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Long-term outcomes of kidney and bladder function in patients with a posterior urethral valve

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Abstract

We investigated long-term functional changes in the kidney and bladder of patients with posterior urethral valve (PUV) who underwent fetal intervention or postnatal surgery.

We retrospectively reviewed the medical records of 28 consecutive patients treated for PUV at our institution. Detailed data on medical and surgical histories, particularly on pre- and postnatal treatment modality, including fetal vesicoamniotic shunt, endoscopic valve ablation, and vesicostomy, were collected and analyzed. Long-term renal function was evaluated based on serum levels of creatinine (sCr), estimated glomerular filtration rate (eGFR), and renal scans. Voiding function was evaluated in urodynamic tests.

Vesicoamniotic shunting was performed in 12 (42.8%) patients. Although the mean initial sCr was significantly higher in patients in whom a fetal shunt was placed than in others (2.04 vs 1.17 mg/L, $P = .038$), the sCr at long-term follow-up was not significantly different between them (0.64 vs 0.40 mg/L, $P = .186$). The mean maximum detrusor pressure was significantly lower in patients with a fetal shunt than in others (37.7 vs 73.0 cm H_2O, $P = .019$). Postnatal vesicostomy was performed in 14 patients, and primary valve ablation was performed in 13 patients. The mean initial sCr was higher in patients in the vesicostomy group than in the primary valve ablation group (2.08 vs 0.86 mg/L, $P = .014$). However, no significant differences were found in sCr (0.9 vs 0.3 mg/L, $P = .252$) or GFR (59.1 vs 68.5 mL/min/1.73 m^2, $P = .338$) at long-term follow-up. Bladder capacity was greater and residual urine volume was less in the vesicostomy group than in the primary valve ablation group, but without statistical significance.

Vesicostomy is more beneficial in the recovery of renal function and is not inferior in terms of bladder function, even in patients with severe PUV disorder. It is a reliable surgical option that can spare renal function and guarantee adequate bladder function in the long term.

Abbreviations: CKD = chronic kidney disease, sCr = serum creatinine, eGFR = estimated glomerular filtration rate, ESRD = end-stage renal disease, PLUTO = percutaneous vesicoamniotic shunting versus conservative management for fetal lower urinary tract obstruction, PUV = posterior urethral valve, USG = ultrasonography, UTI = urinary tract infection, VUR = vesicoureteral reflux.

Keywords: fetal therapies, glomerular filtration rate, long-term care, posterior urethral valve, urethra, urinary bladder

1. Introduction

Posterior urethral valve (PUV) disorder is the most common cause of lower urinary tract obstruction with bilateral hydronephrosis in boys. PUV causes pulmonary hypoplasia with oligohydramnios in the prenatal period, and it is associated with perinatal mortality and morbidity by causing disorders of renal development.[1,2] In addition, PUV causes urinary tract disorders of various clinical features due to urethral obstruction even after birth and is the most common cause of chronic renal failure in boys.[3]

Vesicoamniotic shunting can help prevent chronic oligohydramnios, which can affect renal parenchymal damage and pulmonary development. This procedure can increase survival in PUV.[4–6] The Percutaneous Vesicoamniotic Shunting Versus Conservative Management for Fetal Lower Urinary Tract Obstruction (PLUTO) study investigated the effects of vesicoamniotic shunting using a randomized controlled method and demonstrated that there is an improvement in perinatal survival.[5] However, the study did not elucidate the effects of vesicoamniotic shunting on the function of the lower and upper urinary tract during long-term follow-up.[5,7]

Prenatal diagnosis of PUV is increasing with the widespread use of prenatal ultrasonography (USG). In patients with PUV, primary valve ablation is considered a standard treatment of choice.[8] However, temporary vesicostomy with delayed valve ablation may be considered depending on the condition of patients.[9] A large number of patients with PUV have renal dysfunction associated with postnatal bladder dysfunction.[10–12] However, few studies have addressed the long-term prognosis of renal function and lower tract function during long-term follow-up, and the effects of prenatal or postnatal interventions are unclear. In this study, we investigated the differences in renal and

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lower-tract functions according to treatment method in the prenatal and neonatal periods.

2. Materials and methods

We retrospectively reviewed the medical records of patients treated for PUV disease from July 1995 to January 2014 at our institution. This study was performed with the approval and supervision of the Institutional Review Board of the Asan Medical Center, Seoul, Republic of Korea. The need for informed consent was waived due to the retrospective nature of the study. We enrolled 28 patients with PUV. They were divided according to 2 criteria: whether fetal intervention was performed and whether primary valve ablation or temporary vesicostomy and delayed valve ablation was performed in the neonatal period. We evaluated clinical features, including hydronephrosis, vesicoureteral reflux (VUR), renal function, urinary tract infections (UTIs), and the findings of urodynamic tests.

2.1. Method of prenatal intervention: vesicoamniotic shunt (double-basket catheter or pigtail catheter)

Amnioinfusion was performed during vesicoamniotic shunting to allow the distal segment of the shunt catheter to be located in the amniotic fluid pocket. After injecting antibiotics and local anesthetics, a 5-Fr guide needle was inserted into the upper part of the bladder of the fetus, using a color Doppler for visual guidance. After urine was collected, the components were confirmed through the needle, and a double-basket catheter was pushed into the bladder of the fetus. The proximal half of the catheter was inserted into the bladder of the fetus, and the distal half was placed in the amniotic cavity. Both ends of the catheter are designed to prevent migration. A similar procedure was used for the pigtail catheter.[13]

2.2. Method of postnatal intervention (vesicostomy vs primary valve ablation)

Vesicostomy was performed by making an incision in the skin in the middle of the umbilicus and symphysis pubis. Through this incision site, the bladder dome was brought up and another incision is made. When prenatal intervention was performed, the shunt instrument was removed, and the bladder dome was attached to the skin. The usual size of the vesicostomy is 24 Fr. Urine was effectively drained, and bladder posterior wall prolapse was prevented. Primary valve ablation was performed with an 11-Fr resectoscopy using a cold knife or bugbee electrode after cystoscopic examination of obstructive urethral lesions using an 8-Fr pediatric cystoscope. Obstructive membranes were incised at 5, 7, and 12 o'clock, and cystoscopic forceps were used to remove the shunt instrument that was used for prenatal intervention. Additional cystostomy could be performed if drainage through the urethra is likely to be incomplete after the procedure.

2.3. Evaluation of renal function and bladder function

The assessment of renal function was performed by comparing serum levels of creatinine (sCR) and estimated glomerular filtration rate (eGFR). eGFR (mL/min/1.73 m^2) was estimated according to the method of Schwartz et al[14] (36.2 × height in cm)/creatinine in μmol/L. Chronic kidney disease (CKD) was defined as an eGFR <60 mL/min/1.73 m^2 and end-stage renal disease (ESRD) was defined as an eGFR <15 mL/min/1.73 m^2 or the need for renal replacement therapy.

Estimated bladder capacity for age was calculated using the formula (age in years + 1) × 30 mL. Decreased bladder capacity was assessed as a reduction of >65% of bladder volume identified based on a voiding diary or estimated bladder capacity in uroflowmetry analyses.

We quantitatively evaluated patients based on the International Continence Society guidelines.[15] Detrusor overactivity was defined as an increase in detrusor pressure of >15 cm H_2O. Continence was defined as no need for diapers without getting wet during the day and night. Periodic follow-up was performed to assess the presence of voiding dysfunction, including self-voiding and urinary incontinence.

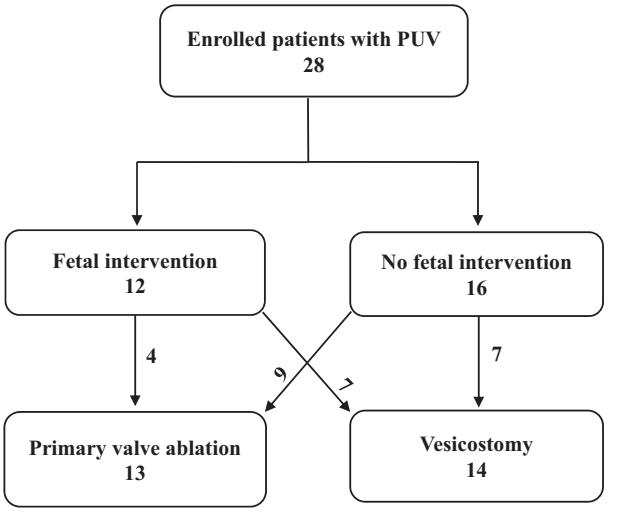
2.4. Statistical evaluation

Data were statistically analyzed using IBM SPSS 20 software (IBM SPSS Inc, Armonk, NY) with *t* test and chi-square test, and results were statistically significant at 95%.

3. Results

We enrolled 28 patients with PUV. Among the 28 patients enrolled, 1 patient was diagnosed with PUV prenatally and was born after fetal intervention, but no neonatal surgery was performed (Fig. 1). Fetal intervention was performed in 12 patients, but not in 16 patients; initial serum creatinine (sCr) was significantly higher in the intervention group than in the nonintervention group. No significant differences were observed in sCR or eGFR between the groups after follow-up. Moreover, the ratio of patients with exacerbated renal function of CKD3 or higher was not significantly different between the 2 groups (Table 1).

Decreased bladder capacity was observed in 5 patients in the fetal intervention group (5/12, 41.6%) and 3 in the nonintervention group (3/16, 18.7%). Urodynamic tests were performed in 4 patients in each group. Residual urine volume was greater in the nonintervention group, but this difference was not statistically



PUV, posterior urethral valves

Figure 1. The flow diagram of patients with PUV. PUV = posterior urethral valve.

Table 1

Initial and follow-up change of renal function according to prenatal intervention.

Number of patients (n)	Total 28	Fetal intervention 12	Nonintervention 16	*P*
Characteristics at birth				
Gestational age, mo	34.2 (28–40)	32.9	35.6	.084
Median follow-up, mo	50 (4–214)	39.8	53.7	.679
Serum creatinine, mg/L	1.50 ± 1.23	2.04 ± 1.51	1.17 ± 0.76	.038
Follow-up (n)	**28**	**12**	**16**	
Serum creatinine, mg/L	0.50 ± 0.43	0.64 ± 0.65	0.40 ± 0.11	.186
eGFR, mL/min/1.73 m^2	49.3 ± 31.4	55 ± 25.7	69 ± 12.5	.147
CKD 3 or higher	6 (21%)	4 (33%)	2 (13%)	.096

CKD = chronic kidney disease, eGFR = estimated glomerular filtration rate.

significant. Bladder detrusor contractility was significantly less in the intervention group than in the nonintervention group. No significant differences were noted in hydronephrosis, VUR, incontinence, or UTI (Table 2).

Vesicostomy was performed in 14 patients, and primary valve ablation was performed in 13 patients as first neonatal procedures. Initial sCR was higher in the vesicostomy group than in the ablation group ($P = .014$). No significant differences were found in sCR or eGFR between the groups after follow-up. However, the sCR tended to be lower after follow-up, although without statistical significance (Table 3). No statistical differences were noted in terms of decreased bladder capacity or incontinence between the groups. In urodynamic tests, in terms of residual urine volume, there was no statistical difference between the vesicostomy group and the primary ablation group (Table 4).

During the follow-up period, 6 patients progressed to CKD. Of these, 4 patients were in the intervention group, 3 were in the vesicostomy group, and 1 was in the ablation group. One patient underwent intervention and vesicostomy and required renal replacement therapy due to ESRD. One patient underwent intervention and vesicostomy and required hemodialysis due to ESRD. One patient each in the nonintervention and ablation groups constantly required clean intermittent clearance. We lost 1 patient who had previously been treated with intervention and vesicostomy (Table 5). The median follow-up period was 50 months.

4. Discussion

The prognosis of patients with PUV has been drastically improved due to early detection by USG screening and development of delicate pediatric instruments with miniaturization. However, in the PLUTO study, of the 3 patients who underwent conservative treatment for prenatal PUV and were followed up to 2 years, 2 had renal insufficiency and one had end-stage renal failure.[5] Although fetal intervention increases survival in PUV, a large percentage of patients have renal dysfunction associated with heterogeneous conditions with multiple etiologies including bladder dysfunction.[10–12]

Fetal interventions are performed in patients with severe PUV accompanied by a distended bladder called a keyhole, which is a sign in USG of severe bilateral hydronephrosis and oligohydramnios. In these patients, intervention is performed only if renal function is salvageable. These procedures are not considered if there is renal dysplasia in ultrasound scans or an incompatible urine biochemical marker was detected (urine sodium, urine chloride, urine osmolality, or urine β2-microglobulin).[4,6,13] Such fetuses develop pulmonary hypoplasia and renal failure, resulting in very high perinatal mortality due to neonatal renal failure. The cohort of this study included patients with mild clinical manifestations of PUV in whom prenatal intervention was not performed. Initial sCR levels were significantly higher in the intervention group than in the nonintervention group. After follow-up, the sCR and eGFR results were relatively poor and the CKD ratio was higher in the intervention group than in the nonintervention group. Despite the inclusion of patients with poor initial clinical manifestation, the intervention group had a favorable bladder function with low detrusor pressure and relatively low residual urine in urodynamic tests than the nonintervention group. The vesicostomy group also had a better bladder function similar to low detrusor pressure and residual urine was observed in urodynamic tests compared to the

Table 2

Initial and follow-up change of bladder function according to fetal intervention.

Follow-up (n)	Total 28	Fetal intervention 12	Nonintervention 16	*P*
Decrease bladder capacity (n)	8 (29%)	5 (42%)	3 (21%)	.340
Incontinence (n)	5 (18%)	2 (17%)	3 (19%)	.887
(n)	14 (50.0%)	6 (50.0%)	8 (50.0%)	1.000
No. of performed USG (n)	**20**	**8**	**12**	
SFU grade 3 (%)	7 (35%)	3 (37.5%)	4 (33.3%)	.446
No. of performed VCUG (n)	**18**	**8**	**10**	
VUR (%)	7 (38.9%)	3 (37.5%)	4 (40.0%)	1.000
No. of performed UDS (n)	**8**	**4**	**4**	
Maximum flow rate, mL/s		9.0 ± 4.0	9.0 ± 4.1	.778
Decreased bladder capacity (n)		0	1	1.000
Postvoided residual urine, mL		19.2 ± 6.1	33.4 ± 14.6	.081
Maximum pressure of detrusor, cm H_2O		37.7 ± 13.9	73.0 ± 13.0	.019
Detrusor overactivity (n)		4 (100%)	3 (75%)	1.000

SFU = Society for Fetal Urology, UDS = urodynamic studies, USG = ultrasonography, UTI = urinary tract infection, VCUG = voiding cystourethrography, VUR = vesicoureteral reflux.

Table 3

Initial and follow-up change of kidney function according to neonatal procedure.

	Total	Vesicostomy	Primary valve ablation	
Number of patients (n)	**27**	**14**	**13**	***P***
Characteristics at birth				
Gestational age, mo	34.2 (28–40)	33.1	35.6	.87
Median follow-up, mo	51 (4–214)	63	37	.18
Serum creatinine, mg/L	1.50 ± 1.23	2.08 ± 1.34	0.86 ± 0.71	.014
Follow-up (n)	**27**	**14**	**13**	
Serum creatinine, mg/L	0.44 ± 0.34	0.9 ± 1.4	0.3 ± 0.1	.252
eGFR, mL/min/1.73 m^2	50.3 ± 31.7	59.1 ± 24.7	68.5 ± 13.2	.338
CKD 3 or higher (n)	5 (17%)	3 (21%)	2 (15%)	.926

CKD = chronic kidney disease, eGFR = estimated glomerular filtration rate.

Table 4

Initial and follow-up change of bladder function according to neonatal procedure.

	Total	Vesicostomy	Primary valve ablation	
Follow-up (n)	**27**	**14**	**13**	***P***
CKD 3 or higher (n)	5 (17%)	3 (21%)	2 (15%)	.926
Decrease bladder capacity (n)	8 (29%)	4 (28%)	3 (23%)	.951
Incontinence (n)	5 (18%)	3 (21%)	2 (15%)	.825
UTI (n)	13 (50.5%)	9 (64.3%)	4 (33.3%)	.238
No. of performed USG (n)	**20**	**8**	**12**	
SFU grade 3 (n)	6/20 (30%)	5 (45.5%)	1 (12.5%)	.082
No. of performed VCUG (n)	**17**	**10**	**7**	
VUR (n)	6/17 (35.3%)	4 (40.0%)	2 (28.6%)	1.000
No. of performed UDS (n)	**8**	**4**	**4**	
Maximum flow rate, mL/s		9.2 ± 4.0	9.4 ± 4.1	.952
Decreased bladder capacity (n)		1	0	1.000
Postvoided residual urine, mL		20.0 ± 6.6	32.6 ± 29.6	.131
Maximum pressure of detrusor, cm H_2O		41.3 ± 14.6	61.5 ± 25.3	.278
Detrusor overactivity (n)	7	3 (75%)	4 (100%)	1.000

CKD = chronic kidney disease, SFU = Society for Fetal Urology, UDS = urodynamic studies, USG = ultrasonography, UTI = urinary tract infection, VCUG = voiding cystourethrography, VUR = vesicoureteral reflux.

primary valve ablation group. As a result of this study, fetal intervention and vesicostomy did not adversely affect long-term bladder function.

The main treatment strategy for patients with PUV is to relieve urinary obstruction and reduce complications associated with bladder and kidney function. The usefulness of vesicostomy is diminishing because the bladders of patients with PUV can be drained efficiently and primary valve ablation can be performed. The first treatment of choice in patients with PUV is primary valve ablation.[8] In addition, initial urinary diversion in patients with PUV may lead to bladder dysfunction,[16] by interfering with the physiologic bladder cycle, leading to complications associated with stoma. However, the usefulness of primary valve ablation and temporary vesicostomy with delayed valve ablation is controversial. Compared to these procedures, high urinary diversion has superior efficiency in that it stabilizes biochemical parameters of the blood more efficiently than a urethral catheter or suprapubic catheter,[17,18] leading to improvements in 90% of cases even with upper urinary tract problems.[17] Previous studies on primary valve ablation and temporary vesicostomy with delayed valve ablation for patients with PUV have also reported favorable outcomes for vesicostomy assessed according to sCr and eGFR.[19]

Many boys with PUV develop a deterioration of renal dysfunction related to bladder dysfunction.[10–12] Bladder

Table 5

Long-term morbidity outcomes among the study patients with posterior urethral valve.

	Fetal intervention	Vesicostomy	Primary valve ablation	Decreased bladder capacity
Chronic kidney disease (n = 6)	4 (67%)	3 (50%)	2 (33%)	0 (0%)
		Fetal intervention		**Operation**
One patient of ESRD		Yes		Vesicostomy
One patient needs CIC		No		Primary valve ablation
One patient		Yes		Vesicostomy

CIC = clean intermittent catheterization, ESRD = end-stage renal disease.

dysfunction has been reported to occur at rates of up to 75%, even with successful primary valve ablation.[20] Bladder dysfunction after primary valve ablation is caused by the gradual deterioration of bladder contractility due to secondary lower urinary tract obstruction and eventually to myogenic bladder failure.[21] In a study of infants who underwent temporary vesicostomy for VUR, after vesicostomy repair, low urinary tract function recovered and vesicostomy alone did not decrease bladder function.[22] In our current study, bladder dysfunction was not observed in patients who underwent vesicostomy as a first procedure.

Our study has several limitations. The retrospective nature and the small sample population limit the generalizability of our results. Moreover, there was no analysis between patients who underwent vesicostomy (7 patients) and those who underwent primary valve ablation (4 patients) after fetal intervention. In addition, in patients without fetal intervention, those who underwent vesicostomy (7 patients) were not compared with those who had primary valve ablation (9 patients). In order to overcome the limitation of the number of patients, we classify the patients according to the fetal intervention or postnatal operation and obtain analytical data and statistical analysis in this classification (Fig. 1).

Although patients who underwent fetal intervention had a higher sCr and higher rate of progression to CKD3 after follow-up, we could not conclude that the patients were exacerbated by procedure, because the initial clinical manifestation was worse.

In conclusion, vesicostomy is more beneficial in the recovery of renal function and is not inferior in terms of bladder function. Even in patients with severe PUV, it is a reliable surgical option that can spare renal function and guarantee adequate bladder function in the long term. We hope that this study will provide a clue as to the prospective study of prenatal and postnatal surgery to preserve bladder function and renal function in PUV patients.

Author contributions

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