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Progression to end-stage renal disease in children with posterior urethral valves

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Abstract. Diagnostic and therapeutic strategies in boys with congenital posterior urethral valves (PUV) have much improved in past decades, but the impact of these changes on the progression to end-stage renal disease (ESRD) has rarely been investigated. We followed renal function in 20 boys with PUV from diagnosis to ESRD. From the first observation period (1969–1978) to the second period (1979–1992) we found a marked drop in age at diagnosis, at valve resection, at first increase of serum creatinine (SCr), and at onset of ESRD. The progression was analyzed by calculating the slope of 1/SCr and the probability of renal survival. In all patients combined, renal survival at the age of 10 years was 35%. In children undergoing valve resection in the 1st year of life, renal survival was worse than in those undergoing later surgery (15% vs. 65% after 10 years, P=0.006). Patients with a SCr>1.2 mg/dl before the age of 12 months progressed more rapidly to ESRD than those attaining this level later. The lower the minimum level of SCr observed after initial surgery, the older the patient at the onset of ESRD. The presence of renal dysplasia or hypoplasia, but not of vesicoureteric reflux, was associated with a more rapid progression. Mean body height at ESRD was −2.3±1.3 standard deviation score compared with controls, and was lower if PUV was diagnosed before the age of 6 months.

Key words: Posterior urethral valves – Chronic renal failure – Obstructive uropathy – Serum creatinine – Renal function – Renal dysplasia/hypoplasia – Body growth

Introduction

Congenital posterior urethral valves (PUV) are the most-common obstructive lesions of the urinary tract in children [1]. Despite advances in diagnosis and in surgical and medical treatment, chronic renal failure (CRF) develops in many children with PUV. In our center, 14% of pediatric patients reaching end-stage renal disease (ESRD) had congenital obstructive uropathy as the primary kidney disease [2]. In the last decade many centers have introduced pre- and perinatal ultrasound screening for the early detection of congenital obstructive uropathies. The impact of this policy on the outcome of PUV has already been investigated [3–5]. The aim of the present study was: (1) to estimate the rate of deterioration of renal function in children with PUV who, in contrast to earlier studies, were followed from diagnosis to ESRD and (2) to determine which factors influence the prognosis of the disease.

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Patients and methods

The records of 20 boys with PUV reaching ESRD who were treated in our hospital between 1969 and 1994 were reviewed. These patients were selected from a larger group which includes children with PUV who did not reach ESRD before 21 years of age. Ten patients were born and diagnosed before 1978 (group A) and 10 between 1978 and 1992 (group B). Initial clinical manifestations included insufficient weight gain or dystrophy (8 patients), convulsions (6), urinary tract infections (4), increased abdominal circumference (3), abdominal pain (3), unexplained fever (3), enuresis (2), macrohematuria (2), and acute renal failure (1). Obstruction of the urinary tract was suspected by prenatal ultrasound in 4 patients of group B. After birth, 3 infants required artifical ventilation and some suffered from acidosis and hyponatremia: 1 was born with prune-belly syndrome.

The diagnosis of PUV was established by voiding cystourethrogram and/or urethroscopy in 9 patients at the age of less than 1 month, in 6 between 1 month and 12 months, and in 5 between 1 and 13 years. All children in group A and half in group B were below 1 year at the time of diagnosis. The mean age at diagnosis was 4.6 years in group A and 0.2 years in group B. Renal dysplasia, hypoplasia, or aplasia was noted in 1 of 10 children in group A and 9 of 10 in group B, either by imaging techniques (intravenous urography, ultrasonography) or by pathoanatomical examination. Primary vesicoureteric reflux (VUR) was observed in 12 patients (unilateral 5, bilateral 7). Unilateral nephrectomy was performed before the start of dialysis therapy in 6 patients.

All patients underwent valve resection. In addition, urinary diversion was performed in 17 patients either prior to resection (5), at the time of (7) or after resection (5). Urinary diversion procedures consisted of nephrostomies (5), ureterostomies (16), cystostomies (16), and conduits (2).

Progression of CRF was analyzed by evaluating the age at the first increase in serum creatinine (SCr) above 1.2 mg/dl and at onset of ESRD (start of dialysis treatment or death from uremia) and calculating the slope of all individual reciprocal SCr values combined before ESRD [6]. Cr was determined by a modified Jaffé reaction. Altogether 767 SCr values were available for analysis in the 20 patients. Renal survival was calculated from birth to ESRD using the Kaplan-Meier method. Body height at onset of ESRD was evaluated according to the reference standards of the Zurich

Table 1. Clinical data of 20 boys with posterior urethral valves progressing to end-stage renal disease (ESRD) observed from 1969 to 1994[a]

Patients	Age at diagnosis (years)	Age at time of valve resection (years)	Age at first increase of SCr>1.2 mg/dl (years)	Age at start of ESRD (years)	Dysplasia (D)/ hypoplasia (H)	VUR +unilateral ++bilateral	Nephrectomy	Height at start of dialysis (SDS)
Group A								
1	0	0	0	8.9 died[b]	–	++	+	–5.1
2	0.1	0.2	0	8.8	D bilateral	–	–	–3.0
3	0.1	0.3	1.0	13.6	–	–	–	–2.8
4	0.3	0.3	1.5	12.7	–	+	–	–3.1
5	0.5	0.5	7.3	14.7	–	–	–	–3.5
6	2.5	2.5	2.5	8.7	–	++	+	–2.0
7	5.3	5.3	5.3	11.0	–	+	+	–2.5
8	9.4	10.3	7.9	10.7	–	++	+	–2.3
9	13.1	13.9	13.1	20.8	–	++	–	–1.1
10	14.8	15.0	4.1	18.1 died[c]	–	++	–	+0.4
Median	1.5	1.5	3.3	11.4				–2.5
Mean	4.6	4.8	4.3	12.8				–2.5
Group B								
11	0.0 P	0.1	0	1.1	H L	–	–	–2.7
12	0.0	0.1	0.1	5.5	H L	–	–	–1.6
13	0.0 P	0.5	0	0.5 died[c]	D R	–	+	–4.2
14	0.0 P	1.4	0	1.0	D bilateral	+	–	–3.4
15	0.0 P	3.5	0	3.0	D bilateral	–	–	–2.3
16	0.1	0.5	0.1	4.7	D bilateral	–	–	–2.7
17	0.2	0.3	0.1	7.9	D bilateral	++	–	GH
18	0.2	0.3	3.0	4.2	D bilateral	+	+	–1.3
19	0.9	0.8	0.9	6.6	H L	+	–	–0.4
20	0.9	0.9	0	1.7	–	++	–	–0.7
Median	0.2	0.5	0.05	3.5				–2.3
Mean	0.2	0.8	0.4	3.6				–2.1

P, Prenatal diagnosis; VUR, vesicoureteric reflux; GH, growth hormone treatment; SCr, serum creatinine; SDS, standard deviation score; L, left; R, right

[a] Group A: diagnosis in 1962–1977; group B: diagnosis in 1978–1992; [b] From uremia; [c] On dialysis

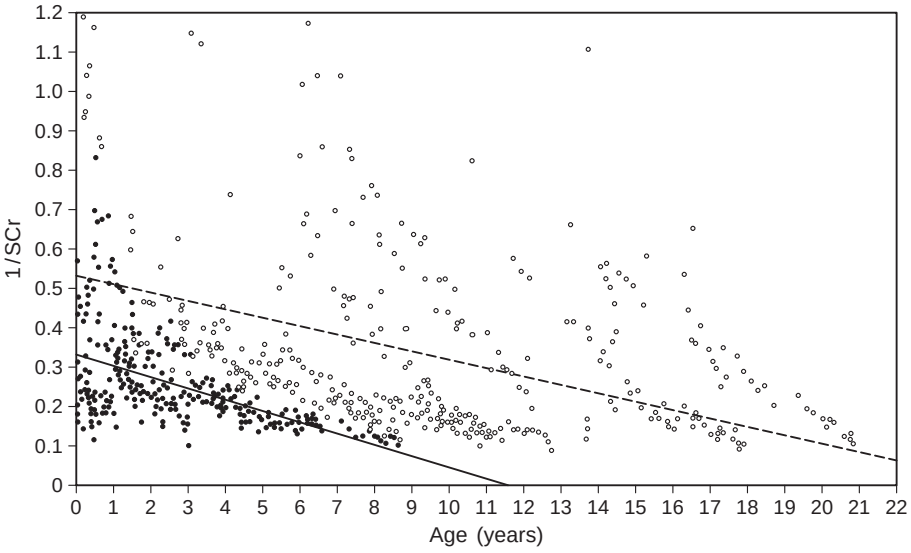

Fig. 1. Serial reciprocal serum creatinine levels (1/SCr) (mg/dl) related to age in 20 boys with posterior urethral valves progressing to end-stage renal disease (ESRD). The slopes of the two age groups were calculated from all individual 1/SCr values combined. *Dots* and *solid line*: individual 1/SCr values and corresponding slope (–0.15) in patients reaching SCr>1.2 mg/dl *before* the age of 12 months. *Circles* and *dashed line:* individual 1/SCr values and corresponding slope (–0.07) in patients reaching SCr >1.2 mg/dl *after* the age of 12 months. The difference between the two groups was not significant

longitudinal growth study [7]. For comparison of groups, Student's *t*-test was used. Correlations were assessed by Spearman's coefficient of correlation.

Results

Despite extensive surgical treatment, all 20 patients reported here developed ESRD before the age of 21 years (Table 1). Complications of CRF included renal anemia, hypertension, and osteodystrophy in almost all children. Three patients underwent parathyroidectomy and 3 orthopedic reconstruction. In addition, 3 children developed a convulsive disorder requiring anticonvulsive medication.

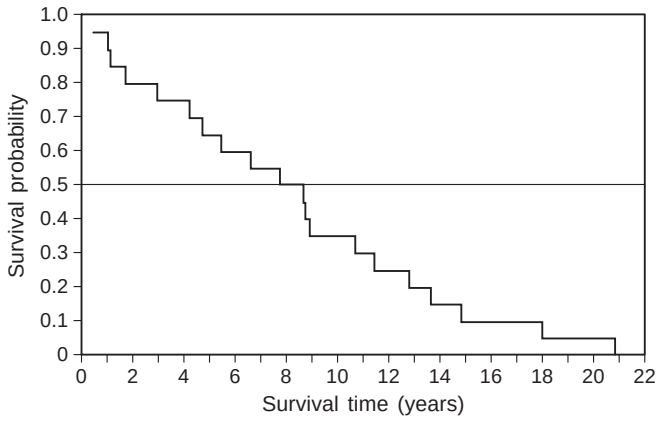

Fig. 2. Probability of renal survival in 20 patients with urethral valves

Mean height standard deviation score (SDS) at the onset of ESRD (±3 months) was –2.3±1.3, excluding 1 patient receiving growth hormone; it was lower in patients diagnosed at <6 months than later (–3.0±1.0 vs. –1.4±1.1 SDS) (Table 1). There was a correlation between height SDS and age at diagnosis (r=0.52, P=0.02) or at valve resection (r=0.50, P=0.03), but not with the age at first increase of SCr or at onset of ESRD, and the presence of renal dysplasia or hypoplasia or VUR.

Median age when SCr first exceeded 1.2 mg/dl was 0.5 (0–13) years in all patients combined; this was decreased markedly in group B compared with A (P<0.05) (Table 1), with a shorter mean duration of predialysis CRF (3.2±2.5 years vs. 8.4±3.5 years, P=0.001) and an earlier onset of ESRD in group B than in group A (3.6±2.5 vs. 8.4±3.5, P<0.0001). There was a correlation between the age when SCr first increased above 1.2 mg/dl and the age at onset of ESRD (r=0.72, P=0.0003). Although the rate of deterioration, as assessed by the slope of 1/SCr, was faster in children reaching a SCR >1.2 mg/dl before than after 12 months, this difference was not statistically significant (Fig. 1).

The overall probability of renal survival was 35% at the age of 10 years and 10% at 15 years (Fig. 2). Median age at renal death was 8.3 years. Those children who exceeded a SCr level of 1.2 mg/dl before 12 months had a shorter 50% cumulative survival than those with a later onset of CRF (4.5 years vs. 12.9 years, P=0.0003) (Table 2). All patients were started on chronic dialysis treatment, except 1 microcephalic, mentally retarded boy (patient no. 1) who died from uremia at the age of 8.9

Table 2. Effect of age at onset of increased SCr levels, age at valve resection, presence of renal dysplasia/hypoplasia, or vesicoureteric reflux on the course of chronic renal failure in 20 boys with posterior urethral valves[a]

		n	Age at first increase of SCr>1.2 mg/dl (years)	Age at onset of ESRD (years)	Time from first increase of SCr>1.2 mg/dl to ESRD (years)	Slope of 1/SCr
Age of increase of SCr>1.2 mg/dl	<1.0 year	11	0.1±0.3 (0–0.9)	4.5±3.3 (0–9)	4.4±3.3 (0–9)	–0.15±0.09
	>1.0 year	9	5.0±4.0 (1–13)	12.9±5.0 (4–21)	7.8±4.5 (1–14)	–0.07±0.03
	P		0.001	0.0003	0.074	NS
Age at valve resection	<1.0 year	13	0.9±2.0 (0–7)	7.7±4.9 (0–15)	6.0±4.2 (0–13)	–0.1±0.26
	>1.0 year	7	4.8±4.0 (0–13)	10.6±7.2 (1–21)	5.8±4.3 (1–14)	–0.07±0.02
	P		0.009	NS	NS	NS
Renal dysplasia/ hypoplasia	Present	10	0.4±1.0 (0–3)	4.3±3.0 (0–9)	4.0±3.2 (0–9)	–0.14±0.29
	Absent	10	4.2±4.3 (0–13)	12.3±5.3 (2–21)	8.0±4.0 (2–14)	–0.06±0.02
	P		0.014	0.0006	0.023	NS
Vesico-ureteric reflux	Uni-/bilateral	12	3.2±4.1 (0–13)	9.5±5.9 (1–21)	6.3±4.2 (1–14)	–0.09±0.04
	Bilateral	7	4.0±2.9 (0–13)	11.1±6.4 (2–21)	7.1±4.0 (2–14)	–0.06±0.01
	Absent	8	1.0±2.4 (0–7)	6.5±5.6 (0–15)	5.4±4.2 (0–13)	–0.18±0.31
	P		NS	NS	NS	NS

NS, Not significant;
[a] Mean values±SD (range in parentheses)

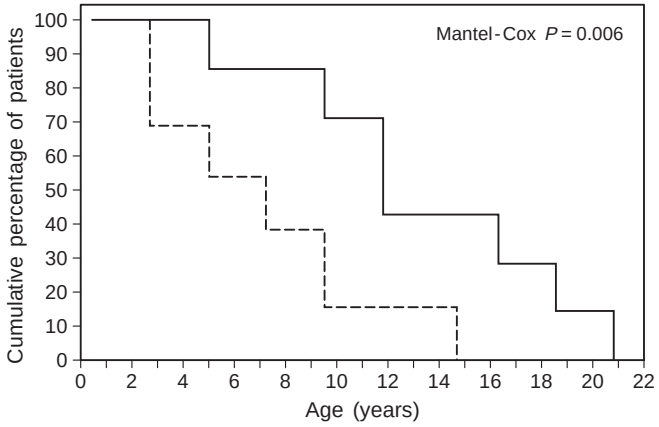

Fig. 3. Probability of renal survival in 13 boys undergoing valve resection before 12 months and in 7 boys after the age of 12 months. –, Valve resection after 12 months; – – –, valve resection before 12 months. The lines are significantly different (Mantel-Cox test P=0.006)

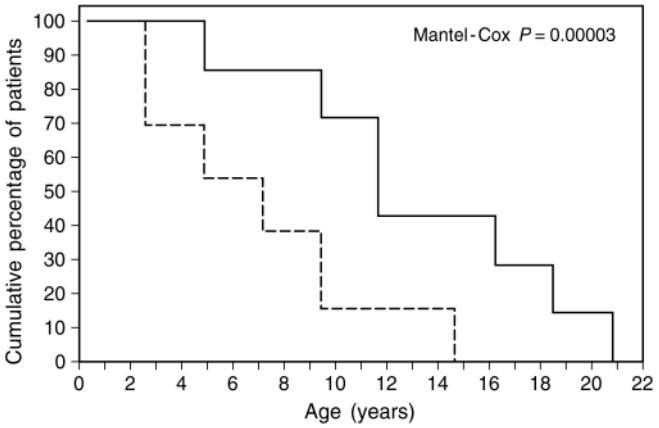

Fig. 4. Probability of renal survival in 10 boys with posterior urethral valves in the presence of renal dysplasia/hypoplasia and in 10 patients in the absence of these lesions. –, Without dysplasia; – – –, with dysplasia. The lines are significantly different (Mantel-Cox test P=0.00003)

years. In addition, 2 patients died some months after initiation of dialysis. Fourteen patients were subsequently transplanted.

The course of CRF and the probability of renal survival were further analyzed in relation to the age at the time of valve resection and the presence of renal dysplasia/hypoplasia or of VUR. No significant differences were found between the duration from first SCr>1.2 mg/dl to ESRD and between the slopes of 1/SCr in children undergoing valve resection either before or after the age of 12 months, but children with early resection had a shorter renal survival (Fig. 3).

The presence of renal dysplasia or hypoplasia was associated with an earlier onset of CRF and ESRD compared with patients without such lesions (Table 2, Fig. 4). In addition, the mean time from the first SCr>1.2 mg/dl to ESRD was half in the presence of renal dysplasia or hypoplasia. The slopes of 1/SCr were not significantly different in patients with early or late valve resection or those with or without renal dysplasia or hypoplasia. The presence of primary VUR (uni- or bilateral) had no significant influence on any variables describing the course of CRF (Table 2). In 14 patients with sufficient postoperative SCr data, a highly significant inverse relation (r=0.72, P<0.001) was found between the nadir SCr determined after the first reconstructive operation and the age when ESRD was reached (Fig. 5).

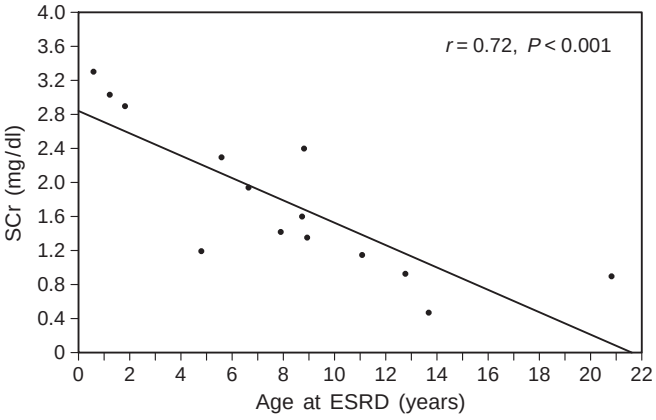

Fig. 5. Minimum nadir serum creatinine levels (SCr) after the initial reconstructive surgical intervention on 14 boys with posterior urethral valves leading to ESRD. An inverse relationship is present between the nadir SCr and the age at onset of ESRD

Discussion

Diagnostic and therapeutic strategies in patients with PUV have much improved over past decades, associated with a dramatic fall in mortality from about 30% to less than 5%, but mortality still remains high in infants compared with older children [1, 5, 8–12]. Previous studies on the prognosis of PUV have included patients with wide variations in age at presentation, proportion of associated anomalies of the urinary tract, such as hydronephrosis, renal dysplasia, VUR, or non-compliant bladder, initial renal function, and pulmonary complications. In addition, the type and timing of surgical interventions and duration of follow-up were different. This might explain why the proportion of PUV patients progressing to CRF varied in different series between 30% and over 50% [5, 10, 12, 12–14].

This paper deals with the minority of PUV patients with early and *severe forms* of PUV entering ESRD during childhood or adolescence. The proportion of this population varies according to different reports from around 10% [13, 15–18] to 32% [10], excluding centers which accept patients primarily for renal replacement therapy [14, 19, 20]. The mean age at onset of ESRD (renal death) was 8.2 years in our patients, which is similar to other series of PUV children [17, 19] and also comparable to other congenital/hereditary nephropathies analyzed by the same statistical method [21, 22].

The *natural history of PUV* has greatly changed over past decades and this is demonstrated by our comparison

of two separate groups of patients followed over subsequent time periods. Age at diagnosis, at valve resection, and at start of CRF have significantly declined from 1969–1977 to 1978–1992, and consequently the mean age at start of renal replacement therapy has dropped from 12.8 to 3.6 years. It is likely that the advances made in prenatal diagnosis, intensive care, surgical treatment, and postoperative care have all contributed to these changes, so that currently more patients present and survive with severe forms of PUV. These patients are often characterized by an association with primary renoparenchymatous, i.e., dysplastic, lesions. However, more patients with milder forms of PUV now appear to survive without progressing to CRF, although minor impairments of kidney function may persist [23].

Most authors agree that renal function usually improves rapidly after surgical relief of PUV. In the long term glomerular filtration rate (GFR) remains stable or slowly declines [10, 15, 19, 24]. In patients with prolonged survival, GFR and renal concentrating capacity eventually normalize in about 60% [23]. Improvement of renal function is, however, rare when GFR is below 30 ml/min per 1.73 m^2 [14], which agrees with our own experience. The prognosis of these patients in adult life remains questionable.

The *rate of deterioration* of renal function in children with PUV is difficult to evaluate from the literature, mainly because the starting and end points of observation were usually not well defined. We restricted our study to patients followed from the time of diagnosis to the onset of ESRD, which allowed us to estimate better the progression and its determinants. To evaluate the deterioration of renal function, we followed serial reciprocal SCr values from diagnosis to ESRD and calculated the time of renal survival from birth by the Kaplan-Meier method [6]. GFR was not calculated from SCr and body height, because the latter was often not available in earlier years; in addition longitudinal changes in GFR over longer periods may be distorted in individual patients when different K values required for the calculations are used. 1/SCr was also preferred here for better comparison with earlier studies. 1/SCr values over time were widely scattered in our patients; their course was non-linear or oscillating in individual patients, which might be attributed to the effect of surgical interventions and transient electrolyte or clinical disturbances. Similar observations were reported in a small group of PUV children by McLean et al. [25].

Our group analysis of the rate of decline of GFR failed to distinguish patients according to age at valve resection or to the presence of associated urinary tract malformations. In contrast, the assessment of the *age at onset of CRF or ESRD* and the survival analysis revealed some significant differences. An early rise of SCr above the critical level of 1.2 mg/dl was followed by a more rapid course towards ESRD, although the renal functional status at presentation was not related to the outcome, as observed earlier [16, 20]. The prognosis was also correlated with the *age at valve resection.* A valve ablation below 1 year of age was associated with an earlier rise of SCr and a significantly shorter renal survival compared with patients with late valve resection. Our findings are in accordance with the observation of Parkhouse et al. [10], that a "bad" long-term outcome is more frequent in boys presenting with PUV before than after the age of 12 months (41% vs. 15%). It is, however, at variance with a report that the age at presentation is not a significant factor for the prognosis [16] and also contradicts the observation that GFR is better maintained when surgical repair of obstructive uropathies takes place in the 1st year of life [24]. In another study the interval between initial surgery and institution of dialysis was independent of age [19].

The variable results with regard to the role of age at presentation or at first surgical intervention might be explained by a different severity of associated *renal dysplasia or hypoplasia.* The frequent combination of PUV and renal dysplasia has been explained by an early intrauterine obstruction of the urinary tract [26]. Recent studies suggest that after the 20th week of gestation there is a good correlation between clinical, sonographic, and biochemical markers predicting poor prognosis and the severity of structural lesions [27]. Although histological evidence of dysplasia was rarely demonstrated in our patients, imaging revealed cystic dysplasia or hypoplastic kidneys in 50%. Our study indicated that the presence of these lesions was associated with a younger age at onset of CRF and at ESRD and a lower probability of renal survival. Since 5 of the 10 patients with dysplastic or hypoplastic changes also had *bilateral VUR* (vs. 2 of the 10 other patients), it is possible that VUR contributed to the worse outcome in the former group [10]. According to our analysis, uni- or bilateral VUR per se had no influence on the rate of deterioration, which is in contrast to other authors [16, 28] who, however, considered only bilateral VUR. Contributing factors which might have influenced the progression of our patients, such as hypertension, pyelonephritis, and bladder dysfunction [10, 13], were not analyzed in this study.

The effect of different therapeutic strategies on the prognosis of children with PUV is controversial. Various arguments have been put forward in favor of early urinary diversion or primary ablation of PUV [14, 18]. Since only a minority of our patients received urinary diversion as a preparatory procedure for subsequent valve resection, we are unable to evaluate the effect of different strategies of initial surgery on the outcome of PUV.

In the search for a parameter which can easily be used in clinical practice to evaluate the rate of progression in PUV, we observed that the *minimum level of SCr* reached after initial reconstructive surgery is negatively related to the age when ESRD was reached (Fig. 5). This finding supports earlier observations that high nadir SCr levels in the 1st year of life are related to the development of CRF [3, 9]. In a larger series of children with PUV, Merguerian et al. [16] reported that the lowest SCr attained during the postoperative follow-up was significantly higher in children with severe PUV progression to ESRD than in patients maintaining "adequate renal function" (mean SCr 2.0 vs. 0.6 mg/dl) after an observation of at least 10 years. Similar to our patients, progression to ESRD was exceptional in this series in the presence of

previously normal SCr values, which is supported by other studies [3, 9, 29, 30].

Growth has been proposed as a prognostic indicator in children with PUV [20, 31]. Renal function appears to be the main predictor of body growth in PUV [14], but subnormal height in children with PUV or other urinary tract malformations may be found even with normal SCr [5, 29, 32]. Our growth analysis was restricted to the time at onset of ESRD and gave similar results as in other progressive congenital nephropathies with advanced CRF [33]. Growth retardation at the time of ESRD was most severe in PUV children younger than 6 months at the time of diagnosis and with early valve resection. However, another study found no influence of the time of prenatal diagnosis of obstructive uropathy on the later growth pattern [5].

In conclusion, our observations demonstrate an earlier onset of CRF and ESRD in boys with PUV in recent years, despite important advances in the diagnosis and treatment of this condition. We speculate that this change is primarily due to earlier recognition of and surgical intervention in severe forms of PUV which frequently are associated with renoparenchymal lesions such as dysplasia or hypoplasia. Consequently, a greater proportion of these patients survive today, whilst function is better maintained in milder forms of PUV. It must be questioned if further expansion of prenatal and early postnatal diagnosis of obstructive uropathy, better postnatal care, and closer follow-up will be able to delay the progression of children with severe forms of PUV. Recent data suggest that detection of PUV before 24 weeks of gestation predicts a poor outcome, even with optimal care [5]. Our own results show that early valve resection per se is not associated with delayed deterioration of renal function. A high nadir level of SCr after initial surgery, an increase in SCr in the 1st year of life, and the presence of renal dysplasia or hypoplasia appear to be valuable predictors of a rapid progression.

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References

1. Williams DI, Whitaker RH, Barratt TM, Keeton JE (1973) Urethral valves. Br J Urol 45:200–210
2. Reiss U (1990) Nierenersatztherapie bei Kindern und Jugendlichen an der Universitäts-Kinderklinik Heidelberg 1969–1988. Thesis, University of Heidelberg
3. Reinberg Y, Castano I de, Gonzalez R (1992) Prognosis for patients with prenatally diagnosed posterior urethral valves. J Urol 148:125–126
4. Dinneen MD, Dhillon HK, Ward HC, Duffy PG, Ransley PG (1993) Antenatal diagnosis of posterior urethral valves. Br J Urol 72:364–369
5. Hutton KA, Thomas DF, Arthur RJ, Irving HC, Smith SE (1994) Prenatally detected posterior urethral valves: is gestational age at detection a predictor of outcome? J Urol 152:698–701
6. Gretz N (1994) How to assess the rate of progression of chronic renal failure in children. Pediatr Nephrol 8:506–511
7. Prader A, Largo RH, Molinari L, Issler C (1989) Physical growth of Swiss children from birth to 20 years of age. Helv Paediatr Acta [Suppl] 52:1–125
8. Atwell ID (1994) Posterior urethral valves in the British Isles: a multicentre B.A.P.S. review. J Pediatr Surg 18:70–74
9. Warshaw BL, Hymes LC, Trulock TS, Woodard JR (1985) Prognostic features in infants with obstructive nephropathy due to posterior urethral valves. J Urol 133:240–244
10. Parkhouse HF, Barratt TM, Dillon MJ, Duffy PG, Fay J, Ransley PG, Woodhouse CRJ, Williams DI (1988) Long-term outcome of boys with posterior urethral valves. Br J Urol 62: 59–62
11. Churchill BM, McLorie GA, Khoury AE, Merguerian PA, Honle AM (1990) Emergency treatment and long-term follow-up of posterior urethral valves. Urol Clin North Am 17:343–360
12. Walker RD, Padron M (1990) The management of posterior urethral valves by initial vesicostomy and delayed valve ablation. J Urol 144:1212–1214
13. Rittenberg MH, Hulbert WC, Snyder HM, Duckett JW (1988) Protective factors in posterior urethral valves. J Urol 140: 993–996
14. Reinberg Y, Castano I de, Gonzalez R (1992) Influence of initial therapy on progression of renal failure and body growth in children with posterior urethral valves. J Urol 148:532–533
15. Mathieu H, Loirat C, Macher MA, Weisberger G, Guedeney J, Pillion G, Guesnu M (1985) Long-term outcome of children with malformative uropathies. Int J Pediatr Nephrol 6:3–12
16. Merguerian PA, McLorie GA, Churchill BM, McKenna PH, Khoury AE (1992) Radiographic and serologic correlates of azotemia in patients with posterior urethral valves. J Urol 148:1499–1503
17. Groenewegen AAM, Sukhal RN, Nata SJ, Scholtmeyer RJ, Nijman RJM (1993) Results of renal transplantation in boys treated for posterior urethral valves. J Urol 149:1517–1520
18. Smith GH, Canning DA, Schulman SL, Snyder HM, Duckett JW (1996) The long-term outcome of posterior urethral valves treated with primary valve ablation and observation. J Urol 155:1730–1734
19. Warshaw BL, Edelbrock HH, Ettenger RB, Malekzadeh MH, Pennisi AJ, Uittenbogaart CH, Fine RN (1982) Progression to end-stage renal disease in children with obstructive uropathy. J Pediatr 100:183–187
20. Tejani A, Butt K, Glassberg K, Price A, Gurumurthy K (1986) Predictors of eventual end-stage renal disease in children with urethral valves. J Urol 136:857–860
21. Gretz N, Schärer K, Waldherr R, Strauch M (1989) Rate of deterioration of renal function in nephronophthisis. Pediatr Nephrol 3:56–60
22. Manz F, Gretz N (1994) Progression of chronic renal failure in a historical group of patients with nephropathic cystinosis. Pediatr Nephrol 8:466–471
23. Dinneen MD, Duffy PG, Barratt TM, Ransley PG (1995) Persistent polyuria after posterior urethral valves. Br J Urol 75:236–240
24. Mayor G, Genton N, Torrado A, Guignard JP (1975) Renal function in obstructive nephropathy: long-term effect of reconstructive surgery. Pediatrics 56:740–747
25. McLean RH, Gearhart JP, Jeffs R (1988) Neonatal obstructive uropathy. Pediatr Nephrol 2:48–55
26. Gonzalez R, Reinberg Y, Burke B, Wells T, Vernier RL (1990) Early bladder outlet obstruction in fetal lambs induces renal dysplasia and the prune-belly syndrome. J Pediatr Surg 25:342–345
27. Daikha-Dahmane F, Dommergues M, Muller F, Narcy F, Lacoste M, Beziau A, Dumez Y, Gubler MC (1997) Development of human fetal kidney in obstructive uropathy: correlations with ultrasonography and urine biochemistry. Kidney Int 52:21–32

28. Johnston JH (1979) Vesicoureteric reflux with urethral valves. Br J Urol 51:100–104
29. Fischbach M, Simeoni U, Zita K, Di Patrizio C, Bieutz J, Sanvag P, Glisert J (1989) Valves de l' urètre postérieur. Nécéssité de la dialyse dans plus du tiers des cas. J Méd Strasbourg 20:251–255
30. Denes ED, Barthold JS, Gonzales RC (1997) Early prognostic value of serum creatinine levels in children with posterior urethral valves. J Urol 157:1441–1443
31. Krueger RP, Hardy BE, Churchill BM (1980) Growth in boys with posterior urethral valves. Urol Clin North Am 7:265–270
32. Seidel C, Schaefer F, Schärer K (1993) Body growth in urinary tract malformations. Pediatr Nephrol 7:151–155
33. Schaefer F, Wingen A-M, Hennicke M, Rigden S, Mehls O, European Study Group for Nutritional Treatment of Chronic Renal Failure (1996) Growth charts for prepubertal children with chronic renal failure due to congenital renal disorders. Pediatr Nephrol 10:288–293