



Renal function outcomes in pediatric patients with symptomatic reflux into the transplanted kidney treated with redo ureteroneocystostomy

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Summary

Introduction

Asymptomatic post-renal transplant reflux is common but only 5–10% patients are diagnosed with vesico-ureteral reflux in the setting of post-transplant febrile urinary tract infections, requiring redo ureteroneocystostomy (redo-UNC). Here we report the renal function outcomes of 37 such patients, stratified by lower urinary tract (LUT) status.

Objective

We hypothesized that those with pre-transplant LUT dysfunction would have lower glomerular filtration rate (GFR) on follow-up.

Study design

Using procedure codes, 37 patients who underwent renal transplant followed by redo-UNC for transplant reflux at our institution between 1991 and 2014 were identified. Patient characteristics and GFR levels from four different time points were recorded. Comparisons were made between those with and without LUT dysfunction, using Fisher's exact, Wilcoxon rank sum, or signed-rank tests. Generalized estimating equations were constructed to account for the clustered nature of GFR within each LUT group and to assess their change over time.

Results

Twelve patients (32%) had pre-transplant LUT dysfunction. The proportion of males in this group was significantly higher (75% vs. 32%, $p = 0.032$), and there was no statistical difference towards presenting earlier with post-transplant reflux (1.4 vs. 2.3 years, $p = 0.087$). After an average of 4.9 years, the median GFRs were similar between the two groups (53 mg/dL vs. 58 mg/dL, $p = 0.936$). There was no significant difference in GFR at this last follow-up time point in patients with and without LUT dysfunction.

Discussion

Vesicoureteral reflux in the setting of renal transplantation is common and doesn't often require repair. In our series, we found that those with LUT dysfunction did not present statistically sooner with symptomatic transplant reflux. Longer-term follow-up did show a decline in GFR but did not reveal a difference in GFR in patients' with and without LUT dysfunction.

Conclusions

Pediatric post-transplant GFR after open redo ureteral reimplant decreases over time in similar fashion in patients with symptomatic reflux regardless of whether they have LUT dysfunction or normal anatomy. Vigilance should apply to the recognition, treatment, and follow-up of all symptomatic transplant reflux regardless of LUT status.

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Introduction

Febrile urinary tract infections (UTIs) after pediatric renal transplant can cause significant morbidity to both patient and graft function. In renal transplant, the donor ureter is anastomosed to the recipient bladder. Depending on the preference of the transplant surgeon, some would use surgical techniques to recreate the antireflux mechanism while others would not, for fear of creating secondary renal obstruction over the more benign vesico-ureteral reflux.

In fact, asymptomatic post-transplant reflux is common. While the true prevalence in the pediatric population is unknown since routine voiding cystourethrogram (VCUG) after transplant is not standard practice, it has been reported in the adult literature to be 40.7% at hospital discharge [1] and 78% at 12 months after the transplant [2]. Not surprisingly, the likelihood of reflux in transplant recipients increases with time from transplant, and this is true regardless of surgical techniques [3]. Fortunately, the majority of the patients with post-transplant reflux are asymptomatic, and the survival of graft or patient is not affected [1,4,5].

A subset of patients with post-transplant reflux does ultimately develop recurrent febrile UTIs or pyelonephritis. Previous studies have suggested that approximately 5–10% of all pediatric renal transplant patients fall in this subset and require additional surgical procedures to correct the reflux [6,7]. At our institution, the surgical procedure of choice in this setting is extravesical redo ureteroneocystostomy (redo-UNC). Extravesical ureteral reimplants were performed by creating a detrusor tunnel in a 3:1 ratio to the ureter with anastomosis of the ureter to the cystotomy and closure of the overlying tunnel. Further details and short-term clinical outcomes have been previously described [6]. The goals of this procedure being prevention of future infections of the renal graft and preservation of graft renal function.

In this study, we aimed to report the long-term renal functional outcomes in an updated series of pediatric patients with symptomatic post-transplant reflux treated with redo-UNC, stratified by their lower urinary tract (LUT) status. We hypothesized that those with concomitant LUT dysfunction at the time of renal transplant would have lower GFR on follow-up, compared to those without.

Materials and methods

Institutional Review Board committee approval was obtained through the University of California San Francisco for this study.

A total of 558 pediatric patients were identified at our institution who had undergone renal transplantation between 1991 and 2014. Using a combination of diagnosis codes and procedure billing codes, we retrospectively identified 46 pediatric patients (<21 years old) who underwent both renal transplant and redo-UNC at our institution between 1991 and 2014 by a single surgeon. Surgical codes for reimplant searched were CPT codes 50780, 50783, 50785, and 50360. Preoperative evaluations included renal ultrasound and VCUG to assess for VUR. All were done for recurrent urinary tract infections secondary to reflux. After excluding nine patients who either underwent redo-UNC for an indication other than post-transplant reflux or were lost

to follow-up, 37 comprehensive chart reviews were performed. Patient characteristics and procedure-related factors, such as the timing of reflux diagnosis and treatment, were recorded. Additionally, glomerular filtration rates levels from four time points were collected: (1) post-transplant nadir, (2) 1-month pre redo-UNC, (3) 2.5 year post redo-UNC, and (4) most recent or 5 year post redo-UNC.

LUT dysfunction was defined as bladder dysfunction either due to an underlying neurologic cause or a history of obstructive genitourinary anatomy, such as posterior urethral valves and was present in twelve patients. Causes for end-stage renal disease in the 25 patients without lower urinary tract dysfunction (LUTD) differed and included polycystic kidney disease, congenital renal dysplasia, focal segmental glomerulosclerosis, Fanconi syndrome, hemolytic uremic syndrome, immunoglobulin M nephropathy, primary hyperoxaluria, medullary sponge kidney, polyarteritis nodosa, and mesangial sclerosis.

GFR calculations were done utilizing the Bedside Schwarz equation for children <18 years of age at the time of laboratory creatinine testing. For children >18 years old at the time of creatinine testing, GFR was calculated using the Modification of Diet in Renal Disease (MDRD) study equation. Comparisons of the recorded parameters were made between those with and without LUT dysfunction, using the non-parametric Fisher exact test, Wilcoxon rank sum test, or the signed-rank test. A p-value < 0.05 was considered to be statistically significant. Generalized estimating equations were constructed to account for the clustered nature of GFR levels within each LUT group and to assess their change over time.

Results

Table 1 provides a summary of patient characteristics and procedure-related factors in those with post-transplant reflux treated with redo-UNC. Of the 37 patients reviewed, 12 (32%) had pre-transplant LUT dysfunction while 25 (68%) did not. Of the patients with LUT dysfunction, eight (66.7%) were patients with neurogenic bladder secondary to myelomeningocele and four (33.3%) patients had a history of posterior urethral valves. The mean age at the time of renal transplant was 9 years old (± 6 years). The proportion of males in the group with LUT dysfunction was 75% and the proportion of females was 36%. Males presented with symptomatic post-transplant reflux at 1.6 years and females presented at 2.2 years. After an average of 4.9 years of follow-up from time of transplant, the median GFR levels were 53 mg/dL and 58 mg/dL in the male and female groups ($p = 0.936$).

When analyses were done within each group, both demonstrated a decrease in serum GFR from pre-redo-UNC compared with their respective most recent follow-up at approximately 5 years post redo-UNC, but this was not statistically significant ($p = 0.055$). The average length of time from redo-UNC to most recent follow up was 4.9 years. At the 5-year post redo-UNC the GFR was essentially the same for both the patients with and without LUT dysfunction. Of note, the patients without and with LUT dysfunction had nadir GFR 106 ml/min versus 78 ml/min after the renal transplant, although this was not statistically significant. Therefore, the GFR decreased more steeply in the

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