Superior Hypertension Management in Pediatric Kidney Transplant Patients After Native Nephrectomy

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Background. Native nephrectomy in pediatric kidney transplant recipients is performed for multiple indications. Posttransplant hypertension requiring medical management is common, and the effect of native nephrectomy on posttransplant hypertension is poorly studied. Our aim is to evaluate the impact of native nephrectomy on posttransplant hypertension. **Methods.** One hundred thirty-six consecutive pediatric kidney transplant recipients from 2007 to 2012 were studied at a single institution and divided into 2 groups: no nephrectomy and native nephrectomy (unilateral and bilateral nephrectomy). Antihypertensive medication use was evaluated before nephrectomy/transplant, at discharge from transplant and at 1, 3, and 5 years posttransplant. **Results.** In a bivariate analysis, nephrectomy was associated with a significant reduction in the percentage of patients requiring antihypertensive medication at the time of discharge (27.3%) and 1 year posttransplant (10.7%) as compared with patients without nephrectomy (71.7%, and 50%, respectively, $P < 0.05$). This trend toward reduction in antihypertensive medication in the nephrectomy group as compared with the no nephrectomy group persisted at 3 (18.6% versus 43.2%) and 5 years (19.7% versus 37.5%) posttransplant. Multivariable logistic regression demonstrated that patients without native nephrectomy had higher odds of requiring antihypertensive medication at the time of discharge (3.3) and 1 year (5.2) as compared with patients who underwent native nephrectomy ($P = 0.036$ and $P = 0.013$, respectively). **Conclusions.** Native nephrectomy reduces the odds of needing antihypertensive medication after transplant. The impact of native nephrectomy is crucial to the comprehensive management of pediatric transplant recipients where medication compliance is challenging and lifelong hypertension is known to negatively impact cardiovascular health.

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Native nephrectomy before or at the time of transplant is advocated in pediatric kidney transplant recipients with anatomical constraints, congenital anomalies, proteinuria, intractable hypertension, malignancy, and chronic

infection.^{1–3} Specifically, pediatric patients often undergo nephrectomy when there is a perceived risk to the recipient or the graft. Cardiovascular disease is a significant cause of morbidity and mortality in pediatric patients with end-stage renal disease (ESRD) reducing lifespan by as much as 40 to 60 years for children with ESRD.^{4,5} Although renal transplantation improves renal-associated risk factors for cardiovascular disease, more than 50% of these patients still have hypertension after transplant.^{6–8} Even after transplant, the life expectancy of children with hypertension is 25 years shorter than age-matched controls with 25% of deaths due to cardiac morbidity.⁴

The impact of the native kidneys on the developing pathophysiology of pretransplant cardiovascular disease is multifactorial.^{7,9} However, the effects of the native kidney on persistent hypertension and cardiovascular disease after transplant are less clear.^{6,8} It has been postulated that native nephrectomy before or at the time of transplant in patients with ESRD may improve posttransplant hypertension. This largely stems from the idea that the native kidney still may exert inflammatory, hormonal, and biochemical effects on the cardiovascular system. The data on the actual impact of nephrectomy on hypertension is very limited. In a small study, Cavallini et al⁶ suggested that nephrectomy for the indication of hypertension before transplantation did not significantly

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influence long-term blood pressure control or the prevalence of left ventricular hypertrophy (LVH) after kidney transplantation. In another study, a small subset of patients with persistent arterial hypertension and large-volume proteinuria pretransplant had a significant reduction in hypertension after nephrectomy.² These few studies limit our ability to draw a clear conclusion regarding the impact of nephrectomy on hypertension after transplant.

Given the limited findings in the literature, the primary aim of this study was to analyze the impact of native nephrectomy for all indications on posttransplant hypertension in pediatric renal transplant recipients.

MATERIALS AND METHODS

The institutional review board at Stanford University approved this study. We conducted a retrospective study of all pediatric patients younger than 18 years who underwent renal transplantation at Lucile Packard Children's Hospital from 2007 to 2012. Data were gathered from the electronic medical record including demographic data, etiology of ESRD, history of prior transplants or multi organ transplants, history of nephrectomy, hypertensive medications pretransplant and posttransplant, immunosuppression, and biopsy-proven rejection. Indications for nephrectomy included congenital anomalies, proteinuria, polyuria, intractable hypertension, malignancy, and chronic infection. Patients were excluded if they were older than 18 years, had a history of a previous renal transplant (≥ 1) before the study period or underwent multiorgan transplant. If a patient proceeded to graft failure, defined as a creatinine clearance less than 15 mL/min per 1.73 m², or required retransplantation during the study window, data from that time point forward were excluded. The remaining patients ($n = 123$) were categorized into 2 groups: no native nephrectomy ($n = 46$) and native nephrectomy (either unilateral or bilateral, $n = 77$) at discharge. Thirty-three patients were excluded from the study over the 5-year period. Nine patients in the no nephrectomy group and 4 patients in the nephrectomy group experienced graft failure over the 5-year study period ($n = 13$). Thirteen patients in the no nephrectomy group and 7 patients in the nephrectomy group transitioned care to outside hospitals due to relocation or progression to care at an unidentified adult hospital by 5 years posttransplant ($n = 20$). In review of the Scientific Registry of Transplant Recipients database, these patients had continued graft function but no additional data were available regarding their posttransplant management. The number of antihypertensive medications was evaluated immediately before nephrectomy/transplant, at the time of discharge from transplant and at 1, 3, and 5 years after transplant. Diuretics were not included as an antihypertensive medication. For the subset of patients that underwent nephrectomy before transplant, antihypertensive medications were evaluated before nephrectomy, postnephrectomy, and before transplant. Creatinine clearance as determined by the Schwartz formula¹⁰ was evaluated at 1, 3, and 5 years posttransplant.

STATISTICAL ANALYSIS

Univariate descriptive analysis was performed for demographic data and is expressed either as a percentage or a median and range for patients in each group. For bivariate

analysis, the Pearson χ^2 test was used for categorical variables, and the unpaired Student t test or the Mann-Whitney U test were used as appropriate for continuous variables. A 2-tailed analysis was performed in all tests. Multivariable logistic regression was performed to ascertain the effects of age, donor type, steroid-based immunosuppression, nephrectomy status, biopsy-proven rejection, and creatinine clearance on the odds that patients used antihypertensive medication at discharge from transplant and at 1, 3, and 5 years posttransplant. The first 4 variables were used at discharge from transplant, and all 6 variables were used at 1, 3, and 5 years posttransplant. Rejection and creatinine clearance were not included in the regression model at the time of discharge because they were not clinically relevant. For all statistical tests, an a priori critical P value less than 0.05 was used to determine significance. All statistical analyses were performed using IBM SPSS Statistics Version 24.0.

RESULTS

Demographics and Etiology of ESRD

Of the 136 pediatric patients who underwent pediatric renal transplant between 2007 and 2012, 7 patients were excluded given prior kidney transplant and 6 patients were excluded as they received a multiorgan transplant. Of the remaining 123 patients, 77 underwent native nephrectomy before or at the time of transplant and 46 did not undergo nephrectomy. Of the 77 patients who had a native nephrectomy, 39 underwent a unilateral nephrectomy and 38 underwent a bilateral nephrectomy. The majority of patients who underwent unilateral nephrectomy had the nephrectomy performed at the time of transplant (38 of 39 patients). In patients who had bilateral nephrectomies, 33 of 38 patients had both kidneys removed simultaneously with 26 patients having bilateral nephrectomies before kidney transplant and 7 patients at the time of transplant. Five patients underwent staged bilateral nephrectomies, 4 of which were completed before transplant.

Between the 2 groups, there was no significant difference in sex or percentage of patients with a body mass index (BMI) of 85th percentile or greater at the time of transplantation (Table 1). HLA matches were compared between groups; the average HLA match was 1.8/6 for the no nephrectomy group and 2.1/6 for the nephrectomy group (data not shown, $P = 0.262$). Age at transplant, donor origin (deceased versus living), steroid-based immunosuppression, creatinine clearance and biopsy-proven rejection were significantly different between groups (Table 1, $P < 0.05$). Given these findings, the above variables were included in a multivariable logistic regression model to determine their relative impact on the use of antihypertensive medication at the time of discharge from transplant and at years 1, 3, and 5 posttransplant (Table 4A and B, Table 5A and B). These data will be discussed in greater detail below.

Among all patients, the most prevalent known etiology of ESRD was congenital anomalies of the kidney and urinary tract (CAKUT) followed by glomerulonephritis (Table 2). The 3 most common indications for nephrectomy were urologic/infectious reasons (27%), anatomic constraints (space for allograft, 20%) and proteinuria (14%). Refractory hypertension accounted for 5.2% of the patients in the study (Table 3).

TABLE 1.**Demographic and clinical characteristics at each timepoint**

(A)							
Independent variables	Units	Discharge		P	Year 1		P
		No nephrectomy	Nephrectomy		No nephrectomy	Nephrectomy	
No. patients	n	46	77	—	46	75	—
Sex	M:F	24:22	38:39	n.s.	24:22	38:37	n.s.
Age at transplantation	Median age (range)	16.3 (11-18)	5.73 (1-18)	< 0.05	16.3 (11-18)	5.7 (1-18)	< 0.05
Steroid-based immunosuppression	% (on steroids)	17 (37%)	15 (19.2%)	< 0.05	19 (41.3%)	15 (20%)	< 0.05
Acute rejection	n (%)	N/A	N/A	N/A	13 (28.3%)	9 (12.0%)	< 0.05
Transplant origin	Deceased/living	35:11	40:37	< 0.05	35:11	38:37	< 0.05
Creatinine clearance	Median (range)	N/A	N/A	N/A	71.4 (40.4-113.6)	82.3 (39.9-186.7)	< 0.05
Patients with BMI >85th Percentile at the time of transplant	%	15 (32.6%)	26 (33.8%)	n.s.			

(B)							
Independent variable	Units	Year 3		P	Year 5		P
		No nephrectomy	Nephrectomy		No nephrectomy	Nephrectomy	
No. patients	n	37	70	—	24	66	—
Sex	M:F	21:16	36:34	n.s.	15:9	35:31	n.s.
Age at transplantation	Median age (range)	16.3 (11-18)	5.6 (1-17.7)	< 0.05	15.8 (11-17.9)	5.3 (1-17.2)	< 0.05
Steroid-based immunosuppression	% (on steroids)	21 (56.8%)	18 (25.7%)	< 0.05	15 (62.5%)	17 (25.8%)	< 0.05
Acute rejection	n (%)	20 (54.1%)	15 (21.4%)	< 0.05	12 (50%)	13 (19.7%)	< 0.05
Transplant origin	Deceased/ Living	29:8	36:34	< 0.05	18:6	33:33	< 0.05
Creatinine clearance	Median (range)	64.7 (16.7-95.2)	73.1 (23-139.4)	< 0.05	61.8 (33.6-87.2)	69.1 (22.6-137.3)	< 0.05
Patients with BMI >85th Percentile at the time of transplant	%						

Hypertension

There was no difference between the percentage of patients on antihypertensive medication in either the nephrectomy (63.6%) and no nephrectomy (73.9%) groups before transplant or nephrectomy (Figure 1). However, there was a

significant reduction in the percentage of patients requiring antihypertensive medication at the time of discharge from transplant whom underwent nephrectomy (27.3%) as compared with patients without nephrectomy (71.7%, $P < 0.001$). At 1 year posttransplant, only 10.7% of patients that underwent nephrectomy remained on antihypertensive medication as compared with 50% of the patients in the no nephrectomy group (Figure 1, $P < 0.001$). Multivariable logistic regression analysis demonstrated that patients who did not undergo native nephrectomy had a 3.3 higher odds of requiring antihypertensive medication at the time of discharge from transplant compared with patients that underwent nephrectomy (Table 4A, $P = .036$). This difference

TABLE 2.**Etiology of ESRD**

Etiology of ESRD	Total (N = 123)	No nephrectomy (n = 46)	Nephrectomy (n = 77)
	No. patients (%)	No. patients (%)	No. patients (%)
CAKUT	46 (33.8%)	14 (30.4%)	32 (41.6%)
Glomerulonephritis	19 (13.9%)	14 (30.4%)	5 (6.5%)
Unknown	13 (9.6%)	10 (21.7%)	3 (3.9%)
FSGS	9 (6.6%)	4 (8.7%)	5 (6.5%)
Other	7 (5.2%)	0 (0.0%)	7 (9.1%)
ARPKD	5 (3.7%)	0 (0.0%)	5 (6.5%)
CNS	9 (6.6%)	0 (0.0%)	9 (11.7%)
HUS	3 (2.2%)	1 (2.2%)	2 (2.6%)
Nephronophthisis	3 (2.2%)	0 (0.0%)	3 (3.9%)
Alport syndrome	3 (2.2%)	3 (6.5%)	0 (0.0%)
Wilms tumor	1 (0.7%)	0 (0.0%)	1 (1.3%)
Denys-Drash syndrome	3 (2.2%)	0 (0.0%)	3 (3.9%)
Cystinosis	2 (1.5%)	0 (0.0%)	2 (2.6%)

FSGS, focal segmental glomerulosclerosis; ARPKD, autosomal recessive polycystic kidney disease; HUS, hemolytic uremic syndrome; CNS, congenital nephrotic syndrome.

TABLE 3.**Nephrectomy indications of the 77 patients who underwent nephrectomy**

Total (n = 77)	
Indication for nephrectomy	No. patients (%)
Urologic/infectious	21 (27.2%)
Anatomic	20 (26%)
Proteinuria	14 (18.2%)
Polyuria	9 (11.7%)
Malignancy	8 (10.4%)
Refractory hypertension	4 (5.2%)
Congenital anomalies	1 (1.3%)

FIGURE 1. Percentage of patients on antihypertensive medication pretransplant, at discharge from transplant, 1, 3, and 5 years after transplant. Black indicates no nephrectomy and gray indicates nephrectomy. Specific *P* values between groups at a given time point are denoted with bars as determined by the Pearson χ^2 test.

persisted out to 1 year posttransplant, where patients in the no nephrectomy group had a 5.2 higher odds of requiring antihypertensive medication compared to patients in the nephrectomy group (Table 4B, $P = 0.013$).

After nephrectomy, we saw a trend toward reduction in the use of antihypertensive medication in the nephrectomy group as compared to the no nephrectomy group at years 3 (18.6% vs 43.2%) and 5 (19.7% vs 37.5%) posttransplant (Figure 1). However, these data were not statistically significant in our multivariable regression at 3 and 5-years posttransplant (Table 5A and B). These findings may be

influenced by a 27% loss to follow up at 5 years, as 33 patients were excluded from analysis by year 5 post-transplant (13 due graft failure and 20 secondary to transitions in care). Given this, we did not have significant power to assess the impact of nephrectomy on hypertension at these later time points.

As 31 of 77 patients underwent native nephrectomy before receiving their kidney transplant, we conducted a separate analysis to investigate if use of antihypertensive medication in these patients changed after receiving a pretransplant nephrectomy or after undergoing their subsequent kidney transplant. Twenty-three of 31 patients who received a pre-transplant nephrectomy displayed a decreased use of antihypertensive medication by time of discharge from transplant. 55.3% of this decrease in antihypertensive medications occurred after nephrectomy but before transplantation.

Impact of Immunosuppression and Rejection on Hypertension

All patients received induction immunosuppression with antithymocyte immunoglobulin or daclizumab. Tacrolimus and mycophenolate mofetil were used for maintenance immunosuppression. Patients received steroid-based immunosuppression based on preoperative sensitization status and donor compatibility. Steroid-based immunosuppression was defined as the use of steroids as part of the daily immunosuppression regimen for each recipient after discharge from transplant. If patients were transitioned to steroid-based immunosuppression at a later time point, they were then included in the steroid-based group starting from that time point forward.

Thirty-seven percent of patients that did not undergo nephrectomy were started on maintenance steroid-based immunosuppression as compared to 19.5% in the native nephrectomy group ($P < 0.05$). This approximately twofold increase in steroid-based immunosuppression within the

TABLE 4.

Multivariate regression at discharge (A) and year 1 (B) after transplant

(A) Logistic regression predicting likelihood of antihypertensive medication use at discharge from transplant

	B	SE	Wald	df	P	Odds ratio	95% CI for odds ratio	
							Lower	Upper
No nephrectomy	1.205	0.574	4.404	1	0.036	3.338	1.083	10.291
Steroid-based immunosuppression	1.392	0.497	7.853	1	0.005	4.022	1.519	10.644
Deceased donor	0.318	0.465	0.468	1	0.494	1.375	0.552	3.423
Age at transplant ≥ 14 y	0.813	0.560	2.108	1	0.147	2.255	0.752	6.759
Constant	0.213	0.272	0.615	1	0.433	1.237		

(B) Logistic regression predicting likelihood of antihypertensive medication use at year 1 posttransplant

	B	SE	Wald	df	P	Odds ratio	95% CI for odds ratio	
							Lower	Upper
No nephrectomy	1.655	0.670	6.103	1	0.013	5.232	1.408	19.448
Steroid-based immunosuppression	1.221	0.507	5.795	1	0.016	3.389	1.255	9.154
Deceased donor	0.766	0.576	1.763	1	0.184	2.150	0.695	6.655
Age at transplant ≥ 14 y	0.136	0.735	0.034	1	0.853	1.145	0.271	4.832
Acute rejection	-0.009	0.595	0.000	1	0.988	0.991	0.309	3.182
Creatinine clearance	-0.017	0.014	1.355	1	0.244	0.983	0.956	1.011
Constant	0.288	1.098	0.043	1	0.836	1.256		

95% CI, 95% confidence interval.

TABLE 5.**Multivariate regression at year 3 (A) and year 5 (B) after transplant****(A) Logistic regression predicting likelihood of antihypertensive medication use at year 3 posttransplant**

	B	SE	Wald	df	P	Odds ratio	95% CI for odds ratio	
							Lower	Upper
No nephrectomy	0.575	0.655	0.771	1	0.380	1.778	0.492	6.149
Steroid-based immunosuppression	1.155	0.524	4.854	1	0.028	3.174	1.136	8.866
Deceased donor	0.400	0.607	0.433	1	0.511	1.491	0.453	4.905
Age at transplant, ≥ 14 y	−0.225	0.717	0.099	1	0.753	0.798	0.196	3.254
Acute rejection	1.124	0.557	4.067	1	0.044	3.076	1.032	9.165
Creatinine clearance	−0.004	0.012	0.139	1	0.709	0.996	0.972	1.019
Constant	−0.548	0.815	0.452	1	0.501	0.578		

(B) Logistic regression predicting likelihood of antihypertensive medication use at year 5 posttransplant

	B	SE	Wald	df	P	Odds ratio	95% CI for odds ratio	
							Lower	Upper
No nephrectomy	0.295	0.694	0.181	1	0.670	1.343	0.345	5.231
Steroid-based immunosuppression	0.693	0.622	1.241	1	0.265	2.000	0.591	6.768
Deceased donor	0.749	0.614	1.486	1	0.223	2.115	0.634	7.048
Age at transplant, ≥ 14 y	0.075	0.741	0.010	1	0.919	1.078	0.252	4.611
Acute rejection	0.758	.613	1.527	1	0.217	2.133	0.641	7.094
Creatinine clearance	0.004	0.014	0.097	1	0.755	1.004	0.978	1.031
Constant	−1.293	0.934	1.919	1	0.166	0.274		

nephrectomy group as compared with the no nephrectomy group persisted at years 1, 3, and 5 posttransplant. In multivariable regression analysis, the use of steroid-based immunosuppression at was associated with a 4.0 and 3.4 higher odds of requiring antihypertensive medication at discharge and 1 year posttransplant, respectively (Table 4A, $P < 0.01$ and $P < 0.02$). At 3 years posttransplant, patients on steroid-based immunosuppression had a 3.2 higher odds of being on antihypertensive medication (Table 5A, $P < 0.05$) but this difference did not persist out to 5 years posttransplant (Table 5B).

Additionally, 13 patients in the no nephrectomy group experienced a rejection episode as compared with 9 patients who underwent nephrectomy ($P < 0.05$) at 1 year. This difference persisted out to years 3 and 5 posttransplant with a ~2.5-fold increase in the percentage of patients who experienced a rejection episode in the no nephrectomy group as compared with the nephrectomy group (Table 1, $P < 0.05$). Multivariable logistic regression analysis demonstrated that acute rejection was associated with a 3.0 higher odds of being on antihypertensive medication at year 3 posttransplant ($P = 0.044$), but was not a significant predictor at all other time points (Table 4&5).

Allograft Function

Using creatinine clearance as a proxy of allograft function, there was superior graft function in the nephrectomy group as compared to the no nephrectomy group at years 1, 3, and 5 after transplant (Table 1, $P < 0.05$). In our multivariable regression model, this difference did not contribute to the use of antihypertensive medication (Table 4B, Table 5).

DISCUSSION

The incidence of native nephrectomy before or at the time of transplant has decreased; however, there is a relative

paucity of evidence regarding the impact of the native kidney on host physiology. Persistent cardiac morbidity and mortality after renal transplant remains a significant concern in the pediatric population and varying reports have implicated the role of nephrectomy in mitigating cardiac factors.^{11–14} To our knowledge, we are the largest study to demonstrate a benefit of nephrectomy on posttransplant hypertension in pediatric renal transplant recipients. We report a reduction in the percentage of patients requiring antihypertensive medication after nephrectomy at discharge from transplant and 1 year posttransplant as well an increased odds ratio for the use of antihypertensive medication in patients who did not undergo nephrectomy. Of added interest, in patients that underwent nephrectomy before transplant, there was a reduction in the use of antihypertensive medications after nephrectomy and preceding transplantation, suggesting a deleterious role of the native kidney independent of the benefits of transplantation. In support of our findings, a recent manuscript by Shumate et al described the benefit of native nephrectomy in autosomal dominant polycystic kidney disease patients.¹⁴ In this study, native nephrectomy was associated with a significant decrease in the defined daily dose of antihypertensive medication as compared to patients without nephrectomy at 24 and 36 months posttransplant.¹⁴

Although we saw a trend toward a decreased use of antihypertensive medication in the no nephrectomy group at 3 and 5 years posttransplant with bivariate analysis, nephrectomy was not an independent predictor of antihypertensive medication. Given the number of patients that were excluded at later time points either to graft rejection or transitions in care, we were not able to determine the independent impact of nephrectomy on hypertension at years 3 and 5. We hope that continued study of this patient cohort over the coming years will provide additional data to ascertain if nephrectomy acts to directly improve long-term hypertension posttransplant.

Cavallini et al⁶ found no difference in mean arterial pressure, number of antihypertensive medications and LVH in a small cohort of pediatric patients who had undergone transplant with or without nephrectomy. Different from our study design, the authors did not evaluate hypertension and use of antihypertensive medications longitudinally after transplant but rather at 1 time point at a variable interval after transplant. Also, the sole indication for all nephrectomies in that study was intractable hypertension, with a greater number of blood pressure medications used in patients before transplant who had undergone bilateral nephrectomies ($n = 14$) as compared with both unilateral ($n = 18$) and no nephrectomy groups ($n = 35$). After transplant, this difference in the number of blood pressure medications was the same across groups. Together, these data suggest that the benefits of nephrectomy were marginalized by the nature of the inclusion criteria and that, as demonstrated in our study, nephrectomy may actually impact the use of hypertensive medications after transplant.

Antihypertensive management in our cohort was initiated by pediatric transplant surgeons, nephrologists and intensivists. After discharge, blood pressures were monitored via home blood pressure measurement as well as resting clinic blood pressures. We recognize that lack of prescription antihypertensive medication may not indicate adequate blood pressure control; however, 24-hour ambulatory blood pressure monitoring data were not available for this cohort. Similarly, echocardiographic measurements of ejection fraction and presence of LVH posttransplant were not available for the majority of our patients. LVH has been shown to be reduced but not necessarily normalized after transplant.¹⁵ Multiple factors pretransplant (uremia, age, and diabetes) as well as posttransplant (inflammatory cascade, immunosuppression, hypertension, anemia, and malnutrition) have been identified as contributors.¹⁶ Hypertension is a modifier of cardiac hypertrophy and remodeling,¹⁷ and given that it is a treatable clinical parameter for cardiac morbidity, we chose this as our primary outcome. We recognize this limitation, specifically in light of the findings by Cavallini et al. Future work to delineate the impact of improved hypertension after nephrectomy as assessed by ambulatory blood pressure monitoring on cardiac remodeling with longitudinal echocardiographic assessment is warranted.

Long-term steroid use is known to predicate the development of hypertension. We did see that steroid-based immunosuppression increased the odds that a patient would be on antihypertensive medication as expected. However, in our multivariable regression, no nephrectomy was actually a stronger predictor of need for antihypertensive medication at 1 year after transplant. Although long-term steroid use is certainly a risk factor for hypertension,^{18,19} our data support that nephrectomy acts as an independent factor in reducing hypertension after transplant.

Arguments against nephrectomy cite the need for attentive pretransplant fluid management, prolonged anesthesia exposure, operative complications (ie, bleeding, infection, and injury to surrounding structures, such as the liver or spleen) and the benefits of having the native ureter available for reconstruction should a complication develop with the transplanted ureters.²⁰ Interestingly, the patients who did undergo nephrectomy in the above study by Fraser et al did so with minimal morbidity and with favorable graft outcomes. These authors did not evaluate any long-term parameters of

cardiac outcomes, and in light of our data, we would favor nephrectomy in the majority of these patients to limit hypertension. As with any surgical indication, careful assessment of each surgical candidate is necessary.

It is also noteworthy that in the pediatric transplant population, there is a high percentage of graft loss secondary to medication noncompliance. Numerous studies have demonstrated that compliance improves with medication simplification^{21,22} and reducing pill burden directly improves overall adherence rates.²³ In the first year posttransplant, medication regimens are often the most elaborate. Fifty percent of patients without nephrectomies required antihypertensive medications compared with approximately 11% in nephrectomy group; reduction in antihypertensive regimens could positively impact adherence and compliance, in turn promoting graft longevity.

In addition to some of the limitations discussed above, this is a retrospective study, and future prospective trials to delineate the role of nephrectomy on hypertension and long-term cardiac morbidity are clearly warranted. Given the data presented here, we continue to support native nephrectomy for appropriate indications in pediatric renal transplant recipients as we demonstrate a positive effect of nephrectomy in reducing hypertension in the posttransplant period. The potential benefit of native nephrectomy on cardiac morbidity in a patient population plagued by decreased longevity with a disproportionate incidence of cardiac-related death should not be dismissed.

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