



Assessment of Age At First Endoscopic Decompression As A Risk Factor For Further Surgical Treatment in The Management of Ureterocele

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ABSTRACT

Introduction: The aim of this study is to investigate whether age at endoscopic decompression (ED) is a risk factor for further surgical treatment (FST)(s) in the management of ureterocele.

Materials and Methods: The data of 29 patients, who underwent surgery for ureterocele, were reviewed retrospectively. 18 of these patients, who had undergone only ED, were categorized under Group 1, the remaining 11 patients, who had undergone further surgical treatment(s) after ED, were categorized under Group 2.

Results: Duplex collecting system (DCS) was detected in 33% and 100%, urinary tract infection (UTI) was detected in 33% and 72%, ectopic ureterocele (EU) was detected in 55% and 81%, and vesicoureteral reflux (VUR) was detected in 77% and 100%, of the patients in Group 1 and 2, respectively ($p<0.05$). The median age at ED was 3 (0-62) and 15 (0-83) months in groups, respectively ($p=0.004$). The capacity of age at ED in predicting the requirement for FST after ED was 77% by using ROC curve analysis. The analyses revealed that the cut off value of "age at ED" was 4 months. The risk for FST who underwent ED before 4 months was 7.6%, whereas 62.5 for patients older than 4 months at ED.

Conclusions: While active surveillance was discussed in the literature about management of patients with ureterocele, the results of this study revealed that the age at endoscopic decompression is an important risk factor for further surgical treatment(s) and that early endoscopic treatment reduces the risk for further surgical treatment.

Key Words: Ureterocele, endoscopic decompression, age, early management, further surgical treatment.

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What is Known:

- Ureterocele management is still a debate in pediatric urology due to complex nature of the disease and insufficient experience due to small number of cases.
- Most of children with ureterocele undergo additional surgeries.
- The risk factors for further surgical treatments are duplex collecting system, vesicoureteral reflux, ectopic location.

What is New:

- Age at first endoscopic intervention is not assessed as an independent risk factor for further surgical treatment (FST). Our results revealed that early endoscopic decompression reduces the risk of FST.
- The capacity of age at ED in predicting the requirement for FST after ED was 77% by using ROC curve analysis.
- The analyses revealed that the cut off value of “age at ED” was 4 months.
- The risk for FST who underwent ED before 4 months was 7.6%, whereas 62.5% for patients older than 4 months at ED.

INTRODUCTION

Ureterocele is an anomaly characterized by congenital dilatation on the distal end of the ureter. It may be associated with duplex collecting system (DCS), vesicoureteral reflux (VUR), non-functioning pole and febrile urinary tract infection (UTI). Management of ureterocele is still a matter of debate in pediatric urology. Nevertheless, endoscopic decompression (ED) is the most preferred method used in initial management^(1,2), which is sometimes supplemented with further surgical treatment (FST)(s) that required in 20% to 90% of cases reported in the literature⁽³⁻⁸⁾. Multiple factors such as UTI, VUR, presentation period (prenatal or postnatal), collecting system anatomy (single or duplex), and localization of ureterocele (intravesical or ectopic) were analyzed in the literature to determine the factors that are associated with the risk of FST^(6,7,9-14). The aim of this study was evaluation of the relation between “age at first ED” and requirement of further surgical treatment.

MATERIAL AND METHODS

After receiving institutional ethics committee approval, we retrospectively reviewed the data of patients with ureterocele who underwent surgery between January 2006 and January 2020 in our department. Patients who did not undergo endoscopic decompression as an initial intervention (n:2) and patients with follow up shorter than 18 months (n:3) were not included in the study. Presentation period (prenatal or postnatal), age at presentation, age at ED,

collecting system anatomy (duplex or single), presence of vesicoureteral reflux and further surgical interventions were recorded. Evaluation tests of the ureterocele included urinary ultrasound, renal scintigraphy with Technetium 99 m-dimercaptosuccinic acid (DMSA), voiding cystourethrography (VCUG), urine tests including urine culture, and renal function tests in serum. Ureterocele was classified as intravesical or ectopic due to the cystoscopic view and the descriptions of the surgeon according to the suggested terminology of the American Academy of Pediatrics Section on Urology⁽¹⁵⁾. VUR was graded by VCUG according to the International Classification System (International Reflux Study Committee)⁽¹⁶⁾. Focal defects in uptake, scar formation, hypo-function, non-function of the moiety or the kidney were considered as renal damage on the nuclear scan. Patients were divided into two groups: Group 1 included patients who underwent only ED, whereas Group 2 included patients who underwent further surgeries after ED. Symptomatic UTIs, upper urinary tract dilatation, renal damage in the upper pole moiety and giant ureterocele that obstruct the bladder outlet were indications for initial endoscopic decompression. Control cystoscopy or repeated ED was not considered as FST. During the follow-up after ED, symptomatic UTIs which could not be prevented with antibiotic prophylaxis, impairment in the hydronephrosis due to inadequate decompression after initial endoscopy and new renal damage on scintigraphy were

the indications for further surgical interventions. Asymptomatic VUR alone was not an indication of FST.

ED was performed with either cauterization using a 3 Fr Bugbee wire electrode for creating holes or short transvers incision on the bottom of the ureterocele with avoiding passing extravescical area. The incision or the puncture, not exceeding the bladder neck provides properly emptying of the ureterocele moiety when the bladder neck is closed and also acts as a valve mechanism against VUR (1,2,6,12,17). Antibiotic prophylaxis was administered in all cases at the time of the diagnosis and continued for at least 6 months. In case of recurrent urinary tract infection that could not be controlled under strict antibiotic prophylaxis, further surgery was performed and prophylaxis continued for 6 months postoperatively. UTI was define as positive urine culture with symptoms. Urine was checked monthly and at every symptomatic attack by urine analysis and urine culture. Urine was collected firstly with a bag and in case of positive urine culture, collected by a catheter. Ultrasound scan was performed once in two months. After uneventful follow-up of the first year, ultrasound scans were performed in every 6 months for long term follow-up. Re-evaluation of renal function was performed by scintigraphy in long term follow-up. VUR presence was re-evaluated with VCUg after ED or further surgical treatment in selected cases who had recurrent febrile UTI, new renal damage or impairment in hydronephrosis.

Statistical Analysis

The data were analyzed using SPSS version 21. Quantitative variables are presented in numbers as mean or median. All p -values < 0.05 were considered statistically significant. The Mann-Whitney U-Test was used to compare age and follow-up time and Pearson Chi-square test and Fischer's Exact test were used to compare categorical variables between groups. Receiver operating characteristic (ROC) curve was performed to analyze the capacity of age at ED in predicting the requirement for further surgical treatment. Probability chart was performed to determine the possibility for further surgical treatment according to age at ED

(months). Univariate and multivariate analyses were performed.

RESULTS

In the study period, 34 patients underwent surgery for ureterocele. Two patients, who underwent ureteroneocystostomy and upper pole heminephrectomy, respectively, and not endoscopic decompression were excluded from the study. Three patients with short follow up were also excluded (Figure 1: Flow chart). Of the 29 patients included in the study, 18 patients underwent only ED (Group 1), and 11 patients underwent further surgery after ED (Group 2). Among the patients included in Group 2, 5 patients underwent ureteroneocystostomy (UNC), 4 patients received sub-ureteric injection for VUR, 1 patient underwent heminephrectomy, and another patient underwent UNC and heminephrectomy. Of the patients that received sub-ureteric injection for VUR, 1 patient underwent UNC and another patient underwent heminephrectomy, in the following period.

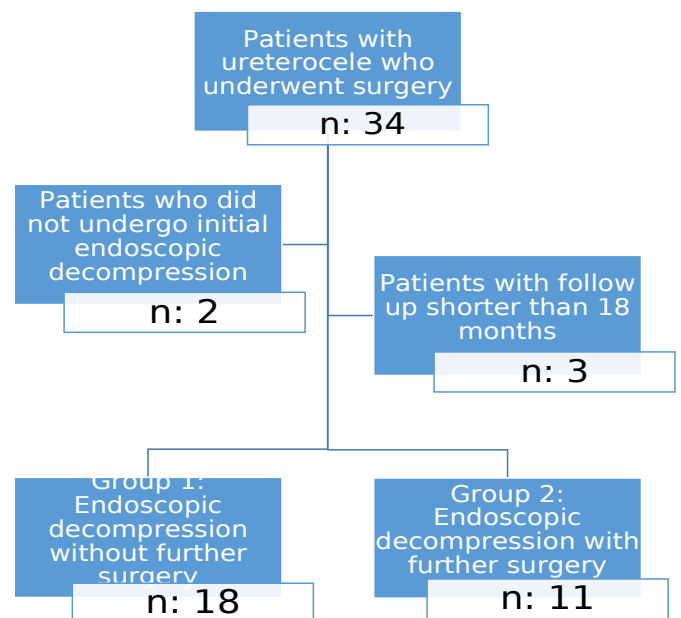


Fig. 1. Flow-chart

The median age at presentation was 1.5 months and 2 months in Groups 1 and 2, respectively. There were no

differences between the groups in terms of age at diagnosis, prenatal diagnosis, side and bilaterality,

Table 1: Details of the patients in groups and p values

	Group 1 (patients underwent only ED) n:18	Group 2 (patients underwent ED and received further surgical treatment) n:11	TOTAL n:29	p value
Median age of presentation (months)	1.5 (min. 0-max.76)	2 (min.0- max.55)	2 (min.0- max.76)	0.674*
Median age at first ED (months)	3 (min.0- max.62)	15 (min.0- max.83)	6 (min.0- max.83)	0.004*
Age at first ED (n)				
• < 4 months	12	1	13	0.002**
• > 4 months	6	10	16	
Antenatal diagnosis (n)	4 (22%)	2 (18%)	6 (20%)	0.794**
Bilateral ureterocele (n)	1	0	1	0.660**
Right ureterocele (n)	6	3	9	
Left ureterocele (n)	11	8	19	
Ectopic ureterocele (n)	10 (55%)	9 (81%)	19 (65%)	0.149**
DCS (n)	6 (33%)	11 (100%)	17(58%)	0.001**
Age at first ED in patients with DCS (n)			17	
• < 4 months	5	1	6	0.005***
• > 4 months	1	10	11	
Hydronephrosis at diagnosis (n)	12 (66%)	8 (88%)	20 (68%)	0.903**
Presence of VUR (n)	14 (77%)	11 (100%)	25 (86%)	0.092**
Febrile UTI (n)	6 (33%)	8 (72%)	14 (48%)	0.039**
Renal damage on nuclear scan (n)	12 (66%)	9 (81%)	21 (72%)	0.376**
Median follow-up time (months)	68 (min. 18- max.189)	51 (min. 26- max.228)	67 (min. 18- max.228)	0.774*

ED: Endoscopic decompression, DCS: Duplex collecting system, VUR: Vesicoureteral reflux, UTI: Urinary tract infection, n: number of patients, min.: minimum, max.: maximum

*Mann-Whitney U test

**Pearson's Chi-squared test

*** Fisher's Exact Test

renal damage on nuclear scan and hydronephrosis, (Table 1). Ratio of males to females were 11/7 and 2/9 in groups respectively (p=0.024). Girls more frequently needed further surgical treatment(s). Ectopic ureterocele was detected in 55% of patients in Group 1 and in 81% of patients in Group 2. This difference did not reach a statistical significance (p>0.05). Ipsilateral

DCS was detected in 33.3% of Group 1 and in all patients of Group 2 (p=0.001). Urinary tract infections were observed in 3 and 8 patients of groups, respectively (p=0.039).

The median age at ED was found as 3 (0-62) and 15 (0-83) months in Group 1 and 2, respectively (p=0,004). The predicting capacity of "age at ED" in the

requirement for further surgical treatment was analyzed by using Roc curve analysis and found 77% (Figure 2). The cut-off value of “age at first ED” was found 4 months. The probability chart is given in Figure 3. Of 29 patients, 13 patients were younger than 4 months and 16 patients older than 4 months at the time of ED in both groups (Table 1). Of 13 patients, twelve patients were in Group 1 (only ED) and 1 patient was in Group 2 (ED with FST). This outcome indicated that the risk of FST for patients younger than 4 months at ED was 7.6%, whereas this risk for patients older than 4 months at the time of ED was 62.5% ($p=0.002$). Febrile UTIs were detected in 4 (30.7%) of 13 patients who underwent ED before 4 months of age and in 10 (62.5%) of the 16 patients who underwent ED after 4 months of age ($p=0.089$). A significant difference was found in terms of endoscopic decompression age between those who had urinary tract infections and those who did not ($p=0.023$).

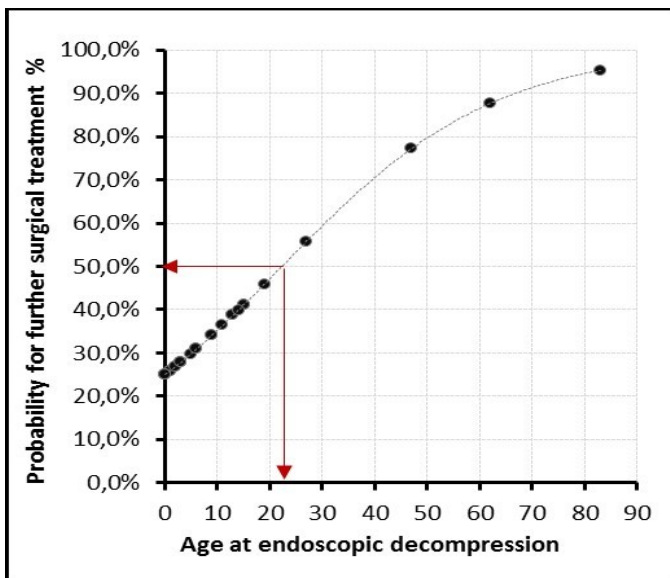


Fig. 2. ROC curve of “age at endoscopic decompression” in predicting the requirement for further surgical treatment

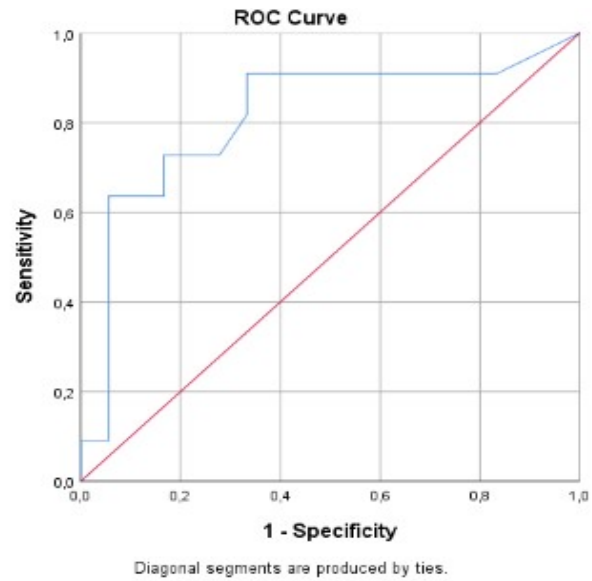


Fig 3. The probability chart of the risk of further surgical treatment after endoscopic decompression (ED) by the age at ED

Since the duplex collecting system is an important risk factor for further surgery and the groups were different in terms of this factor, we performed a further analysis among only patients with DCS. There were 17 patients with DCS in this study; 6 were in Group 1 and 11 were in Group 2. In Group 1, 5 of 6 patients with DCS were younger than 4 months at ED while in Group 2, 10 of 11 patients with DCS were older than 4 months at ED. Only one of the 6 patients with DCS, whose ED was performed before 4 months, required FST (16.6%). Among patients with duplex collecting system whose ED was performed after 4 months of age ($n:11$), 10 needed FST (90.9%) ($p=0.005$).

DISCUSSION

Management of ureterocele includes endoscopic ureterocele treatment, upper pole heminephrectomy, open surgical ureterocele excision and bladder reconstruction, ureteroneocystostomy, combined technique with upper and lower pole reconstruction, endoscopic vesicoureteral reflux correction^(6,18). ED is usually the initial treatment for most of the patients^(1-8, 11,17,19,20). At any age, ED is a good choice of procedure with its simple and less invasive features and can be performed with a very short hospital stay^(3,8). However, FST are required in 20-90% of these patients in the literature⁽⁴⁻⁸⁾. Some patients need even a third or fourth intervention^(5,18). The major challenge is determining how to prevent further surgical requirements after ED.

The risk factors for further surgeries were discussed in the literature extensively. Ectopic ureterocele, VUR and DCS, prenatal vs postnatal presentation are the most analyzed risk factors for further surgeries^(6,7,9-14,21). On the other hand, active surveillance without intervention

has been discussed in recent years. In this study, it was investigated whether age at first ED is an independent risk factor for the requirement of FST and early endoscopic treatment reduces risk for FST or not. While active surveillance has been discussed in recent literature ⁽⁹⁾, our study revealed that early endoscopic treatment provides better result in terms of UTI and lower risk for FST.

Satisfactory outcomes were reported in the literature with patients who underwent ED in young ages. Blyth *et al.* reported the study with 51 ureterocele cases, of whom 31 were younger than 1-years and 19 were newborns at the time of ED and mentioned 89% satisfactory decompression and 21% FST rates ⁽⁷⁾. Chertin *et al.* reported 34 ureterocele cases, of whom 80% were younger than 6 months and presented 94% success rate and 6% FST rates after ED ⁽¹⁾. Although there was no analysis in terms of age at ED for further surgical requirements in these studies, both reported good outcomes after ED in young ages.

On the other hand, the studies in which presenting during the prenatal versus postnatal period was investigated as a risk factor for further surgical intervention might provide some valuable insight in this issue. Upadhyay *et al.* emphasized that prenatal diagnosis was related with younger age at initial intervention (6 vs 31 months) and with lower rate of FST (20% vs 46%) than postnatally diagnosed patients ⁽¹¹⁾. Timberlake and Corbett reported a study and the median age of prenatal and postnatal diagnosis groups were 4 months and 3.5 years, respectively in that study. After ED, the rates of postoperative UTI, secondary puncture, secondary reflux procedure and heminephrectomy were reported higher in their postnatal group ⁽²⁰⁾. Hodhod *et al.* reported 51 patients and determined that antenatal presented cases had lower risk for further surgery ⁽¹³⁾. Overall, none of these studies specifically addressed age at ED as a risk factor for further surgical treatment, but they all reported better outcomes in younger patient groups.

In comparison, in our study, age at first ED was found to be a significant risk factor for FST. The median age of patients who underwent only ED (Group 1) was 3 months at ED, whereas the median age of patients who underwent further surgery (Group 2) was 15 months at first ED. The difference was statistically significant ($p=0.004$). The capacity of age at ED in predicting the requirement for further surgical treatment was 77% calculated by using ROC curve analysis (Figure 2). The analyze revealed that the cut-off value of "age at ED" was 4 months. The risk of further surgery after ED for patients who underwent ED while younger than 4 months was 7.6%, whereas it was 62.5% for patients older than 4 months at the time of ED. To the best of our knowledge, this is the first study in which "age at endoscopic decompression" was assessed as whether it

can be used to predict the risk for further surgical treatment, using ROC curve and probability analyses, and the first study in which the respective cut-off value of age at ED was reported.

In addition, it was reported in the literature that early surgical intervention may reduce the febrile UTI. Chertin *et al.* determined that 23% of patients with postnatally diagnosed ureterocele had UTI, while none of the patients with prenatally diagnosed ureterocele had UTI after ED and conclude that early intervention may result better outcome such as lower UTI as seen in prenatal groups ⁽²²⁾. Castagnetti *et al.* reported that none of the 41 newborns with ureterocele who underwent transurethral incision had UTI during the follow-up ⁽¹²⁾. Upadhyay *et al.* reported lower rate of UTIs in the group of patients diagnosed prenatally (median age of 6 months at first ED) compared to the cases diagnosed postnatally (median age of 31 months at first ED) ⁽¹¹⁾. These studies reveal that early intervention may reduce the febrile UTI. Early endoscopic decompression may be an advantage for resolution of VUR in these cases. Jesus *et al.* reported 60 patients with median age 3 months and demonstrated spontaneous VUR resolution or improvement occurred in 72% postoperatively ⁽²³⁾. Chertin *et al.* reported a study including patients with mean age at ED of 3 months and determined that 59% of VUR resolved spontaneously after ED ⁽¹⁹⁾. Castagnetti *et al.* reported 41 neonates and observed 40 % of VUR resolution after ED ⁽¹²⁾. This high-resolution rates in these studies may be associated with the young age at ED. In our study, six patients (33%) in Group 1 had febrile UTI at the beginning of their follow-up and the febrile UTIs were prevented by regular and strict use of prophylactic antibiotics or changing antibiotics, similar as in the literature ^(4,6,12,17). Additionally, 8 patients (72%) with recurrent UTIs in Group 2, which could not be controlled with prophylaxis, underwent further surgery. Further analyses were carried out using Mann Whitney-U test to determine whether age at ED differed between patients who had febrile UTIs and the ones who did not. Febrile UTIs were observed less in patients who underwent early ED than patients who underwent ED lately ($p=0.023$). The further analyses on the risk of febrile UTIs in patients who underwent ED before and after 4-months of age revealed that this risk was 30.7% and 62.5%, respectively, yet this difference between the groups was not statistically significant ($p=0.89$). Nevertheless, the results of this study suggested that early intervention reduces the risk of febrile UTI.

Results of the multivariate analysis indicated that DCS and having an age older than 4 months at first ED are independent risk factors for further surgical treatment. The fact that VUR was not found to be one of these independent risk factors was attributed to the high reflux ratio in both groups (77% and 100%) and the small number of cases.

The authors sought to express opinions to explain the positive effects of early endoscopic decompression. Firstly; early endoscopic decompression before first year of age of the patients may reduce the risk of FST due to high resolution ratio before one year of age. Secondly; ureterocele may play a role as a mass at the bladder neck and may cause bladder outlet obstruction. Decompression of the ureterocele may provide improvement in the bladder dynamics during opening and closure of the bladder neck. These mechanisms of this positive effect could not prove with this study.

Duplex system is a very important risk factor for FST in ureterocele management ^(4,14). Since the groups were not homogeneous among this important factor, we performed another analysis among only patients with DCS to evaluate the effect of age at ED on the risk of FST. In our study, there were 17 patients with DCS, 6 were in Group 1 and 11 were in Group 2. Among patients with DCS and ureterocele, the risk of FST was 16.6% in patients who underwent ED while younger than 4 months and this risk was 90.9% in patients who underwent ED while older than 4 months (Table 1). Most of patients with DCS and older than 4 months at ED underwent FST ($p=0.005$).

Although the mean presentation ages of patients were 1,5 and 2 months in groups ($p>0.05$), the mean age at ED in groups were 3 and 15 months ($p=0.004$) respectively. The cause of the late endoscopic decompression was evaluated retrospectively and the reasons of this delay were breakthrough urinary tract infections and irregular follow-up.

Nevertheless, there were some limitations to this study. First, it was carried out retrospectively. Secondly, the groups formed were not homogenous due to the variation in the anatomy of ureterocele, and it was not possible to form homogenous groups in terms of variations or risk factors, as the number of patients to be remained insufficient in the subgroups to carry out further analyses. However, these features of ureterocele are also common limitations observed in the literature. There is an ongoing need for large-scale, multi-center, randomized-controlled studies for further investigation.

CONCLUSIONS

The results of this study revealed that age at first endoscopic decompression is an independent risk factor for further surgical treatment. The cut-off value of age at first ED as an independent risk factor for further surgical treatment(s) was found to be 4-months. The risk of further surgical treatment for patients who underwent ED while they were younger or older than 4-months old were found as 7.6% and 62.5%, respectively. Instead of active surveillance, our study revealed that early endoscopic treatment provides lower risk for FST and UTI.

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Conflicts of interest/Competing interests: The authors declare that there is no conflict of interest.

Ethics approval: Ethics committee of Marmara University had approved the study. Number and date of approval: 09.2020.1115 and 02.10.2020.

Availability of data and material: All data of the study is available for re-assessment.

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