Pediatric Kidney Transplant Outcomes in the Steroid-Free Era

Steroids were once a critical part of post-transplant care for children who received a kidney transplant, and were notoriously linked to impaired growth, diabetes, and hypertension. But thanks to today’s steroid-free regimens, the outlook for these patients is brighter.

To paint a clearer picture of just how much better that outlook is, Juhi Kumar, MD, Assistant Attending Physician at NewYork-Presbyterian Hospital/Phyllis and David Komansky Center for Children’s Health and Assistant Professor of Pediatrics at Weill Cornell Medical College, has been leading a study assessing pediatric renal transplant outcomes before and after 2005 — the year when steroids were eliminated from post-transplant care at NewYork-Presbyterian Hospital — to see how outcomes have changed. While data have yet to be published, the results so far suggest that after kidney transplantation, children have greater gains in height than they did during the era of steroids and need less antihypertensive medication, while experiencing similar graft function and survival.

“The use of medications other than steroids after transplant can promote a child’s growth, reduce the need for cholesterol-lowering and blood pressure medications, and lower the risk of post-transplant diabetes,” says Dr. Kumar. “Our transplant team tailors drug regimens to meet the needs of each patient.” Molecular tools developed by the adult transplant team at NewYork-Presbyterian Hospital/Weill Cornell Medical Center are a key part of individualized care, and new anti-rejection medications continue to be studied.

In cooperation with The Rogosin Institute, NewYork-Presbyterian/Weill Cornell has a long and highly successful history of performing pediatric kidney transplants.

Genetic Roots of Kidney Disease in Children May Run Deep

Congenital disorders of the kidney and urinary tract are the most common cause of kidney failure in children. As many as one in five children with these defects has an associated hereditary disorder that can be detected with genomic testing, but is not always performed clinically. Identifying these genetic abnormalities early enables practitioners to better understand each patient’s disorder as well as the risk of other family members carrying the mutation, and clarify the optimal course of care.

That’s the goal of Ali Gharavi, MD, Chief of Nephrology at NewYork-Presbyterian Hospital/Columbia University Medical Center and Professor of Medicine. He is collaborating with pediatric nephrologists, urologists, and medical geneticists at NewYork-Presbyterian/Morgan Stanley Children’s Hospital, as well as genetic counselors, immunologists, and others, to explore the genetic mutations that may not only be linked to a particular urologic abnormality, but may signal a broader syndrome with wider clinical implications that requires a multifaceted regimen of personalized care.

For example, a mutation in the HNF-1β gene causes renal cysts and diabetes syndrome, which causes renal cysts that may be detected in utero. But the damage doesn’t stop there: Over time, patients may also develop early-onset non-insulin dependent diabetes, genital tract malformations, hyperuricemia, and early-onset gout. Armed with the findings of genomic testing, however, clinicians can assemble a plan of care for a child that includes management of diet to prevent obesity and the use of uric acid-lowering medications to avoid further complications.

Already, 80 to 100 mutations have been identified which...
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dispose individuals to kidney and urinary tract disorders. One mutation in the DSYT1K gene was identified by Dr. Gharavi and his colleagues and determined to be a major determinant of urinary tract development (N Engl J Med. 2013;369:621-629). Other mutations are associated not only with urinary tract abnormalities, but autism, schizophrenia, developmental delays, and other neurocognitive defects. A recent grant to the Columbia University George M. O’Brien Urology Cooperative Research Center will fuel the search for more clues regarding the genetics and developmental origins of urinary tract defects, such as vesicoureteral reflux and other congenital urologic disorders.

Because congenital abnormalities of the kidney and urinary tract may represent just one part of a constellation of problems caused by a single genetic lesion, Dr. Gharavi advocates for genomic testing of all children with chronic kidney disease and is applying for federal funding to pursue this research. “Our objective is to bring personalized genomic nephrology from the laboratory into the clinic,” he says. “With recent genomic advances, we now have the opportunity to make a precise genetic diagnosis and personalize care based on the specific molecular mechanism underlying each patient’s disease.”

“Outcomes may be worse in children with genomic syndromes causing multiple health problems, and there is an extra level of care needed for these patients,” adds Fangming Lin, MD, PhD, Chief of the Division of Pediatric Nephrology at NYP/Morgan Stanley Children’s and Associate Professor of Pediatrics and Pathology and Cell Biology. “The sooner we can identify the genetic cause of their abnormalities, the better we can care for them.”

Easing the Transition for Pediatric Kidney Transplant Recipients

“I always intended to be a doctor for patients of all ages.” Those words are fitting for Hilda Fernandez, MD, MSCE, who is both a board-certified internist and pediatrician. Dr. Fernandez completed fellowships in both pediatric nephrology at UCLA Medical Center and adult nephrology at the University of Pennsylvania, and she is currently continuing her training in kidney transplantation at NewYork-Presbyterian/Morgan Stanley Children’s Hospital. Her decision to “double-dip” is benefitting children who have had kidney transplants and are reaching the age when they will need to transition to adult care. That transition is the focus of Dr. Fernandez, who is also Instructor in Medicine at Columbia University College of Physicians and Surgeons.

Thanks to medical and surgical advances developed at NewYork-Presbyterian/Columbia, more people than ever have access to a kidney transplant. While pediatric transplant recipients receive continuous and ongoing care while they are children, many do not maintain the same level of care as they enter their adult years, due to a number of barriers. “As adolescents reach the adult medical world, there is a huge change in their continuity of care,” says Dr. Fernandez. “They’ve only known their pediatric specialists, and they may not feel that adult care practitioners understand their needs as well as their pediatric counterparts.” Indeed, several studies of pediatric allograft recipients who transitioned to adult care showed that this transition may be linked to non-adherence to care and subsequent graft loss.

Armed with a master’s degree in Clinical Epidemiology, Dr. Fernandez is studying outcomes in pediatric kidney transplant recipients to study the association with transition of care. While at the University of Pennsylvania, she and her colleagues at The Children’s Hospital of Philadelphia performed a retrospective chart review to analyze the effects of the transition to adult transplant care on kidney function among 48 patients who had a kidney transplant as a child. They found that the rate of kidney function decline in the year prior to transitioning to adult care was significantly greater than in the year following that transition. When censoring for allograft loss within one year after transition, this interaction was nonsignificant. The results were presented at the 2014 annual meeting of the American Society of Nephrology.

While the results are preliminary, transition of care was not independently associated with acceleration in kidney function loss. A future analysis will investigate factors such as race, age of transition, and prior episodes of allograft rejection as potential risk factors for declines in renal function. To support her research, Dr. Fernandez is the recipient of an NIH National Research Service Award to study the effects of the transition to adult care on outcomes when she completes her kidney transplant fellowship in 2015.

Pediatric nephrologists at NYP/Morgan Stanley Children’s work hand-in-hand with adult nephrologists at NewYork-Presbyterian/Columbia to prepare adolescents and young adults for a safe transition from pediatric to the adult nephrology care, especially among children whose kidney transplantation was preceded by surgery to correct complex congenital anomalies. Says Fangming Lin, MD, PhD, Chief of the Division of Pediatric Nephrology at NYP/Morgan Stanley Children’s and Associate Professor of Pediatrics and Pathology and Cell Biology, “Our goal is to formalize this program to help coordinate that transition and to make it as streamlined and as efficient as it can be.”

For more information about pediatric nephrology at NYP/Morgan Stanley Children’s or to refer a patient, contact (212) 305-5825.
Growth hormone therapy can help children whose growth is impaired by chronic kidney disease (CKD) attain an additional couple of centimeters of height a year. But children who don’t take the subcutaneous injection every day, as prescribed, fail to achieve this benefit at a time when they have the greatest chance to do so. That was one of the findings of a study led by Oleh Akchurin, MD, Assistant Attending Physician at NewYork-Presbyterian Hospital/Phyllis and David Komansky Center for Children’s Health and Assistant Professor of Pediatrics at Weill Cornell Medical College, published in the Clinical Journal of American Society of Nephrology in September 2014 (2014:9:1519-1525).

Impaired growth is one of multiple issues that can affect quality of life in children with CKD, including psychosocial effects associated with short stature. Damaged kidneys can slow a child’s growth by:

• Causing mineral and bone disorder, which occurs when vitamin D is not converted into calcitriol, starving the bones of calcium.
• Creating acidosis, triggering a response by the body to slow growth to focus energy on restoring the balance.
• Decreasing appetite.
• Decreasing the production of erythropoietin and causing anemia.
• Causing polyuria, which disrupts the body’s fluid balance and provokes mineral loss.
• Preventing the body from correctly using growth hormone.

In addition to recombinant human growth hormone, medications that may be used to enhance growth in children with CKD include phosphate binders, alkali, active and nutritional vitamin D, iron, and erythrocyte-stimulating agents. Dr. Akchurin and his co-investigators assessed medication adherence and growth in 834 children with CKD participating in the Chronic Kidney Disease in Children (CKiD) cohort study. Self-reported non-adherence to therapy, relayed during the first seven study visits, ranged from 4 percent for erythrocyte-stimulating agents to 22 percent for nutritional vitamin D.

Children who did not adhere to daily growth hormone therapy did not experience a change in their height z score, while those who did take the hormone as directed demonstrated an increase in height. Nonadherence to other medications did not significantly affect height z score. "Nonadherence to growth hormone therapy was associated with poorer growth velocity in children with CKD, suggesting an opportunity for intervention and improved patient outcomes," the investigators concluded.

To learn more, Dr. Akchurin and other investigators — including Juhi Kumar, MD, Assistant Attending Physician at NYP/Komansky Center and Assistant Professor of Pediatrics — are designing another study to identify novel factors that may influence a child’s response to growth hormone therapy and to further clarify the benefits of this therapy, particularly those related to quality of life. “Clearly some children respond better to growth hormone therapy than others,” Dr. Akchurin notes. “Recent scientific data suggest that there must be other as yet unidentified factors that contribute to growth delay in these children. For example, does inflammation play a role? We want to find out.”

“Growth hormone is the most expensive medication we use to treat children with chronic kidney disease,” adds Eduardo Perelstein, MD, Chief of the Division of Pediatric Nephrology at NYP/Komansky Center and Associate Professor of Clinical Pediatrics. “And its benefits may extend beyond growth, such as increasing muscle mass and reducing inflammation. So we want to learn how to use it wisely.”

For more information or to refer a patient with CKD for care at NYP/Komansky Center, contact (646) 962-4324.

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acclaimed history of performing kidney transplantation, having completed more than 4,200 transplants in the program’s first 50 years. The first transplant in the New York metropolitan area was performed through the program in 1963, as well as the area’s first pediatric kidney transplant in 1964. The team has performed hundreds of pediatric kidney transplants since then. NewYork-Presbyterian/Weill Cornell remains one of the highest volume transplant centers in the Tri-State area, featuring low rates of kidney rejection and high rates of graft survival comparable to national averages.

“We offer a comprehensive and personalized approach to treating children and adolescents who may need a kidney transplant,” says Eduardo Perelstein, MD, Chief of the Division of Pediatric Nephrology at NYP/Komansky Center and Associate Professor of Clinical Pediatrics. “We are fully committed to providing every possible opportunity for transplantation for all of our patients.”

For more information about pediatric kidney transplantation or to refer a patient for a transplant evaluation, contact (646) 962-4324.
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