

# Clinical characteristics and management of children with ureteropelvic junction obstruction and severe vesicoureteral reflux: preliminary results

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**Objective** The aim of this study was to investigate the physiopathology of isolated or coexisting ureteropelvic junction obstruction (UPJ-O) and high-grade vesicoureteral reflux (VUR), including the clinical characteristics and management.

**Summary background data** The association between UPJ-O and VUR was reported more frequently in boys with high-grade VUR; however, the physiopathology of concomitant UPJ-O and VUR is still unknown. Primary pyeloplasty, followed by ureteral reimplantation, if needed, has been widely accepted, although VUR should be treated first (most often by endoscopic treatment) in the presence of a functional obstruction.

**Methods** We reviewed the charts of 78 children with isolated or coexisting high-grade VUR/UPJ-O. Among the children, 14 had isolated UPJ-O, 16 had high-grade VUR/UPJ-O, and 48 had high-grade VUR. Children with other urological or extrarenal conditions were excluded.

**Results** Patients with isolated UPJ-O showed significantly different clinical characteristics compared with the other two groups of patients with high-grade VUR. Among the patients of group 2, 3/13 (23%) showed progression from functional to obstructive UPJ-O after endoscopic treatment. All of them underwent secondary pyeloplasty, which was

complicated at follow-up by VUR recurrence needing further endoscopic injection.

**Conclusion** We suggest that UPJ-O in high-grade VUR patients is just a complication of severe VUR that produces structural changes in predisposed children. The treatment of children with associated high-grade VUR/UPJ-O may be complicated by the progression of urinary flow obstruction or VUR recurrence after pyeloplasty. Endoscopic treatment of high-grade VUR is associated with a high rate of VUR recurrence in children requiring subsequent pyeloplasty. *Ann Pediatr Surg* 9:114–116 © 2013 Annals of Pediatric Surgery.

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## Introduction

Historically, the association between ureteropelvic junction obstruction (UPJ-O) and vesicoureteral reflux (VUR) was reported more frequently in boys with high-grade VUR, with a range from 9 to 14% [1,2]. In a large series including 224 children with UPJ-O, the incidence of ipsilateral VUR was found to be 18%. Further, a five-fold increased risk of UPJ-O in children with high-grade VUR was also reported; however, when all grades of VUR were considered, an increased risk of obstruction was not observed [3]. Furthermore, in another study, records of 143 children with prenatally diagnosed hydronephrosis secondary to UPJ-O as well its association with clinical features such as prematurity, twinning, and urological anomalies were analyzed. It was found that pyeloplasty was required more often in children with associated VUR (54.5 vs. 18.2%) [4].

The physiopathology of concomitant UPJ-O and VUR is still unknown. Several hypotheses have been proposed including, association or causality, early developmental anomalies during the evolutionary process of the ureteral bud ascending toward the primitive metanephric blastema, tortuosity, kinking and inflammation, and primary

or secondary changes of the ureteral barrier at the UPJ. However, none of these hypotheses have been proven yet.

Primary pyeloplasty, followed by ureteral reimplantation, if needed, has been widely accepted. This surgical strategy is justified by two observations: (a) even high-grade VUR may improve spontaneously, (b) primary reimplantation may cause acute deterioration of an already obstructed UPJ [1,2]. In contrast, VUR should be treated first in the presence of a functional obstruction [2]. Actually, the preferred surgical treatment for VUR is by endoscopic treatment (ET) in all grades with a percentage of improvement/resolution greater than 90% [5,6].

The aim of this retrospective study was to investigate the differences in clinical characteristics and management in children with isolated or coexisting UPJ-O and high-grade VUR. Furthermore, we demonstrated that high-grade VUR may play a role in the development of secondary ipsilateral UPJ-O.

## Patients and methods

During a 6-year period, we operated upon 126 children with high-grade VUR or/and UPJ-O. All patients (48/126

patients) with other associated renal (duplex kidney, horseshoe kidney, ureterocele, contralateral VUR, spina bifida, etc.) or extrarenal diseases (down syndrome, calculosis, oesophageal atresia, etc.) were excluded from the study. UPJ-O was diagnosed using renal ultrasounds, voiding urethrocytography, and diuretic  $^{99m}\text{Tc}$  MAG3 renal scans. The diuretic renal scan was performed according to the guidelines for the 'well-tempered' diuretic renogram using a bladder catheter [7]. An injection of 50 Ci/kg of  $^{99m}\text{Tc}$  MAG3 was followed by a 20-min baseline observation (renogram phase). Children who did not eliminate at least 50% of the labelled substance in the pelvis ( $T_{1/2}$ ) underwent furosemide stimulation (1 mg/kg endovenous bolus). Elimination was monitored for another 20 min. Patients who did not achieve  $T_{1/2}$  by the end of the test ( $T_{1/2} > 20$  min) were diagnosed with 'obstructive' UPJ-O, whereas those who achieved  $T_{1/2}$  ( $T_{1/2} \leq 20$  min) were diagnosed with 'functional' UPJ-O. Finally, a normal urinary flow was defined when  $T_{1/2}$  was reached within 10 min from injection of the radionuclide.

Seventy-eight patients were included in the study. The mean follow-up duration was  $35 \pm 17$  months (median 31). The patients were divided into three groups: (a) the isolated obstructive UPJ-O group (14 patients), (b) the coexisting ipsilateral high-grade VUR/UPJ-O group (16 patients), and (c) the isolated high-grade VUR group (48 patients). None of the children with low-grade VUR had UPJ-O. For each group, the following clinical characteristics were studied: age at surgery, sex, affected side, history of urinary tract infection (UTI), bladder dysfunction, and split renal function (SRF) up to 45% (Table 1). Bladder dysfunctions included a reduced capacity and an underactive or overactive bladder requiring medical treatment.

The indications for surgery in UPJ-O included an obstructive slope curve coexisting with (a) SRF of up to 45%, (b) a persistent obstructive curve at the 6 month-follow-up renal scan, or (c) recurrent abdominal pain or UTIs despite antibiotic prophylaxis.

The indications for ET of VUR included (a) recurrent or breakthrough UTI, (b) moderate or high-grade VUR, (c) renal scars on dimercaptosuccinic acid renal scans, (d) SRF, (e) VUR persistence over 5 years of age, and (f) poor compliance to antibiotic prophylaxis. High-grade VUR was defined mainly according the international system of radiographic grading of VUR [8].

However, in patients with coexisting ipsilateral UPJ-O, the main finding used to grade VUR was the dilatation and tortuosity of the ureter, because the pelvicaliceal morphology could have been influenced by UPJ-O.

Pyeloplasty was performed through a mini-flank laparotomy. Thereafter, the child was sent back home on antibiotic prophylaxis (in patients with ipsilateral VUR, a bladder catheter was left in place for a week). The pyelovesical stent was removed during the second post-operative week by cystoscopy.

In this series of patients, polydimethylsiloxane (Macroplastique, MPQ; Uroplasty BV, Geleen, the Netherlands)

**Table 1 Clinical characteristics according to age, sex, laterality of disease, history of UTI, bladder dysfunction, and split renal function  $\leq 45\%$  for all groups of patients**

	Group 1	Group 2	Group 3
Mean age $\pm$ SD (months)	41 $\pm$ 43	42 $\pm$ 33	41 $\pm$ 26
Sex <sup>a</sup>	11 M, 3 F	8 M, 8 F	20 M, 28 F
Laterality <sup>a</sup>	6 RT, 6 LT, 2 BIL	6 RT, 10 LT	11 RT, 22 LT, 15 BIL
UTI (%) <sup>a</sup>	27	75	61
Bladder dysfunction (%) <sup>a</sup>	9	25	39
SRF $\leq 45\%$ (%) <sup>a</sup>	45	92	80

BIL, bilateral; F, female; LT, left side; M, male; RT, right side; SRF, split renal function; UTI, urinary tract infection.

<sup>a</sup>Statistical differences between group 1 versus groups 2 and 3.

was the usual bulking agent for ET in high-grade VUR; however, dextran-hyaluronic acid (Deflux; Oceana Therapeutics Ltd., Dublin, Ireland) was also offered as an alternative implant.

Standard follow-up comprised regular renal ultrasounds every 6 months for 2 years and then every year, cystography, and, more recently, cystosonography or cystoscintigraphy after 3 months and after 1 year. A diuretic  $^{99m}\text{Tc}$  MAG3 renal scan was obtained after 2 years, unless progressive UPJ-O was suspected by a renal US. All patients were operated upon or monitored by the same surgeon who has expertise in homogeneous management and treatment.

### Statistical analysis

Statistical analysis was done using SPSS v.15 (Chicago, Illinois, USA). Quantitative data were analyzed using 1 way ANOVA test; while qualitative data were analyzed using Chi square. The difference was considered significant when *P* value was less than 0.05.

Approval of the ethical committee for this research was obtained.

### Results

Among patients with ipsilateral coexisting UPJ-O/high-grade VUR, urinary flow impairment was graded functional in 13/16 patients (81%) and obstructive in the remaining 3/16 patients (19%). In Table 1, the group-based clinical characteristics of all the three groups are reported (age at surgery, sex, affected side, history of UTI, bladder dysfunction, and SRF  $\leq 45\%$ ). Group 1 was significantly different from groups 2 and 3 with regard to sex ( $P < 0.05$ ), affected side ( $P < 0.05$ ), history of UTI ( $P < 0.01$ ), bladder dysfunction ( $P < 0.01$ ), and SRF of up to 45% ( $P < 0.01$ ). Group 2 did not show significant differences compared with group 3, except for only a slightly higher percentage of history of UTI and SRF up to 45% ( $P = \text{NS}$ ). No age differences were observed among all the three groups.

The treatment options according to the group were: (a) group 1, primary pyeloplasty (100%); (b) group 2, primary pyeloplasty, followed by ET in patients with obstructive UPJ-O (19%) or ET and observation in patients with functional UPJ-O (81%); and (c) group 3, primary ET (100%).

All patients in group 1 had an obstructive UPJ-O.

In group 2, 3/13 patients (23%) with functional UPJ-O/high-grade VUR progressed to obstructive UPJ-O and required secondary pyeloplasty. At 1-year follow-up after secondary pyeloplasty, all of them had recurrent VUR, which was successfully treated by redo ET. All children who underwent redo injection had implant displacement.

The incidence of significant UPJ-O in patients with high-grade VUR was 16/64 (25%). In this study, six (33%) of the 20 patients who underwent pyeloplasty had ipsilateral UPJ-O/high-grade VUR.

In group 3, 45/48 patients (94%) had resolution of VUR/improvement to grade 1 after ET, whereas the other three required ureteral reimplantation.

## Discussion

Our results showed that ipsilateral UPJ-O/high-grade VUR has a higher occurrence compared with what has been reported in the literature (25%). This study also showed that patients with isolated UPJ-O have clinical characteristics different from children with UPJ-O/high-grade VUR and high-grade VUR, whereas no significant differences were seen in both groups with severe VUR (group 2 vs. group 3;  $P = \text{NS}$ ). These findings support the hypothesis that UPJ-O/high-grade VUR may be an evolving process complicating the natural course of patients with severe VUR. In fact, the hypothesis based on association lacks evidence on the basis of the poor statistical probability that both diseases occur simultaneously but act independently. Most likely, causality, that is, one factor influencing the other, may explain how high-grade reflux causes UPJ-O. Previously, it has been proposed that severe reflux causes kinking of the UPJ, which becomes fixed secondary to inflammation. Criticism to this hypothesis was that, in the face of persistent reflux, hydronephrosis would persist despite pyeloplasty, and there would be a risk of recurrent obstruction. Furthermore, ureteric reimplantation would protect against progressive UPJ-O or, as an alternative, would lead to its resolution. In clinical practice, these relationships are often opposite to what is expected as a consequence of the above-mentioned hypotheses. In fact, pyeloplasty is effective despite persistent severe VUR, and treatment of VUR may cause progression from functional to obstructive UPJ-O. In our series, we observed this progression in 23% of patients. This percentage is much lower than that reported by another study in which it was observed that five children with high-grade VUR and functional UPJ-O underwent primary ureteroneocystostomy. All five children developed progressive obstruction requiring subsequent pyeloplasty [3]. In our opinion, this finding may be related to a difference in the antireflux procedure. However, this observation needs at least two answers that have not yet been provided: does ureteric reimplantation produce higher resistance at the ureterovesical junction when compared with ET? And does it (the different pressure gradient at the ureterovesical junction) influence urinary

flow at the ureteropelvic junction, especially if it was already damaged? We hypothesized that damage of the urothelial barrier could play an important role in the progression of functional hydronephrosis into an obstruction [9]. Furthermore, a higher rate of pyeloplasty has been reported in patients with associated reflux compared with patients without VUR. This observation suggests that simultaneous occurrence of UPJ-O and VUR may not be coincidental but rather the consequence of common causality and/or common pathogenesis [4].

Interestingly, all patients successfully treated for primary VUR with coexistent functional UPJ-O who subsequently underwent pyeloplasty developed VUR recurrence. To our knowledge, this finding has not been reported yet. In fact, pyeloplasty in patients with previous ureteroneocystostomy does not cause VUR recurrence. The reason why ureters treated by ET develop VUR recurrence after pyeloplasty is unknown; however, displacement of the implant may play a role. All our patients underwent successful redo ET and had an uneventful follow-up.

## Conclusion

We believe that patients with isolated UPJ-O have clinical characteristics different from those with high-grade VUR or UPJ-O/high-grade VUR wherein obstruction seems to be secondary to severe reflux. The ET of children with associated UPJ-O/high-grade VUR may be complicated by progression of urinary flow obstruction at a lower rate. VUR recurrence after pyeloplasty should be expected if reflux has been managed endoscopically.

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### Conflicts of interest

There are no conflicts of interest.

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