Progression of Renal Insufficiency in Children and Adolescents With Neuropathic Bladder is Not Accelerated by Lower Urinary Tract Reconstruction

Vesna Ivančić, William DeFoor,* Elizabeth Jackson, Shumyle Alam, Eugene Minevich, Pramod Reddy and Curtis Sheldon

From the Division of Pediatric Urology, Cincinnati Children's Hospital, Cincinnati, Ohio

Abbreviations and Acronyms

1/Cr = inverse creatinine

CIC = clean intermittent catheterization

CRI = chronic renal insufficiency

DTPA = diethylenetetramine pentaacetic acid

ESRD = end stage renal disease

GFR = glomerular filtration rate

MDRD = modification of diet in renal disease

Study received institutional review board approval.

* Correspondence and requests for reprints: Division of Pediatric Urology, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave., MLC 5037, Cincinnati, Ohio 45229-3039 (telephone: 513-636-6758; FAX: 513-636-6753; e-mail: Bob.DeFoor@cchmc.org).

Purpose: Children with chronic renal insufficiency and neuropathic bladder resistant to medical management may require lower urinary tract reconstruction before renal transplantation. A low pressure urinary reservoir optimizes the chance of graft survival and may slow native kidney death. We evaluated whether the renal deterioration rate is affected by augmentation cystoplasty.

Materials and Methods: We performed a retrospective cohort study in children who presented to our institution with chronic renal insufficiency and neuropathic bladders from 2005 to 2009. Chronic renal insufficiency was defined as a glomerular filtration rate of less than 60 ml per minute. As a surrogate for renal function change, we used the inverse creatinine trend with respect to time to determine the progression rate of renal insufficiency before and after augmentation.

Results: A total of 11 patients with a mean glomerular filtration rate of 34 ml per minute per 1.73 m^2, mean bladder capacity 168 ml and mean compliance 3.5 ml/cm H_2O met study inclusion criteria. Bladder augmentation or replacement was done at a mean age of 9.7 years with a resultant mean capacity of 486 ml and compliance of 14.7 ml/cm H_2O. Mean followup was 4 years before and 1.9 years after augmentation. There was no statistically significant difference between the preoperative and postoperative slopes of inverse creatinine in 8 of 11 patients (73%). Two of the 3 patients (18%) with different preoperative and postoperative slopes had improving renal function after surgery. There was no statistically significant difference in slopes across all patients.

Conclusions: In our series bladder augmentation did not appear to hasten progression to end stage renal disease in patients with severe chronic renal insufficiency and neuropathic bladder.

Key Words: kidney; urinary bladder, neurogenic; kidney failure, chronic; reconstructive surgical procedures; kidney transplantation

More than 20% to 25% of children with ESRD have associated anatomical or functional lower urinary tract dysfunction.[1,2] Conversely select children with neurogenic bladder eventually have progression to ESRD.[3] The importance of this overlap between upper and lower urinary tract dysfunction is the causal relationship between high pressure, noncompliant bladders and resultant acquired renal failure.

Severe bladder dysfunction has deleterious effects capable of destroying not only native kidneys but also adversely affecting the function of transplanted kidneys.[3–5] For this reason staged lower urinary tract reconstruc-

0022-5347/10/1844-1768/0
THE JOURNAL OF UROLOGY®

Vol. 184, 1768-1774, October 2010
Printed in U.S.A.
DOI:10.1016/j.juro.2010.03.082

tion before renal transplantation has been done for the last 25 years[6] and numerous studies have documented the safety of renal transplantation into an augmented bladder.[7–11] Recent literature showing comparable graft survival in children with a normal bladder and those with a reconstructed lower urinary tract supports the argument that continent reconstruction does not adversely affect renal allograft function or survival.[2,6,12,13]

Nevertheless, controversy still exists about augmentation timing. Some groups argue that even moderate renal insufficiency is a relative contraindication to augmentation since it may hasten ESRD.[14] We studied the progression rate of renal insufficiency in patients with severe lower urinary tract dysfunction and evaluated whether the deterioration rate is affected by augmentation.

MATERIALS AND METHODS

We performed an institutional review board approved, retrospective cohort study in all children who presented to a single pediatric institution with severe upper and lower urinary tract dysfunction from 2005 to 2009.

Study Inclusion and Exclusion Criteria

Our inclusion criteria considered severe CRI to be stage 3 or higher chronic kidney disease, defined as a GFR of less than 60 ml per minute. All patients with severe lower urinary tract dysfunction underwent urodynamic testing and aggressive attempts at conservative rehabilitation with strict CIC and anticholinergic medication. Only those who needed lower urinary tract reconstructive surgery (neobladder or augmentation) due to a persistently hostile bladder (upper tract deterioration or failure to achieve safe bladder capacity/compliance) were chosen for this study. Patients with adequate bladder capacity and a low pressure reservoir in whom continent reconstruction consisted of certain procedures were excluded from analysis, including those with ureteral reimplantation, creation of a Mitrofanoff, Monti or Malone catheterizable channel, urinary undiversion or bladder neck reconstruction without augmentation. We also excluded patients already on renal replacement therapy, whether dialysis or renal allograft, and those who underwent staged, planned reconstruction just before transplantation since the deterioration rate cannot be determined in this population.

Data Acquisition

Patient demographics, urinary tract dysfunction etiology, surgical details, renal outcome and all available laboratory values were abstracted from the patient medical records at our institution and elsewhere. Except for creatinine valid surrogates for renal function accepted in the literature are GFR estimates, as measured by nuclear scintigraphy or more recently cystatin C. GFR estimates measured by ^{99m}Tc-DTPA were available preoperatively but not postoperatively in all patients. These invasive studies are rarely done compared to creatinine measurement, providing inadequate data for statistical analysis. Since the practice of obtaining cystatin C estimates of GFR in patients with CRI is relatively new, in most patients in whom augmentation was done before 2007 such levels were not determined preoperatively. Thus, we chose the change in 1/Cr as a surrogate for renal function, given that creatinine measurements were uniformly available before and after reconstruction, and provided enough data points for meaningful trend analysis.

Statistical Analysis

We plotted 1/Cr for each available data point with time to determine the progression rate of renal insufficiency before and after bladder augmentation. To estimate the linear trend in each patient before and after bladder augmentation we developed a linear model in each patient with a linear term for days (continuous variable), phase (preoperative or postoperative) and the days by phase interaction term. To compare preoperative and postoperative slopes, ie linear trends, we tested the interaction term in each patient at $\alpha = 0.05$. To determine whether there was a significant difference in slope before vs after bladder augmentation across all patients we applied the Wilcoxon signed rank test ($\alpha = 0.05$) using the estimated slopes in each patient. Patient 6 was excluded from these analyses due to inadequate preoperative followup to determine a reliable estimate of the linear trend. Analysis was done with SAS®, version 9.2.

RESULTS

During the study period 11 patients with severe upper and lower urinary tract dysfunction met inclusion and exclusion criteria. Urinary tract dysfunction etiology was cloacal malformation in 6 patients, VATER syndrome in 3, anorectal malformation in 1 and posterior urethral valves in 1. Mean followup before augmentation was 48 months (range 0.3 to 151). Mean followup after augmentation was 23 months (range 7 to 49). Mean age at lower urinary tract reconstruction was 9.7 years (range 3 to 18).

Urinary tract reconstruction included augmentation enterocystoplasty with ileum in 6 patients, a composite augment of gastric plus ileum in 1, gastrocystoplasty in 3 and a composite neobladder in 1. Concomitant procedures included urinary undiversion in 3 cases, a Mitrofanoff neourethra in 2, a Monti neourethra in 9, bladder neck reconstruction in 5, transureteroureterostomy in 3, ureteral reimplantation in 7 and native nephrectomy in 1. All patients were on a strict CIC protocol. Table 1 lists detailed demographic data on the study group.

Table 2 shows estimated renal function. Estimated mean GFR was 34 ml per minute per 1.73 m^2 on ^{99m}Tc-DTPA nuclear scintigraphy done less than 6 months before the surgery date. Postoperative GFR was estimated by repeat nuclear scintigraphy, serum cystatin C measurement or the MDRD Schwartz equation corrected for pediatric patients. The most recent estimated GFRs available are presented as familiar clinical correlates for comparison with 1/Cr trend