Brazilian Journal of TRANSPLANTATION

https://doi.org/10.53855/bjt.v27i1.568_ENG

REVIEW ARTICLE

Particularities in Urinary Tract Management before Pediatric Renal Transplantation in Small Children

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Section editor: Ilka de Fátima Santana F Boin

Received: Feb 07, 2024 | Accepted: Feb 14, 2024

ABSTRACT

The number of renal transplants in small children (infants or under 15 kg) has risen amid improved prenatal diagnosis, earlier referral to specialized centers, and advances in care of kidney failure patients. Most of these patients have congenital anomalies of the kidney and urinary tract, which need correcting prior to transplantation. In order to meet this challenge, the presence of a pediatric urologist working together with an experienced multidisciplinary team is paramount. This study provides a narrative review compiling details on the urological management of the urinary tract of low-weight patients with chronic kidney disease and congenital anomalies of kidney and urinary tract (CAKUT) referred for renal transplantation (RT). **Objectives:** Conduct a narrative review about urologic correction in small children before RT. **Methods:** Articles published in English language over a 20-year period were reviewed. The keywords considered for the research and article selection were pediatric RT or pediatric kidney transplantation and children or small children or small infants or young children or young infants and urinary tract reconstruction and CAKUT. Some articles that are reference to elucidate the urological aspects of the review were also included.

Descriptors: Renal Transplantation; Infants; Low-Weight; Urologic Disease; CAKUT.

Particularidades no Manejo do Trato Urinário antes do Transplante Renal Pediátrico em Crianças Pequenas

RESUMO

O número de transplantes renais em crianças pequenas (bebês ou com menos de 15 kg) aumentou devido à melhoria do diagnóstico pré-natal, ao encaminhamento mais precoce para centros especializados e aos avanços no tratamento de pacientes com insuficiência renal. A maioria desses pacientes tem anomalias congênitas do rim e do trato urinário, que precisam ser corrigidas antes do transplante. Para enfrentar esse desafio, a presença de um urologista pediátrico trabalhando em conjunto com uma equipe multidisciplinar experiente é fundamental. Este estudo fornece uma revisão narrativa compilando detalhes sobre o manejo urológico do trato urinário de pacientes de baixo peso com doença renal crônica e anomalias congênitas do rim e do trato urinário (CAKUT) encaminhados para transplante renal (TR). **Objetivos:** Realizar uma revisão narrativa sobre a correção urológica em crianças pequenas antes do TR. **Métodos:** Foram revisados artigos publicados em língua inglesa nos últimos 20 anos. As palavras-chave consideradas para a pesquisa e seleção de artigos foram TR pediátrico ou transplante de rins e crianças, ou crianças pequenas, ou lactentes pequenos, ou crianças jovens, ou lactentes jovens e reconstrução do trato urinário e CAKUT. Alguns artigos referenciados para elucidar os aspectos urológicos da revisão também foram incluídos.

Descritores: Transplante de Rim; Lactentes; Baixo Peso; Doença Urológica; CAKUT.

INTRODUCTION

Prior to 1980, low-weight pediatric patients, under 15 kg, presenting with kidney failure were not candidates for renal transplantation (RT) and only select cases were treated with dialysis.[1] Although this subgroup of small patients represents only a minority of cases, numbers have been rising, where underlying urological anomalies are the leading cause of renal failure in this population.

Congenital anomalies of kidney and urinary tract (CAKUT) denote a wide array of malformations that can affect the upper urinary tract (kidneys and ureters) and lower urinary tract (bladder, genitalia and urethra) and require individualized treatment. The highly heterogeneous nature of these diseases hampers comparison and interpretation of RT in this population.[2] Complex corrective procedure may be needed to prevent progression of renal disease from the perinatal period or when kidney failure occurs and to make future RT feasible.

The collaborative efforts of a number of specialists (nephrologists, urologists, intensive care physicians, pediatric anesthesiologists, surgeons, and nurses, among others), technical advancements, as well as advances in equipment and materials available to care for small patients have contributed to improved outcomes and a consequent rise in the number of patients eligible for this modality of treatment. The ability to establish a diagnosis during the prenatal period is also a contributory factor, allowing early referral of the most serious cases to specialized centers for managed treatment.

However, despite transplantation being the best therapeutic approach for children with kidney failure, and most experts recommending transplant as soon as possible,[3-5] RT in small children remains a challenge. In addition, the low number of small patients undergoing transplantation hinders training of professionals specialized in this area.[6]

Although there is no consensus on the ideal weight or age at which RT should be carried out,[7] many studies suggest that patients weighing around 6-7 kg can safely receive a graft at specialized centers.[6] Patients with kidney failure have nutritional deficit and, therefore, weight is more important than age in establishing a reference value for small patients. Many centers deem 15 kg as the acceptable weight for RT.[3] The adequate weight for correction of different CAKUT depends on the type of procedure to be performed, where this often commences during the perinatal period.

Correcting urological anomalies prior to RT is necessary for the recipient to have an adequate bladder reservoir, with low storage pressure and good emptying,[8] and low risk of urinary infections, in an effort to preserve residual diuresis and reduce clinical repercussions as much as possible. Also, other associated congenital anomalies, such as anorectal malformations, should be treated prior to transplant to prevent immunosuppression-related complications.

Integrating urological management with transplantation should be the primary goal for these patients in a bid to speed up the process,[3] limit the number of interventions the child must undergo, and to avoid jeopardizing the future graft.[1] This is important because both urological assessment and previous correction of anomalies take time and can delay RT.[3] A fundamental point is that the long-term results of transplantation compared with dialysis therapy prompt the former to be carried out as soon as possible.[9]

The objective of this narrative review is to describe the assessment and care in the urological management performed prior to RT in small children, with an emphasis on correction of CAKUT and individualized care, drawing on the literature and experience of the specialized service for RT in low-weight patients.

Pre-transplant assessment

When the urinary tract is thoroughly assessed and adequately treated before RT, the primary underlying cause of the disease has little impact on the outcome of the transplant itself, even in small children.[10]

Urological assessment prior to transplantation should include a detailed clinical history of the patient,[8,11,12] encompassing the prenatal period and intrauterine procedures, along with urinary diary containing notes on frequency and urinary flow. In small children with urinary stomas, or those still in use of diapers, this information is collected based on the weight and number of diapers used. Description of the aspect of the urinary stream in boys can reveal cases of infravesical obstruction when there is a weak urinary stream, e.g., in cases of posterior urethral valve (PUV).

During physical examination, assessment of the abdomen with description of urinary or intestinal stomas, when present, can help in devising the strategy for surgical correction. The assessment of genitalia can reveal details on the underlying disease, such as ectopic ureter or anorectal anomaly (Fig. 1), or disclose testicular dystopia in boys, which should be corrected before transplantation. The physical examination of the dorsal region should be performed to check for the presence of sacral stigmas, often associated with cases of neuropathic bladder.

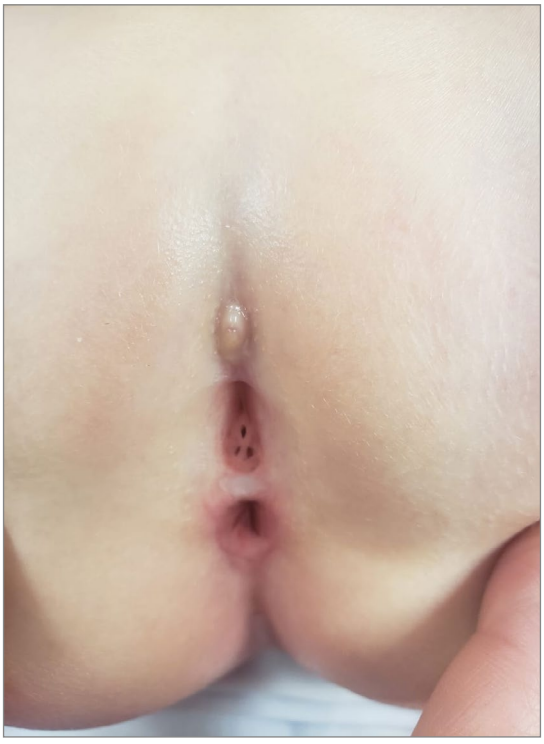

Figure 1. Exam of patient genitalia showing bilateral ectopic ureters associated with anorectal anomaly (rectovestibular fistula).

Ultrasound scans disclosing the upper urinary tract, size of kidneys,[4] degree of hydronephrosis, data on bladder capacity, bladder wall thickness, and postvoiding residual volume should ideally be performed by a radiologist who has experience working with the pediatric population. This exam may require patience by the examiner because young patients can often be uncooperative when asked to empty the bladder for measuring residual volume. Observing more than one cycle of bladder filling and emptying can help determine important data, but requires time and availability on the part of the radiologist and patient´s family.

Contrast-enhanced radiographies, especially a voiding cystourethrogram (VCUG), help show the anatomical aspects of the bladder and urethra and uncover vesicoureteral reflux (VUR).[4] For this test, details of the volume of iodinated contrast infused and images of the urethra without catheter during the voiding phase for more than one view are essential. Contrast-enhanced cystography of urinary stoma, particularly when diversion procedures were performed by other services, may be decisive in establishing the surgical strategy.

Performing a urodynamic study in children, although recommended by some authors prior to RT to disclose important data such as bladder compliance, voiding pressure and postmicturition residual volume[4], can cause anxiety and require careful interpretation by a specialist experienced with the test in this age group.[13,14] The study in small children can be affected by crying, hampering analysis.

Pre-operative preparation

Social and economic aspects should be taken into account when establishing the surgical strategy for correcting urological anomalies.[8] Many of these children will require clean intermittent catheterization to perform adequate bladder emptying, rendering assessment by stoma therapist nurses with experience in urological preparation essential. In the event that catheterization cannot be performed using the urethral route, continent appendicovesicostomy using the Mitrofanoff technique is performed.[15] Training family members who are the direct caregivers of the child and explanation to patients in a playful way can help reduce the anxiety associated with the procedures.

Many individuals with CAKUT also have bladder and intestinal dysfunctions, which can lead to poor bladder emptying and greater risk of urinary infections.[16] Lower urinary tract infections should be identified and treated appropriately,[11] as should constipation issues. Patients with lower urinary tract obstruction, such as those with PUV, urethral atresia, or neuropathic bladder, constitute a high-risk group for bladder dysfunction following transplantation.[17] Evidence shows that reimplantation of the ureter of the transplanted kidney in thick-walled, fibrotic, noncompliant, high-pressure bladders is associated with a higher incidence of graft loss.[12]

Dialysis method

For children with kidney failure, the metabolic and nutritional consequences determine the need for dialysis before transplantation in most of these cases.[17] More severe cases may commence dialysis therapy soon after birth,[2] whereas others start on dialysis after correction of the underlying anomaly due to the metabolic changes promoted by surgical trauma, especially when glomerular filtration rate is at a threshold level.

Urological correction should take into account the modality of renal replacement therapy and hemostasis control should be rigorous, since small patients can have higher levels of bleeding,[10] where loss of only a low volume of blood can have a major effect. In patients on peritoneal dialysis, a temporary or permanent switch in method for hemodialysis may be necessary during procedure involving access to the peritoneal cavity. A reserve of blood components and immediate postoperative monitoring in the intensive care unit are paramount. Having a team of pediatric nephrologists, pediatric, or vascular surgeons experienced in handling venous access and hemodialysis in small patients reduces the likelihood of complications and improves the safety of this form of renal replacement therapy.[18]

Hemodialysis prior to the procedure and immediately after should be done without heparin if it is possible, trying to minimize bleeding in surgical wounds. Despite these precautions, hemorrhage is an expected complication, most often treated conservatively and with replacement of blood components.

Technical principles

The main reason for the rise in number of transplants in low-weight children is the ongoing improvement in care available for neonates and infants with kidney disease who can receive the clinical treatment and dialysis required,[10] besides the improved management of urological anomalies. To this end, teams with expertise in treating small children, use of surgical loupes, and the right material resources are important. When fine instruments for endoscopy are available, procedures such as PUV resection can be carried out patients from the neonatal period. Careful control of intraoperative hemostasis through judicious use of electrocautery and surgical thread with noncutting needles can make a difference in small patients. In cases requiring multiple procedures prior to RT, the sites of incision must be chosen carefully to avoid weakening the vascularization of the abdominal wall, bearing in mind the site of a future transplanted allograft.[4]

Correction of urological anomalies

Many studies reporting the outcomes of RT in CAKUT patients fail to include cases with malformations of the upper urinary tract, probably because bladder pathologies have a greater impact on graft function compared to upper renal and ureter anomalies.[19] Highly-invasive procedures such as nephrectomies are typically performed prior to RT in the presence of difficult to control hypertension, severe proteinuria, and kidneys that are enlarged or at greater risk of infection. In general, tissues of the upper urinary tract can be retained because they may serve for graft rescue in the event of a ureter loss due to ischemia, for example.[8] Especially in small children, management to remove fluids for dialysis can be challenging in anephric patients. This is mainly because, in order to achieve adequate nutrition, patients must consume liquids in the form of infant formulas.[20] Although less common, lithiasis or neoplasms must also be ruled out[12] or treated appropriately.

Correcting ureteropelvic junction (UPJ) obstructions will preserve residual diuresis and reduce the risk of urinary infection. While surgical intervention of the UPJ in children under 6 months of age is relatively rare, this may be required and entails some technical challenges[21] that can be overcome using the right equipment and materials by an experienced team.

In patients with VUR associated with infection or significant urinary stasis, reimplantation should be performed prior to RT, albeit via surgical, laparoscopic, or endoscopic approaches, observing the technical principles used in patients not indicated for renal replacement therapy. In small children, if there is adequate bladder emptying and no urinary tract infection or urinary stasis, the patient may be cleared for transplantation without the need for prior intervention, given the high rate of spontaneous resolution of VUR through maturation of the ureterovesical junction (UVJ) with growth and development. Postectomy is recommended in boys with reflux, and in all others with CAKUT, in order to reduce the risk of urinary infections.[22]

In cases with ectopic ureter, surgical correction also aims to provide urinary continence. In some cases of infants that are still in use of diapers, identifying ectopic ureter requires experience and a trained eye on the part of the examining urologist. Cases with bilateral ectopic ureter can be associated with urinary bladder agenesis (Fig. 2), due to failure of integration of the ureters and mesonephric duct into the trigone during embryogenesis.[23] In such cases, the urinary bladder reservoir must be constructed, preferably using intestine (ileal neobladder), and the Mitrofanoff procedure performed to make RT viable.

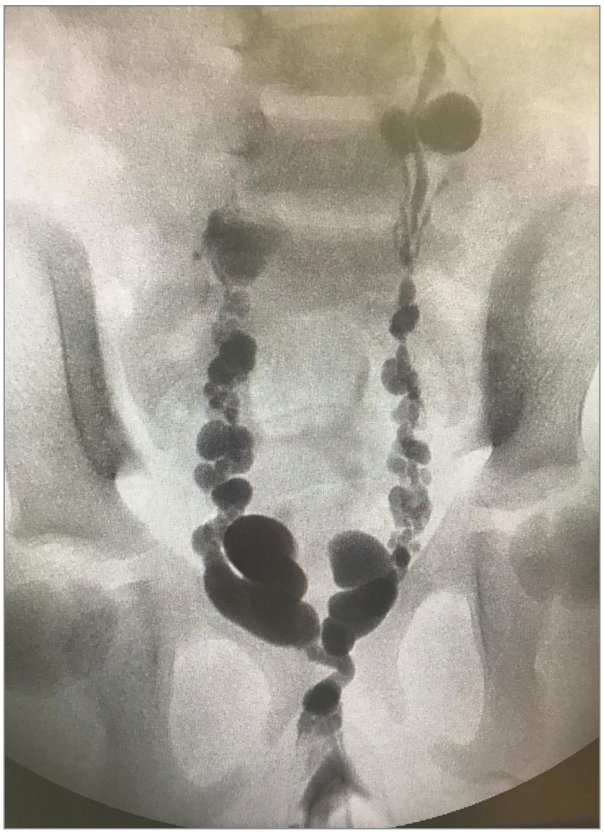

Figure 2. Contrast-enhanced retrograde cystography of patient with bilateral ectopic ureters (draining into urogenital sinus), urinary bladder agenesis associated with Müllerian malformation. There is reflux of contrast to both ureters with primitive appearance (embryonic).

In the management of the lower urinary tract, when there is inadequate urinary bladder emptying, incontinent diversions of the bladder (vesicostomy) can prove a satisfactory method for draining urine in small children. However, this is not the most recommended approach in the context of RT.[8] Although vesicostomy can be present at time of transplantation in some small children, this is the exception rather than the rule.[24,25]

In cases of infravesical obstruction, e.g., in PUV, endoscopic correction is indicated as soon as possible. Nevertheless, even with early ablation of the valve during the postnatal period, urinary bladder dysfunction may persist and lead to recurrent urinary infections and decline in renal function. Alpha-blockers, anticholinergic agents, bladder training, and clean intermittent catheterization with or without night drainage[26] are treatment options for urinary bladder dysfunction.

When effective micturition via the urethral route is not possible, leading to incomplete bladder emptying jeopardizing the future graft, stomas or continent urinary diversions are indicated, taking into consideration the preparation of the patient and family as outlined earlier. The routinely used Mitrofanoff technique can be performed in conjunction with bladder augmentation or neobladders, to ensure more effective emptying.

Controversy exists over the safety of renal grafts when transplanted in patients with bladder augmentation given the higher risk of urinary infections in immunosuppressed patients.[27] However, the risk of transplantation in a nonfunctional bladder is also real and perhaps greater, because of the added problem of high-pressure micturition. Bladder reconstruction should be carried out as soon as abnormal bladder function is identified prior to RT, such that the immunosuppression regimen does not impact the healing process.[27] This procedure can be performed in small children, provided this is done under the right clinical conditions and that the recommendations for training of families are observed. Smaller children are often able to quickly adapt to Mitrofanoff catheterization (Fig. 3) and to the other care procedures, such as flushing out the reservoir to reduce the amount of mucus when augmentation-using intestine has been performed. Generally, although bladder reconstruction is a major operation, patients can be cleared to undergo RT just 3 months after the procedure,[28] following a new contrast-enhanced radiograph to confirm the presence of an adequate reservoir.

In patients with Prune Belly syndrome, the principles for urological preparation for RT are the same as those described earlier, except that, in small children, reconstruction of the abdominal wall (abdominoplasty) should be postponed in order to prevent hypoperfusion of the graft at the time of transplantation due to lack of space in the abdominal cavity.

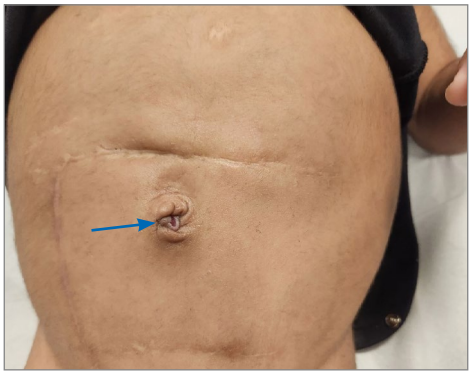

Figure 3. Transplanted low-weight posterior urethral valve (PUV) patient with Mitrofanoff in umbilical region (blue arrow).

CONCLUSION

Urological preparation for RT in small children is feasible and should precede transplantation, particularly when performed within specialized services employing the proper material resources and multidisciplinary team working in unison. Some technical principles should be observed and the presence of a pediatric urologist experienced in handling these patients is vital, whether deployed in assessment before clearance for transplantation, the correction of urological anomalies, or during long-term follow-up after RT. The correction of congenital anomalies should be individualized and should ideally take place before transplantation to allow better healing and reduce the risk of immunosuppression-related infection.

CONFLICT OF INTEREST

Nothing to declare.

AUTHOR'S CONTRIBUTION

Substantive scientific and intellectual contributions to the study: Ascar PCB, Leão JQS, Camargo MFC, Nogueira PCK; **Conception and design:** Ascar PCB, Nogueira PCK; **Data analysis and interpretation:** Ascar PCB, Nogueira PCK; **Article writing:** Ascar PCB, Leão JQS, Nogueira PCK; **Critical revision:** Leão JQS, Camargo MFC, Nogueira PCK; **Final approval:** Camargo MFC.

DATA AVAILABILITY STATEMENT

The data sets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

FUNDING

Not applicable.

ACKNOWLEDGEMENT

Not applicable.

ETHICAL APPROVAL

This article is part of a larger study previously submitted to and approved by the Research Ethics Committee of Hospital Samaritano Higienópolis and by Plataforma Brasil (CAAE permit no. 48790821.8.0000.5487). Free and informed consent was obtained from the guardians of patients whose images are contained in the present article.

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