Original Article

Short-Term Outcomes of Treatment of Boys with Posterior Urethral Valves

Abdulrasheed A. Nasir[1], Adewale O. Oyinloye[1], Lukman O. Abdur-Rahman[1], Kayode T. Bamigbola[2], Nurudeen T. Abdulraheem[1], Olanrewaju T. Adedoyin[3], James O. Adeniran[1]

[1]Department of Surgery, Division of Paediatric Surgery, University of Ilorin/University of Ilorin Teaching Hospital, Ilorin, Nigeria, [2]Department of Surgery, Federal Medical Center, Owo, Nigeria, [3]Department of Paediatric, Division of Nephrology, University of Ilorin/University of Ilorin Teaching Hospital, Ilorin, Nigeria

Abstract

Background: Posterior urethral valve (PUV) is a significant cause of morbidity and mortality among male children resulting in renal failure in 25%–30% before adolescence irrespective of initial treatment. This study aimed at evaluating the early outcomes of children managed for PUV. **Materials and Methods:** This was a prospective study of all children who were treated for PUV between 2012 and 2016 at a single referral institution. Information reviewed included demographic and clinical data, imaging findings, pre- and post-operative serum electrolytes, and postoperative renal outcomes. **Results:** Twenty-nine male children were managed for PUV at a median age of 6 months including 7 (24.1%) neonates. Two (6.9%) patients had antenatal diagnosis. Micturating cystourethrogram confirmed PUV in all patients. Fourteen (48.3%) patients had impaired renal function (IRF) at presentation and 8 (57%) had improved renal function (RF) after initial catheter drainage. The mean creatinine at presentation was 1.86 ± 1.69 mg/dl and the mean serum creatinine following initial catheter drainage was 0. 93 ± 0.49 mg/dl ($P = 0.003$). For those patients with normal RF, the mean creatinine at presentation was 0.81 ± 0.22 mg/dl versus 0.74 ± 0.21 mg/dl ($P = 0.012$), following initial catheter drainage. Children with IRF on admission had mean creatinine at presentation of 2.61 ± 2.00 mg/dl compared to 1.17 ± 0.53 mg/dl ($P = 0.002$) after initial catheter drainage. Valve ablation was achieved with Mohan's valvotome in 26 (96.3%) patients. All patients had good urine stream at a median follow-up of 5 months. Four (13.8%) patients developed IRF at follow-up. Renal outcomes of patients presenting before 1 year and those presenting after 1 year were similar. Two children died preoperative of urosepsis and one out of hospital death given an overall mortality of 10.3% ($n = 3$). **Conclusion:** There was significant improvement in RF after initial catheter drainage. The incidence of IRF at follow-up was 13.8%. Long-term follow-up is necessary to identify patients at risk of end-stage renal disease.

Keywords: Congenital obstructive posterior urethral membrane, posterior urethral valves, renal impairment, vesicoureteric reflux

Introduction

Posterior urethral valve (PUV) is the most common cause of bladder outlet obstruction in male children with recent study suggesting an incidence of about 1:2500–4000 male births.[1] The incidence is unknown in Africa; however, hospital-based studies reported an average of 5–15 cases per annum.[2-4]

PUVs continue to be a significant cause of morbidity, mortality, and ongoing disability among male children, resulting in renal failure in 25%–30% of cases of PUV before adolescence.[5] Moreover, many patients with stable renal function (RF) in childhood may progress into end-stage renal failure after puberty.[5,6] The morbidity associated with PUV extends beyond childhood through adolescence and into adult life, irrespective of the apparent success of initial treatment.[6,7] Early diagnosis and intervention is necessary to reduce urostasis and to stabilize upper tract as a vital step to delay or prevent progression to renal insufficiency.

Valve ablation is the treatment of choice for patients with PUV, and the potential for recovering of RF is believed to be significant after relief of obstruction. However, long-term

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Address for correspondence: Dr. Abdulrasheed A. Nasir, Department of Surgery, University of Ilorin/University of Ilorin Teaching Hospital, Ilorin, Nigeria.
E-mail: draanasir@yahoo.com

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renal and bladder dysfunction remains a concern in children with PUV. The risk of poor RF has been linked to several factors, including patient age at presentation, prenatal diagnosis, vesicoureteral reflux (VUR), serum creatinine at presentation, nadir serum creatinine after bladder drainage, and nadir creatinine during the 1st year of life.[4,6,8,9] Whether early presentation is associated with improved outcome or not is a matter of ongoing controversies.[10-12]

The purpose of the present study was to assess the short-term functional outcome of patients with PUV at our center. In addition, we sought to evaluate the possible impact of serum creatinine and age at presentation on renal outcome.

Materials and Methods

Consecutive children managed for PUV between 2012 and 2016 at our institution were prospectively studied. Patients with clinical suspicion of PUV without radiological confirmation were excluded. The preoperative evaluation included history, clinical examination, RF assessment with serum electrolytes (urea and creatinine), urinalysis, and urine culture. Initial renal ultrasonography was done and empirical antibiotics (Unasyn 150 mg/kg) were commenced. At admission, catheter drainage of the bladder was achieved by passing a transurethral (nonballoon) feeding tube (size 5 or 6 Fr gauge). Voiding cystourethrogram was done when patients became clinically stable. Voiding cystourethrogram showing dilated and elongated posterior urethra and radiolucent valve cusps was considered diagnostic of PUV [Figure 1]. After stabilization of RF and correction of electrolytes and acid base imbalances, patients were taken for cystoscopy [Figure 2a]. Primary valve ablation was done using Mohan's valvotomy[13] in all cases except one patient that had electrocautery fulguration with Bugbee electrode. Adequacy of ablation was checked by applying suprapubic pressure on the bladder filled with saline to observe the caliber and force of urine stream. This was followed by a check cystoscopy [Figure 2b]. After valve ablation, the urethral catheter was left *in situ* for 72 h to allow edema to subside. Urine output was monitored and intravenous fluids were given equal to urinary output plus insensible loss of the previous hour till diuresis subsided. Electrolytes and serum creatinine were also monitored. The patients were observed voiding after the removal of the urethral catheter and at the follow-up visit at the outpatient clinic. Patients were discharged with antibiotic prophylaxis. Postvoid residual urine volume (PVR) was monitored by abdominal ultrasound done 4-week postoperative and then every 3 months. Patients with significant PVR (>10% of expected bladder capacity) were placed on doxazosin (an α adrenergic blocker) 0.5 mg/kg/day. The grade of hydronephrosis by ultrasound was not consistent and therefore excluded from analysis. Primary outcomes were death and serum creatinine <1.2 mg/dl at the last follow-up. Other outcome measures included improvement in RF after initial catheter drainage, good urine stream after valve ablation, and bladder emptying. Renal outcome was defined as favorable when serum creatinine was normal and impaired when ≥1.2 mg/dl (106 μmol/L).

Analysis

Statistical analysis was performed using IBM-SPSS Statistics 21.0 (SPSS, Inc., Chicago, IL, USA). Values were expressed as proportion, means ± standard deviation, median, and interquartile range. Continuous variables were compared with Student's *t*-test or Mann–Whitney U test as appropriate, and discrete variables were analyzed with Chi-square test and Fisher's exact test where appropriate. All statistical tests were two sided. $P \leq 0.05$ was considered statistically significant.

Results

Twenty-nine male children were managed for PUV over the 5-year period; the median age at presentation was 6 months, range 3 days to 9 years. There were 7 (24.1%) neonates and 12 (41.4%) infants. Table 1 summarizes the demographic and clinical characteristics of the patients. Twenty-eight (96.6%) of the patients presented with poor urinary stream, 11 (37.9%)

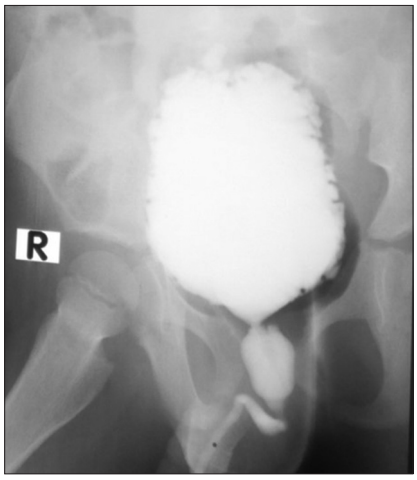

Figure 1: Micturating cystourethrogram of a child with posterior urethral valve demonstrating elongated and dilated posterior urethral, and irregularity of the bladder wall from trabeculations

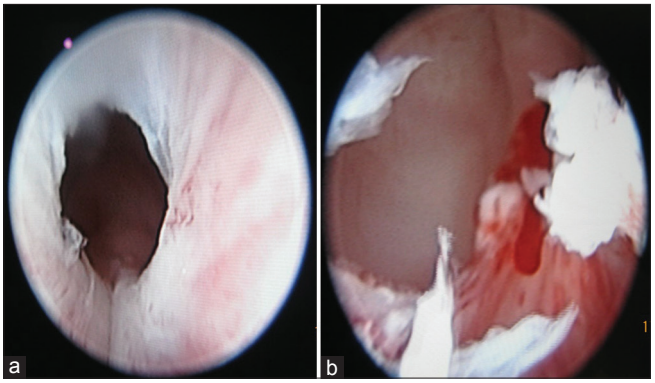

Figure 2: (a) Urethrocystoscopic view of a child with posterior urethral valve demonstrating obstructing posterior urethral valve arising from verumontanum, Type 1, (b) Urethrocystoscopic view after valve ablation showing torn valves

recurrent urinary tract infection, 11 (37.9%) urosepsis, 9 (31%) with dribbling of urine, and 5 (17.2%) patients with hematuria.

Two (6.9%) patients were diagnosed in the antenatal period; one patient was referred to us after initial vesicostomy, valve ablation, and bladder closure with recurrent features of obstruction and the other child presented for the evaluation of PUV suspected antenatally. Voiding cystourethrogram confirmed PUV in all patients. All the patients had bilateral hydronephrosis at presentation. Vesicoureteric reflux (VUR) was present in 13 (44.8%) patients and was unilateral in 10 (7 right and 3 left) and bilateral in 3, representing 16 renal units. Fourteen (48.3%) patients had impaired RF (IRF) at presentation. Eight (57%) of these patients had improved RF after initial catheter drainage, $P = 0.004$. An 11-month-old patient who had renal failure at presentation had peritoneal dialysis preoperatively for 3 months before definitive ablation. The mean creatinine at presentation was 1.86 ± 1.69 mg/dl and the mean serum creatinine following initial catheter drainage was 0. 93 ± 0.49 mg/dl ($P = 0.003$). For those with normal RF, the mean creatinine at presentation was 0.81 ± 0.22 mg/dl and the mean serum creatinine following initial catheter drainage was 0. 74 ± 0.21 mg/dl ($P = 0.012$). Children with IRF on admission had mean creatinine at presentation of 2.61 ± 2.00 mg/dl and the mean serum creatinine following initial catheter drainage dropped to 1.17 ± 0.53 mg/dl ($P = 0.002$).

Table 1: Clinical and demographic characteristics of patients

Variables	*n* (%)
Number of patient	29
Age	
Less 1 month	7 (24.1)
1-12 months	10 (34.5)
>1 year	12 (41.4)
Presentation	
Poor steam	28 (96.6)
Urinary tract infection	11 (37.9)
Urosepsis	11 (37.9)
Dribbling of urine	9 (31.0)
Haematuria	5 (17.2)
Hypertension	3 (10.3)
Mortality	
Preoperative death	2 (6.9)
Out of hospital death	1 (3.5)

Two (6.9%) patients died preoperatively of uncontrolled urosepsis at 7 days and 44 days of life. Cystourethroscopy (size 6/7.5 Fr, Karl Storz) in 27 patients confirmed Type I PUV. Valve ablation was achieved with Mohan's valvotome in 26 (96.3%) patients and 1 (3.7%) had electrocautery fulguration with Bugbee electrode.

There was sustained good postoperative urinary stream in all patients at a median follow-up of 5 months, ranged 1 month to 5 years. Three patients had significant postvoiding residual (PVR) urine volume and were placed on doxazosin which resulted in improved bladder emptying and reduction in PVR. Comparing patients who presented before 1 year and those above 1 year, there was no significant difference in the median serum creatinine at presentation (1.06 vs. 1.14 mg/dl, $P = 0.785$), incidence of VUR (47.1% vs. 45.5%, $P = 0.932$), proportion of patients with IRF at admission (47.1% vs. 50%, $P = 0.876$), patients with nadir preoperative creatinine >1 mg/dl after initial bladder drainage (29.4% vs. 50%, $P = 0.260$), and mean nadir preoperative creatinine (0.92 ± 0.61 vs. 0.95 ± 0.30 mg/dl, $P = 0.878$) [Table 2]. Follow-up serum creatinine was available for 19 patients, of which 4 (13.8%) developed IRF. The median age of patients with IRF was 1.8 years versus 11 months for those with normal RF, $P = 0.089$. One (11.1%) of the patients aged < 1 year developed IRF compared with 3 (30%) of children aged more than 1 year, $P = 0.582$. Patients with VUR were six times more likely to develop IRF compared with those without VUR (37.5% vs. 9.1%, odds ratio [OR] =6.0). There was no IRF in patients with nadir preoperative serum creatinine below 1 mg/dl compared to 44% (4/9) IRF in boys who presented with serum creatinine above 1 mg/dl; OR = 3, confidence interval (CI) =1.47–6.14; $P = 0.033$ [Table 3]. The average preoperative nadir serum creatinine in patients without IRF was 0.85 ± 0.30 mg/dl versus 1.40 ± 0.33 mg/dl in the IRF group ($P = 0.005$; CI: 0.19–0.92). The mean follow-up nadir serum creatinine was 0.64 ± 0.20 mg/dl in boys with normal RF compared with

Table 2: Comparison of the features and outcome of posterior urethral valve between boys that presented before 1 year of age and those that presented after 1 year of age

Variables	Less 1 year	>1 year	OR (CI)	*P*
Median age at presentation	32 days	2.8 years		<0.0001
VUR (%)	8/17 (47.1)	5/11 (45.5)	1.00 (0.23-4.89)	0.932
Unilateral VUR (%)	5/17 (29.4)	5/11 (45.5)	0.50 (0.10-2.43)	0.387
Bilateral VUR (%)	3/17 (17.6)	0/11 (0)	0.82 (0.66-1.03)	0.258
Median serum creatinine at presentation (mg/dl)	1.06	1.14		0.785
Preoperative nadir serum creatinine (mg/dl), mean±SD	0.92±0.61	0.95±0.30		0.878
Preoperative nadir serum creatinine >1 (mg/dl) (%)	5/17 (29.4)	6/12 (50)	0.47 (0.08-1.92)	0.260
IRF at follow-up (%)	1/9 (11.1)	3/10 (30)	0.29 (0.02-3.48)	0.582
Mortality (%)	3/17 (17.6)	0/12 (0)	0.82 (0.66-1.03)	0.246

VUR – Vesicoureteric reflux; SD – Standard deviation; OR – Odds ratio; CI – Confidence interval; IRF – Impaired renal function

Table 3: Comparison of posterior urethral valve patients with impaired renal function at follow-up and those with normal renal function

Variables	Normal	IRF	OR (CI)	*P*
Median age at presentation	11 months	1.8 years		0.689
VUR	1/11 (9.1)	3/8 (37.5)	6.00 (0.49-73.45)	0.262
Median serum creatinine at presentation (mg/dl)	1.06	1.62		0.089
Preoperative nadir serum creatinine (mg/dl), mean±SD	0.85±0.30	1.40±0.33		0.005
Preoperative nadir serum creatinine >1 (mg/dl)	0/10 (0)	4/9 (44.4)	1.46-6.14	0.033
Nadir serum creatinine at follow-up	0.64±0.20	1.85±1.08		<0.0001

SD – Standard deviation; OR – Odds ratio; CI – Confidence interval; IRF – Impaired renal function; VUR – Vesicoureteric reflux

mean follow-up nadir serum creatinine of 1.85 ± 1.08 mg/dl in those with IRF ($P < 0.0001$, CI: 0.63–1.78). One patient had residual valve necessitating reablation and there was one out of hospital death given an overall mortality of 10.3% ($n = 3$) in this study, all aged <1 year, $P = 0.232$.

Discussion

PUVs can be detected by routine prenatal ultrasound, with detection rate of between 20% and 42% in developed countries.[8,14,15] The antenatal detection rate in Nigeria is at best <10%[16,17] similar to 6.5% of cases that had prenatal ultrasound diagnosis of PUV in the present series. The low detection rate in developing countries may be related to limited access to antenatal screening as most antenatal ultrasounds are focused on fetal viability and sex determination. Prenatal diagnosis facilitates prenatal intervention in well-selected patients, provides an opportunity to prevent the severe urosepsis, and permits early intervention for the relief of outlet obstruction.[6,18] However, the impact of prenatal diagnosis on the long-term outcome of PUV is debatable. While some authors suggest improved outcomes with prenatal diagnosis,[19] others on the contrary observed that antenatal diagnosis was associated with poor renal outcomes.[6,8] In the present study, one of the patients with antenatal diagnosis of PUV died postoperatively on the 35th day of life, possibly from urosepsis or renal insufficiency (RI). It is worthy of note that pulmonary hypoplasia contributes significantly to neonatal morbidity and mortality.

About a quarter of the patients presented within the 1st month of life and another third presented between 1 month and a year in the present report. This is not different from previous reports, indicating that only a third are diagnosed in the neonatal period and another third during the remainder of the 1st year of life.[11,12] Several authors have discussed late presentation as a characteristic of patients in developing countries.[16,17] It seems unlikely that presentation in these settings are due to negligence and also partly due to continuous use of diapers in neonate not allowing parents to notice symptoms or less obstructive type of PUV early. Furthermore, individuals with less obstructive PUV might otherwise remain undiagnosed until the later part of the 1st year of life or beyond.[6]

In this study, 48% of our patients had renal impairment at presentation; 1 (3.4%) required peritoneal dialysis for 3 months before valve ablation. This finding is comparable to 46% of renal failure reported by Mirshemirani *et al*.[15] in a review of 98 patients treated for PUV in Iran. The incidence of renal failure of 71% at presentation was also reported by Odetunde in Nigeria and Choudhury in India.[20,21] The nature of renal injury in boys with PUV has been categorized into two distinct components. Some damage, described as obstructive uropathy (glomerular and tubular injury), is caused by persistent high pressure, but it is potentially reversible if the high pressure is relieved early. Other damage, termed renal dysplasia, results from either increased pressure during kidney development or due to abnormal embryologic development. Renal dysplasia is not reversible and therefore the degree of dysplasia is critical in determining eventual RF in valve patients.[7] The other type of injury that coexists is renal scarring due to UTI.

Adequate medical stabilization and relief bladder obstruction are the priorities in the initial postnatal management of PUVs. The bladder drainage has been shown to significantly improve renal status of children with PUVs.[14] In a report of management of 65 patients with PUV over 7 years, Sudarsanan *et al*.[14] documented improvement in 9 (75%) out of 12 patients with renal impairment at presentation.[14] In the present study, 8 (57%) of 14 patients with IRF at presentation had significant improved RF after initial catheter drainage. The improvement in RF following bladder drainage may be related to relief of persistently high pressure causing glomerular and tubular injury, which is usually reversible if the pressure is relieved.

Endoscopic valve ablation has been the gold standard in the definitive management of PUV. However, in developing countries where endoscopic facility is not readily available, use of Mohan's valvotome for primary valve ablation has been reported with significant successes.[3,13,14,22] In this study, valve ablation provided relief of obstruction and improvement in urine stream in all patients without any significant sequelae. However, one patient required a repeat valve ablation for residual valve at 3 months of follow-up to attain satisfactory urine stream.

Long-term RF represents a vital determinant of quality of life in patients with PUVs.[8] Despite continuous improvement in the survival of children with PUV, as many as 20%–50% of patients may have significant RI at long-term follow-up.[4,6,7,23] In a review of 98 boys with PUV boys, Parkhouse *et al*.[12]

showed that 26% of postpubertal patients were in chronic renal failure (CRF) on long-term follow-up. In their study of 100 boys treated for PUV and followed for 11.2 years, Smith *et al*.[23] reported an incidence of end-stage renal disease (ESRD) of 10% at 10 years and 38% at 20 years, with evidence of CRF in 34% and 51% at the same ages.

In the present study, IRF was recorded in 4 (13.8%) of patients after a median follow-up of 5 months. This is similar to 8.6% of patients with ESRD in report by Bilgutay *et al*.[8] Heikkilä *et al*.,[24] in a review of 193 Finnish PUV patients followed to a median of 31 years of age recorded 22.8% rate of ESRD in their cohort. While this is significantly higher than our rate of 13.8%, their follow-up was much longer, with onset of renal failure after the age of 17 years seen in a third of ESRD cases. This emphasizes the importance of lifelong follow-up for PUV patients.

The risk of poor RF has been linked to several factors including patient's age at presentation, prenatal diagnosis, VUR, serum creatinine at presentation, serum creatinine after bladder drainage, and nadir creatinine during the 1st year of life.[4,8,11,25]

We found no significant difference in renal outcome of patients aged <1 year and those older than 1 year at the time of diagnosis. This is similar to the findings of Kibar *et al*.[11] in a review of 42 children with PUV in which the rate of postoperative CRF was not statistically significant between the early and late diagnosed PUV; however, they suggested that diagnosis after 1 year of age is associated with lower risk of future renal insufficiency. [11] This was based on the premise that patients with higher degrees of obstruction are probably detected earlier. The cases detected later are likely to have lower degrees of obstruction and, therefore, rarely progress to permanent CRF and ESRD. Similarly, Parkhouse *et al*. in a review of the RF outcome in 98 boys with PUVs found that 26 (41%) of the 64 boys presenting before 1 year of age had a poor long-term outcome for RF, compared to only 5 (15%) of 34 presenting after 1 year of age.[12] In contrast to the above findings, El-Sherbiny *et al*.[10] in a study of 53 boys with PUV provided evidence of a less favorable outcome with delayed presentation of PUVs relative to those diagnosed in the 1st year after birth.

Notwithstanding the ongoing controversies, late diagnosis of PUV may not be uniformly harmful to every patient. In fact, a late diagnosis may suggest less harm and minor illness, which therefore led to the late presentation. Furthermore, all the three patients that died in our study were infants corroborating the observations that early presentation may connote severe obstruction.[12]

Nadir creatinine after operative intervention for PUVs is a well-known predictor of long-term RF.[8,25] Elevated presenting creatinine has also been associated with poor renal outcomes.[4,26] Denes *et al*.[26] proposed creatinine at initial treatment as a predictor for long-term RF. In their cohort of 35 PUV patients, they demonstrated that those who progressed to chronic kidney disease (CKD) had significantly higher creatinine not only at nadir but also at presentation and after catheterization when compared to patients with preserved RF at the last follow-up.

In this study, we found that nadir serum creatinine after valve ablation was a very important prognostic indicator for the final renal outcome after a mean follow-up of more than 5 months. The initial serum creatinine levels were higher among boys with poor follow-up renal outcome than in cases with normal RF, but this does not reach statistical level ($P > 0.05$). Nadir preoperative serum creatinine >1 mg/dl is thrice more likely to result in IRF (OR: 3.0, $P = 0.033$). Our findings suggest that the levels of serum creatinine after initial bladder drainage are a more reliable reflection of functional kidney mass than those obtained before. Our results are comparable with those of Sarhan *et al*.,[4] who found that a return of serum creatinine of <1 mg/dl is predictive of a favorable outcome. Although Bilgutay *et al*.[8] demonstrated an association between creatinine at presentation and final RF, our results did not show any significant association between serum creatinine at presentation and final renal outcomes.

Vesicoureteric reflux (VUR) occurs in 50%–70% of PUV patients at the time of PUV diagnosis.[5,7,9] This VUR is usually secondary to increased intravesical pressure and loss of ureterovesical junction competence. High-grade reflux is mostly associated with a severe degree of dysplasia and has been associated with high morbidity and poor renal outcome.[9,12] In the present series, reflux was present in about 45% of patients and was six times more likely to develop IRF at follow-up. This seems similar to the findings by Ansari *et al*., where high-grade reflux turned out to be strongly associated with a high incidence of CKD and ESRD.[9] In the final analysis, all our patients had good urinary stream at follow-up and 75.9% of our cases achieving improvement of RF, which is comparable with the results from more developed countries.[6,7,23] We recorded overall mortality of 10.3% compared to 5.1%–12.9% in previous studies, [3,6,15,16] although other studies reported no mortality.[11,14]

Limitation of study

This study is limited by the small number of cases studied. Other limiting factors include patient loss to follow-up and short duration of follow-up in some of our cases. We also do not have facility for renograms.

Conclusion

Our results suggest preoperative nadir serum creatinine after initial bladder drainage to be significantly associated with renal outcomes on short-term follow-up. Importantly, this study indicates that late age at diagnosis is not associated with worse renal outcomes, although early detection and intervention is crucial to delay or prevent ESRD. Longer follow-up is needed to identify patients at risk for late progression to CKD or ESRD.

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Conflicts of interest

There are no conflicts of interest.

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