



Role of vesicoureteral reflux on pediatric kidney allograft function

Kelsi Alexander¹ · Sharon M. Bartosh¹ · Weixiong Zhong¹ · Rachel M. Engen¹

Received: 30 May 2024 / Revised: 22 August 2024 / Accepted: 23 August 2024
© The Author(s), under exclusive licence to International Pediatric Nephrology Association 2024

Abstract

Background Vesicoureteral reflux (VUR) is a common urologic complication of pediatric kidney transplant, though there is little data on the effect of VUR on histologic graft changes or graft survival.

Methods All pediatric patients who received a kidney transplant from 2007 to 2020 were selected for retrospective chart review. All participants underwent a voiding cystourethrogram (VCUG) at a 6-month post-transplant. Patients were then categorized into two groups based on vesicoureteral reflux grade: no/low-grade VUR (grades 0–2) and high-grade VUR (grades 3–5). Outcomes collected included graft failure rates, graft function, urinary tract infections (UTIs), proteinuria, and Banff scores at 3- and 12-month post-transplant surveillance kidney biopsies.

Results There were 74 pediatric patients who received a kidney transplant in the designated time-period, and of those 39 had no/low-grade VUR and 35 had high-grade VUR. There was no difference in graft failure among the two groups over time when stratified for age ($p=0.389$, CI 0.53–5.08). Patients with high grade VUR had a higher risk of UTI development overall (RR 1.89, 95%CI 1–3.6, $p=0.041$), mostly accounted for from increased development of febrile UTI (RR 1.66, 95%CI 1.1–2.6, $p=0.038$).

Conclusions Unselected pediatric kidney transplant recipients with high-grade vesicoureteral reflux on VCUG at a 6-month post-kidney transplant are more likely to have febrile UTI compared to those in the low-grade VUR group. There is no difference in graft survival among the two groups.

Keywords Pediatrics · Vesicoureteral reflux · Histology · Kidney transplant · Outcomes

Background

Vesicoureteral reflux (VUR) occurs commonly after pediatric kidney transplant. The reported incidence of post-transplant VUR is highly variable, with reports from 2 to 86%, based on patients selected for testing due to post-transplant urinary tract infections (UTI) [1]. Risk factors have been well-described and include kidney and bladder anatomy prior to transplant and surgical technique used [2, 3]. VUR leading to febrile UTI is the most well-studied outcome. A 1987 study by Dunn et al. [4] of 67 pediatric kidney transplant recipients found that when all patients received voiding cystourethrogram, those with VUR had higher rates of UTI (46%) compared to those without (33%). More recent studies have shown an incidence of UTI post-transplant of 39–78%

despite common use of anti-reflux surgical procedures [5]. Reflux associated with UTI is usually considered a late complication of transplant, with most patients being diagnosed with UTI 6 months or more after transplant [6].

Little data has been gathered on the effect of VUR on graft health or survival. In 1999, a study of 170 pediatric transplant patients conducted by Fontana et al. [7] showed no significant change in measures such as creatinine or length of graft survival among patients with and without reflux. In 2008, Jung et al. [1] reported that in 75 adult patients who underwent VCUG at a 1-year post-transplant, acute cellular rejection occurred more often in transplanted patients with VUR (44%) compared to patients without VUR (20%), though this difference was not significant, and reflux had no effect on graft function.

Lack of data regarding the relationship between VUR and graft outcomes is relevant, as many therapies, including conservative non-surgical treatment, endoscopic, and surgical fixation, exist for the management of VUR for transplanted patients. Understanding the relationship between VUR,

✉ Kelsi Alexander
alexander.kelsi@outlook.com

¹ Department of Pediatrics, University of Wisconsin-Madison, Madison, USA

histologic changes, and graft outcomes could further guide monitoring and management of transplanted patients for preservation of the allograft.

The goal of this study is to demonstrate the relationship between VUR and graft survival. We also seek to explore the relationship between VUR post-transplant and inflammation on 12-month protocol biopsies.

Methods

We performed a retrospective cohort study of all pediatric patients who received a kidney transplant at The University of Wisconsin-Madison from 2007 to 2020. Data were collected via a retrospective chart review of the electronic medical record. Inclusion criteria were age less than 18 at the time of transplant, at least 1 year of a follow-up post-transplant, surveillance biopsies obtained at 3- and 12-month post-transplants, and a voiding cystourethrogram (VCUG) performed at a 6-month post-transplant (± 2 months).

Patients in the cohort were divided into two groups based on the results of their VCUG at a 6-month post-transplant: patients with no/low-grade VUR and patients with high-grade VUR. The no/low-grade VUR group had grades 0–2 VUR and the high-grade VUR group had grades 3–5 VUR. The primary outcome of interest was graft survival. Graft failure was defined as return to dialysis or repeat transplantation. Secondary outcomes of interest included association of VUR with post-transplant biopsy findings, particularly interstitial and tubular inflammation and fibrosis. Other outcomes studied included graft function over time, proteinuria, and development of UTI. Graft function was determined by measuring the estimated glomerular filtration rate (eGFR). eGFR was calculated using a modified Schwartz equation based on creatinine and height obtained during outpatient follow-up appointments at 3-month, 12-month, 3-year, and 5-year post-transplants [8]. Proteinuria was defined as $> 1+$ protein on urine dipstick or random urine protein-to-creatinine ratio > 0.2 mg/mg. Confounding variables such as pre-transplant cause of chronic kidney disease, pre-transplant kidney and bladder anatomy, presence of pre-transplant anuria, and intermittent catheterization status pre-transplant were also collected in data review.

Vesicoureteral reflux surveillance and management

During surgical implantation of the transplanted kidney, nearly all (93%) patients underwent the Lich–Gregoir non-refluxing technique for ureteral implantation and had a ureteral stent placed. Ureteral stents were removed 4–6-weeks post-transplant. All patients included in the cohort underwent a surveillance fluoroscopic VCUG at a 6-month post-transplant unless they required a VCUG for cause prior to

that. Patients who did not have a VCUG within that time frame were excluded from the study. The International Grading System for vesicoureteral reflux was used to diagnosis VUR based on the VCUG [9]. Patients with evidence of VUR at 6 months underwent education and timed voiding training. Most patients with VUR continued Bactrim past 12 months as UTI prophylaxis, though a few patients discontinued prophylaxis due to side effects such as neutropenia.

General transplant management

Nearly all (77%) patients received induction immunosuppression with alemtuzumab, and maintenance immunosuppression was primarily with tacrolimus (goal trough level 8–10 ng/mL for the first 12 months, 6–8 ng/mL month 13–24, and 4–8 ng/mL thereafter) and mycophenolate mofetil. Prednisone was included in the maintenance immunosuppression regimen for patients with pre-transplant immunosuppression therapy or who were highly sensitized. All patients included in the study underwent surveillance biopsies at 3- and 12-month post-transplants, and those who did not were excluded from the study. Protocol biopsies were scored under the Banff Classification System by a single kidney pathologist [10]. Patients with biopsy-proven acute cellular rejection underwent treatment with methylprednisolone. Patients with antibody-mediated rejection were treated with methylprednisolone, intravenous immunoglobulin, and rituximab.

Patients were maintained on *Pneumocystis jirovecii* prophylaxis with trimethoprim-sulfamethoxazole or pentamidine until a 12-month post-transplant. Patients also received antifungal prophylaxis with nystatin for a 3-month post-transplant and antiviral prophylaxis with cytomegalovirus (CMV) immunoglobulin $\times 2$ doses post-transplant and valganciclovir for a 12-month post-transplant.

Analysis

Descriptive statistics report median and interquartile range (IQR) for continuous variables and counts and percentages for categorical variables. Kaplan–Meier methods and Cox proportional hazards regression compared transplant recipients with low/no grade VUR and high-grade VUR for time to graft failure. Outcomes were adjusted for confounding based on age at transplant. A Mann–Whitney *U* test was used to compare outcomes of GFR, proteinuria, and Banff score changes, and chi-square testing was used to compare the incidence of hypertension.

This study was approved by the University of Wisconsin Institutional Review Board, Study #2014–1072.

Results

Incidence of vesicoureteral reflux

A total of 75 patients receiving kidney transplant were reviewed between 2007 and 2020 (Table 1). One patient was excluded from the study due to not having undergone VCUG after transplant. Of the 74 patients remaining in the study population, 39 had grades 0–2 VUR (52%) and 35 had grades 3–5 VUR (48%). Overall, 29 patients (39%) had no VUR, one patient (1%) had grade 1 VUR, 15 patients (20%) had grade 2 VUR, 23 patients (31%) had grade 3 VUR, 11 patients (15%) had grade 4 VUR, and one (1%) patient had grade 5 VUR (Table 2). One patient in the high-grade VUR group required surgical intervention for reflux in the 5-year study period. The two groups were similar in demographic make-up including sex of patient, race/ethnicity, and age at transplant.

There were a similar number of urologic vs. non-urologic cause for kidney failure in each group. Urologic causes included chronic pyelonephritis/reflux nephropathy, congenital obstructive uropathy, and prune belly syndrome. In the no/low-grade VUR group, urologic causes made up 46% of the group, compared to 60% in the high-grade VUR group, a difference that was not statistically significant. The breakdown of urologic causes per VUR group is represented in Table 1. There was little difference between groups in other notable characteristics of kidney disease including dialysis prior to transplant (VUR 0–2, 37%; VUR 3–5, 43%), prior kidney transplant (VUR 0–2, 10%; VUR 3–5, 5%), and clean intermittent catheterization prior to transplant (VUR 0–2, 13%; VUR 3–5, 17%).

Histologic outcomes

Of the 74 patients who underwent VCUG at a 6-month post-transplant, 56 had protocol biopsies obtained at 3- and 12-month post-biopsies. Patients in the high-grade VUR group did not have more acute inflammation at a 3-month post-transplant (16.7%) compared to those with the no/low-grade VUR (9.1%) ($p = 0.390$). A t score > 0 (acute tubulitis) was seen in 16.7% of patients in the high-grade VUR group compared to 3% of the no/low-grade VUR group ($p = 0.072$).

Patients in the high-grade VUR group also did not have more acute histologic changes between 3- and 12-month post-transplants, with 21.7% of patients with a high-grade VUR having an increase > 1 of their acute tubulitis (t) and acute inflammation score (i). The no/low-grade VUR group showed a change > 1 in their t and i scores in 20% and 13.3% of patients, respectively ($p = 0.877$ and

0.419, respectively) (Table 3). There was no difference in fibrosis (both tubular atrophy and interstitial fibrosis) at a 12-month post-transplant among the two groups (ci $p = 0.069$, ct $p = 0.206$).

There was no statistically significant difference in rates of rejection between the two groups. Patients with no/low-grade reflux had an incidence of T-cell-mediated rejection of 41% compared to 34.3% in the high-grade VUR group (RR 0.84, 95%CI 0.46–1.5, $p = 0.551$). Similarly, antibody-mediated rejection occurred in 18% of patients with the no/low-grade reflux and 20% of the high-grade reflux (RR 1.11, 95%CI 0.43–2.9, $p = 0.822$) (Table 3). There was also no significant difference in time to first episode of acute cellular rejection, with both groups having a median of 1 year to the first episode of acute T-cell-mediated rejection ($p = 0.976$). The median time to first episode of antibody-mediated rejection was 6.6 years with the no/low-grade reflux group compared to 3.5 years in the high-grade VUR group ($p = 0.428$).

Functional outcomes

When assessing graft survival using a Kaplan–Meier curve, patients with a high-grade VUR had a higher rate of graft failure over time when stratified for age ($p = 0.389$, CI 0.53–5.08), though this was not statistically significant (Fig. 1).

Markers of graft health and function were assessed including the change in glomerular filtration rate over time and the development of hypertension and proteinuria. Among those with 5 years of post-transplant follow-up ($n = 64$), there was no statistically significant difference in the change in eGFR over time between the two groups, with the no/low-grade VUR group showing a median decrease in eGFR of 1.33 ml/m²/min compared to a decrease of 12 ml/m²/min in the high-grade VUR group over the 5-year follow-up period ($p = 0.192$).

There was no difference in the development of hypertension at 1-year or 5-year post-transplant between the two groups. Eighty-one percent of patients in the no/low-grade VUR group developed hypertension at a 1-year post-transplant compared to 70% of patients in the high-grade VUR group ($p = 0.305$). At a 5-year post-transplant, 78% of patients with the no/low-grade VUR developed hypertension and 69% of patients with the high-grade VUR developed hypertension ($p = 0.410$). There was also no difference in the development of proteinuria at a 1-year post-transplant (VUR 0–2, 61%; VUR 3–5, 77%; $p = 0.148$) (Table 4).

Patients in the no/low-grade VUR group developed ten episodes of UTI (25.60%) over the follow-up period, with eight febrile UTI (20.5%) compared to a total 17 UTI (48.6%), and 15 febrile UTI (42.9%) in the patients with the high-grade VUR. Patients with the high-grade VUR had a higher risk of UTI development overall (RR 1.89, 95%CI

Table 1 Demographic and clinic factors of 74 pediatric kidney transplant recipients at the University of Wisconsin Madison, 2007–2020, by grade of vesicoureteral reflux (VUR)

	VUR 0–2 (<i>n</i> = 39)		VUR 3–5 (<i>n</i> = 35)		<i>p</i>
	<i>n</i> /median	%/IQR	<i>n</i> /median	%/IQR	
Male	28	71.8%	20	57.1%	0.187
Age at transplant	12.4	7.9–16.6	11.4	5.3–14.2	0.112
Race/ethnicity					0.393
White	34	87.2%	32	91.4%	
Black	1	2.6%	2	5.7%	
Native American/Pacific Islander	1	2.6%	1	2.9%	
Asian	1	2.6%	0		
Unknown	2	5.1%			
Hispanic	2	5.1%	4	11.4%	
Cause of kidney failure					
Non-urologic	18	46.2%	21	60%	0.338
Urologic	12	30.8%	8	22.9%	0.492
Congenital obstructive uropathy	6	15.4%	6	17.1%	
Prune belly syndrome	2	5.1%	1	2.6%	
Reflux nephropathy	4	10.2%	1	2.6%	
Unknown	9	23.1%	6	17.1%	0.067
Blood type					
A	18	46.2%	12	34.3%	
B	5	12.8%	2	5.7%	
AB	3	7.8%	0		
O	13	33.3%	21	60%	
Previous kidney transplant	4	10.3%	2	5.7%	0.467
Previous liver transplant	1	2.6%	1	3.6%	0.829
Previous pancreas transplant	0	0.0%	1	3.6%	0.232
Donor age	32	23–40	35	28.5–40.5	0.421
Donor type					0.092
Living	26	68.4%	23	82.1%	
Deceased	12	31.6%	5	17.9%	
Anuria prior to transplant	13	33.3%	9	25.7%	0.474
Dialysis prior to transplant	13	37.10%	14	43.8%	0.512
Clean intermittent catheterization	5	13.2%	6	17.1%	0.635
Induction immunosuppression					0.365
Alemtuzumab	30	76.90%	27	77.10%	
Basiliximab	7	18%	8	22.90%	
Thymoglobulin	2	5.10%	0	0%	
Maintenance immunosuppression					
Tacrolimus and mycophenolate	34	97.10%	31	88.6%	0.949
Maintenance steroids	9	25.70%	9	29%	0.763
Delayed graft function	3	7.7%	0	0%	0.094
Oxybutynin prescription	11	28.2%	5	14.3%	0.146
Doxazosin prescription	1	2.6%	3	8.6%	0.254
Lich–Gregoir technique	31	91.2%	33	100%	0.072
Ureteral stent placement	38	97.4%	35	100%	0.34
3-month protocol biopsy	33	84.6%	24	69%	0.11
12-month protocol biopsy	32	82.1%	24	69%	0.188
Follow-up at 5-years post transplant	33	84.6%	31	88.6%	0.619

Table 2 Grade of vesicoureteral reflux (VUR) by voiding cystourethrogram (VCUG) at 6 months of post-kidney transplant. A percentage of 52% had a low/no-grade VUR and 48% had a high-grade VUR

Vesicoureteral reflux grade	n	%
0	23	31%
1	1	1%
2	15	20%
3	23	31%
4	11	15%
5	1	1%

1–3.6, $p=0.041$) with that risk accounted for mostly from their increased development of febrile UTI (RR 1.66, 95%CI 1.1–2.6, $p=0.038$).

Discussion

This study presents a comprehensive assessment of the incidence of VUR after pediatric kidney transplantation using protocol VCUG in patients as well as protocol biopsies, which has not been performed in over 20 years. Our study showed no differences in graft survival, graft function, inflammation on kidney biopsy, or graft fibrosis related to VUR. As has been described in the literature previously, patients with the high-grade VUR were at higher risk of

developing febrile UTI compared to patients with the no/low-grade VUR.

Two studies have performed VCUG for all pediatric kidney recipients to investigate incidence of VUR. In 1987, Dunn et al. [4] reported a 36% incidence of VUR in pediatric kidney transplant recipients, with considerable variation by anastomosis technique, and in 1999, Fontana et al. [7] reported an overall incidence of VUR in 34% of 73 patients using the Lich–Gregoir technique. Both of these older reports are considerably lower than the 69% incidence of VUR reported in this study. Some of this may be due to differences in assessment; for example, Dunn et al. [4] used radionucleotide voiding studies in an unknown portion of their population. There may also be differences in patient population; for example, Dunn et al. [4] excluded all patients with neurogenic bladder and Fontana et al. [7] did not report the patients’ cause of kidney disease or bladder history.

Our study did not find differences in graft survival among patients with the no/low and high-grade vesicoureteral reflux. There were also no differences in graft function or histologic changes on post-transplant biopsies. These results are consistent with similar prior studies and suggest that VUR does not significantly impact the health of the graft over time, except for development of UTIs. In fact, a 2023 review by Hewitt et al. [5] concluded that while post-transplant VUR is common, in the absence of infection it does not appear to cause concern otherwise.

Table 3 Banff scores on protocol kidney biopsies at 3- and 12-month post-kidney transplants and rates of rejection among groups. Also shown are changes in biopsy scores between the two sets of protocol biopsies

Biopsy results for high-grade vs. low-grade VUR	VUR grade 0–2		VUR grade 3–5		Missing n	p
	n	%	n	%		
3-month biopsy results						
<i>t</i> > 0	1	3%	4	16.7%	17	0.072
<i>i</i> > 0	3	9.1%	4	16.7%	17	0.390
<i>ct</i> > 0	12	39.4%	12	50%	17	0.303
<i>ci</i> > 0	11	33.3%	11	45.8%	17	0.339
12-month biopsy results						
<i>t</i> > 0	6	18.8%	6	25%	18	0.573
<i>i</i> > 0	4	12.5%	6	25%	18	0.227
<i>ct</i> > 0	25	78.1%	18	75%	18	0.784
<i>ci</i> > 0	23	71.9%	16	64%	18	0.675
Change in Banff score in the 3-month to 12-month post-transplants						
<i>t</i> increase ≥ 1	6	20%	5	21.7%	21	0.877
<i>i</i> increase ≥ 1	4	13.3%	5	21.7%	21	0.419
<i>ct</i> increase ≥ 1	18	60%	8	34.8%	21	0.069
<i>ci</i> increase ≥ 1	17	56.7%	9	39.1%	21	0.206
TCR incidence	41%		34.3%		0.551	
ABMR incidence	18%		20%		0.822	

VUR vesicoureteral reflux, *t* acute tubulitis, *i* acute inflammation, *ct* chronic tubulitis, *ci* chronic inflammation, TCR T-cell-mediated rejection, ABMR antibody-mediated rejection

Fig. 1 Kaplan–Meyer curve demonstrating graft survival post-transplant between the no/low-grade VUR and high-grade VUR groups

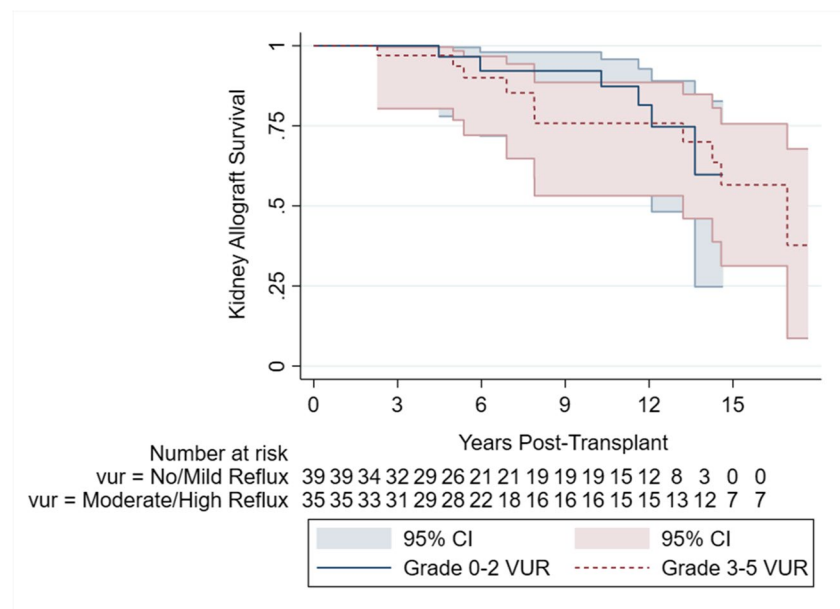


Table 4 Secondary outcomes among no/low-grade and high-grade VUR groups

	VUR grade 0–2		VUR grade 3–5		Missing	RR	<i>p</i>
	<i>n</i> /median	%/IQR	<i>n</i> /median	%/IQR			
UTI prophylaxis prescription	22	57.9%	30	85.7%	2		0.009
UTI within 5 years of post-transplant	10	25.6%	17	48.6%	0	1.89	0.041
Febrile UTI	8	20.50	15	42.90%		1.66	0.038
Afebrile UTI	6	15.4%	8	22.9%		1.27	0.413
eGFR 3 months	69.5	52.3–99.1	76	59–103	0		0.196
eGFR 1 year	63.4	52.2–84.9	78.2	60.9–98.2	8		0.076
eGFR 3 years	67.9	53.1–86.7	73.7	61.1–93.2	9		0.447
eGFR 5 years	61.0	45–85.5	68.7	56–82.0	10		0.773
Change in eGFR 3 months to 12 months	1.4	–9.9–8.6	0.4	–16.5–8.7	8		0.805
Change in eGFR 3 months to 3 years	4.9	–12.9–20.9	-8.5	–17.9–2.0	9		0.079
Change in eGFR 3 months to 5 years	–1.33	–19.0–16.7	–12.0	–27.9––0.65	10		0.192
HTN 1 year	31	82%	25	70%	1		0.305
HTN 5 year	22	79%	20	69%	17		0.410
Proteinuria 1 year	24	62%	27	77%	0		0.148

VUR vesicoureteral reflux, UTI urinary tract infection, eGFR estimated glomerular filtration rate, HTN hypertension

Our study found that patients with the high-grade VUR were more likely to go on to develop febrile UTI. Similar past studies have shown conflicting evidence for association of VUR and UTI. A 2000 retrospective cohort study by Ranchin et al. [11] examined UTI associated with cystography findings at a 8-month post-transplant and found that patients with VUR to the transplanted kidney developed more episodes of acute pyelonephritis than those without. In 2019, a study by Morrison et al. [3] also demonstrated that VUR associated with UTI was the most common urologic complication in their cohort of 224 pediatric kidney transplant recipients, and that only a small percentage (4%) of

their patients without VUR went on to develop UTI. However, a 2008 study by Jung et al. [1] of 75 pediatric transplant patients showed no difference in the development of UTI among patients with VUR vs. those without. Association of VUR with UTI is important, as interventions may become necessary for patients with recurrent UTI. Wu et al. [12] demonstrated that patients with VUR and recurrent UTI were frequently managed with dextranomer/hyaluronic acid injections or ureteral reimplantation. Similarly, Morrison et al. [3] found that of the 26 patients with VUR and UTI, six required injections or reimplantation, and the remaining 20 patients required aggressive catheterization, bladder/bowel

regimens, and antibiotic prophylaxis. Therefore, the association of VUR with febrile UTI is important as it suggests an increased risk of illness, hospitalization, and post-transplant surgical intervention.

Little is known about the histologic changes associated with VUR. In native kidneys, limited data is available describing tubulointerstitial nephritis, tubular atrophy, and Tamm-Horsfall protein as histologic findings associated with VUR, though few studies have correlated the post-transplant reflux with histologic findings directly [13, 14]. In transplanted kidneys, a 2009 study by Akioka et al. [15] reported that interstitial fibrosis and tubular atrophy were not associated with VUR and further concluded that development of Tamm-Horsfall protein was more closely associated with UTI, rather than VUR alone. Although our study showed a trend toward more early acute inflammation in patients with the higher grade VUR, this was not statistically significant.

The strengths of this study include long term follow-up of our cohort and the use of the post-transplant surveillance biopsy in most patients. Critically, VUR was comprehensively assessed in every transplant recipient, rather than only those with infections. This protocol at our institution allowed for the design of our study to accurately investigate the relationship between reflux and histology. Additionally, all the biopsies were reread, for the purpose of this investigation, by a single kidney pathologist, eliminating variation in histologic scoring. There was also no variation in surgical implantation technique at our institution, which if present, may have altered the incidence in reflux reported. Potential limitations of this study include a relatively small sample size, lack of histology beyond a 12-month post-transplant and the known variation in reflux grading inherent to VUCG [16]. We also recognize that transplant patients at our institution with VUR are maintained on antibiotic prophylaxis for UTI indefinitely after transplant, which may bias our association between VUR and UTI towards the null. This may also bias our outcomes assessment toward the null. Our cohort also represents a predominately White, suburban population, which may make its applicability to more diverse or urban populations limited.

Despite an increased risk of febrile UTI, pediatric patients undergoing kidney transplant who had the high-grade VUR post-transplant have no change in graft survival, function, or inflammation on short-term biopsy compared to patients with the no/low-grade VUR.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s00467-024-06516-0>.

Funding This project was funded by the University of Wisconsin, Department of Pediatrics Resident and Fellow Research and Development Grant.

Data availability The datasets generated during and/or analyzed during the current study are not publicly available due to institutional review

board restrictions but may be available from the corresponding author on reasonable request.

Declarations

Competing interests The authors declare no competing interests.

References

- Jung GO, Chun JM, Park JB et al (2008) Clinical significance of posttransplantation vesicoureteral reflux during short-term period after kidney transplantation. *Transplant Proc* 40:2339–2341. <https://doi.org/10.1016/j.transproceed.2008.06.027>
- Amesty MV, García-Vaz C, Espinosa L, Martínez-Urrutia MJ, López-Pereira P (2021) Long-Term renal transplant outcome in patients with posterior urethral valves Prognostic factors related to bladder dysfunction management. *Front Pediatr* 9:646923. <https://doi.org/10.3389/fped.2021.646923>
- Morrison CD, Shannon R, Rosoklija I et al (2019) Ureteral complications of pediatric renal transplantation. *J Urol* 201:810–814. <https://doi.org/10.1016/j.juro.2018.08.082>
- Dunn SP, Vinocur CD, Hanevold C, Wagner CW, Weintraub WH (1987) Pyelonephritis following pediatric renal transplant: increased incidence with vesicoureteral reflux. *J Pediatr Surg* 22:1095–1099. [https://doi.org/10.1016/s0022-3468\(87\)80716-9](https://doi.org/10.1016/s0022-3468(87)80716-9)
- Hewitt IK, Montini G, Marks SD (2023) Vesico-ureteric reflux in children and young people undergoing kidney transplantation. *Pediatr Nephrol* 38:2987–2993. <https://doi.org/10.1007/s00467-022-05761-5>
- Maison POM, Smit S, McCulloch M et al (2017) Urological complications following unstenosed pediatric renal transplantation. *Pediatr Transplant* 21(7):e13045. <https://doi.org/10.1111/ptr.13045>
- Fontana I, Ginevri F, Arcuri V et al (1999) Vesico-ureteral reflux in pediatric kidney transplants: clinical relevance to graft and patient outcome. *Pediatr Transplant* 3:206–209. <https://doi.org/10.1034/j.1399-3046.1999.00017.x>
- Schwartz GJ, Muñoz A, Schneider MF, Mak RH, Kaskel F, Warady BA, Furth SL (2009) New equations to estimate GFR in children with CKD. *J Am Soc Nephrol* 20:629–637. <https://doi.org/10.1681/ASN.2008030287>
- Lebowitz RL, Olbing H, Parkkulainen KV, Smellie JM, Tamminen-Möbius TE (1985) International system of radiographic grading of vesicoureteric reflux. *International Reflux Study in Children. Pediatr Radiol* 15:105–109. <https://doi.org/10.1007/BF02388714>
- Loupy A, Haas M, Roufosse C et al (2020) The Banff 2019 Kidney Meeting Report (I): Updates on and clarification of criteria for T cell- and antibody-mediated rejection. *Am J Transplant* 20:2318–2331. <https://doi.org/10.1111/ajt.15898>
- Ranchin B, Chapuis F, Dawhara M, Canterino I, Hadj-Aïssa A, Saïd MH, Parchoux B, Dubourg L, Pouillaude JM, Floret D, Martin X (2000) Vesicoureteral reflux after kidney transplantation in children. *Nephrol Dial Transplant* 15:1852–1858. <https://doi.org/10.1093/ndt/15.11.1852>
- Wu HY, Concepcion W, Grimm PC (2018) When does vesicoureteral reflux in pediatric kidney transplant patients need treatment? *Pediatr Transplant* 22:e13299. <https://doi.org/10.1111/ptr.13299>
- Cendron M (2008) Reflux nephropathy. *J Pediatr Urol* 4:414–421. <https://doi.org/10.1016/j.jpuro.2008.04.009>
- Jones C, Eddy A (1992) Tubulointerstitial nephritis. *Pediatr Nephrol* 6:572–586. <https://doi.org/10.1007/BF00866512>

15. Akioka Y, Chikamoto H, Horita S et al (2009) Screening of vesicoureteral reflux in pediatric patients with kidney transplantation showing non-specific interstitial fibrosis and tubular atrophy with interstitial Tamm-Horsfall protein deposits in protocol allograft biopsy. *Clin Transplant* 23(Suppl 20):2–5. <https://doi.org/10.1111/j.1399-0012.2009.01000>
16. Schaeffer AJ, Greenfield SP, Ivanova A et al (2017) Reliability of grading of vesicoureteral reflux and other findings on voiding cystourethrography. *J Pediatr Urol* 13:192–198. <https://doi.org/10.1016/j.jpuro.2016.06.020>

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.