RESIDENT'S CORNER

Posterior urethral valves in Eastern Ontario - a 30 year perspective

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Introduction: *Posterior urethral valves (PUV) are the most common cause of male pediatric obstructive uropathy. Recent advancements in antenatal ultrasound and endoscopy have altered the presentation and management of PUV. Herein we describe the presentation, management and outcome of PUV patients in Eastern Ontario/Western Quebec over the last 3 decades. A comparison analysis of those cases identified pre and post widespread utilization of antenatal ultrasound diagnosis was performed to discern the clinical evolution of PUV with respect to long-term outcome.*

Methods: *Retrospective systematic chart review of all PUV cases diagnosed and treated at the Children's Hospital of Eastern Ontario over the last 3 decades. Charts were reviewed for initial presentation, method of diagnosis, radiological and clinical findings at diagnosis, initial management, and long-term clinical outcome. The evolution of PUV was interpreted by dividing the cohort into two groups chronologically delineated by the first case detected by antenatal ultrasound in the mid-1980s. These pre- and post- antenatal ultrasound eras were compared with respect to the parameters outlined above.*

Results: *Fifty-three cases were reviewed - 21 prior to widespread antenatal ultrasound screening in the mid-1980s and 32 after. There were 13/53 cases (32%) discovered by prenatal ultrasound evidence of hydronephrosis, none prior to 1985. VCUG confirmed the diagnosis in all cases. Mean age at presentation in the remaining post-natally diagnosed patients was 33 months. Of the cases diagnosed post-natally, ultrasound investigation complemented VCUG findings in 19/40 cases (47%), whereas IVP was utilized in 14/40 (35%). IVP has not been utilized for this purpose since 1987. Overall, 26/53 cases (49%) had documented VUR - 16/26 (62%) bilateral; 42/53 (79%) had hydronephrosis on ultrasound - 37/42 (88%) bilateral; 26/53 (49%) had radiological evidence of renal parenchymal damage at diagnosis; 41/53 (77%) cases had a thickened bladder wall on ultrasound at diagnosis, and 23/53 (43%) had at least one bladder diverticulum. Techniques of initial management comprised: valve ablation 32/53, vesicostomy 11/53, and high diversion 10/53. Clinically significant bladder dysfunction was found in 31% of cases, ranging from bladder instability to myogenic failure. Globally impaired renal function, as determined by significantly elevated serum creatinine levels, reduced GFR, or both, was found in 12/53 (23%). 6/53 (11%) progressed to ESRD, of which 4 received transplants. Two patients died - one from complications related to renal failure. Of the six cases of myogenic bladder failure identified, three (50%) had concurrently significant renal impairment. Average length of follow-up was 8.3 years, varying between 1 month and 18 years.*

Conclusions: *The presentation of PUV is variable, and currently antenatal detection is the most common mode. Despite this, it still does not make up the majority of diagnoses. Complete radiological work up should include abdominal and pelvic U/S in conjunction with VCUG. Concurrent VUR in 50% of boys mandates suppressive antibiotic use. Primary valve ablation remains the gold standard for treatment of PUV, with vesicostomy reserved for selected cases. Long-term bladder and renal dysfunction is common in this population, and mandates long-term urological and nephrological follow-up.*

Key Words: posterior urethral valves, presentation, treatment, long-term follow-up

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Introduction

Posterior urethral valves (PUV) are the most common cause of pediatric obstructive uropathy, with an

estimated incidence of 1/5000 to 1/8000 male births.[1] More important is the observation that a considerable proportion of these boys either present with or progress to significant bladder and/or renal dysfunction.

Since the foundation of the Children's Hospital of Eastern Ontario (CHEO) 29 years ago, the presentation, diagnosis, and management of PUV has evolved considerably. With the advent and widespread utilization of miniaturized endoscopes in the early 1970's, the use of supravesical and vesical diversion was diminished in favor of primary valve ablation.[2-6] The next major technological advancement to impact the management of PUV came with the widespread employment of antenatal ultrasound in the mid-1980s.[7] Fetuses found to have antenatal hydronephrosis could thus be assessed and managed for PUV antenatally or immediately post-partum, in the hope of yielding better long-term outcomes.[8]

The purpose of this study was twofold: to summarize the experience with PUV at CHEO over the past 3 decades, and to discern what impact, if any, antenatal ultrasound has had in altering the natural history of the disorder. This was accomplished by performing a comparison analysis of those cases identified pre- and post- the widespread use of antenatal ultrasound in the mid-1980s.

Methods

A retrospective systematic chart review of all cases of PUV diagnosed and treated at CHEO was performed. Each case was evaluated along an axis for seven different parameters pertinent to the clinical picture of PUV. These were: age at presentation, mode of presentation, radiological findings (bladder and upper tracts) at diagnosis, initial and subsequent surgical management, long-term bladder outcome, and long-term renal function outcome. Boys discovered to have PUV as a result of work-up for antenatal hydronephrosis were designated diagnosed at birth. Mode of presentation was sub-divided into four gross categories, namely antenatally detected hydronephrosis, failure to thrive, documented UTI, or voiding dysfunction. Voiding dysfunction was defined as persistent childhood nocturnal enuresis or daytime incontinence sufficient to warrant specialist consultation at CHEO. Initial management was broken down into endoscopic valve ablation, vesicostomy, or high diversion. High diversion may have been in the form of unilateral or bilateral cutaneous ureterostomy. Long-term renal function outcome was evaluated and classified into four categories. On one end of the spectrum was globally normal function as defined by age-appropriate serum creatinine or creatinine clearance at last follow-up. Cases with globally impaired renal function or clinical evidence of chronic renal failure (CRF) were grouped together. Impaired function was defined as persistent significant elevation in serum creatinine or decline in creatinine clearance, whereas CRF was defined as having clinical signs and symptoms of uremia or persistent hypertension requiring pharmacological intervention. The third category consisted of those boys requiring dialysis or having received a renal transplant. The last category was reserved for those deceased. Long-term bladder outcome was likewise subdivided into four categories, namely: clinically normal function in childhood, impaired function, bladder failure, and unknown. Impaired function included all boys with evidence of instability, poor compliance, or voiding dysfunction as described above. Bladder failure patients included those requiring clean intermittent catheterization, surgical augmentation, or both. Unknown function was reserved for cases with insufficient follow-up or still in the pre-toilet trained stages of development.

The entire cohort was then divided chronologically into two distinct groups based on date of presentation. The cut-off for this division was arbitrarily chosen to coincide with the first antenatally detected case of PUV by ultrasound in 1985. The data was then analyzed to determine if there was any significant difference in presentation, management, and outcome for PUV between the pre- and post-ultrasound eras.

Results

A total of 53 cases of PUV were reviewed - 21 in the pre-ultrasound (U/S) era and 32 in the post-U/S era as defined by the cutoff with the first case picked up via antenatal ultrasound in 1985. Overall, 32% were discovered by prenatal ultrasound evidence of hydronephrosis, none prior to 1985. VCUG confirmed the diagnosis in all prenatally detected cases. Mean age at presentation in the remaining 68% of cases was 33 months, decreasing from 3.3 to 1.3 years between the pre- and post-U/S cohorts, respectively.

Forty-one percent of all post-U/S era cases were picked up by antenatal U/S, compared to 43% and 33% as neonates or children over 5 years, respectively, prior to the mid-1980s Figure 1. The most common presentation in the pre-U/S era was failure to thrive. Although the most common presentation since the mid-1980s has been antenatal U/S detection (41%), the majority of boys still present later on, most commonly following work-up for UTI (38%) Figure 2.

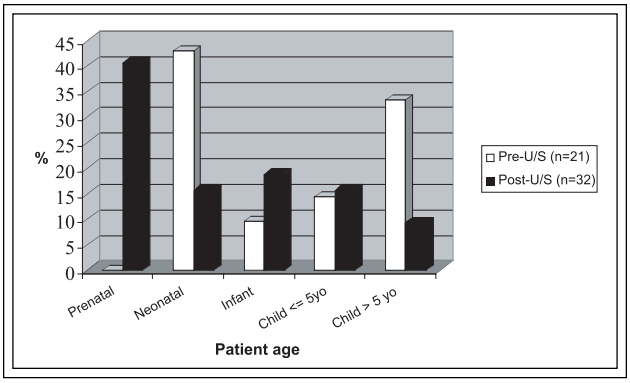

Figure 1. Frequency distribution of age of presentation of PUV for population at CHEO as a function of five distinct chronological groups. The first case of prenatal ultrasound diagnosis in 1985 was used as the determinant of pre- and post-ultrasound eras.

37/40 (93%) of all post-natally discovered cases were diagnosed by VCUG. U/S investigation complemented VCUG findings in 19/40 cases (47%), whereas IVP was utilized in 14/40 (35%). IVP has not been utilized for this purpose since 1987. Overall, 26/53 cases (49%) had documented VUR - 16/26 (62%) bilateral; 42/53 (79%) had hydronephrosis on U/S - 37/42 (88%) bilateral; 26/53 (49%) had radiological evidence of renal parenchymal damage at diagnosis; 41/53 (77%) had a thickened bladder wall on U/S at diagnosis, and 23/52 (43%) had at least one bladder diverticulum. Figures 3 and 4.

Initial management comprised valve ablation (32/53), vesicostomy (11/53), and high diversion (10/53) Figure 5. Since implementation of antenatal

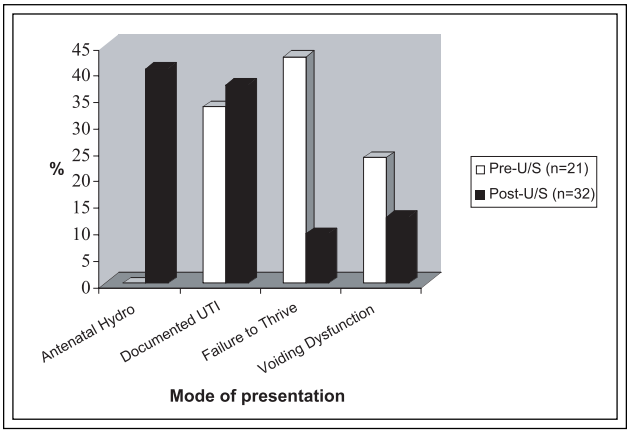

Figure 2. Frequency distribution of mode of presentation of PUV at CHEO divided into four clinical categories, comparing pre- and post- antenatal ultrasound era cohorts. (UTI = urinary tract infection)

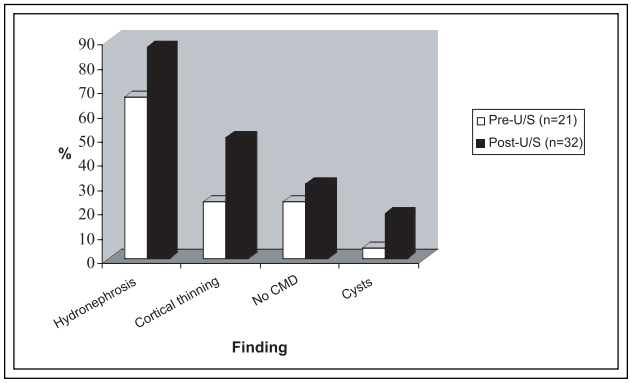

Figure 3. Frequency distribution of renal radiographic findings at diagnosis of PUV, comparing pre- and post-antenatal ultrasound era cohorts. Hydronephrosis is the most common finding overall and was bilateral 88% of the time when present. (CMD = corticomedullary differentiation)

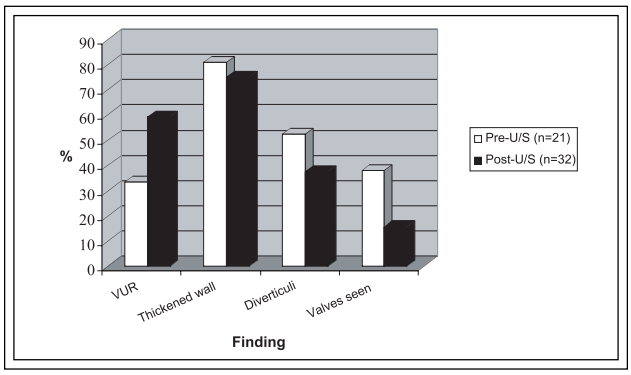

Figure 4. Frequency distribution of bladder radiographic findings at diagnosis of PUV, comparing pre- and post-antenatal ultrasound era cohorts. (VUR = vesicoureteral reflux)

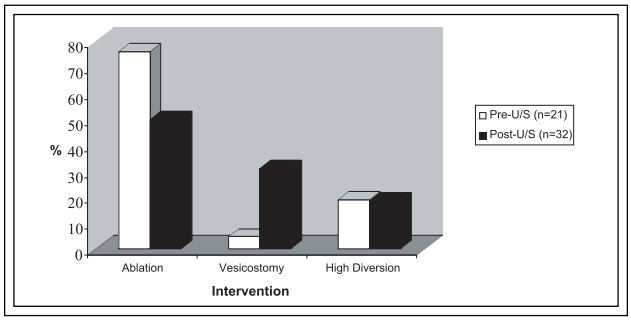

Figure 5. Frequency of primary therapeutic intervention for PUV at CHEO divided grossly into three procedures. Comparison is made between pre- and post- antenatal ultrasound era cohorts. The majority of all cases treated at CHEO employed primary valve ablation (32/53 = 60%).

U/S in the mid-1980s, the proportion of boys treated by primary valve ablation has declined (76% and 50% for pre- and post-U/S eras, respectively). Vesicostomy evolved as the preferred alternative therapy to primary valve ablation (5% of pre-U/S and 31% of post-U/S era cases), with high diversion reserved for complicated cases. Primary high diversion has not been employed since 1995, and all cases eventually received endoscopic valve ablation except one (98%).

At initial presentation, 53% of all boys had normal renal function (48% in the pre-U/S and 56% in the post-U/S eras, respectively). In comparison, 62% of all boys had normal renal function at last follow-up. All of the 38% of cases with abnormal renal function at last follow-up initially presented with objective findings of impaired renal function. Globally impaired renal function, as determined by persistently elevated serum creatinine, reduced GFR, or both, was found in 12/53 (23%). 6/53 (11%) progressed to ESRD, of which 4 received transplants. Two patients died - one from complications related to renal failure Figure 6. Clinically significant bladder dysfunction was found in 31% of cases, ranging from bladder instability to myogenic failure. Of these, 38% (6/16) had evidence of concurrent renal impairment. Of the six cases of myogenic bladder failure identified, three (50%) were found to have renal impairment. Also, all six cases of myogenic failure requiring intermittent catheterization or surgical augmentation were diagnosed and treated in the post-U/S era Figure 7. Overall, average length of follow-up was 8.3 years, ranging between 1 month and 18 years.

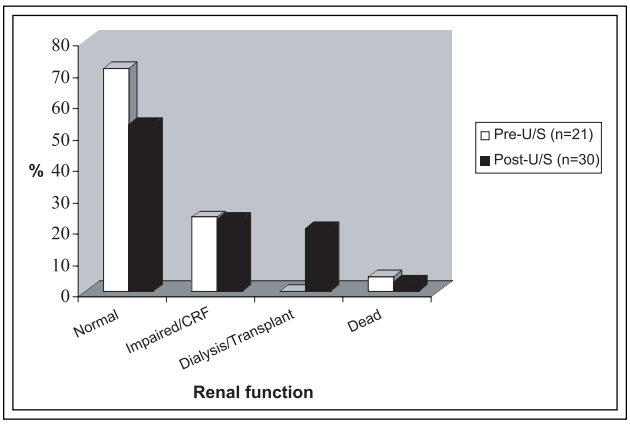

Figure 6. Summary of global renal function at last follow-up for males with PUV at CHEO. Pre- and post- antenatal ultrasound era cohorts are compared. Overall, 62% of boys had normal renal function at last follow-up. Two patients in the post-antenatal ultrasound cohort were lost to follow-up immediately following neonatal treatment. (CRF = chronic renal failure)

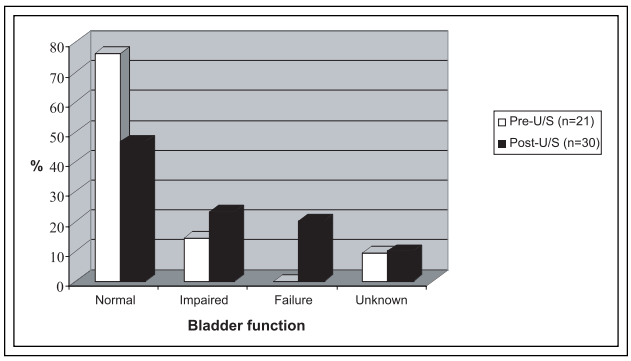

Figure 7. Summary of global bladder function at last follow-up for males with PUV at CHEO. Pre- and post-antenatal ultrasound eras are compared. Overall, 60% of boys had normal bladder function at last follow-up. Unknown bladder function was reserved for those cases with insufficient follow-up or still in the pre-toilet trained stages of development. Two patients were lost to follow-up immediately following neonatal treatment.

Discussion

Since the widespread employment of routine antenatal U/S in the mid-1980s, the average length of time to detection of PUV has declined an average of 2 years (3.3 to 1.3 years of age, respectively). And while proportionately fewer boys are presenting with neonatal complications or over 5 years of age, it is unclear whether or not this has had a positive prognostic effect on long-term renal and bladder outcome. Prior to widespread implementation of antenatal U/S, it was observed that a younger age at diagnosis was associated with a worse prognosis.[7] This finding could simply be explained by milder disease going undetected for a longer period of time. It was thought that the advent of prenatal U/S would change this pattern, on the premise that early diagnosis and treatment of PUV would yield better long-term renal and bladder outcomes. However, our experience seems to suggest just the opposite, with the cohort of boys presenting in the post-U/S era faring worse overall in the long-term. This finding is congruent with other studies in the literature.[9,10] One proposed explanation is that more severe obstruction producing compromised renal function and oligohydramnios is necessary for antenatal detection.[11] Another possible explanation is that, in effect, a historical selection bias has taken place. Prior to our ability to detect antenatal hydronephrosis boys with severe disease may have become acutely ill and died without a diagnosis of PUV being entertained. Likewise, boys presenting later with voiding

dysfunction may have been under-evaluated and progressed to renal failure and nephrological follow-up without PUV being diagnosed as the underlying etiology. This is more plausible considering that the majority of PUV cases reviewed exhibited bilateral hydronephrosis and VUR at diagnosis, thereby affecting both kidneys and increasing the risk of global renal dysfunction.

In the contemporary post-U/S era where all cases of significant antenatal hydronephrosis are worked up immediately post-partum, the majority of boys with PUV (59%) are still presenting with UTI, failure to thrive, or voiding dysfunction at a later age. This lends to the notion that despite routine antenatal U/S screening, the presentation of PUV remains highly variable and that a normal antenatal U/S is not necessarily predictive of valves not presenting later on.

While early primary valve ablation has been, and remains, the standard of care for initial treatment of PUV,[2-6] the more recent post-U/S cohort had proportionately fewer boys treated in this manner compared to the pre-U/S cohort. Deferring valve ablation after primary vesicostomy has been shown to be at least as effective as primary valve ablation.[12] At CHEO, vesicostomy was often performed due to lack of appropriately sized endoscopic instruments for valve ablation in smaller, antenatally diagnosed infants. An 8.5 Fr Wolf resectoscope was not acquired until 1999. Even with new miniature instruments, some of our antenatal cohort are delivered pre-term, and primary valve ablation is not technically feasible due to the small size of the premature infant. However, the decision to perform primary vesicostomy has to be weighed against the risks and increased morbidity of exposing boys to an additional invasive operation that may be unnecessary. Our current preference is for primary valve ablation if technically possible.

The proportion of cases treated by primary high diversion remained essentially unchanged between the two cohorts, which was not altogether surprising considering there remained a number of proponents for this modality well into the 1990's.[8] The concept that bladder cycling is important for long-term bladder function, thus advocating low diversion and primary ablation, is now more widely accepted. Moreover, the initial concept behind high diversion was optimizing renal functional outcome. It is now thought that the renal functional outcome is largely determined prenatally by the degree of renal dysplasia that is present. Thus the rationale for high diversion has waned. In support of this is the observation that no cases since 1995 have been treated with primary high diversion at CHEO.

The observation that 79% of all cases of PUV had hydronephrosis at diagnosis, of which 88% were bilateral, supports the premise that renal U/S is a helpful modality for detecting PUV. However, the differential diagnosis of bilateral hydronephrosis in the pediatric male population is extensive, including prune belly syndrome, high grade bilateral VUR, bilateral UPJ obstruction, and bilateral UVJ obstruction. When hydronephrosis is found in conjunction with a thickened bladder wall, the likelihood of PUV is increased.

Despite earlier detection via antenatal U/S, the proportion of boys exhibiting VUR was increased in the post-U/S cohort. In addition, a considerable proportion of these boys exhibited bilateral reflux. This observation supports the use of suppressive antibiotics in all children suspected of having PUV. Of the 38% of boys with some form of impaired renal function, all initially presented with compromised renal function, and all six with more severe disease requiring dialysis or transplant were found in the post-U/S cohort. Nine percent of boys initially presenting with impaired renal function subsequently improved with acute resuscitation and definitive valve management, as evidenced by a normal renal function profile at last follow-up. This observation supports the premise that with proper diagnosis and treatment, at least some boys with PUV may be spared the sequelae of long-term renal impairment.

Proportionately less boys from the post-U/S era had normal bladder function at last follow-up. Again, all six cases of myogenic bladder failure warranting surgical augmentation or intermittent catheterization were found in the post-U/S cohort. Also, the high proportion of boys with concurrent bladder and renal impairment (38% of all boys with bladder involvement and 50% of those with myogenic failure have some degree of compromised renal function), supports the premise that long-term bladder dysfunction is often indicative of long-term renal dysfunction. These observations reinforce the absolute necessity for long term urological and nephrological follow-up in this patient population.

PUV is a congenital anatomic abnormality with a widely variable clinical picture, ranging from urinary incontinence to end-stage renal and bladder failure. And while abundant effort and report has focused on the evolution of PUV with advancing technology, the long-term endpoints of renal and bladder dysfunction have not changed for the better when moderate or severe disease is present.

Conclusion

The presentation of PUV is variable, and currently antenatal detection is the most common mode. Despite this, earlier U/S detection does not appear to have had a positive prognostic impact in this series. Also, the majority of diagnoses are still made post-partum. Complete radiological work up should include abdominal and pelvic U/S in conjunction with VCUG. Hydronephrosis and a thickened bladder wall are the most common U/S findings, with VCUG adding valuable information concerning VUR, bladder diverticulae, and direct visualization of valves. Concurrent VUR in 50% of cases mandates suppressive antibiotics in all boys. Primary valve ablation remains the gold standard of treatment, with vesicostomy reserved for complicated cases. When renal involvement occurs, often both kidneys are affected. Bladder involvement is highly variable, ranging from normal function to myogenic failure requiring intermittent catheterization, surgical augmentation, or both.

Significant bladder and renal dysfunction is common in this population, mandating long term urological and nephrological follow-up. Advances made in earlier detection of PUV may indirectly play a role in this observation. □

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