VURD Syndrome—Does it Really Preserve Long-Term Renal Function?

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Purpose: VURD (posterior urethral valves, unilateral vesicoureteral reflux and renal dysplasia) syndrome is the combination of persistent unilateral vesicoureteral reflux associated with an ipsilateral dysplastic, poorly functioning kidney in patients with posterior urethral valves. It was postulated that this syndrome may result in preservation of long-term renal function due to a pressure release pop-off mechanism. We determined the effects of VURD long-term renal outcomes.

Materials and Methods: We retrospectively reviewed the records of boys diagnosed with posterior urethral valves between 1983 and 2009 at a single pediatric tertiary hospital. Patients were divided into those with and those without VURD syndrome. The outcome of interest was renal impairment, defined as stage 3 or greater chronic kidney disease (glomerular filtration rate less than 60 ml/min/1.73 m^2).

Results: We identified 89 patients, of whom 23 (26%) had VURD. Median followup was 77 and 57 months in the VURD and nonVURD groups, respectively. Seven patients (30%) with and 26 (39%) without VURD had significant renal impairment. Survival analysis using a Cox proportional hazard model showed no association between VURD and renal impairment (HR 1.05, 95% CI 0.65–1.70). The main predictors of renal function were the creatinine nadir and patient age at diagnosis.

Conclusions: VURD syndrome does not seem to have a long-term protective effect on renal function.

Key Words: kidney; urethra; abnormalities; vesico-ureteral reflux; renal insufficiency, chronic

Abbreviations and Acronyms

GFR = glomerular filtration rate
PUV = posterior urethral valves
UTI = urinary tract infection
VUR = vesicoureteral reflux
VURD = posterior urethral valves, unilateral vesicoureteral reflux and renal dysplasia

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THE relationship between PUV, renal dysplasia and resultant renal impairment is well known, although the specific mechanism of dysplasia development is not fully understood.[1,2] There is much heterogeneity in long-term renal function among patients with PUV. Some require renal replacement therapy (dialysis/renal transplantation) while in others renal impairment may be minimal or absent.[3] Also, there are several known independent prognostic indicators for renal impairment associated with PUV. Bladder dysfunction, greater age at diagnosis, nadir serum creatinine greater than 88 μmol/l, bilateral grade 3 or greater VUR and recurrent febrile UTIs are predictors of poor long-term renal function.[4–7]

VURD syndrome was first identified in 1982 by Hoover and Duckett,[1]

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and described in 1983 by Greenfield et al.[8] It is defined as persistent unilateral VUR and renal dysplasia in boys with PUV.[9] It was thought that unilateral VUR would lead to dysplasia in the affected kidney while sparing the contralateral kidney, portending a potentially more favorable long-term prognosis for renal function.[9] Another 2 studies support the notion of renal protection secondary to VURD syndrome and the pop-off mechanism that it provides.[10,11] The proposed mechanism is that the ipsilateral kidney bears the brunt of increased upper tract pressure and the resultant prevention of high bladder pressure is transmitted to the nonaffected contralateral kidney.

The relationship between VURD syndrome and renal dysfunction is a controversial issue. Criticisms have been raised and the renal protective effect of VURD syndrome has been contended based on methodological issues in the mentioned studies.[10,11] It was subsequently reported that VURD syndrome might not benefit renal function outcomes as originally thought.[12]

We determined whether VURD syndrome provides protection from long-term renal impairment in boys with PUV.

MATERIALS AND METHODS

We retrospectively reviewed the records of boys diagnosed with PUV between 1983 and 2009 at a single tertiary pediatric urology institution. Patients diagnosed with PUV were divided into 2 groups for comparison, including those with and those without diagnostic criteria for VURD syndrome, in a retrospective cohort design.

The PUV diagnosis was based on a combination of cystoscopy and voiding cystourethrogram. VURD syndrome criteria were persistent, unilateral high grade (IV or V) VUR and renal dysplasia on imaging or evidence of poor ipsilateral function (less than 30%) on nuclear medicine scan. Charts were reviewed to determine which patients had renal impairment, defined as chronic kidney disease stage 3 or greater (GFR less than 60 ml/min/1.73 m^2). We used radionuclide renal scans or serum creatinine to determine GFR. When GFR was estimated based on creatinine, we used a validated, center specific equation.[13]

Several additional variables were recorded, including patient age and creatinine at diagnosis, treatment type, nadir creatinine in year 1 after treatment and UTIs. Mean followup was determined using time to the event of interest (renal impairment), defined as the initiation of renal replacement therapy in boys with renal impairment. The date of last followup was used to calculate mean followup in boys without renal impairment. Descriptive statistics were generated with measures of dispersion and centrality, as indicated. We used univariate and multivariate Cox proportional hazards with time to event and censoring as described. Statistical analysis was done using SPSS®, version 20.

RESULTS

We identified 89 patients for review who met study inclusion criteria, including 79 diagnosed prenatally. Of the patients 53 (59%) had VUR with a median grade of IV (range II to V) and 21 (24%) had bilateral VUR. All except 2 patients had bilateral moderate to severe hydronephrosis. Of these 89 patients 23 (26%) had VURD syndrome. Significant renal impairment developed in 7 of 23 patients (30%) with and 26 of 66 (39%) without VURD, although this difference failed to attain statistical significance ($p = 0.07$). Median age at diagnosis was 1 month. Mean followup was 77 months (range 2 to 184) in the VURD group and 57 months (range 1 to 239) in the nonVURD group. Table 1 lists the baseline characteristics of the 2 cohorts.

Of the 89 patients 36 (40%) underwent a form of urinary diversion vs transurethral valve ablation. The treatment modality did not affect long-term renal function ($p = 0.19$). More than 1 documented febrile UTI developed in 32 of the 89 patients (36%). Although febrile UTIs were associated with a poor renal outcome ($p < 0.001$), we did not introduce this factor into analysis because there was a high proportion of missing data.

Interestingly, we noted no association between VURD and febrile UTIs. On univariate analysis no statistically significant relationship was identified between VURD syndrome and the presence or absence of renal impairment (HR 1.05, 95% CI 0.65–1.70, see figure). On multivariate analysis younger age at diagnosis and lower nadir creatinine were independent favorable prognostic indicators of long-term renal function ($p < 0.001$, table 2).

Patients were also compared based on high grade or any grade of VUR regardless of VURD status. The presence of high or any grade reflux did not affect the renal outcome ($p = 0.5$ and 0.9, respectively).

DISCUSSION

It is well recognized that renal dysplasia is associated with renal dysfunction and ipsilateral renal dysplasia develops in patients with VURD syndrome. However, to our knowledge the effect, if any, of the pressure release pop-off mechanism on overall renal function remains unknown. It is plausible to

Table 1. *Cohort baseline characteristics*

	VURD	No VURD
Median μmol/l creatinine at birth (range)	95 (30–451)	108 (20–570)
Nadir creatinine (μmol/l)	88	82
% Febrile UTI	43	23
% Primary diversion	68	56
% Stage 3 or greater chronic kidney disease	30	39 (26 pts)