlı bir şekilde incelemektir.

Gereç ve Yöntem: Haziran 2017 ile Haziran 2022 tarihleri arasında pediatrik nefroloji ünitesine başvuran EB tanısı konmuş hastaların klinik kayıtları geriye dönük olarak değerlendirildi.

Bulgular: Bu çalışmada, hastaların %41,20'sinde (n: 61) çapraz ektopik (ÇE) böbrekler bulunmaktaydı. En yaygın çapraz ektopi türü inferior ÇE idi (n: 33, %56,9). En sık görülen bulgu boş renal fossa idi (%7,40, n: 11). İlk değerlendirme

sırasında hastaların %18,91'inde (n: 28) hidronefroz mevcuttu, çoğunluğu hafif (SFU 1-2) idi. Üriner vezikoüreteral reflü (VUR), hastaların %7,4'ünde mevcuttu. Ortalama DMSA (dimercaptosuccinic acid) alımı, EB'lerde (40,37±7,31) ortotopik böbreklere göre daha düşüktü. Basit ve ÇE böbreklerin hidronefroz, VUR ve EB'lerin diferansiyel fonksiyonu açısından karşılaştırılması benzer sonuçlar gösterdi. Her iki grupta da serum kreatinin düzeyleri ve tahmini glomerüler filtrasyon hızı (eGFR) korunduğu görüldü.
Sonuç: Ektopik böbreklere sahip hastalar genellikle renal ve ekstrarenal anomalilerle birlikte gelirler. Hidronefroz sık görülen bir durum olmasına rağmen, genellikle hafif ve geçicidir ve vezikoüreteral reflü insidansı düşüktür. Orta vadede renal fonksiyonun korunması göz önüne alındığında, her bir hastanın tam bir ürolojik muayene için ihtiyacının vaka bazında değerlendirilmesi daha uygun olabilir.

Introduction

The human kidney goes through different stages during embryonic development. Normally, the development of the kidney and urinary tract begins with the formation of a nephric duct (ND) from the intermediate mesoderm. Formation of a permanent mature kidney requires complex interactions between different cell lineages consisting of epithelial cells of the ureteric bud, mesenchymal cells of nephric blastema, and endothelial cells of capillaries (1). As morphogenesis progresses, the kidney simultaneously undergoes an ascent from its lower pelvic position to its typical intraabdominal location. The formation of the kidney and outflow tracts necessitates a complex interplay of various factors, including genetic, epigenetic, and environmental influences from both the maternal and fetal aspects of organogenesis (2-4). Distruption of convergence between genetic and environmental factors can lead to congenital anomalies of kidney (CAKUT).

CAKUT is the leading cause of chronic kidney disease in children. It presents with diverse phenotypes based on the timing of disrupted embryonic development and the type of affected segment. CAKUT can be classified according to abnormalities in kidney number (renal agenesis, aplasia), size, and morphology (hypoplasia, multicystic dysplastic kidney - MCDK, dysplasia), outflow tract abnormalities (ureteropelvic junction obstruction - UPJ, vesicoureteric reflux - VUR, duplex collecting system, ureterovesical stricture, posterior urethral valve), as well as abnormalities in kidney rotation and position (horseshoe kidneys, ectopic kidney, and fusion anomalies) (2-5).

The failure of the normal ascent of the kidney can result in an ectopic kidney located in the pelvis, lower abdomen, or even rarely in the thoracic cavity. When a kidney is situated on the opposite side of its ureteric implantation in the urinary bladder, it is termed 'crossed ectopia.' Occasionally, abnormally ascending kidneys may partially fuse to create 'crossed fused ectopia' or form a 'horseshoe kidney' by complete fusion, sometimes referred to as 'pancake pelvic kidneys (6). Regardless of the phenotype, ectopic kidneys may be associated with conditions such as UPJ (ureteropelvic junction) obstruction, VUR (vesicoureteral reflux), MCDK (multicystic dysplastic kidney), renal stone formation, and other related anomalies (7).

Previous studies on renal ectopia and kidney fusion anomalies have been limited by a small number of patients. This study aims to assess the clinical profiles, associated anomalies, and renal outcomes in children with ectopic kidneys at a referral center in the eastern part of Turkey.

Materials and Methods

We conducted a retrospective evaluation of patients admitted to the pediatric nephrology unit at Van Regional Training and Research Hospital between June 2017 and June 2022. We searched the hospital database system and polyclinic records using ICD codes Q63.2. Duplicate records, patients with inconclusive ultrasound or DMSA scan results, and patients horseshoe kidneys connected by a thin isthmus were excluded. We gathered information from the medical records, including the chief complaint at the time of diagnosis, age, sex, weight, height, body mass index, and corresponding standard deviation scores (SDSs) of the patients (8). Additionally, we recorded creatinine levels, and estimated glomerular filtration rate (eGFR) for patients older than 24 months. Ethical approval was obtained from the Van Training and Research Hospital Clinical Research Ethics Committee (date: 01.11.2014 approval number: VEAH KAEK).

The type of ectopia, whether simple or crossed, and the location of EKs (lower abdominal, pelvic,

or thoracic) were evaluated through ultrasonography and DMSA scans (Figure 1). Additionally, renal and extrarenal anomalies beyond ectopia, such as hydronephrosis (HN) and vesicoureteral reflux (VUR), as well as other system involvement, were recorded.

A standardized nuclear DMSA study protocol was already conducted for all patients and those DMSA results were categorised as 'no pathological uptake,' 'photopenic region,' 'multiple photopenic region,' ' scarring,' 'multiple scars,' or 'globally diffuse decreased uptake.'

In cases of hydronephrosis, we reported its severity as mild (SFU 1-2) or moderate to severe (3-4) using the SFU grading system and measured the anteroposterior diameter of the renal pelvis. VUR was graded according to the International Reflux Study in Children (9,10).

Statistical Analysis

Data analysis was performed using IBM SPSS version 21. Categorical data were presented as numbers and percentages, and continuous variables were presented as means and standard deviations. The chi-squared test was used to compare categorical data. The distribution of continuous data was evaluated using tests and graphs. The Mann-Whitney U test was used to compare data that did not have a normal distribution. The Wilcoxon test was used to compare dependent variables. $p<0.05$ was considered statistically significant.

Results

Among the 148 patients diagnosed with EKs in this study, 58.80% (n:87) had simple ectopic (SE) kidneys, while the remaining 41.20% (n:61) had CE kidneys. Among the CE kidneys, 95% (n:58) were cross-fused, while three of them were non-fused CE. The most common subgroup among CE fused kidneys was the inferior type, accounting for 56.9% (n:33), followed by L-shaped (17.20% - n:10), disc (12.10% - n:7), sigmoid (8.6% - n:5), and lump (5.2% - n:3) types, respectively.

Most of the ectopic kidneys were localized in the pelvic region, representing 60.10% (n:89), while the remaining 39.20% (n:58) were localized in the lower abdomen. Only one patient (0.7%) had a kidney localized in the thoracic cavity. Upon admission, all patients had serum creatinine levels within normal limits (0.40±0.15). Demographic data is provided in Table 1.

The most common identifiable presenting feature was empty renal fossa 7.40 % (n:11) and suspected renal agenesis 7.40 % (n:11). 10 % (n:15) of patients suffered from abdominal pain as a presenting symptom, but most patients with ectopic kidneys were detected incidentally while being evaluated for another reason (n:75 50.8%). Presenting features and complaints were given in Table 2.

Table 3 provides details on urological abnormalities. Out of the 148 patients, 18.91% (n:28) had hydronephrosis during their initial evaluation. Among these patients, 22 had mild hydronephrosis (SFU 1-2), with 77.2% (n:17) detected on the EK and 22.8% (n:5) on the contralateral (orthotopic) side. Additionally, there were six patients with moderate to severe hydronephrosis (SFU 3-4), with four on the ectopic side and two on the orthotopic kidney. Most cases of hydronephrosis (n:15, 68%) showed improvement during follow-up. At the last visit, six patients had mild hydronephrosis, and one patient had moderate to severe hydronephrosis. Surgical intervention was required in only one patient who underwent temporary double J

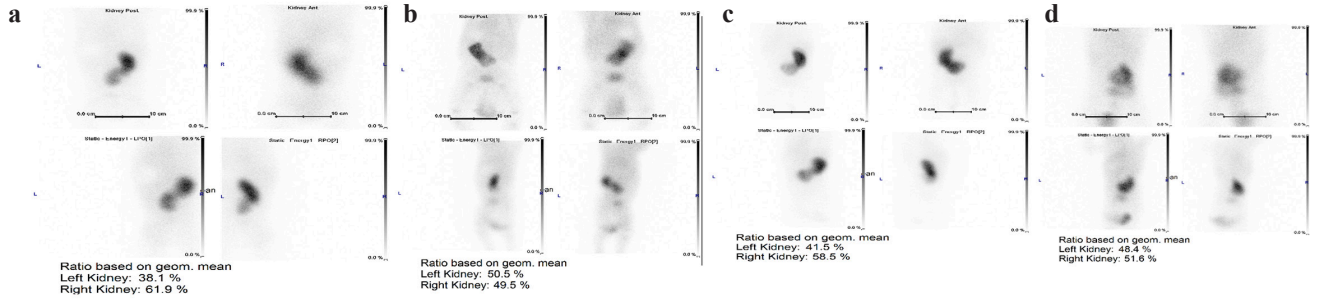

Figure 1. Examples of crossed ectopic kidney types (a-d)

catheter placement due to UPJ obstruction. Voiding cystourethrogram (VCUG) results were available for 34 patients, revealing VUR in 11 patients (32.3%). Among these patients, nine had low-grade VUR, and two had high-grade VUR. A comparison of ectopic and orthotopic kidneys showed that eight patients had VUR in the EK, two in the orthotopic kidney, and one had bilateral VUR. Among the patients with VUR, six were managed conservatively and showed spontaneous recovery, 2 underwent endoscopic treatment, one received ureteroneocystostomy, and two were lost to follow-up. Other abnormalities included hypospadias (n:2, 1.3%), calyceal diverticula (n:1, 0.7%), undescended testis (n:4, 2.7%), neurogenic bladder (n:1, 0.7%), and UPJ obstruction (n:1, 0.7%).

Table 1. Demoghraphic data and patient characteristics

Variables	n (%) or Mean±SD
Sex	
Male	83 (56.10)
Female	65 (43.90)
Age at diagnosis (months) [median-IQR]	42 [97.13]
Weight SDS at admission	-0.59±1.17
Height SDS at admission	-0.65±1.17
BMI SDS at admission	-0.22±1.16
Laterality of EK	
Left to right	72 (48.60)
Right to left	65 (43.90)
Bilateral	11 (7.40)
Localisation of EK	
Pelvic	89 (60.10)
Lower abdominal	58 (39.20)
Thoracic	1 (0.70)
Type of EK	
Simple	87 (58.80)
Cross unfused	3 (2.00)
Cross fused	58 (39.20)
Inferior	33 (56.90)
Sigmoid or S-shaped	5 (8.60)
Lump	3 (5.20)
Disc	7 (12.10)
L-shaped	10 (17.20)
Superior	0 (0.00)

SDS: Standard deviation score, BMI: Body mass index, EK: Ectopic kidney

In the entire group, the mean DMSA uptake was significantly lower in EKs (40.37±7.31) compared to orthotopic kidneys (59.53±7.40) ($p<0.001$). However, the differential functions were similar between simple EKs (40.44±6.12) and cross-fused EKs (40.27±8.90) ($p<0.447$). Among EKs, more than half (n:84, 57.5%) exhibited some degree of pathological DMSA uptake patterns, including hypoactive areas/scarring (n:36, 24.65%) or globally diffuse decreased uptake (n:48, 32.87%). However, there was no significant difference between simple and cross-fused ectopic kidneys in terms of DMSA uptake patterns (see Table 4).

Comparison of simple and cross-fused ectopic kidneys revealed similar results regarding the presence of any degree of hydronephrosis, VUR, and the differential function of ectopic kidneys (see Table 5).

Extrarenal malformations were identified in 14.9% (n:22) of patients. The most common abnormalities had cardiac origins, affecting 5.4% of patients (n:8). These cardiac abnormalities included atrial septal defect (ASD) (n:1), coarcation of aorta (CoA) and (atrioventricular septal defect) AVSD (n:1), Tetralogy of Fallot (n:1), ventricular septal defect (VSD) (n:1), CoA (n:1), and bicuspid aortic valve (n:1). Additionally, four patients (2.7%) exhibited VATER association (Table 6).

Table 2. Clinical presentations and complaints

Chief complaint	n (%)
Suspected renal agenesis	11 (7.43)
Family history	3 (2.02)
Antenatal empty renal fossa	11 (7.43)
Congenital HN	2 (1.35)
Growth retardation	5 (3.37)
Enuresis	5 (3.37)
Dysuria	1 (0.67)
Hematuria	1 (0.67)
Hypospadias	2 (1.35)
Urinary tract infection	6 (4.05)
Abdominal pain	15 (10.13)
Syndromic appearance	10 (6.75)
Spina bifida	1 (0.67)
Tuberose sclerosis	1 (0.67)
Incidental finding	75 (50.67)

Table 3. Urological abnormalities accompanying ectopic kidneys					
			Ectopic kidney n (%)	**Contralateral kidney n (%)**	**Bilateral n (%)**
VUR(+)		Low grade (GI-III)	6 (17.6)	2 (5.8)	1(2.9)
		High grade (GIV-V)	2 (5.8)	-	-
Hydronephrosis	**Admission**	SFU I-II	17 (11.50)	5 (3.40)	-
		SFU III-IV	4 (2.70)	2 (1.40)	-
		SFU 0	127 (85.80)	141 (95.20)	-
	Last visit	SFU I-III	6 (4.1)	-	-
		SFU III-IV	1 (0.7)	-	-
		SFU 0	141 (95.2)	148 (100)	-
VUR: Vesicoureteral reflux, SFU: Society of Fetal Urology					

Table 4. DMSA uptake patterns of ectopic kidneys with respect to type of ectopia				
DMSA*		**Simple EK**	**Cross EK**	**p-value****
		n (%)	**n (%)**	
DMSA Normal		35 (23.97)	27 (18.49)	0.507
DMSA Abnormal		52 (35.62)	32 (21.92)	0.098
Hypoactivity/scar		24 (16.44)	12 (8.22)	
Global diffuse decreased uptake		28 (19.18)	20 (13.70)	
VUR	present	8 (23.5)	3 (8.8)	0.067
	absent	9 (26.4)	14 (41.2)	
Hydronephrosis admission	absent	75 (62.5)	45 (37.5)	0.057
	present	12 (42.9)	16 (57.1)	
*2 patients'DMSA were inconclusive due to disc-shaped kidney, **Chi-square test				

Table 5. Comparison of simple and cross ectopic kidneys			
Variables	**Simple ectopia**	**Cross ectopia**	
	Mean±SD	**Mean±SD**	**p-value**
Diagnosis time (month)	56.46±59.68	58.88±55.19	0.675
Follow-up time (month)	66.76±61.39	68.25±65.64	0.623
Cre admission	0.41±0.15	0.39±0.15	0,569*
Cre last admission	0.43±0.14	0.43±0.17	0,630*
GFR admission	135.63±28.19	152.00±35.02	0,169*
GFR last visit	159.68±35.52	161.52±30.52	0.929*
DMSA fxn EK	40.44±6.12	40.27±8.90	0.447
Cre: Creatinine, *Mann Whitney U test			

Table 6. Extrarenal anomalies accompanying ectopic kidneys	
	N (%)
Cardiac	8 (5.4)
VATER	4 (2.7)
GIS	2 (1.3)
GUS	2 (1.3)
Orthopedic	1 (0.6)
CNS	1 (0.6)
MMC	1 (0.6)
External ear anomaly	2 (1.3)
Rhabdomyoma	1 (0.6)

GIS: Gastro intestinal system, VATER: Vertebral defects, anal atresia, cardiac, tracheoesophageal fistula, renal vertebral anorectal TGUS: Genito urinary system CNS: Central nervous system

Discussion

This study aimed to provide a comprehensive overview of ectopic kidneys and associated renal and extrarenal anomalies. In our study group, simple ectopia was more common than crossed ectopia, with the pelvic region being the most common location. Although left-to-right ectopia (48.60%) appeared slightly more frequent than right-to-left (43.90%), there was no significant difference in terms of laterality. These findings align with previous reports by Arena et al. (11).

In our cohort, the most common type of cross-fused ectopic kidney was the inferior type, representing 56.90%. This corresponds to the fusion of the upper pole of the ectopic kidney to the inferior pole of the orthotopic kidney, consistent with findings in the literature (12). Cross-fused ectopic kidney has been classified by McDonald and McClellan (13) into six different types. The type of fusion anomaly and anatomical details may be important, especially in cases requiring surgical intervention. Glodny et al. (14) reported that CE kidneys may exhibit variations in vasculature (15). Identifying these complex anomalies through appropriate radiological investigations can assist in devising treatment strategies.

In this study, the most common urological abnormalities observed were hydronephrosis and VUR, with hydronephrosis evident in 23.6% of patients at admission. Current reports in the literature vary in terms of the prevalence of hydronephrosis, the existence of VUR, and the necessity for surgery. For instance, Gleason et al. (16) reported a hydronephrosis prevalence of 56% among patients with ectopic kidneys, and the need for surgical intervention was relatively frequent in their cohort, affecting 44 out of 82 ectopic kidneys (54%) .Surgical interventions included procedures such as nephrectomy, pyeloplasty, ureterocalicostomy, and ureteric reimplantation. Kramer and Kelalis et al. (17) reported that out of 49 children with renal ectopy, 51% had hydronephrosis, and 35% of patients required surgical intervention. However, Guarino et al. (18) reported that the need for surgical intervention was approximately 1% of ectopic kidneys. Engelhard et al. (19) reported that one-quarter of their patients required surgical intervention due to various factors such as VUR, pelvic ureteric junction obstruction, or nephrectomy. Calisti et al. (20) also reported that the need for surgical intervention in patients with CAKUT, including solitary, small, or ectopic kidneys, was less common compared to previous reports. In our study, 34 patients underwent VCUG, and reflux was detected in 11 of them (32.3%). Among these 11 patients with VUR, 2 underwent endoscopic treatment, and 1 underwent ureteroneocystostomy. Presence of VUR was similar between simple and cross-ectopic kidneys in our study, but since not all patients in our cohort underwent VCUG this comparison may not be sufficient to make definitive conclusions. In our study group, the proportion of patients requiring any surgical intervention was relatively low compared to previous reports. This might be partially explained by the limited number of patients who underwent VCUG. Fortunately, most cases of hydronephrosis resolved with close follow-up without the need for surgical intervention. Only one patient required temporary double J stent placement without further need for pyeloplasty.

One of the most striking findings in this study was that the differential functions measured by DMSA were decreased in ectopic kidneys compared to contralateral kidneys. Sarhan et al. (12) reported that impaired renal function was found in 34% of patients with ectopic kidneys, but they did not specify DMSA uptake patterns in their cohort. In our study, more than half of the ectopic kidneys exhibited some degree of pathological DMSA uptake, either in the form of hypoactive areas/scarring or globally diffuse decreased uptake. In most cases, despite abdominal and pelvic

ultrasonography being the initial diagnostic tool, it can be insufficient to fully evaluate ectopic kidneys. Therefore, complementary diagnostic tools such as DMSA scans or cross-sectional imaging modalities are often needed.

Beyond providing anatomical details, a DMSA scan can offer insights into differential functions, (the presence of renal scarring related to past pyelonephritis, and can guide the follow-up of kidney functions in affected individuals. As such, performing a DMSA scan may be a part of the evaluation for these patients. Comparing simple and cross ectopic kidneys revealed similar results regarding kidney functions. It's worth noting that the use of eGFR has limitations in patients younger than 24 months due to changing normal clearance values. Therefore, comparisons based on eGFR values were limited to patients older than 24 months.

In both groups with simple EC and crossed EC, serum creatinine levels and eGFR levels were well preserved at the last visit (156.74±28.90) compared to admission (142.80±32.37) ($p<0.05$). Throughout the entire group, after 66 months of follow-up, there was only one patient whose eGFR was <60 ml/min/1.73m² among patients who were 24 months old or older at admission.

Van den Bosch et al.(21) reported that 22% of patients in their cohort exhibited a glomerular filtration rate less than 90 ml/1.73/m², although they didn't specify whether the age of the patients was taken into account. As mentioned earlier, the use of eGFR has limitations in younger patients. Based on our results, we can speculate that the overall renal prognosis was favorable in the mid-term period. In contrast to the report by Van den Bosch et al.(21), where incidental diagnosis of ectopic kidneys constituted only 17% of patients, in our study, the most common presenting feature was the incidental detection of ectopic kidneys. This difference may be explained by the widespread use of ultrasonography in our center. Performing Urinary US during screening for developmental dysplasia of the hip may explain this difference. In addition to the presence of hydronephrosis and VUR, a wide range of renal and extrarenal anomalies often accompanies ectopic kidneys, either as a component of a syndrome or as isolated involvement. In this study, accompanying extrarenal anomalies were observed in 14.9% of patients, which aligns with previous reports(11). The most common extrarenal abnormality observed was of cardiac origin, seen in 5.4% of patients, and the most common association was VATER association, detected in 2.7% of patients. Other system involvements included Sprengel deformity (n:1), meningomyelocele (n:1), rhabdomyoma due to tuberous sclerosis (n:1), external ear anomalies (n:2), cerebellar dysgenesis (n:1), uterus didelphis (n:1), urachal cyst (n:1), diaphragmatic hernia (n:1), and cleft palate (n:1). In the literature, varying rates of extrarenal malformations have been reported (12,16,22).

Study Limitations

Our study has some limitations. Firstly, since this is a retrospective study, missing data may have a limiting effect. Additionally, the selection of patients for whom VCUG was performed was based on the clinician's judgment rather than a standardized protocol, which could result in the underestimation of VUR. Secondly, despite DMSA scans providing valuable information, fused ectopia can present challenges in assessment due to non-discrete renal boundaries in some cases. Therefore, anatomical variations may limit interpretations.

Conclusion

Patients with ectopic kidneys often present with renal and extrarenal anomalies. Although hydronephrosis is a common occurrence, it is usually mild and transient, and the incidence of vesicoureteral reflux is low. Considering the preservation of renal function in the mid-term period, it may be more appropriate to evaluate each patient's need for a complete urological examination on a case-by-case basis. We believe that further studies are also necessary to determine long-term risk factors in larger patient groups and to stratify patients accordingly.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Van Training and Research Hospital Clinical Research Ethics Committee (date: 01.11.2014 approval number: VEAH KAEK).

Footnote

Conflict of Interest: None of the authors has any financial ties that might create a conflict of interest related to the content of the manuscript.

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