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Posterior urethral valves: Risk factors for progression to renal failure

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Summary

Introduction
Posterior urethral valves (PUVs) are the most common etiology for congenital urethral obstruction and congenital bilateral renal obstruction. PUVs produce a spectrum of urologic and renal sequelae. Our aims were to assess outcomes of PUV patients, to determine whether vesicoureteral reflux (VUR) is a risk factor for progression to renal failure, and to identify other risk factors for poor outcomes.

Materials and methods
We conducted a retrospective analysis of PUV patients from 2006 to 2014. Data collected included demographics, initial renal ultrasound (RUS) findings, creatinine at presentation and nadir, pre- and postoperative VUR status, presence or absence of recurrent urinary tract infections (UTIs), and surgical intervention(s). Univariate and multivariate analyses were used to determine risk factors for renal failure.

Results
Of 104 patients, 42.3% (44/104) were diagnosed prenatally, 31.8% (14/44) of whom underwent prenatal intervention. Postnatally, 90.4% (94/104) initially underwent transurethral resection of PUVs (TUR-PUVs). Vesicostomy was the next most common index surgery (4.8%). Forty-two percent (44/104) required >1 surgery. The predominant second surgery was repeat TUR-PUV in 16 patients. At last follow-up (mean 28.8 months after initial surgery), 20.2% had chronic kidney disease (CKD) of at least stage IIIA, and 8.6% had progressed to end-stage renal disease (ESRD). Antenatal diagnosis, prematurity, abnormal renal cortex, and loss of corticomedullary differentiation (CMD) on initial RUS were associated with CKD and ESRD on univariate analysis, as were elevated creatinine on presentation and at nadir. Presence of pre- or postoperative VUR and recurrent UTIs were associated with the need for multiple surgeries, but not with poor renal outcomes. On multivariate analysis, nadir creatinine was the only independent predictor of final renal function.

Conclusions
Our finding that creatinine is the only independent risk factor for poor renal outcomes in PUV patients is consistent with the literature. The effect of VUR has been controversial, and our finding that VUR is associated with need for multiple surgeries but not with CKD or ESRD is novel. Limitations include biases inherent to retrospective studies and relatively small sample size. The majority of patients with PUVs (56.7%) required one surgery and maintained renal function with CKD II or better (79.8%) up to 2 years after initial surgery. While multiple factors were associated with poor renal outcomes, nadir creatinine was the only independent predictor. VUR and recurrent UTIs were not associated with poor renal outcomes. Longer follow-up is necessary to identify risk factors for delayed progression of renal disease.

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Table Summary of results.

	A. Predictors of ESRD	*p*-value
Categorical	Prematurity	0.010
	Prenatal diagnosis	0.034
	Abnormal renal cortex on initial RUS	0.011
	Loss of CMD on initial RUS	<0.001
Continuous	Presenting creatinine: mean non-ESRD pts vs ESRD pts: 1.3 vs 2.9	<0.001
	Nadir creatinine: mean non-ESRD pts vs ESRD pts: 0.4 vs 2.7	<0.0001
	B. Predictors of CKD	*p*-value
Categorical	Prematurity	0.038
	Prenatal diagnosis	0.014
	Abnormal renal cortex on initial RUS	<0.001
	Loss of CMD on initial RUS	<0.001
Continuous	Presenting creatinine: mean non-ESRD pts vs ESRD pts: 1.3 vs 2.9	<0.0001
	Nadir creatinine: mean non-ESRD pts vs ESRD pts: 0.4 vs 2.7	<0.0001
	C. Predictors of >1 surgery	*p*-value
Categorical	Prematurity	0.028
	Prenatal diagnosis	0.027
	Symptomatic presentation	0.048
	Recurrent UTIs	<0.001
	Pre-op VUR	0.006
	Post-op VUR	0.049
	Loss of CMD	<0.001

CKD, chronic kidney disease; CMD, corticomedullary differentiation; ESRD, end-stage renal disease; RUS, renal ultrasound; UTIs, urinary tract infections; VUR, vesicoureteral reflux.

Introduction

Posterior urethral valves (PUVs) represent the most common etiology for congenital urethral obstruction and the most common congenital cause for bilateral renal obstruction [1,2]. With an estimated incidence of 1/5000 to 1/8000 male births [1], they account for 10% of all prenatally diagnosed urinary obstructions [2]. PUVs produce a spectrum of urologic and renal sequelae. Severe urethral obstruction is a devastating congenital anomaly that can be lethal *in utero* and in the perinatal period [2]. Patients with severe disease often require multiple surgical interventions and may develop long-term complications, including urinary incontinence and loss of renal function [2]. In contrast, mild cases may be nearly subclinical, presenting later in childhood with subtle signs and symptoms. A single surgery may be curative in these cases, with no apparent long-term complications. Predicting outcomes in patients with PUVs remains challenging. To investigate this issue, we assessed outcomes of patients presenting to our institution with PUVs, focusing on the number of surgical interventions required and risk factors for progression to chronic kidney disease (CKD) or end-stage renal disease (ESRD). Proposed risk factors in the literature include abnormalities on presenting renal ultrasound (RUS), elevated creatinine at presentation and at nadir, and presence of vesicoureteral reflux (VUR), although data on the latter have been mixed. We hypothesized that each of these factors would be associated with worse renal function at last follow-up.

Materials and methods

We performed a retrospective analysis of patients presenting with PUVs from 2006 to 2014. Of 208 charts identified by the ICD-9 code, 60 were excluded because they were not cases of PUVs. Of the remaining 148 patients, 44 were excluded because of chart incompleteness and/or lack of follow-up. The remaining 104 charts were reviewed in detail and used for statistical analysis. Data collected for each patient included timing and mode of presentation, creatinine and RUS findings at presentation, pre- and postoperative VUR status, nadir creatinine, type and number of surgeries performed, and renal function at last follow-up. Estimated glomerular filtration rate (eGFR) was calculated from creatinine using the modified Schwartz formula whenever patient height was known [3].

Univariate and multivariate analyses were performed using SAS 9.3 software. Categorical variables were analyzed using Fisher's exact test. Continuous variables were analyzed using Wilcoxon rank-sum and Kruskall—Wallis tests. As eGFR is calculated from creatinine, we could not include both in the multivariate analysis. We elected to include creatinine, as more patients had these data available. Events of interest were relatively rare and were not even observed for some of the categorical variables; therefore, we were unable to include all variables that were significant on univariate analysis into a single multivariate model for each outcome. Instead, we performed multivariate analyses by including the two continuous variables of interest (presenting creatinine and nadir