Survival and Kidney Outcomes of Children with an Early Diagnosis of Posterior Urethral Valves

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Abstract

Background and objectives Posterior urethral valve is the most common cause of bladder outlet obstruction in infants. We aimed to describe the rate and timing of kidney-related and survival outcomes for children diagnosed with posterior urethral valves in United States children's hospitals using the Pediatric Health Information System database.

Design, setting, participants, & measurements This retrospective cohort study included children hospitalized between January 1, 1992 and December 31, 2006, who were in their first year of life, had a diagnosis of congenital urethral stenosis, and underwent endoscopic valve ablation or urinary drainage intervention, or died. Records were searched up to December 31, 2018 for kidney-related mortality, placement of a dialysis catheter, and kidney transplantation. Cox regression analysis was used to identify risk factors, and Kaplan–Meier survival analysis used to determine time-to-event probability. Subgroup survival analysis was performed with outcomes stratified by the strongest identified risk factor.

Results Included were 685 children hospitalized at a median age of 7 (interquartile range, 1–37) days. Thirty four children (5%) died, over half during their initial hospitalization. Pulmonary hypoplasia was the strongest risk factor for death (hazard ratio, 7.5; 95% confidence interval [95% CI], 3.3 to 17.0). Ten-year survival probability was 94%. Fifty-nine children (9%) underwent one or more dialysis catheter placements. Children with kidney dysplasia had over four-fold risk of dialysis catheter placement (hazard ratio, 4.6; 95% CI, 2.6 to 8.1). Thirty-six (7%) children underwent kidney transplant at a median age of 3 (interquartile range, 2–8) years. Kidney dysplasia had a nine-fold higher risk of kidney transplant (hazard ratio, 9.5; 95% CI, 4.1 to 22.2).

Conclusions Patients in this multicenter cohort with posterior urethral valves had a 5% risk of death, and were most likely to die during their initial hospitalization. Risk of death was higher with a diagnosis of pulmonary hypoplasia. Kidney dysplasia was associated with a higher risk of need for dialysis/transplant.

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Introduction

Posterior urethral valves is the most common cause of bladder outlet obstruction in infants, with an estimated prevalence rate in the United States of 1.6 per 10,000 in-hospital live male births (1). With widespread access to antenatal sonography, posterior urethral valves is increasingly confirmed during fetal life or immediately after birth. Despite this, it is difficult to counsel parents on a child's prognosis given known heterogeneous effects on bladder, kidney, and pulmonary function.

Posterior urethral valves can be silent until late childhood, presenting with recurrent urinary tract infections or urinary incontinence; conversely, it is associated with pulmonary hypoplasia, manifestations of oligohydramnios at birth, and even death. Posterior urethral valves can be treated in mild cases by a single valve ablation with minimal long-term sequelae, whereas severe cases can require multiple reconstructive surgeries, lifelong care for loss of bladder and kidney function, kidney replacement therapy, and kidney transplantation. It is important for providers to understand expected outcomes to guide follow-up, treatment, and to counsel parents, yet prognostic measures for posterior urethral valves are imprecise. Epidemiologic data regarding frequency and timing of surgical interventions, hospitalizations, and development of kidney disease are needed, but most studies reporting long-term urologic and kidney outcomes in these patients have been single center, thus limiting sample sizes and generalizability (2–9). Rates of ESKD in the literature, given varied cohort characteristics and lengths of follow-up, range from 6% to 29% (10). We aimed to describe the rate and timing of kidney-related outcomes for children diagnosed early in life with posterior urethral valves in United States children's hospitals, using the Pediatric Health Information System database.

Materials and Methods

Research Design and Data Source

Data for this study were obtained from the Pediatric Health Information System, an administrative database that contains inpatient, emergency department, ambulatory surgery, and observation encounter-level data from over 52 not-for-profit, tertiary care pediatric hospitals in the United States. These hospitals are affiliated with the Children's Hospital Association (Lenexa, KS). Data quality and reliability are assured through a joint effort between the Children's Hospital Association and participating hospitals. Portions of the data submission and data quality processes for the Pediatric Health Information System database are managed by IBM Watson Health (Ann Arbor, MI). For the purposes of external benchmarking, participating hospitals provide discharge/encounter data, including demographics, diagnoses, and procedures. Nearly all of these hospitals also submit resource utilization data (*e.g.*, pharmaceuticals, imaging, and laboratory) into the Pediatric Health Information System. Data are deidentified at the time of data submission, and are subjected to a number of reliability and validity checks before being included in the database. For this study, data from 38 hospitals were included. This study was not considered human subjects research by the Institutional Review Board at Connecticut Children's Medical Center.

Patients

Included were children with an inpatient hospitalization between January 1, 1992 and December 31, 2006 during their first year of life, and an International Classification of Diseases, Ninth Revision (ICD-9) diagnosis code for congenital urethral stenosis (753.6) who either died or had an ICD-9 procedure code for valve ablation (58.3, 58.31, 58.39) or urinary drainage intervention (55.02, 55.03, 55.12, 56.61, 57.17–57.19, 57.21, 57.82, 57.94, 57.95, 59.8). Patients with bladder exstrophy, prune belly syndrome, neurogenic bladder, or spinal dysraphism were excluded.

Data on each patient's initial hospitalization were abstracted, including demographics, comorbidities, dates of intervention, and disposition. As patients can be historically tracked within a hospital by a unique identifier, records were searched forward to December 31, 2018 for kidney-related mortality, placement of a dialysis catheter, and kidney transplantation (Figure 1).

Outcome Definitions

Kidney-related mortality was defined as a discharge disposition of "death" and an International Classification of Diseases Ninth Revision or Tenth Revision (ICD-9/10) diagnosis code for CKD or ESKD (285.21, 584.5, 584.8, 584.9, 585.1–585.9, 586, D63.1, N17.0, N17.8-N17.9, N18.1-N18.9, N19). Kidney-related mortality date was defined as date of discharge. Placement of a dialysis catheter was defined as ICD-9/10 procedure code (38.95, 39.27, 54.93, 03130ZD-01380ZD, 03190ZF, 0W1G0J4–0W14J4, 05HY33Z, 06HY33Z) or Current Procedural Terminology code (36800–36821) for catheter placement during an inpatient or outpatient stay. Kidney transplant was defined as ICD-9/10 procedure code for kidney transplant (55.6, 55.69, 0TY00Z0–0TY00ZE, 0TY10Z0–0TY10Z2) during an inpatient stay. To ensure all kidney transplant events were identified, patients whose initial hospitalization occurred in a hospital without a transplant program in place at the time of that hospitalization were excluded from the transplant analysis. We identified hospitals without transplant programs by searching for kidney transplant codes among all hospitals and for all diagnosis codes. Hospitals with fewer than two kidney transplants for the hospitalization year were considered not to have a transplant program.

Exact dates of kidney transplant or dialysis catheter placement were available in the date of service inpatient Pediatric Health Information System file. Follow-up was defined as date of birth to date of last visit. Potential risk factors for the above outcomes were identified by ICD-9 diagnosis codes from initial visit comorbidities, and included <37 weeks at birth (765.0–765.28); kidney agenesis and dysgenesis (748.5); kidney dysplasia (753.15); agenesis, hypoplasia, and dysplasia of lung (748.5); and sepsis (38.0–38.9, 670.2, 771.81, 785.52, 995.91, 995.92, 999.3).

Statistical Analyses

Univariate comparisons were made using *t* test or the Fisher exact test. Cox regression analysis were performed to evaluate risk factors for all outcomes in unadjusted and multivariable models. Risk factors were selected *a priori* on the basis of biologic plausibility. Kaplan–Meier survival analysis was used to determine time-to-event probability. Outcomes used in the Kaplan–Meier analysis were mortality and ESKD intervention, a composite outcome of dialysis catheter placement and/or transplant. Subgroup survival analysis was performed with outcomes stratified by the strongest risk factor identified in multivariable Cox regression analysis, and Mantel–Cox log-rank test used for between group comparisons. As some patients experienced multiple dialysis catheter placements and kidney transplants, Kaplan–Meier and Cox regression time to event was defined as the first time an event occurred. Descriptive and survival analysis was conducted using IBM SPSS Statistics 25.0 (IBM Corporation, Armonk, NY), and Cox regression analysis was conducted using SAS 9.4 (SAS Institute Inc., Cary, NC). All tests were two-tailed, with a P value <0.05 considered significant.

Results

The study cohort included 685 children from 38 hospitals, after excluding for bladder exstrophy (n=4), prune belly (n=91), and neurogenic bladder/spina bifida (n=66). The majority of participants (45%) were white, with a median age at initial hospitalization of 7 days (interquartile range [IQR], 1–37 days). Over 90% (n=623) had an initial hospitalization length of stay of 1 month or less (median 8 days; IQR, 4–14 days).

One third (30%) of participants did not have a subsequent Pediatric Health Information System hospitalization after their initial hospitalization. Patients without subsequent hospitalization(s) were admitted to their initial hospitalization at an older age than those with subsequent visits (12 days versus 6 days; P=0.001), and a smaller proportion were born at <37 weeks of gestation (13% versus 21%; P=0.01) and diagnosed with kidney dysplasia

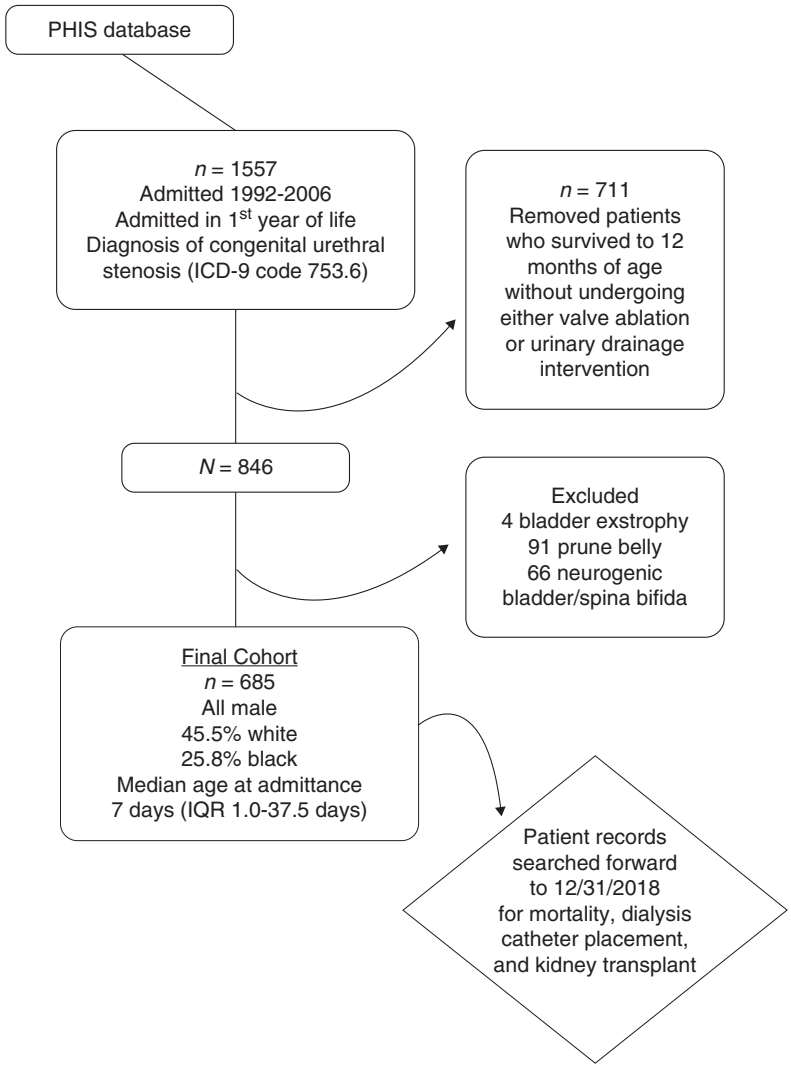

Figure 1. | **Study cohort construction and database query methodology.** PHIS, Pediatric Health Information System database.

(4% versus 20%; $P<0.001$) or pulmonary hypoplasia (3% versus 8%; $P=0.02$) (Table 1). Among those with subsequent visits, median follow-up was 7 years (IQR, 2–14 years).

Over three quarters of participants (87%) did not experience any of the primary outcomes studied (kidney-related mortality, placement of a dialysis catheter, and kidney transplant). Initial hospitalization patient characteristics by outcome are presented in Table 2.

Kidney-Related Mortality Incidence and Risk Factors

Thirty-four children (5%) died during the study period. Of these, over half (n=18) died during their initial hospitalization, and 85% within the first 2 years of life. The multivariable Cox regression model found a diagnosis of pulmonary hypoplasia to be the greatest risk factor for death (hazard ratio, 7.5; 95% confidence interval [95% CI], 3.3 to 17.0); prematurity had a three-fold risk of death (hazard ratio, 3.0; 95% CI, 1.4 to 6.4). Hospital volume of posterior urethral valves cases was found to be protective. Patients whose initial hospitalization occurred in a hospital that treated three or more posterior urethral valves cases per year were 62% less likely to die (hazard ratio, 0.38; 95% CI, 0.17 to 0.82) (Table 3).

Dialysis Catheter Placement Incidence and Risk Factors

Fifty-nine children (9%) underwent one or more procedures for catheter placement for dialysis during the study period. The majority (n=33) underwent their first placement during their initial hospitalization. For the remaining 26 patients, median age was 33 months (IQR, 8–128 months). The latest recorded dialysis catheter placement was at 15 years. Almost half (44%) of children with catheter placement progressed to kidney transplant. Multivariable Cox regression analysis found children diagnosed with kidney dysplasia to have over four-fold higher risk of catheter placement (hazard ratio, 4.6; 95% CI, 2.6 to 8.1). A diagnosis of pulmonary hypoplasia had a three-fold higher risk of catheter placement (hazard ratio, 3.0; 95% CI, 1.6 to 5.7), and children born at <37 weeks of gestation had three-fold higher risk of undergoing catheter placement (hazard ratio, 2.2; 95% CI, 1.1 to 3.9) (Table 4).

Table 1. Initial hospitalization characteristics stratified by subsequent hospitalization status

Initial Hospitalization Characteristic	Total	Subsequent Hospitalization	
		Yes (*n*=477)	No (*n*=208)
Admit age, d, median (IQR)	7 (1–37)	6 (1–30)	12 (2–61)
<37 wk at birth, %	128	101 (78)	27 (22)
Kidney agenesis, %	18	16 (89)	2 (11)
Kidney dysplasia, %	106	97 (91)	9 (8)
Sepsis, %	53	40 (75)	13 (24)
Pulmonary hypoplasia, %	43	37 (86)	6 (14)
Hospital volume			
≤2 PUV case/yr, %	316	235 (74)	81 (26)
>2 PUV cases/yr, %	369	242 (66)	127 (34)

Data given as *n* (%) of row or median (IQR) unless otherwise indicated. IQR, interquartile range; PUV, posterior urethral valves.

Kidney Transplant Incidence and Risk Factors

After excluding patients whose initial hospitalization occurred at a hospital without a transplant program (*n*=154), 36 out of 531 (7%) patients underwent kidney transplant at a median age of 38 months (IQR, 23–97 months). Only one patient underwent transplant during the first year of life. Over half of children (*n*=23) undergoing transplant did so under 5 years of age, with most transplants (*n*=9) occurring during the third year of life. Kidney dysplasia was the strongest risk factor, increasing risk of kidney transplant over nine-fold (hazard ratio, 9.5; 95% CI, 4.1 to 22.2) (Table 4).

Kaplan–Meier Analysis

Kaplan Meier analysis found probability of survival for children with posterior urethral valves to be 98% (95% CI, 97% to 98%) in the first month of life, decreasing to 95% (95% CI, 95% to 96%) probability by 1 year. There was minimal change in survival probabilities after 1 year, with 5- and 10-year survival at 94% (95% CI, 93% to 95%), and 15-year survival at 92% (95% CI, 91% to 94%), as few deaths were reported in later years. Mean survival time was 22 (95% CI, 21 to 22) years. Children with pulmonary hypoplasia had greatly reduced estimated probabilities of survival compared with children without hypoplasia

Table 2. Patient and hospital characteristics present at initial hospitalization stratified by mortality and ESKD intervention

Characteristic	Cohort	Stratified Cohort					
		Mortality		Dialysis Catheter		Kidney Transplant	
		Yes	No	Yes	No	Yes	No
Individual (*n*)	685	34	651	59	626	36	495
Race, %							
White	45	5	95	8	92	7	93
Black	26	4	96	11	89	8	92
Hispanic/Latino	11	3	97	9	91	7	93
Multiracial	11	7	93	5	95	7	93
Other/unknown	7	6	94	11	89	—	100
Insurance, %							
Public	34	4	96	9	91	6	94
Private	44	6	94	9	91	7	93
Uninsured	4	7	93	—	100	—	100
Unknown	18	4	96	8	92	9	91
Admit age, d, median (IQR)	7 (1–37)	2 (0–8)	8 (2–40)	2 (0–17)	8 (2–40)	3 (1–17)	7 (1–39)
<37 wk at birth, %	19	14	86	19	81	11	89
Kidney agenesis, %	3	28	72	11	89	—	100
Kidney dysplasia, %	15	9	91	32	68	69	31
Sepsis, %	8	11	89	24	76	15	85
Pulmonary hypoplasia, %	6	35	65	37	63	24	76
Hospital volume category							
≤2 PUV case/yr, %	15	8	92	11	89	6	94
>2 PUV cases/yr, %	54	2	98	6	94	7	93

Data given as percent of cases across row or median (IQR). IQR, interquartile range; PUV, posterior urethral valves.

Table 3. Risk factors for mortality in unadjusted and multivariable model Cox regression analysis

Initial Hospitalization Characteristic	Unadjusted		Multivariable Model	
	HR	95% CI	HR	95% CI
Admit age, d	1.0	1.0 to 1.0	1.0	1.0 to 1.0
<37 wk at birth	5.2	2.6 to 10.1	3.0	1.4 to 6.4
Kidney agenesis	7.0	2.7 to 18.1	2.3	0.8 to 6.5
Kidney dysplasia	2.0	0.9 to 4.1	0.9	0.4 to 2.0
Sepsis	2.3	1.0 to 5.6	1.1	0.4 to 2.8
Pulmonary hypoplasia	12.5	6.3 to 24.6	7.5	3.3 to 17.0
Hospital volume (reference ≤2 PUV case/yr)				
>2 PUV cases/yr	0.34	0.16 to 0.73	0.38	0.17 to 0.82

HR, hazard ratio; 95% CI, 95% confidence interval; PUV, posterior urethral valves.

(log-rank $P<0.001$). Stratified analysis for children with versus without pulmonary hypoplasia showed survival probabilities of 79% (95% CI, 73% to 85%) versus 99% (95% CI, 98.9% to 99.5%) at 1 month, 71% (95% CI, 63% to 78%) versus 97% (95% CI, 96% to 98%) at 1 year, and 59% (95% CI, 51% to 68% versus 96% (95% CI, 96% to 97%) at 5 years (Figure 2).

Mean ESKD intervention-free survival time was 19 (95% CI, 18 to 20) years. One-year probability of undergoing catheter placement and/or transplant was 7% (95% CI, 6% to 8%), 11% (95% CI, 10% to 13%) at 5 years, 13% (95% CI, 11% to 15%) at 10 years, and 20% (95% CI, 17% to 23%) at 15 years (Figure 3). Probability of undergoing an ESKD intervention was higher with a diagnosis of kidney dysplasia (log-rank $P<0.001$). Stratified analysis for children with versus without kidney dysplasia showed probability of undergoing an ESKD intervention as 27% (95% CI, 22% to 31%) versus 3% (95% CI, 2% to 4%) at 1 year, 38% (95% CI, 32% to 43%) versus 6% (95% CI, 4% to 7%) at 5 years, and 43% (95% CI, 37% to 48%) versus 6% (95% CI, 5% to 8%) at 10 years (Figure 4).

Discussion

This cohort provides a unique opportunity to analyze outcomes for a large number of patients with posterior urethral valves from multiple tertiary care institutions. In these children, we found a 5% mortality rate, with over half dying during the first 2 months of life. Mortality in posterior urethral valves has been difficult to predict given its rarity, but this statistic is important for prenatal and postnatal counseling of parents. Pulmonary hypoplasia had over seven-fold risk of death, and reduced the probability of 5-year survival from 96% to 59%.

A known sequela of lower urinary tract obstructions is oligohydramnios (11), which is a reported risk for ESKD (12). Normal lung development requires amniotic fluid and thus kidney development, and if normal development has not occurred by around 28 weeks, pulmonary hypoplasia ensues. Although the exact mechanism is not fully understood, the link between posterior urethral valves, oligohydramnios, and pulmonary hypoplasia is established (13). It is not surprising that a diagnosis of pulmonary hypoplasia increases the risk of death given that these children often need ventilator support with its inherent risks, and experience delay of surgical intervention for the urinary tract. This association raises the question of utility for antenatal intervention for posterior urethral valves. The use of antenatal vesicoamniotic shunting and fetal cystoscopy are controversial but purported to reduce mortality,

Table 4. Risk factors for dialysis catheter placement and kidney transplant in unadjusted and multivariable model Cox regression analysis

Initial Hospitalization Characteristic	Dialysis Catheter Placement				Kidney Transplant			
	Unadjusted		Multivariable Model		Unadjusted		Multivariable Model	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Admit age, d	1.0	0.99 to 1.0	1.0	1.0 to 1.0	1.0	1.0 to 1.0	1.0	1.0 to 1.0
<37 wk at birth	3.7	2.2 to 6.2	2.2	1.1 to 3.9	2.3	1.1 to 4.7	1.3	0.62 to 2.9
Kidney dysplasia	6.9	4.1 to 11.7	4.6	2.6 to 8.1	8.6	4.4 to 17.0	9.5	4.1 to 22.2
Sepsis	3.2	1.7 to 6.0	1.9	1.0 to 3.6	2.3	0.93 to 5.4	1.0	0.41 to 2.5
Pulmonary hypoplasia	7.3	4.1 to 13.1	3.0	1.6 to5.7	6.1	2.8 to 13.4	2.5	1.0 to 5.9

HR, hazard ratio; 95% CI, 95% confidence interval.

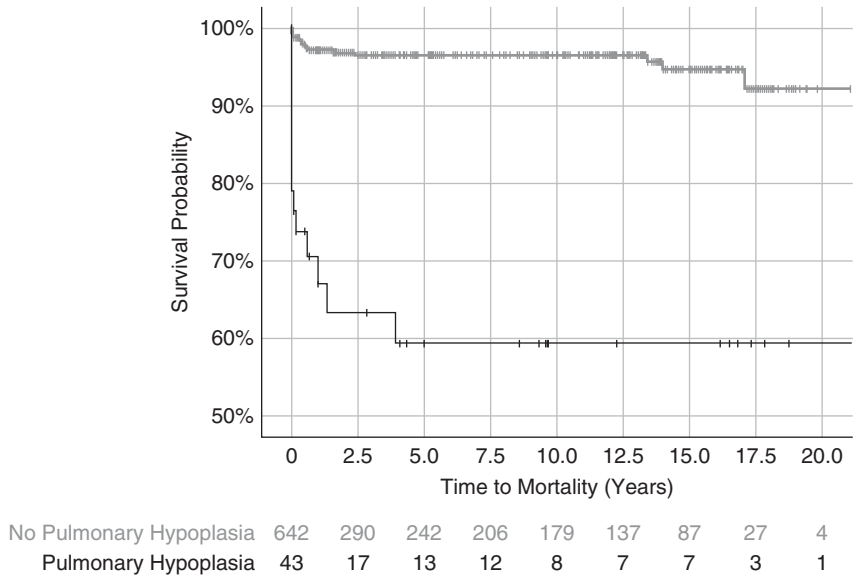

Figure 2. | **Survival among children diagnosed with pulmonary hypoplasia is markedly different than those without the diagnosis**. Five-year survival among those with pulmonary hypoplasia was 59% (95% CI, 51% to 68%) compared with 96% (95% CI, 96% to 97%) for those without pulmonary hypoplasia.

and improve long-term kidney function in some studies (14–16). However, fetal intervention does not come without significant risk, and currently cannot be undertaken before 20 weeks, at which time the fetus may already have abnormal kidney function and be developing pulmonary hypoplasia. Thus, more research is needed to better risk stratify which patients would most benefit from prenatal intervention on the basis of their imaging findings, urinary biomarkers of kidney injury, and serum creatinine and amniotic fluid levels (17).

We found that children admitted to hospitals with greater exposure to posterior urethral valves cases was protective. This finding is consistent with other reports of increased case volume yielding improved outcomes (18–20). The protective effect may be because of improved immediate postnatal planning and management, as

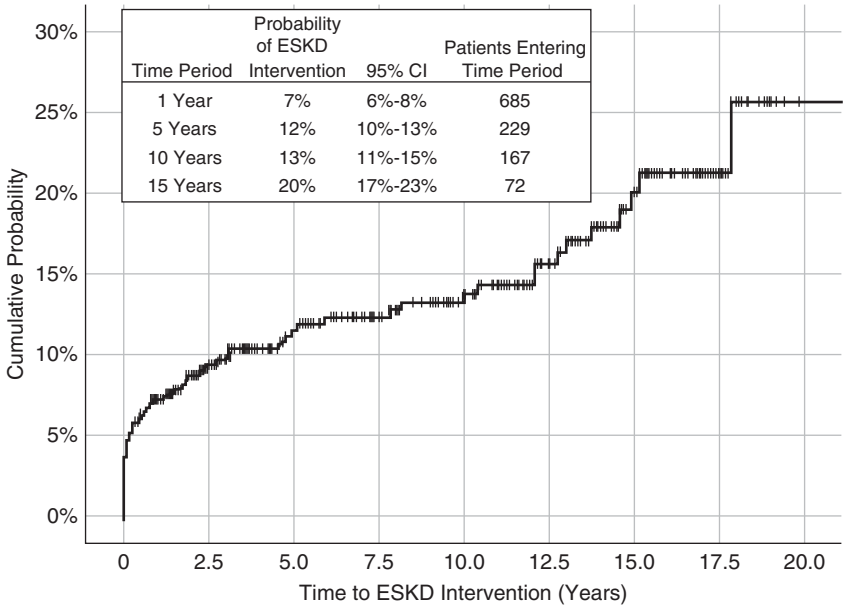

Figure 3. | **Cumulative probability of a child undergoing an ESKD intervention (one-survival) was 7% (95% CI, 6% to 8%) at 1 year, increasing to 13% (95% CI, 11% to 15%) by 10 years of age.**

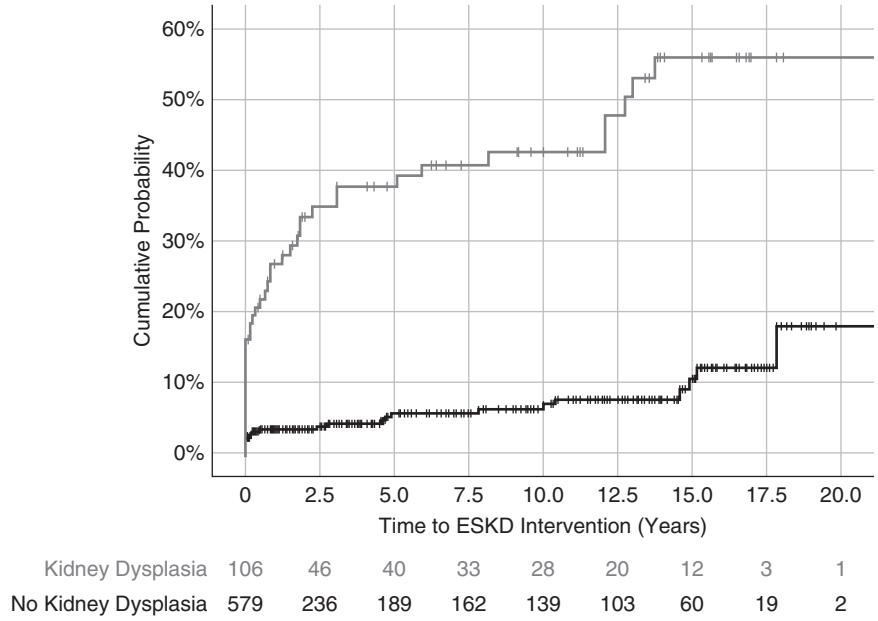

Figure 4. | Cumulative probability of an ESKD intervention (one-survival) occurring for children with kidney dysplasia was significantly higher compared with those without kidney dysplasia (log-rank *P*<0.001). Five-year probability was 38% (95% CI, 32% to 43%) for children with kidney dysplasia compared with 6% (95% CI, 4% to 8%) for children without kidney dysplasia.

exposure to these patients and their complex presentations provides opportunities to develop and improve standardized treatment protocols. A multidisciplinary approach taken between experienced neonatologists, pediatric nephrologists, pediatric urologists, and pediatric radiologists is paramount.

As with mortality, we found that the majority of initial dialysis catheter placement procedures occurred early in life. Of the 59 children (9%) who underwent one or more catheter placements, 69% had them placed during the first year of life, and 83% were placed during the first 5 years of life. This distribution is similar to that observed by McLeod *et al.* (21) in a recent multi-institutional analysis of children with posterior urethral valves. However, our overall rate of dialysis was lower, at 9% in our series versus 15% in theirs. Kidney dysplasia was found to be the strongest risk factor for undergoing dialysis catheter placement, with adjusted risk between two- and eight-fold higher. This is consistent with the known correlation between congenital kidney dysplasia and ESKD (22).

Kidney dysplasia was also the biggest risk factor for undergoing kidney transplantation, with an adjusted risk nine-fold higher than children without the diagnosis. Kidney dysplasia raised the probability of undergoing ESKD intervention from 6% to 38% by 5 years of age, and from 6% to 43% by 10 years of age. The presence or degree of kidney dysplasia truly relies on kidney biopsy, but ultrasonography and nuclear scintigraphy are often relied on for making this diagnosis. It is likely that the diagnosis of kidney dysplasia in our patients was made on the basis of imaging studies. Hyperechoic kidneys have been reported to portend a higher risk for kidney insufficiency and death in children with fetal diagnosis of lower urinary tract obstruction (11). Kidney parenchymal area (simply put as the total calculated kidney area minus the area of the pelvicalyceal system) has been associated with a higher risk of progression to ESKD in boys with posterior urethral valves (7). Quantity and quality of kidney parenchyma radiographically act as surrogate markers for kidney dysplasia, and our results strongly corroborate the relationship between kidney dysplasia and progression to ESKD. Interestingly, Matsell *et al.* (23) showed that, although patients with posterior urethral valves and radiographically defined kidney hypodysplasia do progress to CKD/ESKD at significant rates, they have relatively large kidney size compared with other children with kidney hypodysplasia. These findings indicate that the correlation between kidney size and development of ESKD in these children is complex and not fully understood. Our data show the importance of development of novel imaging tools and potentially biomarkers for kidney dysplasia to aid in risk stratification of patients.

The strength of this study is that it offers an analysis from a large database approach, allowing for stratified analysis of a large number of patients from multiple centers. The study does have limitations, the majority due to inherent limitations of the Pediatric Health Information System database, as well as the acknowledged limitations of retrospective cohort studies.

As the Pediatric Health Information System only contains data on hospitalizations, important information is missing, such as timing of clinic visits and results from laboratory and diagnostic testing. Consequently, disease laterality and/or severity, which may provide insight into treatment thresholds, is unknown. There is likely a broad range of treatment thresholds for dialysis and kidney transplant represented in this cohort, which may affect external validity.

Use of diagnostic codes for the presence risk factors can lead to heterogeneity in the cohort considered to be at risk. There is no standardized definition of kidney dysplasia or dysgenesis, nor is there a standardized definition for pulmonary dysplasia or hypoplasia. Patients were given these diagnoses likely on the basis of multiple parameters. Further research focused on patient-level data could discern a true threshold for dysplasia or dysgenesis on the basis of radiographic or pathologic findings.

As dialysis is sometimes delivered outside the hospital setting and therefore not reflected in the Pediatric Health Information System dataset, we used dialysis catheter placement as a surrogate. This may represent an overestimate of need for dialysis, as sometimes catheters are placed in a preventative fashion in concordance with valve ablation or urinary diversion if the need for dialysis is suspected. Of the 59 children who had a dialysis catheter placed, 33 (56%), did not undergo kidney transplantation. Of those 33, 24 (73%) had their dialysis catheter placed during their initial hospitalization. We believe this discrepancy to be secondary to early concern for need for dialysis that may not ultimately be needed, or less likely, may be needed only during the initial hospitalization.

Although the statistical methods used in this study adjust for different lengths of follow-up, actual follow-up is unknown as clinical follow-up is unavailable. We chose a conservative approach in calculating hazard ratios and estimated survival probabilities by defining follow-up as date of birth to date of discharge for the last known hospitalization. The 30% of patients who had no subsequent visits after their initial hospitalization may represent a healthy cohort who were followed clinically without need for additional hospitalizations. The subgroup analysis comparing risk characteristics between those with and without subsequent visits suggests this may be the case for some patients. However, we could not quantify what proportion of this group were successfully followed clinically and what proportion were in need of hospital care that was subsequently sought outside of their Pediatric Health Information System hospital. To better understand the accuracy of results, we compared hazard ratio and survival probability 95% CIs between models, using (*1*) follow-up on the basis of the last hospitalization, and (2) follow-up assuming all patients were followed until the end of the study period with no additional outcome events. We found confidence intervals overlapped for all adjusted hazard ratios and all survival probabilities up to 10 years. However, after 10 years, survival model confidence interval results began diverging and may not capture the true probability.

In conclusion, children with posterior urethral valves in this large, multi-institutional cohort had a 5% mortality rate, the majority dying within the first 2 months of life. Dialysis catheter placement was performed in 9% of patients, and 7% underwent kidney transplantation. Risk of death was higher with a diagnosis of pulmonary hypoplasia and kidney dysplasia had a higher risk ESKD intervention. These findings contribute to a better understanding of the natural history of posterior urethral valves. This knowledge is not only important for counseling of parents and assisting providers in developing individualized management plans, but also underscore the need for research to identify novel markers for poor kidney outcomes in children with posterior urethral valves.

Disclosures

Dr. D'Alessandri-Silva is a Scientific Advisory Board Member for Advicene. Ms. Herbst, Dr. Lockwood, Ms. Mosha, Dr. Tomlinson, and Dr. Wang have nothing to disclose.

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