

POSTERIOR URETHRAL VALVE, PARTE OF CONGENITAL OBSTRUCTIVE UROPATHIES; PROGNOSTIC FACTORS IN LONG TERM FOLLOW UP

Roxana Alexandra Bogos¹, Radu Russu², Iuliana Magdalena Stârcea^{1,2}, Mihaela Munteanu², Maria Adriana Mocanu^{1,2}, Doina Nedelcu³, Iulia Ciongradi^{1,3}, Ioan Sârbu^{1,3}, Georgiana Scurtu¹, Mirabela Smaranda Alecsa¹, Ingrith Crenguța Miron¹, Ovidiu Ionel Bărbuță³

Abstract

Background: The posterior urethral valve (PUV) is an important cause of lower urinary tract obstruction in boys, with a wide spectrum of presentations, different degrees of severity, and in 25-45% of patients end with stage kidney failure. **Objective:** Monitoring the children diagnosed and operated for PUV and identifying the predictive factors for the evolution towards chronic kidney failure. **Material and method:** Retrospective analysis of children treated for PUV at Children' Hospital "St. Mary" Iasi during 2004-2014. We followed: age, clinical presentation, recurrences of urinary tract infection (UTI), association with/without vesicoureteral reflux (VUR), serum creatinine levels (at diagnosis, after valve resection and at the end of follow-up) and correlation with the degree of impaired of renal function over time. **Results.** Of the 18 boys diagnosed between 2 days and 12 years old; 11 were admitted for recurrent UTI, and 5 were presented for the investigation after antenatal diagnosis of hydronephrosis. 11 cases presented grade IV and V VUR, bilateral in 6 cases. Impairment of renal function was present at initial diagnosis in all patients in various degrees and at the end of follow-up period 5 patients were with end stage kidney disease with creatinine clearance less than 60 ml/min/1.73 sqm. Two of them were in end stage of renal insufficiency under dialysis and one in the predialytic stage. Unfavorable prognostic factors were late diagnosis with recurrent UTI, association with VUR, and persistent increased creatinine after valve resection. **Conclusion.** The study reveals the persistence of recurrent urinary tract infection as the main criteria to identify the posterior urethral valve (11/19). Late diagnosis along with the persistence of increased creatinine after valve resection were the main factors of unfavorable prognosis of renal function.

Keywords: posterior urethral valve, children, urinary tract infection, chronic kidney diseases

The posterior urethral valves (PUV) are the leading cause of lower urinary tract obstruction in male children as a 1 in 8000 – 25000 live births (1). The severity spectrum and the clinical presentation are variable. Severe forms are presented with urinary tract abnormalities; a few are life-threatening condition in neonatal period. Many of these patients have long-term complications regarding urinary continence and impaired kidney function even under a correct and continuous management. It is known that 25-40% of cases develop chronic kidney disease (CKD) at different ages (2). The causes of renal injury in PUV are: associated irreversible dysplasia, respectively persistent obstructive aeropathy, scars after repeated/recurrent UTI and detrusor dysfunction that can be influenced by early and correct medical-surgical treatment.

Objective

Monitoring the evolution of children operated for the posterior urethral valve and identifying the factors that influence the development of renal failure.

Material and method

Retrospective analysis of observation records of 18 children who were diagnosed and treated for the posterior urethral valve at Pediatric Nephrology and the Pediatric Surgery Division "St. Mary" Children's Hospital Iasi during 2004-2014. We followed: the clinical presentation; main complain at diagnosis, age at diagnosis, recurrences of urinary tract infection (UTI), association with vesicoureteral reflux (VUR), association with dysuria, serum creatinine level (at diagnosis, the minimum value in the first year after surgery and at the end of follow-up). We studied the association of above mentioned parameters with the level of impairment of renal function. The patients were classified based on the creatinine clearance calculated by the Schwarz formula, in stages III (GFR: 60-30 ml / min / 1.73 sqm), stage IV (GFR: 30-15 ml / min / 1, 73 sqm) and V (GFR < 15 ml / min / 1.73 sqm) of chronic kidney disease at the end of follow-up.

Introduction

¹ Mother & Child Department, „Grigore T. Popa „, University of Medicine and Pharmacy Iasi, Romania

² Nephrology Division, St. Mary's Emergency Children Hospital Iasi, Romania

³ Second Pediatric Surgery Division, St. Mary's Emergency Children Hospital Iasi, Romania

Email: bogos.roxana@gmail.com, radurussu@yahoo.com, magdabirm@yahoo.com, mihaelamunteanu2001@gmail.com, scurtugeorgiana8@gmail.com, ingridmiron@hotmail.com, adriana_baltag@yahoo.com, iuliaciongradi@gmail.com, ioansarbu@yahoo.com, doinanedelcu2002@yahoo.com, subotnicu_mirabela@yahoo.com, ovidiubarbuta74@gmail.com

Results and discussion

The series includes 18 boys aged between 4 days and 3 years at diagnosis, followed by 6 to 120 months. All patients received primary endoscopic resection of the valve except in one case where initially vesicostomy was performed and after 2 months the resection. At diagnosis creatinine was increased > 1 mg% in all patient at diagnosis, except for one, and at the end of follow-up 5 patients (27.7%) had stage III CKD or greater, of whom 2 patients (11.1%) entered the extra renal dialysis and 1 (5%) before starting dialysis. Severe VUR was noted in 12 cases (66%) bilateral in 7 of 12 cases. Recurrent UTI were present in 13 of 18 cases (72%). Micturition dysfunction was identified clinically and by ultrasound in 9 of 18 cases (50%).

The age at diagnosis shows that 38.9% of patients were diagnosed in the neonatal and infant period, 27.8% were diagnosed between 1 and 2 years, and 33.3% after the age of 2 years, results that attest to a late diagnosis.

By analyzing the average age at diagnosis differentiated for the years of the studied period (fig.1) it is noted the improvement in diagnosis after 2010; so in 2014 the average age of diagnosis was 0.9 months. These data reflect the improvement the early diagnosis in the recent period.

Age at presentation: in 61% of patients were diagnosed after having at least one episode of UTI and only 27.8% of cases by evaluation of antenatal hydronephrosis (ANH). By analyzing the way of clinical presentation separately for the

years studied (fig.2) there is a sharp increase in cases of PUV that are diagnosed after investigating newborns with ANH. This tendency towards early diagnosis is probably also due to the increase number of pregnancies that benefit from antenatal echographia with the more frequent detection of antenatal hydronephrosis. Results are close to literature data which reveals that in the last 20 years antenatal ultrasound identification has become predominant in developed countries (3).

Analysis of postoperative serum creatinine indicates a significant association of its increased value with the advanced stages of CKD at the end of follow-up. (fig.3)

The literature reveals that the minimum value of creatinine in the first year after valve resection (≤ 0.8 mg / dL) correlates with good long-term renal function (4). Other studies have found creatinine threshold value of ≤ 1 mg / dL (6). In patients who presented more than 3 recurrent UTIs, it was noted a significant association with the evolution to CKD stages III-V ($p = 0.00224$ - Spearman Rank R). The presence of severe bilateral VUR was significantly associated with CKD stages III-V (Chi-square = 19.25, $p = 0.032103$). The role of reflux in PUV is debatable. Some authors consider that bilateral IV-th and V-th grade VUR correlates significantly with the prognosis (7). Analysis of the presence of micturition dysfunction showed a significant association with CKD stages III – V (Chi-square = 8.45, $p = 0.016777$).

Box&Whisher Plot: age of diagnosis
 $F(7,14)=9.6487$, $p=0,02102$, $Kruska-Wallis-H(7,22)=9,8648$, $p=0,05556$

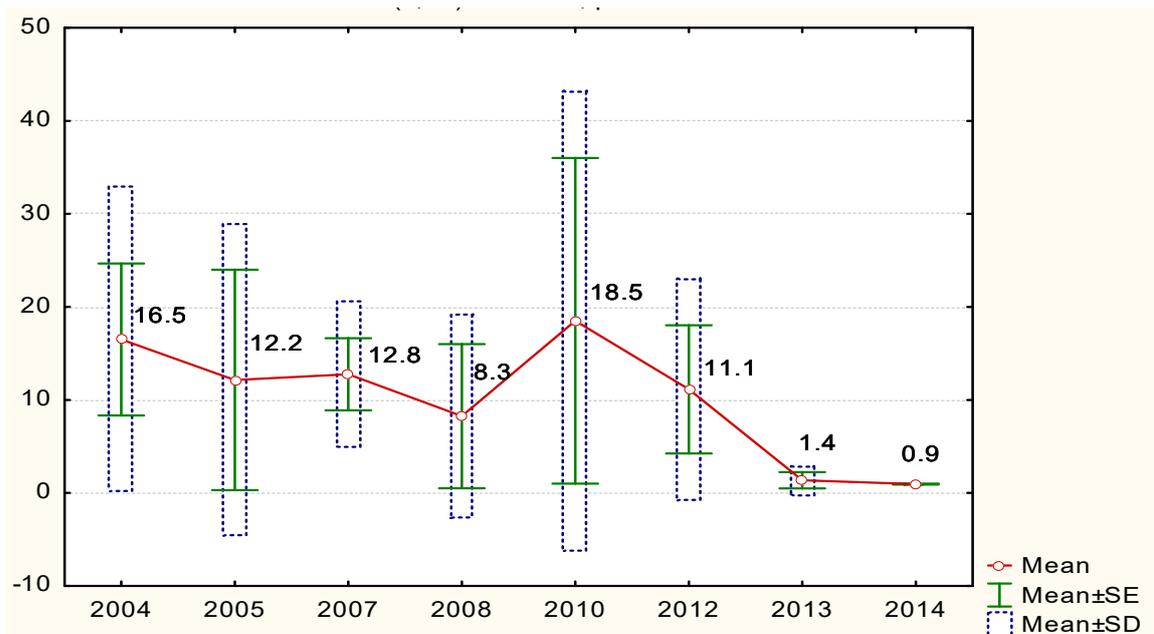


Fig.1. Age at diagnosis in the studied period

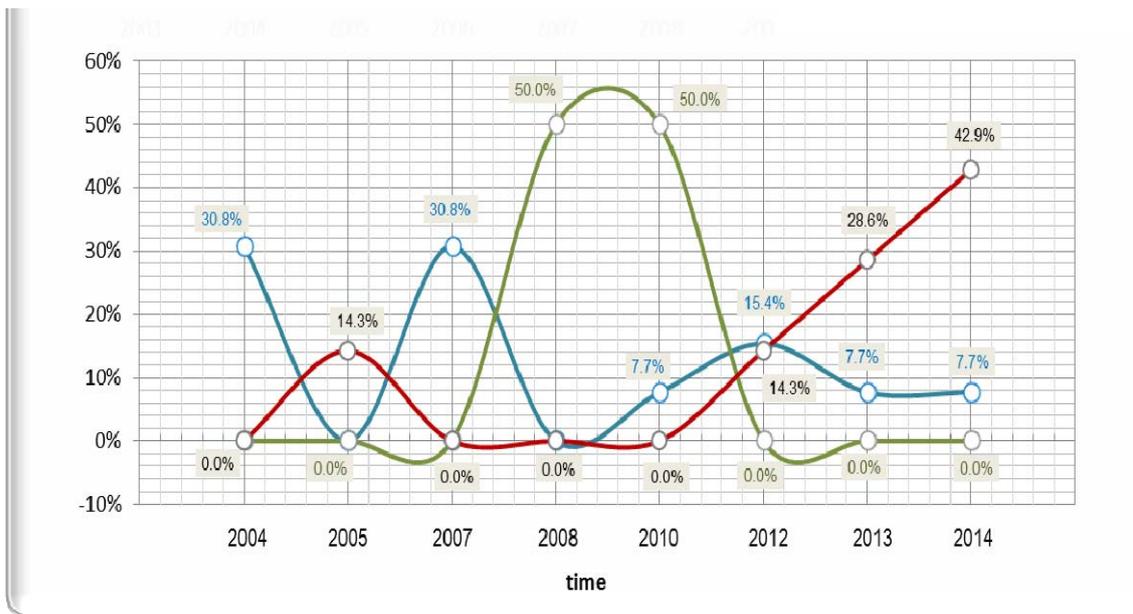


Fig.2. Ways of presentation depending on the period studied

Red – AHN, *green* – urinary ascites, *blue* – UTI

Box&Whisher Plot: age of diagnosis
 $F(4,13)=5,1755$, $p=0,0102$, $Kruska-Wallis-H(4,18)=12,0699$, $p=0,0168$

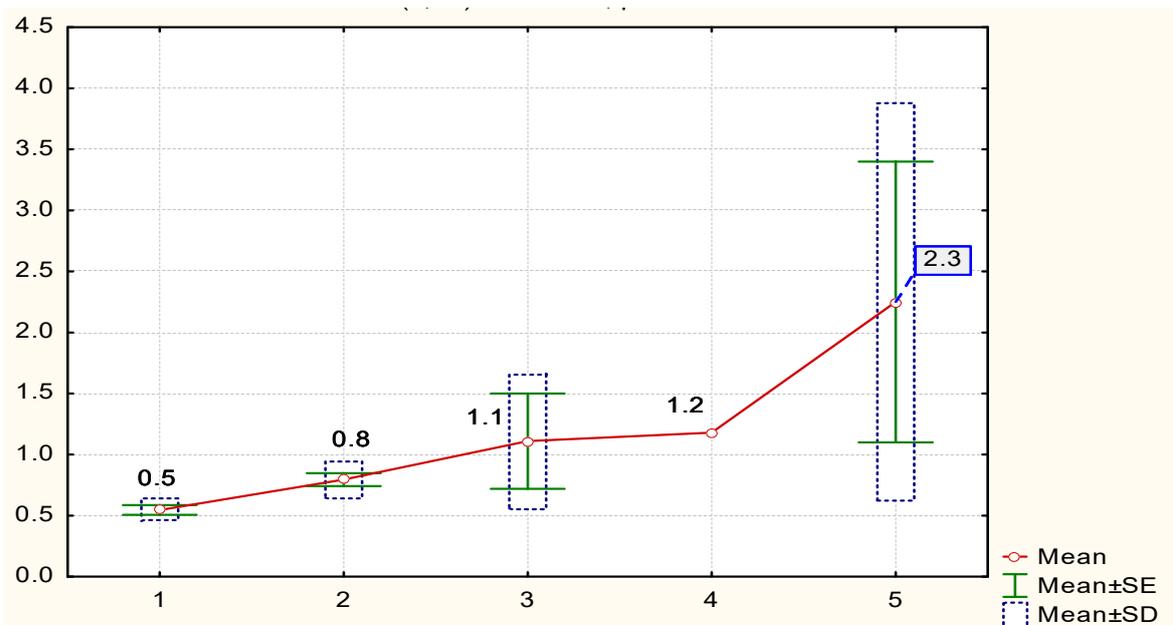


Fig.3. Relationship between postoperative serum creatinine – CKD stage at the end of follow-up

MULTIVARIATE ANALYSIS	Beta	SE	Wald	Sig. p	Hazard Ratio Exp(β)	95% CI for Exp(B)	
						Lower	Upper
Increased creatine	5.002	0.047	11.57	0.001	5.147	2.987	6.987
Post-diagnosis UTI number	4.871	0.024	9.846	0.002	4.806	2.241	5.091
VUR	4.969	0.256	7.817	0.034	4.548	1.946	6.724
urinary dysfunction	1.568	0.155	5.681	0.021	2.645	1.987	3.541
old age at diagnosis	5.871	0.241	6.884	0.037	3.461	1.764	5.975
ways of clinical presentation	1.664	0.367	1.578	0.069	1.576	0.579	2.564

χ^2 statistical test = 5.691 (the degree of fit of the model); df = 5; p = 0.0178; 95%CI.
 CI – confidence interval, df- degrees of freedom , HR- hazard rate (risk ratio), SE- standard error

Fig.4. Multivariate analysis

The patterns of micturition dysfunction described in children with VUP are diverse and changes over time: in infants it is characterized by low compliance, after 1 year, bladder instability, and after puberty the muscular insufficiency of the detrusor is noticed. Along with the ultrasound examination (detrusor thickness, post-micturition residue), the assessment of micturition behavior through urodynamic studies is necessary in order to assess the effectiveness of treatment (8, 9). In children with severe urinary dysfunction, with recurrent UTI and risk of early deterioration of renal function, the solution of Mitrofanoff vesicostomy and intermittent catheterization is viable. Multiple studies have supported this (10, 11).

Multivariate analysis indicated that the prognostic factors for CKD severity were increased creatinine (HR = 5.1), post-diagnosis UTI number (HR = 4.8), VUR (HR = 4.5), urinary dysfunction (HR = 2.6), and old age at diagnosis (HR = 3.46) (fig.4). The literature indicates as predictive factor the plasma renin activity, increased in children with obstructive nephropathy secondary PUV, but the assessment was not accessible to this series of patients (12).

Conclusions

Urinary tract infection was the main way of diagnosing VUP, but in recent years the detection by antenatal echography of gravida as well as postnatal evaluation of ANH has increased significantly the early diagnosis. Severe bilateral VUR, the high number of recurrent UTIs and the presence of micturition dysfunction were significantly associated with the advanced stages of CKD. The main unfavorable prognostic factor for CKD was creatinine level in the first postoperative year > 0.8mg%. Children with PUV, including those operated in neonatal age, require long-term follow-up to identify and treat early complications of CKD.

Acknowledgments

All authors approved the final manuscript and agree to be accountable for all aspects of the work. This original study was performed in accordance with Declaration of Helsinki (the latest revision) and approved by the local hospital ethics committee. Informed consent was obtained from the parents of reported pediatric patient. All the data presented can be available upon request. We would especially like to thank Prof. Dr Gabriel Ionescu for his guidance in writing of this paper.

References

- Nasir A, Ameh E, Abdur-Rahman L, Adeniran J, Abraham M, Posterior urethral valve, World J Pediatr., 2011 Aug;7(3):205-16.
- El-Ghoneimi A, Desgrippes A, Luton D, et all, Outcome of posterior urethral valves: to what extent is it improved by prenatal diagnosis? J Urol. 1999 Sep;162(3 Pt 1):849-53.
- Roth K, Carter W.H, Chan J.C, Obstructive nephropathy in children: long-term progression after relief of posterior urethral valve, Pediatrics, 2001 May;107(5):1004-10.
- Deshpande A, Current strategies to predict and manage sequelae of posterior urethral valves in children. Pediatr Nephrol. 2018 Oct;33(10):1651-1661

5. Ansari MS, Kumar Nunia S, Bansal A, et al, Bladder contractility index in posterior urethral valve: A new marker for early prediction of progression to renal failure. *J Pediatr Urol.* 2018 Apr;14(2):162.e1-162.e5.
6. 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 Feb;6(1):11-4.
7. Bingham G, Rentea R, Posterior Urethral Valve. In: *StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan.2021 Jun 9.*
8. Alsaywid BS, Mohammed AF, Jbril S, Renal outcome among children with posterior urethral valve: When to worry? *Urol Ann.* 2021 Jan-Mar; 13(1): 30–35.
9. Kim SJ, Jung J, Lee C, Park S, Song SH, Won HS, Kim KS., Long-term outcomes of kidney and bladder function in patients with a posterior urethral valve, *Medicine (Baltimore).* 2018 Jun;97(23):e11033.
10. Ezel Çelakil M, Ekinci Z, Bozkaya Yücel B, Mutlu N, Günlemez A, Bek K., Outcome of posterior urethral valve in 64 children: a single center's 22-year experience, *Minerva Urol Nefrol.* 2019 Dec;71(6):651-656.
11. Sharma S, Joshi M, Gupta DK, Abraham M, Mathur P, Mahajan JK, Gangopadhyay AN, Rattan SK, Vora R, Prasad GR, Bhattacharya NC, Samuj R, Rao KLN, Basu AK, Consensus on the Management of Posterior Urethral Valves from Antenatal Period to Puberty, *J Indian Assoc Pediatr Surg.* Jan-Mar 2019;24(1):4-14.
12. Divya Bhadoo, Minu Bajpai, and Shasanka Shekhar Panda, Posterior urethral valve: Prognostic factors and renal outcome, *J Indian Assoc Pediatr Surg.* 2014 Jul-Sep; 19(3): 133–137.

Correspondence to:

Iuliana Magdalena Stârcea
Nephrology Division, St. Mary's Emergency Children Hospital
Iasi, Romania
E-mail: magdabirm@yahoo.com
Tel: +40726704612