EARLY PROGNOSTIC VALUE OF SERUM CREATININE LEVELS IN CHILDREN WITH POSTERIOR URETHRAL VALVES

ENRIQUE D. DENES, JULIA SPENCER BARTHOLD AND RICARDO GONZÁLEZ
From the Department of Pediatric Urology, Children's Hospital of Michigan, Wayne State University School of Medicine, Detroit, Michigan

ABSTRACT

Purpose: We evaluated the prognostic value of serum creatinine level at initial treatment for future renal function in children with posterior urethral valves.

Materials and Methods: We reviewed the records of 35 patients with posterior urethral valves presenting in the first year of life and treated initially at our institution between 1973 and 1990 with valve ablation or vescicostomy. Initial assessment included serum creatinine determination, urine culture, renal ultrasonography and voiding cystourethrography. After 4 or 5 days of catheter bladder drainage renal ultrasound and serum creatinine measurements were repeated. At the end of followup patients were divided into 2 groups according to glomerular filtration rate calculated by the Schwartz formula: group 1—69 ml. or less per minute per 1.73 m.² (median 15) and group 2—greater than 70 ml. per minute per 1.73 m.² (median 110). Median followup was 102 months (8.5 years, range 50 to 219 months).

Results: Mean serum creatinine at diagnosis plus or minus standard deviation was 3.60 ± 2.01 and 1.3 ± 0.7 mg/dl. in groups 1 and 2, respectively (normal 0.1 to 0.6, p <0.01). Mean serum creatinine after catheterization was 2.4 ± 1.1 and 0.6 ± 0.2 mg/dl. in groups 1 and 2, respectively (p <0.01). Mean nadir creatinine during the first year of life was 1.7 ± 0.6 and 0.4 ± 0.2 mg/dl. in groups 1 and 2, respectively (p <0.01). All differences were statistically significant. Linear regression analysis of creatinine after catheterization and glomerular filtration rate at last followup demonstrated a correlation coefficient of -0.7 (p <0.01).

Conclusions: Although it is well known that nadir creatinine in the first year of life correlates with prognosis, the correlation of long-term renal function with creatinine at valve ablation or vescicostomy is more useful to the clinician. These data indicate that serum creatinine level 4 to 5 days after the initial diagnosis correlates strongly with long-term renal function in children with posterior urethral valves.

Key Words: kidney, creatinine, urethra, bladder, abnormalities

Significant controversy still surrounds the choice of initial management of posterior urethral valves. Of the many variables that may impact on ultimate renal function in these infants, only the extent of renal dysplasia is believed to be beyond the potential influence of postnatal treatment. It has been suggested that the type of initial surgical management (high urinary diversion versus primary ablation or vescicostomy) can affect long-term outcome, although conclusions based on controlled randomized protocols are not available.

Several criteria have been identified as predictive of future renal function, including prenatal diagnosis, renal dysplasia, nadir creatinine during the first year of life, vesicoureteral reflux, upper tract obstruction, bladder dysfunction and urinary tract infections. However, most of these parameters can only be ascertained after initial treatment and more or less prolonged followup. Thus, when a patient initially presents with posterior urethral valves, most of this information is not yet available and these criteria are not helpful for predicting outcome or deciding initial treatment. Therefore, we performed a retrospective study of 43 patients born with posterior urethral valves to determine the elements present before initial surgical treatment that are predictive of future renal function.

Accepted for publication August 23, 1996.
Supported by a grant from the Argentine American Medical Association of the Midwest.

MATERIAL AND METHODS

We reviewed the records of 43 male infants with posterior urethral valves presenting in the first year of life who were initially treated at our hospital from 1973 to 1990. Median followup was 102 months (8.5 years, range 50 to 219 months). In 32 patients (74%) the diagnosis was established in the newborn period and 11 (26%) presented between 1 month and 1 year old (median age 3 months). A total of 15 cases (35%) was diagnosed prenatally and a vesico-ureteral shunt was placed in 1. Presenting symptoms and signs in cases diagnosed postnatally varied with age at presentation. The majority of newborns presented with nonspecific gastrointestinal symptoms, respiratory distress, or abdominal distension or mass, whereas most older infants presented with urinary tract infection or an abdominal mass. Initial assessment included the determination of serum creatinine, urine culture, renal ultrasonography and voiding cystourethrography. A urethral catheter was then left indwelling for 4 to 5 days, and renal ultrasound and serum creatinine measurement were repeated.

Four patients (9%) died within the first 3 days of life due to severe pulmonary hypoplasia before surgical treatment and 1 died of severe associated cardiomyopathy. Surgery was performed in 38 patients, including supravesical diversion by cutaneous pyelostomy or ureterostomy in 3 (8%), cutaneous vescicostomy in 7 (18%) and valve fulguration in 28 (74%). For the purpose of analysis only patients who underwent primary ablation or vescicostomy were considered, excluding 3 with
high diversion. Nadir creatinine during the first year of life was recorded.

Glomerular filtration rate was calculated by the Schwartz formula, height × K/serum creatinine, where K = 0.45 for patient ages 0 to 1. 0.55 for 1 to 13 and 0.7 for 13 to 21 years. Patients were divided in 2 groups based on glomerular filtration rate at last followup: group 1 (16 patients) = 69 ml per minute or less per 1.73 m² (median 15) and group 2 (19 patients) = greater than 70 ml per minute per 1.73 m² (median 110). Median followup in groups 1 and 2 was 100 and 95 months, respectively (not statistically significant, p = 0.34).

Statistical analysis was done using the Student t test, chi-square test and regression analysis as appropriate.

RESULTS

Of the 16 patients in group 1 glomerular filtration rate was less than 30 ml per minute per 1.73 m² in 11, including 5 who received a renal transplant and 2 who died of complications of chronic renal failure. Primary surgical management was valve fulguration in 13 cases and vesicostomy in 3. In addition, in 5 of these 16 patients the primary therapeutic approach was considered unsuccessful because of unresolved renal failure or urinary tract infection and they eventually underwent high diversion. One child died of chronic renal failure and 1 underwent renal transplantation.

Of the 19 patients in group 2 glomerular filtration rate was greater than 100 ml per minute per 1.73 m² in 11. Primary surgical treatment was vesicostomy in 4 cases and valve fulguration in 15. When the outcome of patients diagnosed as newborns was compared to that of patients diagnosed in the first year of life, no statistically significant differences were found. At diagnosis all patients presented with bilateral hydronephrosis on renal ultrasonography. Bilateral high grade reflux was present in 10 patients in group 1 and 4 in group 2 (p < 0.01), whereas unilateral high grade reflux was present in 5 in group 1 and 6 in group 2. A total of 14 patients in group 1 and 6 in group 2 had symptomatic urinary infections during followup (p < 0.01).

Mean serum creatinine at diagnosis plus or minus standard deviation was 3.60 ± 2.01 and 1.3 ± 0.7 mg/dl. in groups 1 and 2, respectively (normal 0.1 to 0.6, p < 0.01, see table). Mean serum creatinine after catheterization was 2.4 ± 1.14 and 0.6 ± 0.18 mg/dl. in groups 1 and 2, respectively (p < 0.01). Both differences were statistically significant. Only 1 patient in group 2 had serum creatinine of 0.8 mg/dl. after catheter drainage. We also analyzed the percent decrease in serum creatinine between levels at diagnosis and after catheterization, and no statistical difference was noted (17 ± 52 and 40 ± 20% in groups 1 and 2, respectively, p > 0.05).

Mean nadir creatinine during the first year of life was 1.7 ± 0.6 and 0.44 ± 0.19 mg/dl. in groups 1 and 2, respectively (statistically significant, p < 0.01). Linear regression analysis of creatinine after catheterization and glomerular filtration rate at last followup showed a correlation coefficient of −0.7 (p < 0.01), whereas the correlation coefficient of nadir creatinine during the first year of life and glomerular filtration rate at last followup was −0.55 (p < 0.01, see figure).

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<th>Mean serum creatinine levels plus or minus standard deviation</th>
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<td>Group 1 (16 pts.)</td>
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<td>Mg/dl. creatinine at diagnosis</td>
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DISCUSSION

Posterior urethral valves is a heterogeneous disorder with sequelae ranging from voiding dysfunction without renal impairment to early onset of renal failure and death. Ultimate renal function status of children with posterior urethral valves depends on a number of well-known factors. Severe obstruction, particularly in neonates and infants, has been associated with a high mortality rate but with improved diagnosis and aggressive treatment survival has improved significantly. However, as many as 28 to 45% of patients may have significant renal insufficiency at long-term followup. The risk of poor renal function has been linked to patient age at presentation, prenatal diagnosis, renal dysplasia, nadir creatinine during the first year of life, vesicoureteral reflux, upper tract obstruction, bladder dysfunction and urinary tract infections. 1-8 Rittemberg et al described protective factors associated with improved prognosis, such as unilateral vesicoureteral reflux with dysplasia, urinary ascites, urinoma and large vesical diverticula. 9 Controversy exists regarding the optimization of ultimate renal function in infants treated for posterior urethral valves. It is unclear whether transurethral destruction of valves is optimal initial therapy in all cases and, if not, which patients, if any, would benefit from other forms of therapy, specifically vesicostomy or high urinary diversion. 10,11

It remains difficult to predict from the initial evaluation the patients who will have an unfavorable clinical outcome. Hulbert et al showed that corticomедullary differentiation on renal ultrasonography was associated with a serum creatinine level of 0.8 mg/dl. or less at long-term followup.12 Churchill et al proposed objective criteria to guide practical early management and determine prognosis.13 After the institution of bladder drainage a decrease in serum creatinine of 10% daily correlated with improved renal function.14 In patients diagnosed after birth with azotemia who had normal serum creatinine Warshaw et al reported that those with posterior urethral valves and nadir creatinine of 0.8 mg/dl. or less during the first year of life were likely to have good long-term renal function.14

Although the prognostic value of nadir creatinine in the first year of life is well established and our data support this concept, to our knowledge there are no published guidelines for prognosis for the clinician treating a newly diagnosed patient other than the sonographic appearance of the kidneys and rate of creatinine decrease. These criteria are not universally accepted. In our retrospective study we divided the patients into 2 groups according to glomerular filtration rate at last followup, and then evaluated nadir creatinine in the first year of life and creatinine after at least 4 days of bladder drainage. Clinical significance of the presenting serum creatinine level is limited, since it parallels the maternal level in newborns, and it usually decreases within 96 hours to a concentration consistent with normal infantile levels.

The cutoff point of 70 ml per minute per 1.73 m² is arbitrary but it seems appropriate, since mean glomerular filtration rate in patients with renal insufficiency (group 1) and good renal function (group 2) was 15 and 110 ml per minute per 1.73 m², respectively, with no values between 70 and 80 ml per minute per 1.73 m². These data suggest that creatinine after catheterization of less than 0.8 mg/dl. (0.6 ±
0.2) after at least 4 days of catheter drainage correlates with an excellent prognosis. The only exception to this rule in our series was a patient diagnosed at age 5 months who underwent primary ablation of the valves, was lost to followup and presented several years later with a urinary tract infection.

In contrast, higher levels of serum creatinine after bladder drainage correlated with a decreased glomerular filtration rate later in life. Creatinine after catheterization also correlated well with nadir creatinine during the first year of life but the correlation of creatinine and final glomerular filtration rate was better than that of nadir creatinine and final glomerular filtration rate. Our data also show that the percent decrease in serum creatinine after catheter drainage was of no prognostic value. As in other studies, patients with the worst prognosis also had a higher incidence of massive bilateral reflux at presentation and urinary tract infections later in life. In addition, other factors, such as bladder dysfunction, glomerulosclerosis and hyperfiltration, may contribute to progressive renal damage.

Renal dysplasia is widely blamed for early irreversible renal failure. Parenchymal dysplasia in association with posterior urethral valves has 2 forms: pandysplasia, attributed to a ureteral bud anomaly, and peripheral cortical cystic dysplasia, likely the result of obstruction early in gestation.

The role of early bladder dysfunction in the development of further renal damage is not clear. For example, Jaureguizar et al reported a 37.5% incidence of a normal glomerular filtration rate in 15 patients treated with valve ablation versus 70% in those initially treated with high diversion who underwent undiversion at age 17 months. This study and our data suggest that at least some patients with creatinine greater than 0.8 mg/ml after catheterization may benefit from early high diversion, since in our series they were treated with valve ablation alone and had a universally poor prognosis. It is possible that vesicostomy may benefit patients with bilateral reflux. A study designed to answer these questions may be a useful step in trying to decrease the still unacceptably high rate of renal insufficiency in these children.

REFERENCES