Volume 6
Issue 1
January 2022
ISSN:5101195-3

KOSOVA JOURNAL OF SURGERY

PAPERS PRESENTED AT THE FIRST CLINICAL CONGRESS OF THE KOSOVA COLLEGE OF SURGEONS SEPTEMBER 24-26, 2021

Editorial: RIFAT LATIFI: The First Chapter of the New Book of Kosova College of Surgeons

RUSSELL ANDREWS: The Importance of Surgical Care to Achieve the United Nations Sustainable Development Goal for Healthy Lives by 2030

BELLAL JOSEPH: Breaking the Frailty Code: Emergency General Surgery in the Elderly

DEMETRIUS LITWIN: Hand-Assisted Laparoscopic Living Donor Hepatectomy

LIOR LEVY, ABASS SMILEY, RIFAT LATIFI: Independent Predictors of In-Hospital Mortality in Patients Undergoing Emergency Admission for Arterial Embolism and Thrombosis in the USA: A 10-Year National Dataset

LIOR LEVY, ABBAS SMILEY, RIFAT LATIFI: Mortality in Emergently Admitted Patients with Empyema: An Analysis of 18,033 Patients

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Endoscopic Treatment of the Vesicoureteral Reflux in Children

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Abstract

Introduction: Vesicoureteral reflux (VUR) is the most common uropathy affecting children. Compared to children without VUR, those with VUR have a higher rate of pyelonephritis and renal scarring following urinary tract infection (UTI). Vesicoureteral reflux (VUR) is a common and treatable problem in pediatric urology/nephrology. It is a retrograde flow of urine from the bladder to the upper urinary tract. The incidence of VUR is 0.4-1.8% in the pediatric population. Reflux tends to occur spontaneously. In some cases, it allows the infection to spread from the lower to the proximal parts of the urinary tract, causing pyelonephritis, scarring of the kidneys, and even progressive loss of kidney function. Options for treatment include observation with or without antibiotic prophylaxis and surgical repair. Surgical intervention may be necessary in patients with persistent reflux, renal scarring, and recurrent or breakthrough febrile UTI. Both endoscopic and open approaches to reflux correction are successful and reduce the occurrence of febrile UTI.

Objectives: The aim of this study was to analyze the endoscopic treatment of vesicoureteral reflux in children under 16 years of age and to point out any differences and reasons for the effect achieved.

Material and Methods: This research is a retrospective controlled study conducted at the Clinic for Pediatric Surgery in Prishtina, in the period from January 2015 to December 2020. The study included children diagnosed with primary, congenital vesicoureteral reflux (VUR) up to fifth degree. The diagnosis of VUR was made by Voiding cystouretrography (VCUG) as the gold standard for obtaining accurate anatomical details and gradation of reflux. The sample of respondents was randomized by respecting the set inclusion and exclusion criteria. Patients in the study group, 78 of them, were treated with endoscopic treatment -"STING," and " Hit1 + Hit 2." It is a popular endoscopic procedure and it is less invasive than open surgical techniques. The intervention is performed as a one-day surgery.

Results: After endoscopic treatment of 106 ureters, results were obtained without VUR in 78 ureters or 73.6%. In addition, in 9.4% or in 10 ureters after endoscopic treatment we have obtained a first grade VUR. The rest of 18 ureters (17%) were unsuccessfully treated. The goal of endoscopic procedure was achieved in 78 ureters (73.6%).

Conclusion: Endoscopic treatment of vesicoureteral reflux is a safe and effective method that should be promoted as the method of choice for treating VUR in children.

Keywords: vesicoureteral reflux (VUR), treatment, children, endoscopy

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Introduction

VUR affects 1 - 2% of all children and up to one-third of children with VUR will experience urinary tract infection (UTI).[1]1. Hains DS, Cohen HL, McCarville MB, Ellison EE, Huffman A, Glass S, et al. Elucidation of Renal Scars in Children With Vesicoureteral Reflux Using Contrast-Enhanced Ultrasound: A Pilot Study. *Kidney Int Rep*. 2017 May;2(3):420-424. Acute pyelonephritis, associated with VUR, can lead to renal scarring and, ultimately, chronic kidney disease known as reflux nephropathy. In severe cases of reflux nephropathy, 10 - 25% of patients may develop end-stage kidney disease requiring dialysis or kidney transplant.[2]2. Prasad MM, Cheng EY. Imaging studies and biomarkers to detect clinically meaningful vesicoureteral reflux. *Investig Clin Urol*. 2017 Jun.;58 (Suppl 1):S23-S31.

Nevertheless, the severity of VUR varies greatly and clinical presentation is variable. Most patients are either asymptomatic, or present with hydronephrosis or pyelonephritis. Spontaneous resolution is common. Conservative therapy is based on two principal approaches: active surveillance and antibiotic prophylaxis to reduce the risk of bacterial infection of the bladder while reflux is present. Surgical management of VUR can be done with either endoscopic treatment or open/laparoscopic/robotic surgical techniques

Early diagnosis and vigilant monitoring of VUR are the cornerstones of management, but controversy surrounds the starting point of the evaluation for VUR. Guidelines conflict on whether to focus on assessing the condition of the kidneys ("top-down") or identifying the presence of VUR ("bottom-up").[3]3. Abdelhalim A, Khoury AE. Critical appraisal of the top-down approach for vesicoureteral reflux. *Investig Clin Urol*. 2017 Jun. 58 (Suppl 1):S14-S22. Current research efforts are directed towards better understanding of the genetics of VUR, by refining the diagnostic criteria in order to better identify patients who seem to be at increased risks for renal damage, and, then, by determining who would benefit the most from definitive therapy.

Diagnosis of VUR

The clinical picture in the pediatric population can be quite large nonspecific. The most frequent sign is fever. Other symptoms may be: poor progression, vomiting, anorexia, diarrhea, and lethargy. Temperature may be the criterion for orientation, whether it is cystitis or pyelonephritis (usually associated), but should not be considered as a sure sign. Children with pyelonephritis have a significantly higher temperature compared to children who have cystitis only. Temperature higher than 38^0C- 39^0C indicates possible pyelonephritis. They are candidates for further radiological evaluation. Perform urinalysis and urine culture in all neonates born with antenatal or postnatal hydronephrosis to rule out UTI. More than 90% of newborns vomit within the first 24 hours. The serum creatinine level of a neonate reflects that of maternal creatinine. Laboratory tests are performed on blood and urine samples. Ultrasound and possibly VCUG can be considered as initial protocols for initial evaluation of UI in the pediatric population. Today, MR urography has completely replaced IVP. Literature[4]4.Jothilakshmi K, Vijayaraghavan B, Paul S, MatthaiJ. Radiological evaluation of the urinary tract in children with urinary infection. *Indian J Pediatr*. 2001;68(12); p.1131-3.[5]5. Schmiemann G, Kniehl E, Gebhardt K, Matejczyk MM, Hummers-Pradier E. The Diagnosis of Urinary Tract Infection A Systematic Review. *DtschArztebl Int*. 2010;107(21); p. 361– 367. prescribes that in each UI in infants and young children (most commonly up to three years), there is a need for such an evaluation. Urodynamic tests are extremely important in UI evaluation[6]6. Mazieres L, BagnisCI.Urodynamics in recurrent urinary tract infections. *Rev Prat*. 2014;64(7); p.974-6..

VUR is a disease, wherein due to incompetence of the ureterovesical (UV) junction there is more or less abnormal retrograde flow of urine from the lower to upper urinary tract. Most of the published papers list two basic types of VUR, primary and secondary.[7]7. Ninoa F, Ilaria M, Noviello C, et al. Genetics of Vesicoureteral Reflux. *Curr Genomics*. 2016; 17(1):70-9.

9. Medical versus surgical treatment of primary vesicoureteral reflux: report of the International Reflux Study Committee. *Pediatrics*. 1981 Mar; 67(3):392-400.

10. Läckgren G, Kirsch AJJU. Surgery Illustrated - Surgical Atlas Endoscopic treatment of vesicoureteral reflux. *Int*. 2010 May;105(9):1332-47.

11. Bailey RR. Vesicoureteral reflux in healthy infants and children. *Reflux Nephropathy*. 1979;59–61. This division is not sufficiently complete to explain all possible types of VUR, the mechanisms of occurrence and treatment.

Primary VUR: the disorder primarily occurs as incompetence of the UV junction anti-reflux mechanism

Secondary VUR: damage to the UV junction occurs as a consequence of another disease (infravesical obstruction, neuropathic bladder, jatrogenic injuries, etc.)

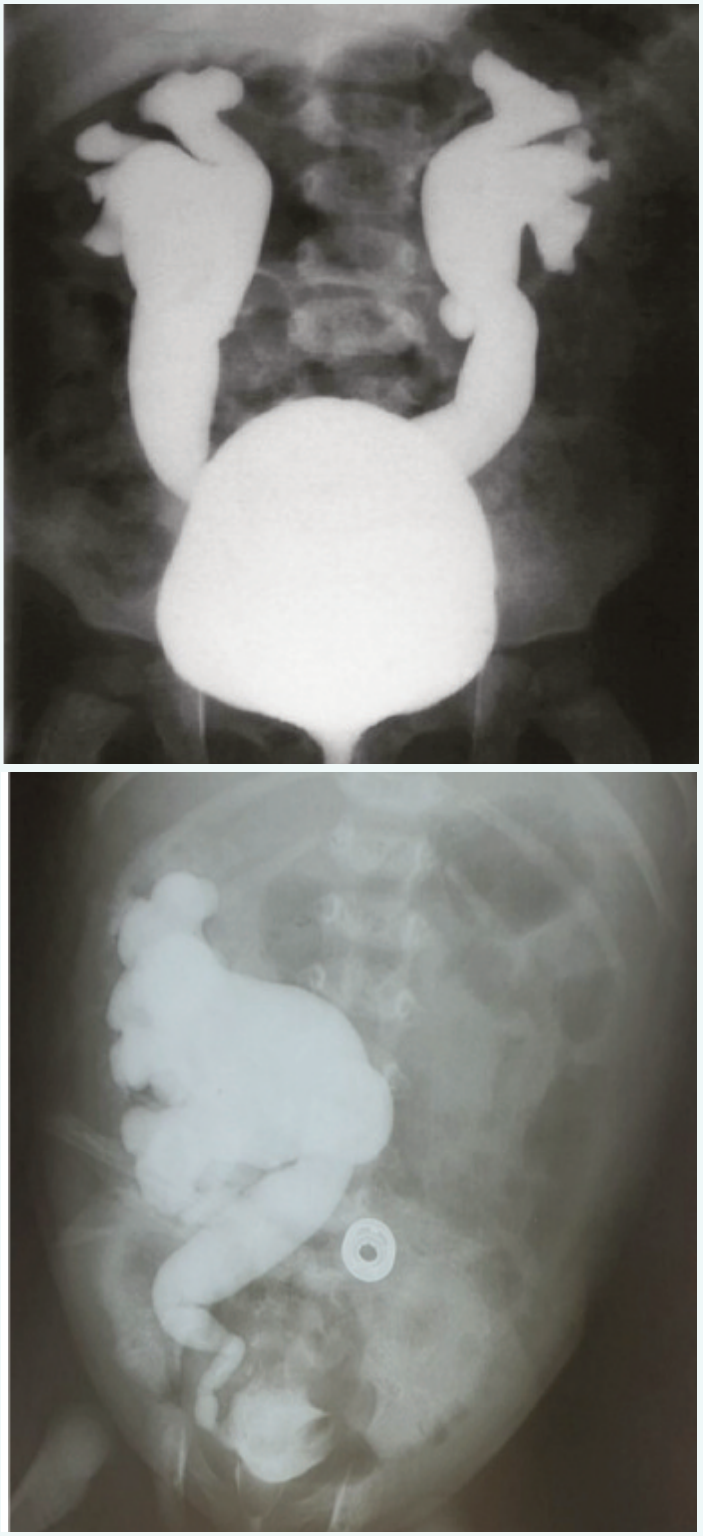


Fig. 1. VCUG unilateral and bilateral VUR

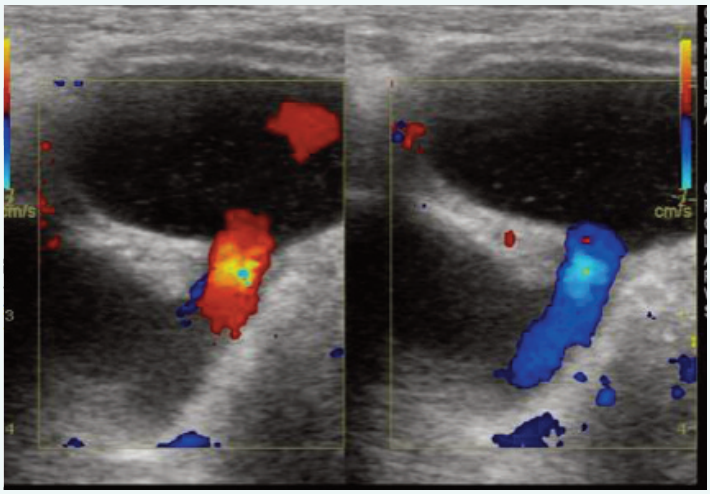


Fig. 2. VURdooplerultrasongraphy

Staging

The International Reflux Grading system classifies VUR into 5 grades (fig. 3.), depending on the degree of retrograde filling and dilatation of the renal collecting system. This system is based on the radiographic appearance of the renal pelvis and calyces on avoiding cystogram, as follows:

- **Grade I**: Urine backs up into the ureter only, and the renal pelvis appears healthy, with sharp calyces.
- **Grade II**: Urine backs up into the ureter, renal pelvis, and calyces. The renal pelvis appears healthy and has sharp calyces.
- **Grade III**: Urine backs up into the ureter and collecting system. The ureter and pelvis appear mildly dilated, and the calyces are mildly blunted.
- **Grade IV**: Urine backs up into the ureter and collecting system. The ureter and pelvis appear moderately dilated, and the calyces are moderately blunted.
- **Grade V**: Urine backs up into the ureter and collecting system. The pelvis is severely dilated, the ureter appears tortuous, and the calyces are severely blunted.

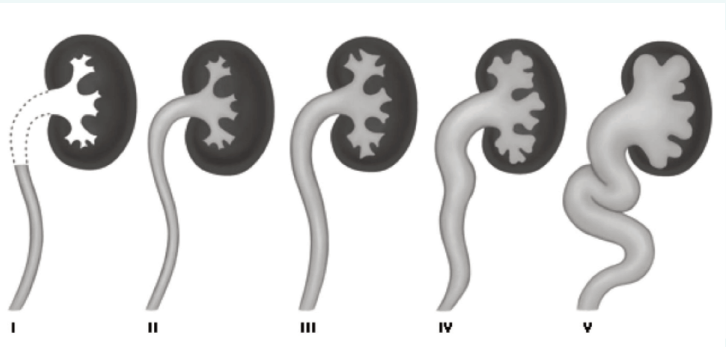


Fig. 3. International classification of Vesicoureteral reflux[9]

Endoscopic Repair

Endoscopic repairing prevents reflux by injecting a bulking agent to allow elevation and coaptation of the ureteral orifice and ureteral wall.[10] Benefits include outpatient surgery, lower cost, and decreased patient morbidity. Various methods of injection (sub-ureteral and intra-ureteral) and injectable materials have been described. In a systematic meta-analysis evaluating endoscopic treatment of pediatric VUR, the estimated success rate for endoscopic therapy after a single injection was 83. [11]

Sub-Ureteral – "STING"

The endoscopic treatment of VUR has been described first by O'Donnell and Puri in 1984 (Fig. 4.). They performed subureteric Teflon injection (STING) in patients with reflux. A total of 78% had resolution of reflux after a single injection.[12]

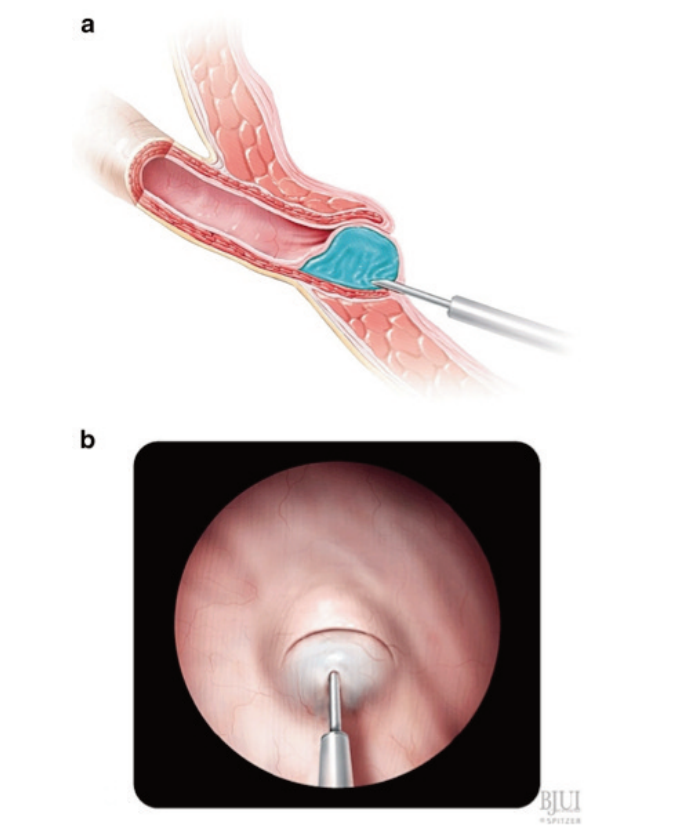


Fig. 4. STING Procedure

Intraureteral – "HIT"

In 2004, Kirsch described a modification called the "hydrodistention implantation technique" (HIT) (Fig.5.). The needle is advanced into the ureteral tunnel and Dx/Ha is injected along the entire length of the detrusor tunnel for maximal coaptation. A total of 89% of patients undergoing HIT had resolution of reflux versus 79% undergoing standard STING.[13]

HIT was further modified to include two intraureteral injections (proximal and distal), for total ureteral tunnel coaptation. The goals of "double HIT" are to create a "mountain range appearance" of the ureteral tunnel and to eliminate hydrodistention.[14]

Success rates ranged from 70 to 95%.

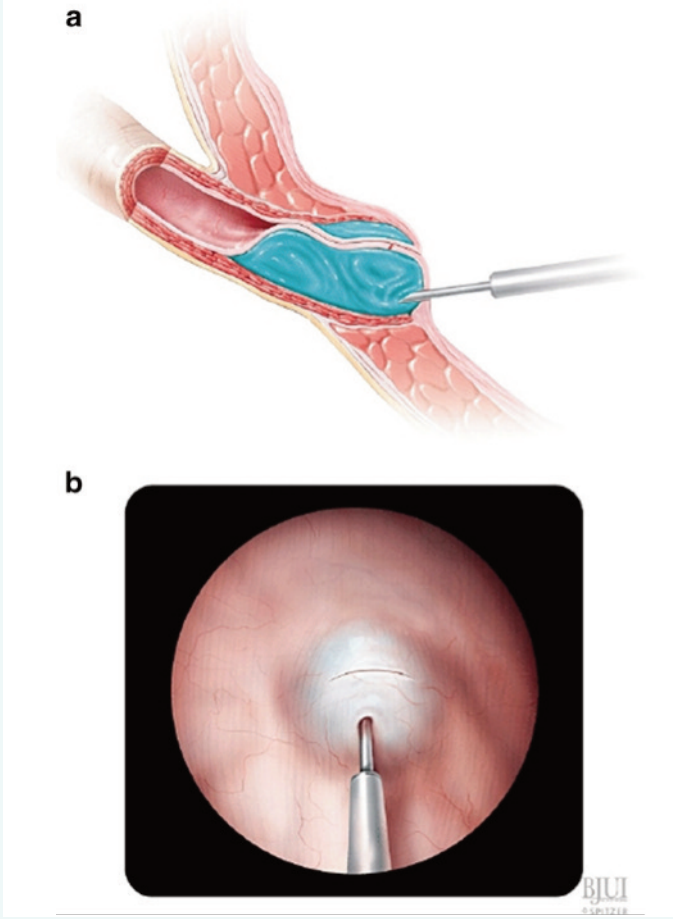


Fig. 5. Double HIT

Factors that have been evaluated as potential predictors of endoscopic injection success include pre-operative reflux grade, functional/anatomic abnormalities, voiding dysfunction, injected volume, mound morphology/location, surgeon factors/experience, and duration of follow-up.[15],[16]

Results

This study included 78 patients with VUR or 106 refluxive ureters treated endoscopically. Females are present with 62% and males with 38%. In patients with VUR, family history was registered in 10.3% of mothers, 6.4% of fathers, 7.7% of both parents, and

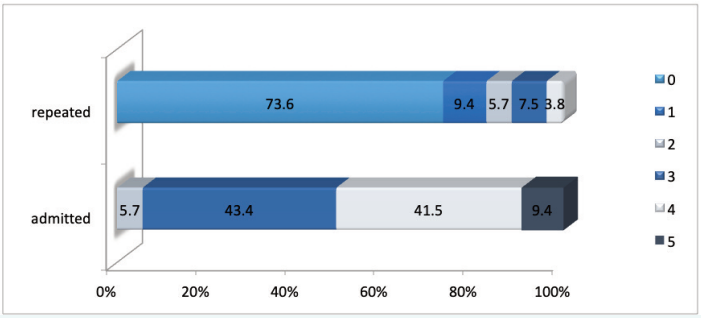
24.4% of siblings. In our study, the largest VUR percentage is represented with 38.5% the left side, 35.9% bilaterally, and 25.6% the right side. On admission, dilatation of the collection system was registered in 85.9% of cases, while during the therapeutic evaluation, dilatation of the collection system was registered in 32.1%. Normal anatomy of the bladder wall was registered in 89.7% of cases upon admission. With changes, it was decreased up to 10.3%. During the therapeutic evaluation, normal anatomy of the bladder wall was registered in 94.9%, and not in 5.1%.

Fever associated with urinary tract infections is registered in 98.0%. Bacteriuria was registered in 78.2% of the patients, and not in 21.8%.

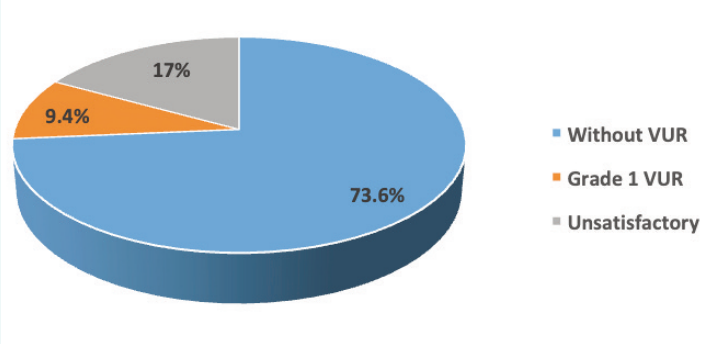
After endoscopic treatment of 106 ureters, results were obtained without VUR in 78 ureters or 73.6%. In addition, in9.4% or in 10 ureters after endoscopic treatment, we have obtained a first grade VUR. The rest of 18 ureters (17%) were unsuccessfully treated. (Table and Graph.1.). The goal of endoscopic procedure was achieved in 78 ureters (73.6%). (Graph. 2.)

Grade	On admission		After treatment	
	Count of ureters	Percent	Count of ureters	Percent
0-no	0		78	73.6
1	0		10	9.4
2	6	5.7	6	5.7
3	46	43.4	8	7.5
4	44	41.5	4	3.8
5	10	9.4	0	
total	106	100.0	106	100.0

Table 1. Overview of the Degree of Hydroureters, Before and After Endoscopic Treatment According to VCUG



Graph.1. Overview of the Degree of Hydroureters Before and After Endoscopic Treatment According to VCUG



Graph. 2. Results of Endoscopic Treatment of VUR After Endoscopic Treatment According to VCUG

After endoscopic treatment of VUR in 73.6% of cases, results were obtained without VUR, in 9.4% grade 1 VUR, and, in 17 % unsatisfactory.

Discussion

We analyzed 78 patients with primary VUR (106 refluxing ureters), who were treated with Deflux injection. Success was defined as resolution of VUR after first injection on postoperative voiding cystourethrogram, performed 2 -3 months following endoscopic treatment.

The number of patients studied in this research, with primary VUR, showed a cure rate of 73.6 % after one Deflux injection. The success rate in our patients confirms success rate reports in other studies other studies.[17] Lee reported success rate of 73% after the first injection.[18] Pinto et al. reported success rate of 84%,[19] while Puri et al. reported success rate of 94% [20] (Table 2).

Our results are very close to the success rate achieved with open surgical treatment. Capozza et al demonstrated that endoscopic treatment with dextranomer/hyaluronic acid copolymer proved to be effective and well-tolerated during long term follow up (7.5 years) in children with vesicoureteral reflux.[21] In our study, patients were followed up with mean duration of twenty-eight months. Patients treated with Deflux injection experienced few complications, out of 106 treated ureters, 8 of them or 7.54 % registered complications after endoscopic treatment. Of these are: contralateral reflux in 4 or 3.8 %, dysfunctional disorders are registered in 3 or 2.8%. Transient ureteral obstruction is registered in 1 ureter or 0.94 %. Moore and Bolduc[22] reported obstruction in 5 ureters in 275 patients after VUR endoscopic treatment.

The average duration of postoperative hospital stays is 1.1 ± 0.3 days, minimum 1 and maximum 3 days. The injected materials migrated to a medial or caudal direction in relation to the ureteral orifice. It might be due to the bulking agent being injected in the wrong position.

Table. 2. Outcomes of single endoscopic injection with DHA[8]

Study	Year	Patients/ ureters	Pre-op VUR grade	Success rate	Last VCUG years after Tx	Patients/ureters w/late VCUG	Recurrent VUR No ureters (%)	Febrile UTI No patients (%)	NF-UTI No patients (%)
Läckgren	2001	221/334	3–5	54%*	2–5	49/77	13 (17%) G3-4	8/221 (3.5%)	11/221 (4.8%)
							20 (26%) G2-4		
Oswald	2002	38/56	2–4	71.4%*	1	22/32	10 (31.2%)	–	–
				62.5%**					
Kirsch	2003	180ζ/292	1–4	72%**	–	–	–	–	–
Elderc	2006	5,527/8,101	1–5	75.7%***	–	–	–	0.0075	0.06
Lee	2009	219/337	1–5	73%**	1	–/150	39 (26%)	–	–
Chertin	2009	507/696 PTFE or DHA	1–5	68%**	1–12	11/-	8 (72.7%)ψ (3 DHA)	11/507 (2.2%) (3 DHA)	28/507 (5.6%)
Hsieh	2010	166/265	1–5	86.4%**	1	44/-	–	0/44 (0%)	11/44 (25%)
Holmdahl	2010	66/82	3–4	54.5%*	2	52/63	30 (47.6%) G2-4	14/66 (21%)	–
Brandströ				52%**		66/-	13 (20%)ψ G 3-4		
Routh	2010	–/7,303	1–5	77%***	–	–	–	–	–
Our study	2021	78/ 106	1-5	73.6%	1-5	15/23	18(17%)	22/106 (23.3%)	

The volume of the injected deflux was lost and it resulted in loss of volcano shape of periureteral orifice mucosa.

Conclusion

Endoscopic treatment of VUR has gained great popularity owing to several obvious benefits, including: short operative time, short hospital stay, minimal invasiveness, high efficacy, low complication rate, and reduced cost. Initially, the success rates of endoscopic treatment have been lower than that of open antireflux surgery. However, because injection techniques have been developed, a recent study showed higher success rates of endoscopic treatment than open surgery in the treatment of patients with intermediate- and high-grade VUR. Despite the controversy surrounding its effectiveness, endoscopic treatment is considered a valuable treatment option and viable alternative to long-term antibiotic prophylaxis.

The success rate shows that this treatment is very effective and with many advantages compared to open surgery. In our center, the endoscopic treatment is the first step of treatment in children with primary VUR. We started with endoscopic treatment in 2006. Our clinic is the only clinic in Kosova that deals with VUR treatment with Deflux, and despite the modest experience, the results are very good.

Conflict of Interest:

The author declares that there is no conflict of interest.

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