

# The Long Term Follow-Up Results of the Direct Nipple Ureteroneocystostomy Technique: A Prospective Study\*

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Received May 26, 2013; revised June 27, 2013; accepted July 5, 2013

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## ABSTRACT

**Objective:** To evaluate the long term follow-up results of the direct nipple ureteroneocystostomy technique. **Materials and Methods:** We studied a total of 16 patients (19 renal units) who underwent direct nipple ureteroneocystostomy. The mean age was 43 years and 3 patients had bilateral disease. In five units the ureters had been ligated during gynecological surgery, 11 renal units were obstructive and three units were reflexive megaureters. The ureters were spatulated for about 2 cm and folded back. Nipples 2 to 2.5 cm long were prepared. In two cases the ureters were thin-walled (2 mm or less) and they were not spatulated but folded back onto themselves. In one case the ureter could not be everted since it had a thick and fibrotic wall. The distal 2 to 2.5 cm segment of this ureter was directly inserted in to the bladder. Postoperative follow-up was at 3 month intervals for the first year at 6 month intervals for 2 - 3 years and yearly thereafter. At the time of follow-up serum creatinine, urine culture, ultrasound, intravenous urography, voiding cystoureterography, nuclear renal scintigraphy and cystometric evaluations were performed. The functions of 11 and 15 renal units were evaluated scintigraphically and stereologically, respectively, in the both preoperative and postoperative first year follow-up. The Wilcoxon Signed Ranks test was used for statistical evaluation and  $p < 0.05$  was considered statistically significant. **Results:** Mean follow-up was 49 months. Three renal units had Grade III reflux (two of them during voiding) and one unit had Grade IV reflux. At follow-up this patient developed in the ureteral stricture. No patients had urinary tract infection, pyelonephritis or ureteral stricture follow-up period. Between the preoperative and postoperative first year, there was an increase in postoperative split renal function based on renal scintigraphy but this difference was not statistically significant. The stereologically calculated decrease in pelvicaliceal dilatation was statistically significant. **Conclusion:** Ease of application and no need to taper or plicate the ureter or prepare a sub-mucosal tunnel may be the reasons to consider the direct nipple ureteroneocystostomy technique for megaureters of different etiologies.

**Keywords:** Megaureter; Nipple; Technique; Ureter; Vesicoureteral Reflux

## 1. Introduction

Primary obstructed megaureter (POM) is a result of obstruction or an adynamic ureteral segment in the ureterovesical junction. Megaureter can be classified as 1) reflux megaureter obstructed megaureter; 2) nonreflux and nonobstructed megaureter and 3) megaureter with obstruction and reflux [1].

POM is occurs 3/12 to 5 times more often in males [2]. Although it is generally unilateral, it may be seen bilaterally in 15% to 25% of cases. Besides excretory urogra-

phy (IVU), diuretic renography and antegrade pyelography are valuable tools for its diagnosis. As treatment, the adynamic ureteral segment is excised and ureteroneocystostomy is performed with different surgical techniques. However, the results may be far from ideal [3,4].

Ureteric injury is one of the most serious complications of gynecologic operations in the pelvis [5]. Ureteric damage has significant morbidity and can present as ureteric stenosis or obstruction and cause variable degrees of impaired renal function in some cases [6]. When the diagnosis of injury is made postoperatively then either open surgery or endourologic procedures can be employed. Delayed repair has been suggested based on

\*There is no financial disclosure of any of the authors.

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the view that this will reduce inflammation and tissue edema [7].

The treatment of vesicoureteral reflux (VUR) is individualized. Before recommending surgery, consideration is given to the severity of the reflux, possible underlying risk factors including bladder dysfunction, age at presentation, and duration of the disorder. A variety of techniques have been described for the correction of VUR. These are anatomically categorized as extravesical, intravesical, or combined, depending on the approach to the ureter [2]. In this study we evaluated the long term follow-up results of the direct nipple ureteroneocystostomy technique.

## 2. Materials and Methods

A total of 16 patients (19 renal units), seven males and nine females, with a median age of 43 years (21 - 73) who underwent nipple ureteroneocystostomy operation were enrolled in this study. Three cases underwent bilateral repair. Eight of the 19 renal units were on the right side and 11 were on the left side. Three of the repaired renal units were reflux megaureter, 11 were obstructed megaureter, and 5 were units at the lower end of the ureter which were ligated at previous gynecologic operations. Neurogenic bladder cases and cases with surgical wound infection were excluded. Preoperative evaluation consisted of urine culture, serum creatinine, urinary system ultrasonography, renal Technetium-99 m-Dimercaptosuccinic Acid (DMSA) scintigraphy, cystoscopy, voiding cystourethrography (VCU), intravenous urography (except for two cases), antegrade pyelography and Whitaker test (Life-Tech, Stafford, Texas) in 4 cases with percutaneous nephrostomy, and cystometric assessment (Life-Tech, Stafford, Texas) in 5 cases with voiding dysfunction. Cases with proliferation in urine culture were not operated on until after their urine became sterile and other cases were operated on after a course of antibiotic therapy with intravenous 3rd generation cephalosporins. In the Whitaker test, a pressure gradient above 22 cm H<sub>2</sub>O between the renal pelvis and bladder during administration of 10 ml isotonic saline is considered diagnostic for obstruction while 15 - 22 cm H<sub>2</sub>O suggests obstruction, and below 15 cmH<sub>2</sub>O indicates no obstruction [8]. All cases were operated on under general anesthesia. A direct nipple ureteroneocystostomy (DNU) operation was carried out with a lower middle incision in cases where bilateral repair was undertaken and with a Gibson incision for the rest of the cases [9].

A follow-up was planned at every three months in the first year, at every 6 months between the 1st and 3rd years and yearly thereafter. Follow-up tests included urine culture, serum creatinine, ultrasonography (USG), VCU, IVU (if creatinine was normal), DMSA scintigraphy, endoscopy (at postoperative 3rd month), and uro-

dynamic examination in cases with dysfunctional micriturition. A sample of the lower ureteral end of 9 renal units was evaluated pathologically. In cases attending regular follow-ups, preoperative and postoperative 1st year DMSA results and amount of pelvicaliceal dilatation in the IVU of the unit that underwent surgery were compared statistically (by counting the dots falling on the pelvis and calices using stereologic methods which use transparent acetates with 3 mm inter-grid distances [10-12]).

Inter-IVU image differences between IVUs taken at different centers were resolved by using the value found by counting the dots falling on the 4th lumbar vertebra in both films and proportioning the results with each other as the multiplier. Measurable values were expressed as means + standard deviation. Preoperative and postoperative values were compared using the Wilcoxon signed rank test. A p value less than 0.05 was accepted as statistically significant.

## 3. Results

The results of a median 49 months follow-up of the 19 renal units that underwent DNU operation were assessed. One reflexive and two obstructive cases underwent bilateral repair. While two cases with an excessively dilated and thin-walled (2 mm or less) ureter were anastomosed by folding back without spatulation, one case with a ureter with an excessively thick and fibrotic wall was directly anastomosed without being everted and spatulated, with a 2 to 2.5 cm part being free in the bladder. In one obstructive case there was a 6 cm stone at the lower end of the ureter. As the ureter of this case undergoing ureterolithotomy and DNU operations was so thick and fibrotic, excessive ureter dissection was avoided to preserve circulation and the bladder was attached to the tendon of the ipsilateral psoas minor muscle by using the Psoas hitch method. Urine cultures of the cases were free of proliferation. All cases underwent preoperative VCU and no reflux was observed except for 3 units. Two cases did not undergo IVU (one of these cases had a serum creatinine level of 1.9 mg/dl and the other was at the early postpartum period). The Whitaker test was applied to 4 cases with percutaneous nephrostomy and the test results of these 4 cases were consistent with obstruction. The test was repeated on the 14th day after the operation and the test results were negative. These cases also underwent postoperative antegrade pyelography which revealed that the contrast material readily passed to the bladder and no obstruction existed, and their nephrostomies were removed. Drains were removed on the 3rd - 5th days. Cases underwent VCU on the postoperative 14th day, which revealed extravasation in no patients. In most of the cases the filling defect caused by the nipple was evident in the bladder in the VCU taken postoperatively

(**Figure 1(A)**). Filling defects seen on the left and right sides of the bladder belong to the nipple while that on the base is of the balloon of the urethral catheter. Five cases whose ureteral lower ends were bound due to previous gynecologic operations were followed up for 8 weeks after the operation for inflammation, edema, and suture reabsorption if they were sutured with an absorbable suture; however, these cases were taken to nipple ureteroneocystostomy as no recovery took place. Urethral catheters of the cases were removed 14 days after VCU.

The flank pain of the patients being followed up abated. One case attended the first month follow-up but quit thereafter. Another case, on the other hand, was admitted for the first appointment on the postoperative 54th day. The high preoperative creatinine level of one case persisted during the postoperative period. Other cases had normal creatinine levels (Normal: 0.6 - 1.3 mg/dl).

Five cases in which had a preoperative cystometry had normal control cystometric examination and this test was not repeated at follow-up. Four out of 19 units (21%) were diagnosed with reflux. While 3 cases had Grade III reflux occurring only during voiding, another case had Grade IV reflux. While one case with voiding-associated Grade III reflux had a preoperative Grade V reflux, other cases had obstructive megaureters.

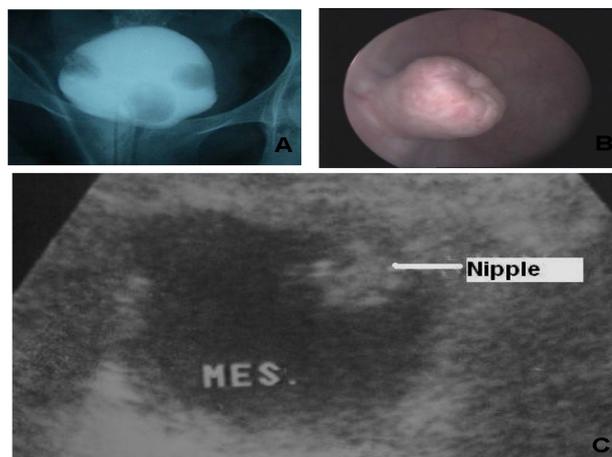
Two of 3 units operated on for obstructive MGU were diagnosed with Grade III reflux during voiding whereas one case had Grade IV reflux. The latter had a severe stenosis in the bulbous urethra in control endoscopy and an optic urethrotomy was performed.

No case attending follow-ups had a retracted nipple in endoscopic examinations. A 2 to 2.5 cm nipple ureter was found to be moving freely inside the bladder and the endoscope could easily pass to the lower end of the ureter (**Figure 1(B)**).

Comparison of the preoperative and postoperative USGs revealed that dilatations decreased in size and thus the cases benefited from surgery but residual dilatations persisted. Radiologists were informed that the nipple occupies space in the bladder and resembles a soft tissue mass and could easily be misdiagnosed as a solid mass (**Figure 1(C)**).

Among those patients who underwent preoperative renal scintigraphy and attended regular follow-up appointments in the postoperative period, preoperative and postoperative first year the Tc99m-DMSA renal scintigraphic results of 11 renal units were statistically compared.

There was a postoperative increase in renal functions, albeit statistically insignificant (**Table 1**). IVU showed that the dilatations decreased, no obstructions were present, and the pelvicaliceal structures of the units that were observable only at the nephrogram phase of the late films in preoperative IVU became visible. Dilatations of the pelvis and calices of 15 renal units in the preoperative



**Figure 1.** (A) Fourteenth day cystographic image of the case that underwent bilateral DNU. (B) Endoscopic appearance of the bladder at postoperative 6th month of a case that underwent DNU operation. (C) USG appearance of the bladder at postoperative 6th month of a case that underwent DNU operation. The nipple appears inside the bladder lumen as if it were a soft tissue mass.

and postoperative 1st year IVUs were compared statistically by counting the dots on these regions. Postoperatively the dilatations significantly diminished (**Table 2**). Samples of the lower end of the ureter of 9 units which were excised at operation and sent for pathology were examined and only two were diagnosed with an aganglionic segment. The lower end pathologies of the remaining 7 units were reported as chronic inflammatory process and fibroadipose tissue.

#### 4. Discussion

Many methods have been defined in megaureter surgery. The main principle is to practice an ureteroneocystostomy suitable for the antireflux technique. Absence of reflux and obstruction, resolution of upper urinary system dilatations, recovery or stabilization of renal functions, regression or elimination of preoperative symptoms, a sterile urinary culture, regression or normalization of serum urea and creatinine levels are all considered as evidence of treatment success. It is not necessary to fulfill all criteria for treatment success. For instance, treatment success may be accepted to exist when the patient is asymptomatic postoperatively and the urinary system is seen to have recovered radiologically [13].

The main problem is the anastomosis of excessively dilated ureters. Hendren applied an anastomosis by forming a submucosal tunnel after constricting and then excising the ureter from the antimesenteric side in 169 patients and reported a reflux rate of 5% and stenosis rate of 7% [14]. Stenosis and obstruction in this study were attributed to intraoperative damage to branches of the inferior vesical artery and hypogastric artery supplying

**Table 1. Comparison of preoperative and postoperative 1st year renal DMSA scintigraphies of the cases.**

	Preoperative (n:11) Mean + standard deviation	Postoperative first year (n:11) Mean ± standard deviation	P
Scintigraphy (%)	55.2 ± 26.1	55.8 ± 29.7	0.721

**Table 2. Comparison of dilatations of pelvis and calices of the cases in preoperative and postoperative 1st year IVU by stereologic grid counting method.**

	Preoperative (n:15) Mean ± standard deviation	Postoperative first year (n:15) Mean ± standard deviation	P
Area	353.0 ± 367.4	246.4 ± 261.1	0.003

the ureter [4].

An alternative option to relieve dilatation is to scale down the distal ureteric diameter by plication. Ehrlic applied submucosal ureteroneocystostomy after ureteric plication in 74 ureters and reported an obstruction rate of 1.4% and a reflux rate of 4% [4]. Perovic applied ureteroneocystostomy to 167 megaureters and performed an anastomosis with the extravescical submucosal tunnel technique without plicating and excising the ureter. He reported stenosis in 2 cases and reflux in 3 patients after a median follow-up of 2.5 years. In addition he reported that a ratio of submucosal tunnel length/ureter diameter of 3/1, or even 2/1 can prevent reflux. He argued that even this ratio is high and the dilated ureteric lumen folds back onto itself inside the tunnel and is easily placed between the detrusor and the mucosa [15].

Hill *et al.* formed a new cuff by folding on approximately 1 cm distal part of the ureter back onto itself and anastomosed it to the new hiatus in 16 renal units in dogs. No nipple could be seen in 2 units at 3-month follow-up while hydronephrosis developed in 4 units with no reflux. They held that retraction and atrophy of the muscles of cuff wall were responsible for not being able to see the nipple. The advantages of this technique have been reported as being easy and rapid use and its forming a permanent intraluminal papilla [16].

Sagalowsky performed anastomosis in 46 ureters with the split-cuff nipple technique and observed a reflux rate of 2.4% at the early period and 5% in the postoperative second year; however, they observed no obstruction at all [17]. Turner-Warwick *et al.* reported that the nipple they formed can cause ischemic necrosis due to constriction if not spatulated and it also leads to outside shifting of the inner wall of the nipple since the everted part would not fully adhere to the ureter [18].

Al-Shukri and Alwan repaired 114 of 560 ureters with bilharziasis-induced stenosis with the nipple ureteroneocystostomy technique [13]. They reported a success rate of 94.7% at 6 months, % at 3 years and argued that a 6-month follow-up is sufficient in the postoperative period. The main difference between that study and our study was the anastomosis site of the ureter. While it was suggested in that technique that the ureter must be anastomosed to a region as close to the original hiatus as pos-

sible, our technique involves an anastomosis performed in the upper posterolateral region, as in psoas hitch technique. In our opinion, an anastomosis to this region is more easily performed [9,13]. It has been reported that it is very challenging to form a tunnel to the ureter without performing constriction or excision in adult megaureters [15].

The two main complications following megaureter repair are reflux or obstruction. In some cases, on the other hand, a temporary obstruction may be observed in the early postoperative period. A short tunnel and excessive lateral anastomosis of the ureter have been held responsible for postoperative reflux formation [14]. Persistent VUR results from inability to form an insufficient tunnel length or to provide the ureter with sufficient muscle support. Fibrotic ureters may not be completely closed due to intravesical pressure and cause persistent reflux. Also, inability to identify and treat secondary causes of reflux results in recurrences [2].

Lee *et al.* reported that increased Type III collagen in megaureters with reflux decreases surgical success and forms an intrinsic solid structure in the ureter [19]. Residual ectasia in the upper urinary system may cause an apparently high reflux grade. Scintigraphically, no new scar formation was evident in kidneys at the side of the operated ureters; no pyelonephritis attack developed and the urine remained sterile during follow-up. Except for case with a high creatinine level in the preoperative period (preoperative: 1.9 mg/dl, postoperative: 1.9 - 2.2 mg/dl), no case developed an increase in biochemical parameters in the postoperative period.

The phenomenon rendering vesicoureteral reflux important is that it causes parenchymal damage. Reflux can damage the kidneys only when it is intrarenal. Hydrostatic pressure of the intrarenal reflux, the age of the patient, and whether or not the urine is infected are decisive on the severity of the scarring in kidney parenchyma [20].

In one study conducted by the Birmingham Reflux Working Group both groups randomized to surgical and conservative treatment approaches had the same kidney scarring rate at study entry whereas subsequent follow-up revealed that the new scarring rate was 20% in the conservative group and 24.1% in the surgical group and

while the progressive scarring rate was 10.5% in the surgical group and 11.6% in the conservative group. No significant difference was noted between the two groups in terms of infection rates [21]. In the "International Reflux Study Group" study in which centers from America and Europe collaborated 60% of cases had scarring at the beginning, with subsequent new scarring rates of 14.6% and 14.5% in surgical and conservative groups, respectively [22].

It has been reported, and many authors agree, that modest refluxes following megaureter surgery may recover by themselves in a period of 2 - 3 months, and thus require no therapy [23]. As further surgery in patients with residual reflux carries the risk of ischemia and is technically demanding, endoscopic substance infusion is recommended. A success rate of 80% has been reported following a single endoscopic injection to 20 ureters with ongoing reflux (Grade III or above in 13 ureters) following ureteroneocystostomy [24].

Obstruction, the other common complication, is the result of fibrosis due to deranged ureter blood supply particularly following excisional constriction or plication. Entry of the ureteric hiatus into the bladder from an excessive cranial and lateral aspect also causes obstruction. In such a situation a second operation is needed. Temporary obstruction seen postoperatively, on the other hand, is the result of edema at the lower end of the ureter and nephrostomy usually suffices. Although our sample size was small, we did not observe obstruction or stricture development, suggesting that a minimal trauma to the ureter ensues. No infection or worsening of renal function due to residual urine in the pelvicaliceal system was observed after surgery. King reported that there is no need for constriction to repair ureter peristalsism [1]. In Whitaker test, a pressure gradient above 22 cm H<sub>2</sub>O between the renal pelvis and the bladder during administration of 10 ml isotonic saline is considered diagnostic for obstruction while 15 - 22 cm H<sub>2</sub>O suggests obstruction, and below 15 cm H<sub>2</sub>O indicates no obstruction [8]. In one study it has been suggested that administration of isotonic saline at a rate of 10 ml/min may not suffice to show obstruction in dilated urinary systems and a rate of 12 - 20 ml/min may be more appropriate [25].

The nipple appears as a smooth-bordered filling defect in the bladder in postoperative cystograms and IVUs while it is observed as a soft tissue mass in the bladder in USG. Endoscopically, the nipple prolapsing into the lumen is easily seen on the lateral superior wall of the bladder and it is easy to advance through the ureter with a cystoscope in the postoperative period. It has been clinically and cystometrically shown that the nipple inside the bladder does not produce symptoms of bladder irritation. None of the patients had irritative symptoms in the preoperative period.

## 5. Conclusion

As the technique is an easy-to-perform one, the learning curve is substantially short. Unlike the previously mentioned techniques, this method does not need a submucosal tunnel, ureteric plication, or tapering, thus shortening surgical time and anesthetic complications, and limiting the frequency of major surgical complications such as ureteral stenosis. Lack of the need for a ureteral stent protects the patient from stent-induced irritation and an additional endoscopic procedure. A readily seen nipple in the bladder and easily performed endoscopy in the postoperative period facilitates intervention. Its potential to be performed in obstructive and reflexive megaureter cases including ureter dilatations caused by a variety of etiologies such as iatrogenic ureteric lower end dilatation may be cause to prefer the direct nipple ureteroneocystostomy technique.

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