



# Long-term fate of the upper tracts following complete primary repair of bladder exstrophy

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## Summary

### Introduction

Complete primary repair of bladder exstrophy (CPRE) is widely used for classic bladder exstrophy (CBE) closure. Long-term renal function with or without dilation in these patients is poorly characterized and may be impacted by bladder storage parameters or recurrent urinary tract infections (UTIs).

### Objective

We sought to assess our long-term experience with CPRE and investigate factors that may influence upper-tract deterioration.

### Study design

A retrospective review of patients at our institution with CBE undergoing CPRE from 1990 to 2015 was performed. Patients were considered included if age at the last renal ultrasound was at least 5 years. Renal imaging and renal function were reviewed. The Society of Fetal Urology (SFU) and Upper Tract Dilation (UTD) grades were retrospectively assigned to all available ultrasounds with hydronephrosis (HN). Additionally, outcomes related to vesicoureteral reflux and lower urinary tract function were assessed. Descriptive and comparative statistical analyses were performed to assess factors influencing HN and renal function at follow-up.

### Results

Thirty patients (57% male) had a median follow-up of 9.7 (3.9–22.3) years. The table shows the HN status and

grade for the entire group, stratified by gender, continence, and surgical reconstruction in. The mean creatinine was 0.50 mg/dL (0.2–1.0) and the mean estimated glomerular filtration rate (eGFR) was 106.8 mL/min/1.73 m<sup>2</sup>. No patient had greater than stage 2 chronic kidney disease. Male gender was associated with worse renal outcomes, including overall rate of HN ( $p < 0.001$ ), severity of HN ( $p = 0.004$ ) and worse eGFR ( $p = 0.05$ ). Lower tract reconstruction, urodynamic parameters, and continence were not associated with differences in upper-tract outcomes. Ureteral reimplantation was performed in 22 patients (73%) at a mean age of 22 months for indications of persistent VUR (10), worsening HN (1), or recurrent UTI (11).

### Discussion

HN is common following CPRE, although severe HN is seen infrequently. Overall long-term renal outcomes are similar to those of other techniques presented in the literature. However, male gender portends a higher risk for long-term upper-tract deterioration as measured by HN and eGFR. Ureteral reimplantation and the status of the lower urinary tract were not associated with differences in upper-tract outcomes.

### Conclusions

Prospective, standardized approaches to characterize upper-tract outcomes are needed to follow children with bladder exstrophy into adulthood. We believe higher-risk patients should be assessed early and managed more aggressively with attention paid towards accurately assessing renal function and lower tract anatomy.

**Table** Presence of hydronephrosis (HN) and Society of Fetal Urology (SFU) grade stratified by gender, continence, and surgical reconstruction by ureteral reimplantation and bladder neck reconstruction (N, %).

	No HN	SFU 1–2	SFU 3–4	N/A <sup>a</sup>
<b>All (N = 30)</b>	14 (47)	11 (37)	4 (13)	1 (3)
<b>Gender</b>				
Male (N = 17)	3 (18)	9 (53)	5 (29)	–
Female (N = 13)	11 (85)	1 (8)	0	1 (8)
<b>Reimplant</b>				
Yes (N = 22)	10 (45)	7 (32)	4 (18)	1 (5)
No (N = 8)	4 (50)	4 (50)	0	0
<b>Continent<sup>b</sup></b>				
Yes (N = 12)	6 (50)	5 (42)	1 (8)	–
No (N = 15)	8 (53)	5 (33)	2 (13)	1 (7)
<b>Bladder neck reconstruction</b>				
Yes (N = 15)	6 (40)	4 (27)	4 (27)	1 (7)
No (N = 15)	8 (53)	7 (47)	0	–

<sup>a</sup> One patient had reported HN but images not available for SFU grading.

<sup>b</sup> Two patients had inadequate documentation to assess continence status.

## Introduction

Bladder exstrophy is a rare but resource-intensive condition with significant impact on long-term urological outcomes. Successful bladder exstrophy closure is defined by volitional voiding with urinary continence and safe storage parameters for the upper urinary tracts. Although most of the recent focus of maturing contemporary exstrophy series has been on continence outcomes [1–3] an equally critical eye, if not more so, must also be turned towards the status of the upper tracts.

Children with classic bladder exstrophy (CBE) are typically born with normal renal function. Complete primary repair of bladder exstrophy (CPRE) performed early following birth seeks to normalize pelvic anatomy and allow early bladder cycling to potentially enhance volitional voiding and continence. However, the upper urinary tract may be exposed to higher bladder pressures earlier in life following this approach. Short-term outcomes of the CPRE suggest up to 70% of renal units will have hydronephrosis (HN), of which half proved to be transient. Likewise, vesicoureteral reflux (VUR) may increase the likelihood for pyelonephritis. Thus, up to 28% of patients will have pyelonephritis, 20% may develop cortical renal scarring, and an additional 10% will develop nephrolithiasis [4,5]. Additionally, promising early series of CPRE are limited by shorter-term follow-up [6].

In this series, we sought to assess our long-term outcomes of the CPRE with attention specifically towards upper-tract outcomes and risks for deterioration. We hypothesized that long-term renal function would be associated with ureteral reimplantation and function of the lower urinary tract.

## Methods

### Patients and procedure

Following institutional review board approval (IRB no. 15680), we reviewed all CBE patients undergoing CPRE at our institution from 1990 to present. Patients were considered eligible for inclusion if age at last renal ultrasound was at least 5 years. Duration of follow-up was defined by age at last renal ultrasound.

Our technique for CPRE has been previously described [6,7]. Osteotomies were performed by an orthopedic surgeon at the discretion of the operative team. Epispadias repair was performed using either complete penile disassembly, modified Cantwell–Ransley, or planned staged repair with buccal mucosal graft [8,9]. Patient demographic and initial operative techniques and perioperative complications were recorded.

### Follow-up and outcomes

Upper-tract outcomes based on imaging and renal function tests measured by serum creatinine and estimated glomerular filtration rate (eGFR, Schwartz formula) were reviewed [10]. Serum creatinine after 6 months of age was available in 20 patients and eGFR could be calculated with

**Table 1** Demographic and early perioperative outcomes of included cohort.

Mean age at CPRE, days (SD)	3.7 (10.2)
<b>Gender, N, %</b>	
Female	13 (43)
Male	17 (57)
<b>Osteotomy, N, %</b>	
Yes	10 (33)
No	18 (60)
OP Note Unavailable	2 (7)
<b>Complications, N, %</b>	
Dehiscence	2 (7)
Fistula	4 (13)
Other	1 (3)
None	23 (77)

CPRE = complete primary repair of bladder exstrophy.

available height and weight in 14. One of two pediatric urologists (J.E., J.A.) reviewed imaging studies to retrospectively assign Society of Fetal Urology (SFU) [11] and Upper Tract Dilation (UTD) [12] grades to all available ultrasounds with HN. One patient had HN reported but ungraded and images were not available for review. Indications for ureteral reimplantation were determined based on operative reports and surgical outcomes for VUR were assessed.

Lower urinary tract function was assessed by fluorourydynamics, continence status, and need for bladder neck reconstruction. The determination for need for urodynamics studies or bladder neck reconstruction was at the discretion of the treating surgeon. Continence was defined as dry with volitional voiding every 3 h [1]. Maximum detrusor pressure was measured in the absence of a detrusor contraction [13].

Descriptive and comparative statistical analyses were performed as appropriate. Continuous variables were assessed using a Student's *t*-test assuming unequal variances while categorical variables were compared using chi-squared tests. All statistical analysis was performed using SAS (v9.4, Cary NC).

## Results

Of the 52 patients undergoing CPRE at our institution for CBE, 30 (58%) were considered eligible for review based on 5-year follow-up with imaging studies, the remainder being ineligible because of age <5 (*N* = 12) or lost to follow-up (*N* = 10). Table 1 displays demographic information of the included cohort. Median follow-up of this cohort was 9.7 (5–22.3) years.

The mean creatinine for the cohort was 0.4 mg/dL (SD = 0.2), at a mean age of 8.5 years. Mean eGFR for the available cohort was 106 mL/min/1.73 m<sup>2</sup>. Four patients had chronic kidney disease (CKD) stage 2, with no patient showing CKD stages 3–5. No patient developed end-stage renal disease during follow-up. HN was noted in 16 (53%) patients at last follow-up, with nine showing bilateral HN. HN severity, renal size, and renal function are shown in Table 2 as are the outcomes stratified by gender and

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