Published in final edited form as:

J Pediatr Urol. 2016 June ; 12(3): 179.e1–179.e7. doi:10.1016/j.jpuro.2015.10.009.

Posterior urethral valves: risk factors for progression to renal failure

Aylin N. Bilgutay^{a,b}, David R. Roth^{a,b}, Edmond T. Gonzales Jr.^{a,b}, Nicolette Janzen^{a,b}, Wei Zhang^a, Chester J. Koh^{a,b}, Patricio Gargollo^{a,b}, and Abhishek Seth^{a,b,*}

^a Texas Children's Hospital, Houston, TX, USA

^b Scott Department of Urology, Baylor College of Medicine, Houston, TX, USA

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.

* Corresponding author. Baylor College of Medicine/Texas Children's Hospital, Clinical Care Center, Suite 620, 6701 Fannin Street, Houston, Texas, 77030–2399 aseth@bcm.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflict of interest

Chester Koh, MD is an advisory board member for HD Sono, Inc. The remaining authors have no conflicts of interest to declare.

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.

Keywords

Urethra; Urethral obstruction; Prenatal diagnosis; Patient outcome assessment

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 Kruskal-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 creatinine) with a single categorical variable at a time, resulting in multiple multivariate analyses per outcome. We applied the Firth logistic regression for bias reduction of maximum likelihood estimates to correct for the rarity of certain events [4,5]. All tests were two-tailed, with findings considered significant at $p < 0.05$.

Ethical approval

IRB approval was obtained for this study (protocol number H-33575).

Results

Of 104 patients meeting inclusion criteria, 42.3% (44/104) were diagnosed with PUVs antenatally. A further 10.6% had abnormal prenatal ultrasounds leading to postnatal workup, but had an incorrect or no specific diagnosis prior to birth. These patients were not considered to have been prenatally diagnosed. Fourteen patients underwent prenatal intervention, representing 31.8% (14/44) of those antenatally diagnosed and 13.5% (14/104) of our entire cohort. Shunt placement (vesicoamniotic and/or vesico-peritoneal) was the most common prenatal intervention; this was performed in 10 patients, with or without additional interventions. Several patients required more than one shunt. Two patients underwent attempted PUV ablation *in utero* prior to shunting, one complicated by prostatic fistula that eventually resolved on its own. Three patients underwent antenatal diagnostic vesicocentesis alone, and one patient underwent amnioinfusion alone.

Sixty patients in our cohort were diagnosed postnatally, 78.3% (47/60) during infancy. The mean age at diagnosis for these patients was 16.2 months (median 2, range 0–155). Twenty-six patients presented with UTI, representing 43.3% of those diagnosed postnatally and 25% of the entire cohort. Eighty-one percent (21/26) of presenting UTIs were febrile. Additional modes of postnatal presentation included AKI and/or electrolyte abnormalities in 10.6% of our cohort (11/104), lower urinary tract symptoms 3.8%, abdominal distension in 1.9%, hypertension in 1%, and bladder stone in 1%. The remaining patients were asymptomatic, with 10.6% diagnosed on workup for abnormal prenatal RUS in the absence of prenatal diagnosis of PUVs, 2.9% diagnosed incidentally on workup for non-genitourinary anomalies, and 1% diagnosed on VCUG performed because of siblings with VUR.

Thirty-three percent of patients in our cohort were born prematurely (defined as birth prior to 37 weeks gestation), 57.7% were term, and 9.6% were born at unknown gestational age. Of 34 premature patients in our cohort, 11 (32.4%) had undergone prenatal intervention, and 78.6% (11/14) of those who had undergone prenatal intervention were born prematurely.

Our patient population was ethnically diverse. Twenty-five percent (26/104) were Hispanic, 18.3% African American, 15.4% Caucasian, 2.9% Asian/Pacific, 2.9% African, and 1.9% multiracial not otherwise specified (NOS). Twenty-eight percent were non-Hispanic NOS, and 5.8% were of unknown ethnicity. Additional patient characteristics are presented in Table 1.

All patients underwent surgery postnatally, except one with prenatal diagnosis and intervention who died in the neonatal period. Seventy-seven percent (80/104) were circumcised. The mean number of surgeries per patient was 1.68 (median 1, range 0–6). The mean length of follow-up after initial surgery was 28.8 months (median 21.2). Ninety percent (94/104) underwent TUR-PUVs as the initial operation. Vesicostomy was the second most common index surgery, performed in 4.8% (5/104). Three patients underwent cystoscopy and foley placement without formal TUR-PUV in the same setting, one patient underwent bilateral cutaneous ureterostomies as primary surgery, and one patient died before having any surgeries, as previously mentioned. Forty-two percent of patients required more than one operation, with the most common second surgery being repeat TUR-PUV in 16 patients. The next most common second surgery was nephrectomy or nephroureterectomy in eight patients for nonfunctioning kidney (considered to be <10% differential function) in the setting of recurrent UTIs, followed by ureteral reimplantation in seven patients. Antibiotic prophylaxis constituted medical management for VUR. Threshold for surgical intervention is surgeon-dependent. However, in our practice, at least one UTI while on antibiotics is generally considered indication for further workup and/or surgery. Twelve patients required at least one anti-reflux procedure; 10 underwent unilateral or bilateral reimplantation at some point in their disease course, and the other two were managed solely endoscopically. Surgical technique for VUR management was at the surgeon's discretion; however, formal reimplant is generally considered to be indicated in our practice in the setting of higher grade VUR (grade III) or when endoscopic management has failed. At last follow-up, 20.2% (21/104) had CKD of at least stage IIIA, and 8.6% (9/104) had progressed to ESRD, defined as CKD stage V or need for renal replacement therapy.

Univariate analysis

Prematurity, antenatal diagnosis, and unilateral or bilateral loss of CMD were associated with significantly higher rates of CKD, ESRD, and need for multiple surgeries (Table 2). Bilaterally abnormal renal cortex (defined as increased echogenicity or dysplastic appearance on RUS) and bilateral pneumothoraces on presentation were associated with significantly higher rates of CKD and ESRD. Symptomatic presentation, recurrent UTIs (defined as at least two culture-proven UTIs with >100K organisms in 1 year), pre-op VUR, and post-op VUR were associated with need for more than one surgery, but not with poor renal outcomes. Presenting and nadir creatinine, along with their corresponding eGFRs, were all significant predictors of poor renal outcomes but not of need for multiple surgeries (Table 3). Presenting creatinines were obtained from at least day of life 3 to avoid results more reflective of maternal creatinine.

Multivariate analysis

Nadir creatinine was found to be the only independent predictor in each trivariate analysis for the outcome of ESRD, with p -values ranging from 0.0018 to 0.0054 (data not shown). This was also true for CKD, with all p -values < 0.001 . Multivariate analyses were also performed for the outcome of multiple surgical interventions. Of all the categorical variables examined for this outcome, only history of recurrent UTI was significant, with $p=0.013$. Nadir creatinine was not a significant predictor of number of surgeries on six of seven multivariate analyses performed, with p -values ranging from 0.064 to 0.14. However, nadir creatinine did appear to be a statistically significant predictor of needing more than one surgery on one of the trivariate analyses performed for this outcome ($p=0.0354$). This is of unclear clinical significance, as nadir creatinine was not a significant risk factor for this outcome on univariate analysis.

Discussion

Survival of PUV patients has improved in recent decades, while morbidity remains high in spite of advances in prenatal detection and intervention. Quality of life is paramount in any disease process, and in patients with PUVs, long-term renal function represents a vital determinant of this. Nadir creatinine after operative intervention for PUVs is a well-known predictor of long-term renal function [6–8]. On multivariate analysis of factors affecting final renal outcome, we found nadir creatinine to be the only independent prognostic factor. This was also noted by Sarhan *et al.* in 2011 [8]. Different nadir creatinine cutoffs have been suggested for use in predicting long-term renal outcomes, most commonly 1.0 [7,8] or 0.8 [9,10]. Sensitivity and specificity will vary with the cutoff chosen; however, it is clear that increasing nadir creatinine is associated with worse long-term renal outcomes.

Elevated presenting creatinine has also been associated with poor renal outcomes [7,8,10]. In 1997, Denes *et al.* proposed creatinine at initial treatment as a predictor for long-term renal function [10]. In their cohort of 35 PUV patients, they demonstrated that those who progressed to CKD had significantly higher creatinines not only at nadir, but also at presentation and after catheterization when compared with patients with preserved renal function at last follow-up. Linear regression analysis of creatinine after catheterization versus GFR at last follow-up revealed a correlation coefficient of -0.7 ($p<0.01$). Our data similarly demonstrate an association between creatinine at presentation and final renal function. Patients who presented with the highest creatinines tended to have higher nadir creatinines and poor long-term renal outcome.

ESRD rates reported in the literature for PUV cohorts vary widely, ranging from 5.8 to 29% [6,11,15]. Heikkilä *et al.* recently published outcomes of 193 Finnish PUV patients followed to a median of 31 years of age [15]. Only 14.5% of the patients in their cohort were diagnosed prenatally, which is much lower than the 42.3% rate of antenatal diagnosis seen in our series. This may be partly because their study included patients treated several decades earlier. Furthermore, they only included patients treated up to 2003, as they were only interested in evaluating patients followed into adulthood. The rate of ESRD in their cohort was 22.8%. While this is significantly higher than our rate of 8.6%, their follow-up was

much longer, with onset of renal failure after age 17 seen in a third of ESRD cases. This emphasizes the importance of lifelong follow-up for PUV patients.

The effect of prenatal diagnosis has been controversial, with some authors suggesting improved outcomes with prenatal diagnosis [16,17]. In contrast, Heikkilä *et al.* found that patients diagnosed prenatally had a higher risk of progressing to ESRD, consistent with our data [15]. Failure of prenatal diagnosis to improve outcomes has been observed in multiple studies over the years [13,18-21], likely because more severe disease is more likely to be picked up prenatally. We suspect that only the mildest forms will not be caught antenatally if all expectant mothers have equal access to routine prenatal screening. Perhaps studies where prenatal diagnosis was protective were confounded by inconsistent access to prenatal screening. Varying rates of elective pregnancy termination may also be a confounding factor. These rates are uncommonly reported, likely because they are unknown (as in our study). However, elective pregnancy termination has been reported in up to 46% of cases in some PUV cohorts [22], and are not performed at all in others for legal and/or religious reasons [17].

The relationship between VUR and long-term renal function has been unclear. Some authors have reported an association between VUR and poor renal outcomes [6,13,15], while other series have revealed no significant association [8,11]. Our data indicate that patients with VUR are more likely to require multiple surgical interventions, as might be expected when using breakthrough UTI as indication for surgery; however, there was no association with long-term renal function. Renal parenchymal changes on initial RUS have been shown by some authors to be predictive of final renal function [8], while other series have contradicted this finding [14]. Our series supports the conclusion that renal parenchymal changes on initial RUS are predictive of final renal function. This is not surprising, as these sonographic findings in PUV patients may indicate the concomitant presence of irreversible congenital renal dysplasia.

In addition to long-term renal function, the number of operations required to treat PUVs and their sequelae also represents an objective outcome that is relatively easy to assess through chart review and may have quality of life implications for the patient and patient's family. Reoperation rates have been widely studied for many urological interventions, including transurethral incision of ureteroceles [23-25] and proximal hypospadias repair [26-28]. To our knowledge, reoperation rates in PUV cohorts and types of repeat surgeries required have not been reported. The majority of patients in our series (56.7%) underwent a single surgery, and median number of surgeries required was 1 (mean 1.68). Forty-two percent of the patients in our series required more than one surgery, with a maximum of six total related operations required in two patients. The most common reason for second surgery was inadequate PUV resection with evidence of persistent urethral obstruction on postoperative VCUG, leading to repeat TUR-PUV in 16 patients. Predictors of need for more than one surgical intervention included symptomatic presentation, recurrent UTIs, preoperative VUR, and postoperative VUR.

Our study has several limitations. It is retrospective in nature, and includes a relatively small number of patients at a single institution. Although our cohort is ethnically diverse, it is

unclear whether our results are generalizable to other institutions. Patients with inadequate charts or lack of follow-up were excluded, which may be a source of bias. Despite our efforts to include only patients with adequate charts, every patient did not have every study of interest, decreasing the effective sample size when analyzing certain variables and representing another potential source of bias. Longer follow-up is necessary to identify patients at risk for delayed loss of renal function.

Conclusions

Our data underscore the importance of considering multiple variables when evaluating a patient with PUVs. Variables predictive of long-term renal outcomes include presenting creatinine, nadir creatinine, and abnormal renal parenchyma or CMD on initial RUS. On multivariate analysis, elevated nadir creatinine was the only independent risk factor for poor renal outcomes. Importantly, our data indicate that VUR and recurrent UTIs are not associated with worse renal outcomes, although these parameters remain vital in guiding treatment and may influence the number of surgeries a patient undergoes. These findings are invaluable in the counseling of patient families. Further investigation and longer follow-up are needed to identify patients at risk for late progression to CKD or ESRD and to elucidate the effects of potentially modifiable risk factors, such as bladder dysfunction.

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

C. Predictors of >1 surgery	p-value
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.

Acknowledgments

Funding

None.

References

1. Krishnan A, de Souza A, Konijeti R, Baskin LS. The anatomy and embryology of posterior urethral valves. *J Urol*. 2006; 175(4):1214–20. [PubMed: 16515962]
2. Casale, AJ. Posterior Urethral Valves.. In: Kavoussi, LR.; Novick, AC.; Partin, AW.; Peters, CA.; Wein, AJ., editors. *Campbell-Walsh Urology*. 10th ed.. Vol. 4. Elsevier Saunders; Philadelphia: 2012. p. 3389-410.
3. Schwartz GJ, Muñoz A, Schneider MF, Mak RH, Kaskel F, Warady BA, Furth SL. New equations to estimate GFR in children with CKD. *J Am Soc Nephrol*. 2009; 20(3):629–37. [PubMed: 19158356]
4. Firth D. Bias Reduction of Maximum Likelihood Estimates. *Biometrika*. 1993; 80:27–38.
5. Heinze G, Schemper M. A solution to the problem of separation in logistic regression. *Stat Med* 30. 2002; 21(16):2409–19.
6. Ansari MS, Gulia A, Srivastava A, Kapoor R. Risk factors for progression to end-stage renal disease in children with posterior urethral valves. *J Pediatr Urol*. 2010; 6(3):261–4. [PubMed: 19833558]
7. Sarhan O, El-Dahshan K, Sarhan M. Prognostic value of serum creatinine levels in children with posterior urethral valves treated by primary valve ablation. *J Pediatr Urol*. 2010; 6(1):11–14. [PubMed: 19581129]
8. Sarhan OM, El-Ghoneimi AA, Helmy TE, Dawaba MS, Ghali AM, Ibrahim el HI. Posterior urethral valves: multivariate analysis of factors affecting the final renal outcome. *J Urol*. 2011; 185(6 Suppl):2491–5. [PubMed: 21555022]
9. Warshaw BL, Hymes LC, Trulock TS, Woodard JR. Prognostic features in infants with obstructive uropathy due to posterior urethral valves. *J Urol*. 1985; 133(2):240–3. [PubMed: 3968741]
10. Denes ED, Barthold JS, Gonzalez R. Early prognostic value of serum creatinine levels in children with posterior urethral valves. *J Urol*. 1997; 157(4):1441–3. [PubMed: 9120976]
11. Kousidis G, Thomas DF, Morgan H, Haider N, Subramaniam R, Feather S. The long-term outcome of prenatally detected posterior urethral valves: a 10 to 23-year follow-up study. *BJU Int*. 2008; 102(8):1020–4. [PubMed: 18485035]
12. Kibar Y, Ashley RA, Roth CC, Frimberger D, Kropp BP. Timing of posterior urethral valve diagnosis and its impact on clinical outcome. *J Pediatr Urol*. 2011; 7(5):538–42. [PubMed: 20829118]
13. Ylinen E, Ala-Houhala M, Wikstrom S. Prognostic factors of posterior urethral valves and the role of antenatal detection. *Pediatr Nephrol*. 2004; 19(8):874–9. [PubMed: 15179564]
14. Sarhan O, Zaccaria I, Macher MA, Muller F, Vuillard E, Delezoide AL, et al. Long-term outcome of prenatally detected posterior urethral valves: single center study of 65 cases managed by primary valve ablation. *J Urol*. 2008; 179(1):307–12. discussion 312–13. [PubMed: 18006017]
15. Heikkilä J, Holmberg C, Kyllonen L, Rintala R, Taskinen S. Long-term risk of end stage renal disease in patients with posterior urethral valves. *J Urol*. 2011; 186(6):2392–6. [PubMed: 22014822]
16. Dinneen MD, Dhillon HK, Ward HC, Duffy PG, Ransley PG. Antenatal diagnosis of posterior urethral valves. *Br J Urol*. 1993; 72(3):364–9. [PubMed: 8220998]

17. Sarhan OM, Helmy TE, Alotay AA, Alghanbar MS, Nakshabandi ZM, Hafez AT. Did antenatal diagnosis protect against chronic kidney disease in patients with posterior urethral valves? A multicenter study. *Urology*. 2013; 82(6):1405–9. [PubMed: 24139350]
18. Reinberg Y, de Castano I, Gonzalez R. Prognosis for patients with prenatally diagnosed posterior urethral valves. *J Urol*. 1992; 148(1):125–6. [PubMed: 1613851]
19. Jee LD, Rickwood AM, Turnock RR. Posterior urethral valves. Does prenatal diagnosis influence prognosis? *Br J Urol*. 1993; 72(5 Pt 2):830–3. [PubMed: 8080495]
20. El-Ghoneimi A, Desgrippes A, Luton D, Macher MA, Guibourdenche J, Garel C, et al. Outcome of posterior urethral valves: to what extent is it improved by prenatal diagnosis? *J Urol*. 1999; 162(3 Pt 1):849–53. [PubMed: 10458394]
21. Abbo O, Bouali O, Ballouhey Q, Mouttalib S, Lemandat A, Decramer S, et al. [Is there an outcome difference between posterior urethral valves diagnosed prenatally and postnatally at the time of antenatal screening?]. *Prog Urol*. 2013; 23(2):144–9. [PubMed: 23352308]
22. Cromie WJ, Lee K, Houde K, Holmes L. Implications of prenatal ultrasound screening in the incidence of major genitourinary malformations. *J Urol*. 2001; 165(5):1677–80. [PubMed: 11342955]
23. Di Renzo D, Ellsworth PI, Caldamone AA, Chiesa PL. Transurethral puncture for ureterocele- which factors dictate outcomes? *J Urol*. 2010; 184(4 Suppl):1620–4. [PubMed: 20728127]
24. Jesus LE, Farhat WA, Amarante AC, Dini RB, Leslie B, Bägli DJ, et al. Clinical evolution of vesicoureteral reflux following endoscopic puncture in children with duplex system ureteroceles. *J Urol*. 2011; 186(4):1455–8. [PubMed: 21862045]
25. Sander JC, Bilgutay AN, Stanasel I, Koh CJ, Janzen N, Gonzales ET, et al. Outcomes of endoscopic incision for the treatment of ureterocele in children at a single institution. *J Urol*. 2015; 193(2):662–6. [PubMed: 25167992]
26. Arshad AR. Hypospadias repair: Byar's two stage operation revisited. *Br J Plast Surg*. 2005; 58(4): 481–6. [PubMed: 15897031]
27. Stanasel I, Le HK, Bilgutay A, Roth DR, Gonzales ET Jr, Janzen N, et al. Complications following Staged Hypospadias Repair Using Transposed Preputial Skin Flaps. *J Urol*. 2015; 194(2):512–16. [PubMed: 25701546]
28. Yang T, Zou Y, Zhang L, Su C, Li Z, Wen Y. Byars two-stage procedure for hypospadias after urethral plate transection. *J Pediatr Urol*. 2014; 10(6):1133–7. [PubMed: 24931759]

Table 1

Patient characteristics

Variable	N	Mean	Range
Gest age at birth, in weeks, if known (for premature pts)	33	33.7	25.0–36.9
Presenting Cr, if known	92	1.5	0.2–7.3
Presenting eGFR, if known	71	31.5	3.1–132.2
Nadir Cr, if known	88	0.6	0.2–7.1
Max eGFR, if known (eGFR at time of nadir Cr)	64	76.1	4.1–198.2
Most recent postop Cr, if checked (for those not on renal replacement therapy)	86	0.5	0.1–3.7
Most recent postop eGFR, if known (for those not on renal replacement therapy)	70	93.4	7.6–247.8

Table 2

Univariate analysis, categorical variables

Variable	ESRD?			CKD?			# surgeries		
	No	Yes	<i>p</i> -value*	No	Yes	<i>p</i> -value*	1	>1	<i>p</i> -value*
	<i>N</i>	<i>N</i>		<i>N</i>	<i>N</i>		<i>N</i>	<i>N</i>	
Prematurity	27	7	0.010	22	12	0.038	13	20	0.028
Prenatal diagnosis	37	7	0.034	30	14	0.014	19	24	0.027
Prenatal intervention	10	4	0.18	7	7	0.095	6	7	1
Symptomatic presentation	45	2	0.18	40	7	0.33	32	15	0.048
Presented with infection	26	0	0.11	23	3	0.27	17	9	0.37
Recurrent UTIs	14	2	0.63	12	4	0.73	3	13	0.00089
Pre-op VUR, unilateral	28	2		25	5		15	15	
Pre-op VUR, bilateral	18	3	0.53	14	7	0.17	8	13	0.006
Post-op VUR, unilateral	22	1		21	2		10	13	
Post-op VUR, bilateral	21	2	0.84	15	8	0.076	9	14	0.0495
Hydronephrosis, unilateral	13	0		12	1		9	4	
Hydronephrosis, bilateral	71	8	0.71	61	18	0.55	40	38	0.077
ARC, unilateral	12	0		11	1		7	5	
ARC, bilateral	42	9	0.011	33	18	0.00047	24	26	0.0798
Loss of CMD, unilateral	8	0		7	1		1	7	
Loss of CMD, bilateral	27	9	0.0002	21	15	0.00052	15	20	0.00011
Bladder tic and/or patent urachus	49	5	0.72	43	11	1	28	26	0.23
Ascites	12	0	0.59	12	0	0.065	6	6	0.76
Urinoma	3	0	1	2	1	0.51	1	2	0.58
pneumothorax, unilateral	2	0		2	0		1	1	
pneumothorax, bilateral	1	2	0.029	0	3	0.013	0	2	0.34

ARC = abnormal renal cortex.

Table 3

Univariate analysis, continuous variables

Variable	ESRD?					CKD?				
	No		Yes		<i>p</i> -value	No		Yes		<i>p</i> -value
	<i>N</i>	Mean ± SD	<i>N</i>	Mean ± SD		<i>N</i>	Mean ± SD	<i>N</i>	Mean ± SD	
Gest age at birth, in weeks, if known (for premature pts)	26	34.0 ± 2.61	7	32.4 ± 2.23	0.059	21	34.1 ± 2.74	12	32.9 ± 2.18	
Presenting Cr, if known	83	1.34 ± 1.21	9	2.89 ± 1.73	0.0002	71	1.24 ± 1.26	21	2.35 ± 1.26	
Presenting eGFR, if known	65	33.6 ± 32.0	6	7.97 ± 1.42	0.0009	54	37.7 ± 33.5	17	11.7 ± 7.71	
Nadir Cr, if known	79	0.39 ± 0.18	9	2.66 ± 1.95	<0.0001	67	0.35 ± 0.14	21	1.49 ± 1.62	
Max eGFR, if known (eGFR at time of nadir Cr)	57	83.9 ± 38.4	7	12.5 ± 8.51	<0.0001	47	92.1 ± 36.9	17	31.8 ± 20.6	