Review Article

Current Surgical Management of Vesicoureteral Reflux

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Vesicoureteral reflux (VUR), a common congenital urinary tract anomaly, refers to retrograde flow of urine from the bladder into the upper urinary tract. The main goal in the treatment of pediatric VUR is to preserve renal function by preventing pyelonephritis. Many surgical management options are available for pediatric VUR. Open ureteral reimplantation has a high success rate but is invasive and is associated with postoperative pain and morbidity. Endoscopic therapy is minimally invasive but has the disadvantages of decreased short-term success and recurrence of reflux over the long term. Laparoscopic or robotic ureteral reimplantation has become increasingly popular owing to its effectiveness and minimal invasiveness, but long-term outcomes have yet to be documented. Urologists should make an effort to select the appropriate surgical strategy by taking into consideration the individual characteristics of the patient such as age, gender, grade of reflux at presentation, status of renal parenchyma, combined bladder and ureteral circumstances, functional status of the bladder and bowel, and preferences of the patients' family.

Keywords: Pediatrics; Surgery; Therapy; Urinary tract infections; Vesico-ureteral reflux

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INTRODUCTION

Vesicoureteral reflux (VUR) occurs at a frequency of about 30% in children with urinary tract infection (UTI) [1]. The goal in the management of VUR is to prevent ascending infection and to decrease the risk of pyelonephritis and subsequent renal scarring. Surgical indications in children with VUR include recurrent infections, renal scarring, and potentially high-grade reflux [2]. Surgery can also be substituted for continuous antibiotic prophylaxis (CAP), even if it is not clear that CAP is effective.

Over the past 50 years, there have been many advances in the treatment of VUR (Table 1) [2,3]. Until the early 1980s, the main objective in the treatment of VUR was anatomical correction of reflux, and several types of antireflux surgical methods were invented and their success rates and complications reported [4-9]. In the mid-1980s, studies compared CAP with surgical treatment, and several studies concluded that surgical treatment was not superior to CAP at preventing UTI or renal damage in children with VUR [10-12]. Therefore, the goal of VUR treatment changed from removal of reflux to prevention of UTI. In the 21st century, the major controversy has centered on the effectiveness of CAP versus endoscopic therapy (ET) as first-line treatment options for VUR [13]. Recent advances in medical devices and technologies have led to increasing use of laparoscopic and robotic ureteral reimplantation [14-18].

Open ureteral reimplantation has a documented high success rate and low associated morbidity; however, an incision is required, which results in pain and potentially unavoidable bladder spasms. ET clearly has advantages both in terms of decreased morbidity and cosmetic appearance, but these advantages may be at the price of decreased short-term success and recurrence of reflux over the long term. Laparoscopic or robotic ureteral reimplantation is thought to result in decreased morbidity; however, this can be difficult to measure.

OPEN URETERAL REIMPLANTATION

Open ureteral reimplantation was first introduced in the

early 20th century. Bovee [19] first described ureteral reimplantation in a patient with a ureteral injury caused by complications of gynecological surgery. In 1952, Hutch [20] introduced ureteral reimplantation to correct VUR in a paraplegic patient. Since then, numerous ureteral reimplantation techniques have been developed. In 1958, Politano and Leadbetter [4] introduced a unique surgical technique for ureteral reimplantation. The ureter was mobilized intravesically and brought through a new hiatus located in the upper portion of the original orifice, and then a submucosal tunnel was created from the new hiatus to the original orifice. This allowed the new ureteral orifice to be located in the original location and enabled creation of a longer submucosal tunnel, which is useful in higher grades of VUR, but at the risk of ureteral kinking or obstruction and bowel injury. In 1961 and 1964, Lich et al. [5] and Gregoir and Vanregemorter [6] introduced novel techniques for ureteral reimplantation. The ureter was mobilized extravesically along the course of the ureter and the detrusor muscle, excluding the mucosal layer, was divided in the direction of the ureter. After the mobilized ureter was located above the mucosal layer, the divided detrusor muscles were sutured to each other to cover the ureter, creating a submucosal ureteral tunnel. This surgical method does not require opening the bladder; however, there is a possibility of urinary retention in children who undergo bilateral ureteral reimplantation because of pelvic nerve damage. In 1967, Glenn and Anderson [7] introduced a ureteral reimplantation technique in which the submucosal tunnel was made from the original ureteral meatus to the bladder neck. This allows the ureter to follow its natural course without the risk of folding or obstruction of the ureter. However, making a submucosal tunnel by use of this technique is challenging, because of the narrow bladder neck area. Thus, in 1978, Glenn and Anderson [8] introduced an improved surgical method. They incised the detrusor muscle proximally from the original ureteral orifice, which facilitated the creation of a submucosal tunnel. In 1975, Cohen [9] introduced a novel surgical method in which a submucosal ureteral tunnel was created transtrigonally, allowing the new ureteral orifice to be created around the contralateral ureteral orifice. This surgical method is easy to perform and allows creation of a submucosal tunnel of sufficient length. Until now, this has been the most widely used method. However, retrograde ureteral catheterization after surgery is difficult by use of this method.

ENDOSCOPIC TREATMENT

Since the first clinical application of ET for VUR in 1984 employing subureteric polytetrafluoroethylene injection [21], the materials and techniques used in ET have improved considerably [13]. Following the approval of dextranomer/hyaluronic acid (Dx/HA) by the U.S. Food and Drug Administration in 2001, ET for VUR with the use of Dx/HA has become increasingly popular in many parts of the world

[22]. The combination of reasonable success, minimal morbidity, safety profile, and short operative time has strengthened the role of ET in treating VUR. Several improvements in surgical technique have also been made since the first clinical application of ET to treat VUR [13]. O'Donnell and Puri [21] first introduced the subureteric Teflon injection (STING) procedure, which involves injection 2 to 3 mm distal to the ureterovesical junction, 4 to 5 mm advancement of the needle in the submucosal plane, and creation of a mound that elongates the intramural ureter. Kirsch et al. [23] introduced the hydrodistention-implantation technique (HIT); this involves inserting the needle into the floor of the distal ureter after dilation of the ureteral lumen by flushing with irrigation fluid. The goal of this technique is to completely coapt the ureteral tunnel, and this modification can be followed by the STING procedure if coaptation of the ureteral orifice is not achieved. Resolution of VUR by using the HIT has been achieved in 92% of cases compared with 79% of VUR cases operated on by using the standard STING procedure [23]. Recently, the HIT has been modified to include both proximal and distal intraureteric injections (double HIT), which facilitates better coaptation of the intramural tunnel [24].

LAPAROSCOPIC AND ROBOTIC URETERAL REIMPLANTATION

Laparoscopic ureteral reimplantation was initially attempted extravesically. Since Atala et al. [25] first introduced laparoscopic Lich-Gregoir extravesical ureteral reimplantation in 1993, several modified laparoscopic extravesical anti-reflux surgical methods have been reported [26,27]. All of these methods use a transperitoneal approach, because a child's pelvic cavity is too small to allow extraperitoneal surgery. Similarly to open extravesical ureteral reimplantation, there is the risk of urinary retention after laparoscopic extravesical reimplantation in cases of bilateral VUR [16]. In 2001, Gill et al. [28] first introduced the novel technique of laparoscopic intravesical ureteral reimplantation. They inserted two laparoscopic ports into the bladder under direct cystoscopic vision, and performed Cohen ureteral reimplantation. In 2005, Yeung et al. [29] reported a novel laparoscopic ureteral reimplantation technique; they made a pneumovesicum by infusing CO_2 gas into the bladder and inserted one camera port and two laparoscopic instrument ports and performed Cohen ureteral reimplantation. Since then, this pneumovesicoscopic ureteral reimplantation has increased in popularity among clinicians [14,30,31].

Various antireflux surgeries have been tried with the da Vinci Surgical System in an intravesicular or extravesicular manner [18]. Robotic manipulation and magnified visualization enable identification of the pelvic plexus, allowing injury to this area to be avoided as well as ureteral mobilization at the hiatus, which is difficult when performing open and purely laparoscopic procedures [32].

TABLE 1. Advances in the treatment of vesicoureteral reflux

Year	Surgical treatment	Research and medical treatment
1952	Hutch: VUR in paraplegics	
1958	Politano-Leadbetter ureteral reimplantation	
1959	Paquin ureteral reimplantation	
1961	Lich-Gregoir ureteral reimplantation	
1967	Glenn-Anderson ureteral reimplantation	
1975	Cohen: transtrigonal ureteral reimplantation	Smellie: VUR medical treatment
1976	Kalicinski: infolding technique	
1979	Starr: ureteral imbrication technique	Ransley and Risdon: intrarenal reflux and bacteriuria cause renal scarring
1981		International Study Classification by International Reflux Study Committee
1984	Gil-Vernet ureteral reimplantation O'Donnell and Puri: STING	
1987	Zaontz: detrusorrhaphy	Birmingham Reflux Study Group
1993	Laparoscopic extravesical Lich-Gregoir	
1995	Dx/HA	
1997		AUA Pediatric VUR Guidelines Panel Report
2001	Gill: laparoscopic intravesical Cohen ureteral reimplantation under cystoscopic vision	
2004	Kirsch: HIT Peters: robotic assisted laparoscopic ureteral reimplantation	
2005	Yeung: laparoscopic intravesical Cohen ureteral reimplantation under carbon dioxide bladder insufflation	
2008		AUA Pediatric VUR Guidelines Panel Report
2009		Cochrane database of systematic reviews for prophylactic antibiotics
2012		EAU guidelines on VUR in children

VUR, vesicoureteral reflux; STING, subureteric Teflon injection; Dx/HA, dextranomer/hyaluronic acid copolymer; HIT, hydrodistention implantation technique; AUA, American Urological Association; EAU, European Association of Urology.

SELECTION OF THE APPROPRIATE SURGICAL TREATMENT OPTION

The pros and cons of the various surgical methods for VUR can be evaluated on the basis of various parameters. These parameters include efficacy, universal applicability, general availability, minimal invasiveness, and cost-effectiveness.

1. Success and durability
The high success rate of open ureteral reimplantation is well documented. According to the Pediatric American Urological Association Guideline Panel Summary published in 1997 [33], the success rates of open ureteral reimplantation for VUR grades I to V are 99.1%, 99.0%, 98.3%, 98.5%, and 80.7%, respectively. The success rate per patient is 95.1%, and the success rate per ureter is 95.9%. In addition, VUR recurrence is not observed except in those children with severe bladder bowel dysfunction. The success rate of ET is low compared with that of open surgery. Several authors have reported high success rates with injection therapy that are comparable with those of open ureteroneocystostomy [34-36]. However, it should be remem-

bered that these excellent results were attained by expert surgeons and that universally, there is a certain period of time required to overcome the steep learning curve necessary to perform these procedures. The average success rates of injection therapy for primary VUR in children according to reflux grade have been reported to be 79% for grade II VUR, 72% for grade III, 63% for grade IV, and 51% for grade V on the basis of meta-analyses [37]. ET for VUR is not very durable. According to the report of Lackgren et al. [38], reflux recurrence was found in 6 patients (13%) after long-term follow-up of 45 patients who underwent ET for VUR. However, voiding cystourethrography (VCUG) was not performed in all of the children who underwent ET; data were obtained from selective patients who visited the hospital for symptoms such as high fever. Thus, the actual recurrence rate after ET is likely to be higher. Lee et al. [39] reported that a total of 150 ureteral units with initial successful Dx/HA treatment were evaluated at 1 year by VCUG; recurrence was observed in 36 ureters (26%). They therefore suggested postoperative long-term follow-up of patients because significant recurrence is observed at postoperative 1 year, even if reflux is resolved during the initial postoperative period. The success rate of laparoscopic or ro-

botic ureteral reimplantation has been reported to range between 95% and 99% [15-17,40], which is comparable to that of open surgery; however, these values are based on a limited number of reports. Long-term outcomes have yet to be documented.

2. Reduction of febrile UTI

The aim of VUR treatment is to prevent febrile UTI and to reduce subsequent renal damage. From this perspective, it is important to assess the reduction in febrile UTI after antireflux surgery. In a Swedish reflux trial, a total of 203 children with dilating VUR were allocated to ET, CAP, or surveillance groups. When the febrile UTI rate was evaluated after the 2-year study period, a significant difference in recurrence rate was observed among girls with febrile UTI: 19% for CAP, 23% for ET, and 57% for surveillance [41]. Moreover, a recent study reported that even in children with persistent VUR, the number of febrile UTI episodes may decrease after ET. When the febrile UTI rate was evaluated in 75 children with persistent reflux after ET, the febrile UTI rate of 0.76 ± 1.18 per year before injection decreased significantly to 0.20 ± 0.61 per year, despite persistent VUR [42]. The decrement in the rate of postinjection febrile UTI may mainly be a result of the decrease in VUR grade. The clinical significance of downgraded reflux after ET is valuable in light of the fact that the primary goal of treatment of VUR in children is to prevent renal damage associated with recurrent febrile UTIs.

3. Universal applicability

VUR has a different clinical course after surgical treatment according to the associated bladder or ureteral circumstances, even if the grade of reflux is the same. Open ureteral reimplantation entails creation of definite submucosal ureteral tunneling and is therefore applicable to all grades of VUR in all varieties of bladder and ureteral circumstances [33]. Most studies have demonstrated that open ureteral reimplantation is effective in neurogenic bladder, valve bladder, and in patients with a duplication anomaly, ureterocele, or megaureter [33,43]. However, it has been reported that ET is less successful when accompanied by associated bladder or ureteral anomalies such as hutch diverticulum, ureteral duplex, or ureterocele [37,43]. The success rate of ET is also lower in children with bladder bowel dysfunction [43]. Data concerning the universal applicability of laparoscopic or robotic ureteral reimplantation is limited. Valla et al. [14] reported their experience of pneumovesicoscopic ureteral reimplantations in cases of megaureter or ureterocele, which was similar to their experience based on open surgery.

4. General availability

It is not easy to assess the difficulty of individual surgical modalities. Open ureteral reimplantation can be performed either transvesically or extravesically and all procedures can be performed without much difficulty. Furthermore, although the anatomy around the ureter-

ovesical junction area is somewhat complicated, there is a relatively minimal risk of great vessel or nerve injury. ET is definitely easier than open surgery. However, the operator should pay attention to proper surgical technique related to the degree of bladder filling, the angle between the cystoscope and ureteral orifice, the injection site of the needle, the final endpoint of the needle, and the injection volume to improve success rates [44]. To perform laparoscopic or robotic ureteral reimplantation, the surgeon should be skilled in open surgery and should also be familiar with laparoscopic or robotic handling. Thus, laparoscopic or robotic ureteral reimplantation is more technically difficult than the other surgical modalities.

5. Morbidity and hospitalization

Open ureteral reimplantation is associated with the inevitable postoperative symptoms of hematuria or bladder spasm, which result in urinary frequency or dysuria. However, owing to advancements in surgical technique, routine placement of suprapubic catheters, ureteral stents, and surgical drains has been abandoned. McCool and Joseph [45] described a decrease in hospitalization stay from 4 days to 2 days after Cohen open ureteral reimplantation. Other groups reported their experiences with outpatient transvesical reimplantations [46,47]. Extravesical reimplantation performed by making small inguinal incisions allows patients to be discharged within 24 hours. Furthermore, pediatric anesthesia and perioperative management of children undergoing ureteral reimplantation have changed dramatically. Regional blocks or continuous epidural infusions help children recover quickly by providing better pain control. Careful use of anti-inflammatory and anticholinergic drugs decreases narcotic requirements and relieves bladder spasms. ET is minimally invasive compared with other antireflux surgical procedures. It takes less than 15 minutes to perform the entire surgical procedure. Furthermore, ET does not require admission treatment. Complications after ET are reported to be very rare and related mostly to transient ureteral obstruction. Little is known about the long-term sequelae of ET. Laparoscopic or robotic ureteral reimplantation is also minimally invasive compared with open surgery. In pneumovesicoscopic ureteral reimplantation, the incidence of postoperative hematuria and bladder spasm has been reported to be less than the incidence of these side effects after open surgery.

6. Surgical wound

Open surgery inevitably results in a surgical wound. However, open ureteral reimplantation is currently usually performed with only a small surgical incision. In open intravesical ureteral reimplantation, the operation scar is from a Pfannelstiel incision, which is a hidden incision below the belt. Open extravesical ureteral reimplantation is performed by making an inguinal incision less than 2 cm in length, and this incision is also hidden [48]. Surgical scars associated with laparoscopic or robotic surgery are

minimal. However, pneumovesicoscopic ureteral reimplantation requires three small incisions, two for laparoscopic ports located below the belt, and one incision for a camera port in the midline between the umbilicus and the pubic bone [29]. An open question is whether there is a cosmetic advantage in having three small incisions above the belt versus one small incision below the belt.

7. Cost

Injection materials are relatively expensive. However, in contrast with the cost in the United States, the cost of ET in Korea is not excessive because it is covered by national medical insurance. The price of Dx/HA, the most widely used injection material, is about 450,000 KRW per 1 mL. The charge for the patient is only 10% when the child is younger than 6 years old and 20% when the patient is 6 to 15 years old. The rest is covered by the national medical insurance system. In open ureteral reimplantation, the operation fee is reasonable, but longer hospitalization is required, which increases costs. The operation fee for laparoscopic surgery is higher than that for open surgery because of the cost of laparoscopic instrumentation usage, but the period of hospitalization is short. Robotic ureteral reimplantation is the most expensive option in Korea.

CONCLUSIONS

There have been many advances in the surgical treatment of VUR. In the past, open ureteral reimplantation was the standard antireflux surgery because of its high success and durability. Development of optimal injectable materials, advances in video systems and endoscopic instruments, and improved injection techniques have made ET therapy for VUR an important surgical modality. Laparoscopic and robotic ureteral reimplantations are becoming increasingly popular surgical options. Understanding the pros and cons of various antireflux surgeries is important when determining which approach is most effective for treating a child with VUR.

CONFLICTS OF INTEREST
The authors have nothing to disclose.

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