

Association Between Clinical Risk Factors and Progression of Chronic Kidney Disease in Children

Amy O. Staples,* Larry A. Greenbaum,[†] Jodi M. Smith,[‡] Debbie S. Gipson,[§] Guido Filler,^{||} Bradley A. Warady,[¶] Karen Martz,** and Craig S. Wong*

*Department of Pediatrics, University of New Mexico, Albuquerque, New Mexico; [†]Department of Pediatrics, Emory University, Atlanta, Georgia; [‡]Department of Pediatrics, University of Washington, Seattle, Washington; [§]Department of Pediatrics, University of Michigan, Ann Arbor, Michigan; ^{||}Department of Pediatrics, University of Western Ontario, London, Ontario, Canada; [¶]Department of Pediatrics, Children's Mercy Hospital, Kansas City, Missouri; and **Emmes Corporation, Rockville, Maryland

Background and objectives: Children with chronic kidney disease (CKD) have an increased risk of progression to ESRD. There is a need to identify treatments to slow the progression of CKD, yet there are limited data regarding clinical risk factors that may be suitable targets to slow progression.

Design, setting, participants, & measurements: We performed a retrospective cohort study using the North American Pediatric Renal Trials and Cooperative Studies CKD database. There were 4166 pediatric subjects with CKD stages II to IV. Disease progression was defined as a GFR on follow-up of <15 ml/min per 1.73 m² or termination in the registry because of dialysis or transplantation. We used Kaplan-Meier and Cox proportional hazards methods to describe progression rates and determine factors associated with CKD progression.

Results: In the univariate analysis, CKD progression was associated with age, gender, race, primary disease, CKD stage, registration year, hematocrit, albumin, corrected calcium, corrected phosphorus, and use of certain medications. Factors that remained significant in the multivariate analysis were age, primary disease, CKD stage, registration year, hypertension, corrected phosphorus, corrected calcium, albumin, hematocrit, and medication proxies for anemia and short stature.

Conclusions: There are multiple risk factors associated with disease progression in the pediatric CKD population. Factors that may be amenable to intervention include anemia, hypoalbuminemia, hyperphosphatemia, hypocalcemia, hypertension, and short stature. Because of the retrospective nature of our study, confirmation of our results from ongoing prospective studies is warranted before recommending interventional trials.

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There is an urgent need to identify risk factors and develop new methods to halt chronic kidney disease (CKD) progression in children. Progression to ESRD at a young age results in lifelong disability and significant reduction in lifespan. The expected remaining lifetime after ESRD in the 0- to 14-year age group is 30 years (1). Among survivors of childhood ESRD, health-related quality of life, rates of vocational placement, and independence from parents are lower compared with peers in the general population (2,3). Although the dominant causes of CKD in adults are diabetic nephropathy and hypertension, nearly 60 to 70% of children affected with CKD have congenital or inherited kidney disorders. Compared with adults with CKD, pediatric patients with CKD require greater amount of resources, specialized care, and care coordination to achieve optimal outcomes (4).

Significant research emphasis has been placed on early iden-

tification of modifiable factors related to CKD progression. Within the pediatric CKD population, hypertension and proteinuria have been shown to be strong clinical risk factors for renal progression (5-10). Recently, Furth *et al.* (11) reported that anemia and hypoalbuminemia were associated with an accelerated decline of GFR among 23 adolescents with CKD. Additionally, the recently published, prospective Effect of Strict Blood Pressure Control and ACE-Inhibition on Progression of Chronic Renal Failure in Pediatric Patients (ESCAPE) trial found that optimal BP control can slow the progression of CKD (10). The pediatric studies to date have been either limited in range of clinical measures surveyed or sample size. Although the literature is growing, these data within the pediatric CKD population remain sparse, and the reported associations need further validation.

Using the North American Renal Trials and Cooperative Studies (NAPRTCS) Chronic Kidney Disease Registry, we report on multiple clinical factors associated with disease progression in a large pediatric cohort of patients with CKD. Particular attention was paid to potentially modifiable factors that may be targets for future clinical trials to slow CKD progression in children.

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Correspondence: Dr. Amy Staples, University of New Mexico, Pediatrics/ACC-3, MSC10-5590, 1 University of New Mexico, Albuquerque, NM 87131. Phone: 505-272-3887; Fax: 505-272-6620; E-mail: astaples@salud.unm.edu

Materials and Methods

Study Population

Details of the methods used for this analysis are published elsewhere (12). Briefly, patients are eligible for enrollment in the voluntary NAPRTCS database through their 20th birthday. Patients were classified by disease severity into one of five stages using the Kidney Disease Outcomes Quality Initiative (KDOQI) CKD staging system (13). Estimated GFR (eGFR) was determined using the Schwartz equation (14). The original Schwartz equation was used in this analysis because the data analysis was complete before the publication of the revised equation. Disease progression was defined as an eGFR at any follow-up visit of <15 ml/min per 1.73 m² or registry termination because of initiation of dialysis or transplantation (cumulatively referred to as CKD stage V). All patients with CKD stages II to IV at registry entry and any available follow-up data were included in the analysis. Subjects excluded from the study were those with a history of prior kidney transplant or dialysis or those who were <2 years of age, because the KDOQI staging system is not applicable to children <2 years old (13).

Statistical Analyses

Variables examined in the univariate analysis included age, gender, race, primary diagnosis, CKD registry year (before 2000 and after), erythropoietin use, growth hormone use, iron supplementation, hypertension (systolic or diastolic BP >95 percentile for age, gender, and height), anti-hypertensive medication use, parathyroid hormone (PTH), CKD stage, anemia (hematocrit < 33%), height z-score, weight z-score, body mass index z-score, corrected calcium (low, normal, high), age-adjusted phosphorus (normal, high), and albumin (as a dichotomous variable ≤ 4 or >4 g/dl). Serum calcium was adjusted for serum albumin as follows: measured Ca (mg/dl) + 0.8 × [4 – serum albumin (g/dl)]. We defined a calcium value of 8.5 to 10.0 mg/dl as normal. Calcium values <8.5 mg/dl were classified as low, and values >10.0 mg/dl as high. The definition of hyperphosphatemia was adjusted for age in the following manner: ≥ 6.5 mg/dl for 2 to 5 years; ≥ 5.8 mg/dl for 6 to 12 years; ≥ 4.5 mg/dl for 13 to 20 years.

Patients with any missing data were excluded from the multivariate analysis (although included in the univariate analysis for the data that were available). Additionally excluded from the multivariate analysis were height, weight, and body mass index z-scores because they were not significant in the univariate analysis. PTH was not included multivariate analysis because of >1800 missing values. All other covariates were included in the multivariate analysis.

Univariate analysis using Kaplan-Meier time-to-event curves and log-rank tests were used to identify individual covariates associated with disease progression. All significant factors were included in a multivariate Cox proportional hazards regression model. Model selection used backward elimination methods, with final covariates significant at the 0.05 level. The analyses were performed using SAS version 8.2 (SAS Institute, Cary, NC).

Results

Population Demographics

A total of 6133 of the available patients enrolled in the NAPRTCS CKD database had baseline eGFR and hematocrit data available. Of those, 4166 were at least 2 years old, had one set of follow-up data, and had CKD stages II to IV at registry initiation. These patients were included in the initial analysis.

Demographic data for included patients is presented in Table 1. At the time of registration, 79.8% were 6 years of age or older, 60.9% were white, 61.5% were male, and the most common

Table 1. Patient characteristics

	N (%)
Total cases (≥ 2 years)	4166 (100)
Age (years)	
2 to 5	836 (20.1)
6 to 12	1681 (40.4)
>12	1649 (39.6)
Gender	
male	2562 (61.5)
female	1604 (38.5)
Race	
white	2539 (60.9)
African American	786 (18.9)
Hispanic	577 (13.9)
other	257 (6.2)
Primary diagnosis	
obstructive uropathy	837 (20.1)
focal segmental glomerulosclerosis	478 (11.5)
renal dysplasia	529 (12.7)
reflux nephropathy	389 (9.3)
other	1833 (44.0)
Anemia	
hematocrit $\geq 33\%$	2589 (62.1)
hematocrit <33%	1577 (37.9)
CKD stage	
stage II	828 (19.9)
stage III	2162 (51.9)
stage IV	1176 (28.2)
CRI registry year	
before 2000	2795 (67.1)
2000 and after	1371 (32.9)
Erythropoietin use	
yes	557 (13.4)
no	3606 (86.6)
Growth hormone use	
yes	281 (6.7)
no	3878 (93.1)
Calcium (corrected)	
low	214 (5.1)
normal	2728 (65.5)
high	632 (15.2)
Phosphorus	
normal	2654 (63.7)
elevated	1177 (28.3)
Parathyroid hormone	
<2× upper limit	1477 (35.5)
>2× upper limit	853 (20.5)
unknown	1836 (44.1)
Iron supplementation	
yes	997 (23.9)
no	3157 (75.8)
Anti-hypertensive medication use	
yes	1928 (46.3)
no	2230 (53.5)
Albumin	
≤ 4.0 g/dl	1954 (46.9)
>4.0 g/dl	1674 (40.2)
Hypertension	
yes	1954 (46.9)
no	2154 (51.7)

Percents may not total 100% because of missing values.

diagnosis was obstructive uropathy (20.1%). Although 37.9% of patients were anemic (hematocrit < 33%), only 13.4% were receiving erythropoietin and 23.9% supplemental iron. Additionally, 6.7% reported using growth hormone. Almost one half (46.9%) of the patients were hypertensive, whereas 46.3% reported using anti-hypertensive medications. Regarding other laboratory values at registration, 5.1% had a low serum calcium, 28.3% had elevated serum phosphorus, 20.5% had a PTH value greater than two times the upper limit, and 46.9% had a serum albumin \leq 4.0 g/dl. The majority of patients had CKD stage III at registry initiation (51.9%), followed by stage IV (28.2%) and stage II (19.9%).

As described previously, the prevalence of anemia (hematocrit < 33%) was 21% in CKD stage II patients and increased to 59% in CKD stage IV patients (data not shown) (12).

Univariate Progression Rates

The median time to progression for all patients ($n = 4166$) was 53.7 months from registry initiation. Table 2 provides the Kaplan-Meier progression rates (the percent of patients who progress to CKD stage V) at 1 and 3 years from the time of registration, as well as the median months to reach CKD stage V (number of months when 50% of the cases have progressed to CKD stage V). African-American and Hispanic patients had a higher rate of progression compared with white CKD patients (median time to progression, 43.9 and 47.1 *versus* 60.3, respectively). Patients diagnosed with focal segmental glomerulosclerosis had a significantly shorter median time to progression (22.9 months) than did those with obstructive uropathy (67.2 months), reflux nephropathy (88.5 months), renal dysplasia (54.0 months), and other diagnoses (52.3 months).

Laboratory values collected at the time of registration showed anemia, low serum calcium, high serum phosphorus, and low serum albumin were associated with faster rate of progression. Anemic patients progressed appreciably more rapidly than did nonanemic patients (26.2 *versus* 77.3 months). CKD patients with low serum-corrected calcium had a median time to CKD stage V of 29.1 months compared with patients with normal or high serum calcium (respectively, 52.7 and 55.6 months); those with high serum phosphorus levels had a median time to progression of 23.6 months compared with those with normal serum phosphorus, who had a median time of 70.1 months. Hypoalbuminemic patients progressed more rapidly compared with those with a normal serum albumin (respectively, 32.2 and 74.6 months).

Hypertensive patients progressed to CKD stage V almost 2 years sooner than did nonhypertensive patients (respectively, 43.8 and 63.7 months). Additionally, use of erythropoietin and iron (likely indicating anemia) were associated with more rapid progression to CKD stage V compared with nonuse of these medications.

In the univariate analysis, all variables reported in Table 2 were significantly associated with progression to CKD stage V, with severity of CKD and primary diagnosis showing the greatest association. The z-scores for height, weight, and body mass index were not associated with renal progression.

Kaplan-Meier curves for disease progression associated with

CKD stage and anemia are presented in Figures 1 and 2. At 5 years, 23.2% of those with CKD stage II at registry initiation had progressed, whereas 86.4% of those with CKD stage IV at initiation had reached stage V. Also, 71.0% of anemic patients had progressed to stage V by 5 years, whereas only 41.6% of nonanemic patients had progressed.

Multivariate Analysis for Renal Progression

To adjust for differences in CKD stage, primary diagnosis, and other potential confounders, we performed a multivariate proportional hazards regression analysis to evaluate independent risk factors for renal progression (Table 3). Results showed younger age at time of registration was associated with a lower risk of progression compared with older age (hazard ratio [HR], 0.72; 95% confidence interval [CI], 0.61 to 0.84). CKD stages III and IV were associated with higher risk of disease progression compared with stage II (HR, 2.0 and 6.68; 95% CI, 1.64 to 2.42 and 5.46 to 8.18, respectively). Using obstructive uropathy as the referent group, focal segmental glomerulosclerosis was the only diagnosis that was independently associated with a risk of disease progression (HR, 1.77; 95% CI, 1.48 to 2.12).

Independent of the other factors, anemia, hypocalcemia, hyperphosphatemia, and hypoalbuminemia each remained significantly associated with a higher risk for renal progression. We estimate that those with anemia at registration have an associated 52% increase in risk of disease progression compared with the nonanemic patient (HR, 1.52; 95% CI, 1.36 to 1.69). Compared with patients with a normal serum calcium at time of registration, those with hypocalcemia have a 29% higher risk for renal progression independent of other factors (HR, 1.29; 95% CI, 1.06 to 1.58). Furthermore, those with hyperphosphatemia have a 41% increase in risk for renal progression compared with those with normal serum phosphorus (HR, 1.41; 95% CI, 1.25 to 1.59). In the multivariate model, hypoalbuminemia was associated with a 67% higher risk for renal progression (HR, 1.67; 95% CI, 1.49 to 1.86).

Use of erythropoietin and use of growth hormone were considered surrogate indicators of anemia and short stature. The surrogate indicators were associated with renal progression. Anti-hypertensive medication use was not associated with renal progression when hypertensive status is included in the multivariate model (Table 3).

To fully evaluate the relationships between the laboratory measure of anemia and erythropoietin use, we evaluated two interaction terms to identify any possible effect modification: (1) erythropoietin use and anemia and (2) CKD stage and anemia. Although we did find an increased risk of disease progression for those with anemia not on erythropoietin compared with those with anemia using erythropoietin (HR, 2.38 *versus* 1.60), when the term was added to the multivariate regression model, it became nonsignificant ($P = 0.97$; data not shown). Assessment for interaction between anemia and CKD stage with modeling of interactions terms was similarly not significant in the multivariate setting ($P = 0.11$).

Table 2. Time to progression: Kaplan-Meier rates

Patient Variables	1-Year Progression Rate (%)	3-Year Progression Rate (%)	Median Months to Progression
All cases	17.3	39.4	53.7
Age (years)			
2 to 5	11.8	28.6	78.6
6 to 12	16.0	38.4	52.8
>12	21.6	46.9	40.9
Gender			
male	16.5	37.9	57.5
female	18.6	42.0	48.0
Race			
white	16.3	37.5	60.3
African American	19.5	44.1	43.9
Hispanic	17.3	41.2	47.1
other	21.0	41.5	51.8
Primary diagnosis			
obstructive uropathy	10.8	29.4	67.2
focal segmental glomerulosclerosis	31.7	61.7	22.9
renal dysplasia	14.3	39.3	54.0
reflux nephropathy	10.5	28.4	88.5
other	18.2	39.7	52.3
CKD stage			
stage II	3.5	15.4	137.7
stage III	8.6	28.8	67.8
stage IV	43.0	74.5	15.5
Hypertension			
yes	21.0	44.8	43.8
no	14.2	34.5	63.7
Laboratory values at registration			
anemia			
HCT \geq 33%	10.3	28.2	77.3
HCT <33%	29.0	57.6	26.2
calcium			
low	33.5	53.3	29.1
normal	16.9	39.3	52.7
high	17.1	40.3	55.6
phosphorus			
normal	10.9	29.8	70.1
high	32.3	62.5	23.6
albumin			
\leq 4.0 g/dl	24.5	52.2	32.2
>4.0 g/dl	10.4	27.6	74.6
Medication use at registration			
anti-hypertensive medication use			
yes	21.5	45.7	42.7
no	13.7	34.1	64.0
erythropoietin use			
yes	40.9	68.8	17.7
no	13.7	34.8	61.2
iron supplementation			
yes	29.2	56.3	28.8
no	13.5	34.0	63.7

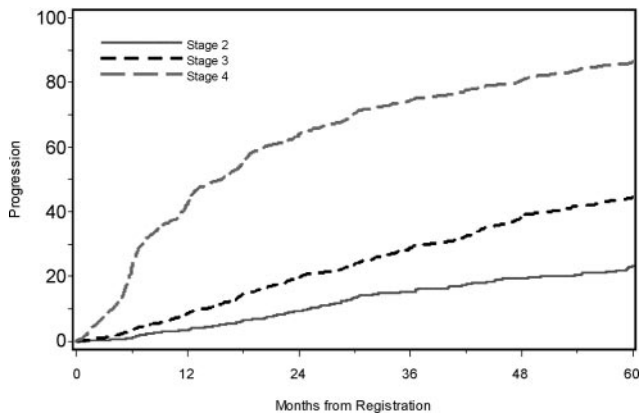


Figure 1. Time to progression by CKD stage at registration.

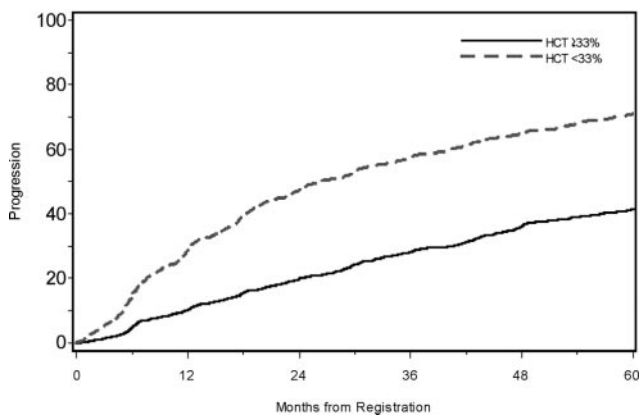


Figure 2. Time to progression by anemia (defined by hematocrit %) at registration.

Discussion

Although there has recently been significant emphasis on factors associated with disease progression in adult CKD populations, little is known about the pediatric population. Our review of a large pediatric CKD cohort identified a number of clinical factors associated with renal progression, several of which are potentially modifiable and provide potential targets for interventional trials aimed at slowing CKD progression. The Kaplan-Meier–based estimates regarding time to progression (Table 2) provide benchmark progression rates for future studies and are potentially useful to provide anticipatory guidance for families affected by childhood CKD. In our multivariate analysis, we found that age at registration, CKD stage at registration, cause of CKD, hypertension, anemia, hypoalbuminemia, hyperphosphatemia, hypocalcemia, and reported medications used to treat anemia and short stature were associated with CKD progression in children.

In adults with CKD, Hunsicker *et al.* (15) identified that renal progression was associated with race, degree of proteinuria, mean arterial pressure, HDL, and underlying diagnosis using data from the Modification of Diet in Renal Disease Study in 1997. Only mean arterial pressure, HDL cholesterol levels, and possibly degree of proteinuria were associated factors found in

Table 3. Multivariate Cox regression analysis of factors associated with CKD progression

Demographic Characteristics	Hazard Ratio	95% Confidence Interval
Age (years)		
2 to 5	0.72	0.61 to 0.84 ^a
6 to 12	0.97	0.85 to 1.10
>12	1.00	—
CKD stage		
stage II	1.00	—
stage III	2.00	1.64 to 2.42 ^a
stage IV	6.68	5.46 to 8.18 ^a
Primary diagnosis		
dysplasia	1.15	0.96 to 1.37
reflux nephropathy	0.85	0.68 to 1.06
focal segmental glomerulosclerosis	1.77	1.48 to 2.12 ^a
other	1.13	0.98 to 1.30
obstructive uropathy	1.00	—
Cohort year		
1994 to 1999	0.78	0.69 to 0.88 ^a
2000 to 2008	1.00	—
Hypertension		
yes	1.26	1.14 to 1.40 ^a
no	1.00	—
Laboratory data at registration		
anemia		
hematocrit <33%	1.52	1.36 to 1.69 ^a
hematocrit >33%	1.00	—
calcium		
<8.5 mg/dl	1.29	1.06 to 1.58 ^b
≥8.5 mg/dl	1.00	—
phosphorus (high)		
high	1.41	1.25 to 1.59 ^a
normal	1.00	—
albumin		
≤4.0 g/dl	1.67	1.49 to 1.86 ^a
>4.0 g/dl	1.00	—
Medication use at registration		
erythropoietin use		
yes	1.30	1.14 to 1.49 ^c
no	1.00	—
growth hormone use		
yes	1.24	1.04 to 1.48 ^b
no	1.00	—

Factors in the multivariate analysis include age, gender, race, hematocrit, albumin, CKD stage, primary diagnosis, cohort year, calcium, phosphorus, anemia, hypertension, iron supplementation, growth hormone use, and erythropoietin use.

^a*P* < 0.0001.

^b*P* < 0.05.

^c*P* < 0.005.

the study of Hunsicker *et al.* that might be amenable to correction. Similarly, Jungers *et al.* (16) identified primary disease and degree of proteinuria as major determinates of renal progression in their adult population of CKD patients without diabetic kidney disease. Although these associated factors may be helpful in predicting the rate of CKD progression for patients, only modifiable factors have the potential of slowing the rate of progression.

Our finding of increased risk of disease progression in patients with hypertension (HR, 1.26) supports the findings of prior studies using the NAPRTCS data. Mitsnefes *et al.* (6) used the NAPRTCS database to evaluate the association of hypertension and disease progression. In their evaluation of 3834 patients with CKD, they found that systolic hypertension was a significant independent risk factor for disease progression with a relative risk of 1.2. Recently additional prospective data from the ESCAPE trial has confirmed that optimal BP control can significantly retard the progression of CKD (10). The ESCAPE study provided firm evidence that higher BP and furthermore high levels of proteinuria increases the rate of renal progression in children. The NAPRTCS database does not collect data on proteinuria, and hence this was not evaluated in our analysis.

Our study confirmed findings of two other recent pediatric studies focused on associated risk factors for renal progression. Soares *et al.* (9) performed a retrospective review of 107 pediatric patients aimed to identify predictive factors associated with CKD progression. Our study confirmed their findings that primary cause of CKD and initial CKD stage were associated with renal progression in children. Although the findings from Soares *et al.* are valuable to the literature, their study was limited in sample size and lacked variables for modifiable risk factors, such as those identified in our study. Similar to what has been reported by Furth *et al.* (11), we found that anemia and hypoalbuminemia were associated with pediatric CKD progression. Although the study by Furth *et al.* was a multicenter prospective study, it was limited in size (only to 23 subjects) and was limited to adolescents and is thus not generalizable to younger CKD patients. Although our study was retrospective, our data included >4000 pediatric patients, with 60% of our population being 12 years of age or younger. Furthermore, Furth *et al.* (11) defined anemia as a hematocrit <36%. Although this may be one definition of anemia, the KDOQI anemia guidelines specify a hematocrit of <33% as the cut-off for anemia (17), which was the defined anemia threshold for our study.

In addition to anemia and hypoalbuminemia, we also identified that hypocalcemia and hyperphosphatemia were independent risk factors for renal progression in these children with CKD. Voormolen *et al.* (18) have previously found an association between hyperphosphatemia and a more rapid decline in renal function (as well as mortality) in the predialysis CKD population. However, their study included only adults with an eGFR <20 ml/min per 1.73 m².

The use of medication in this cohort identified patients who were at risk for renal progression. It is notable that we found an increased rate of progression in patients using erythropoietin compared with those not using erythropoietin (HR, 1.29; 95%

CI, 1.13 to 1.48). This association is likely not caused by the use of erythropoietin itself but rather that this variable served as a surrogate marker for the condition of anemia that is not fully explained by hematocrit alone. Because a very small proportion of patients with anemia are being treated with erythropoietin in our cohort (13%), it may be that those with more significant anemia (possible correlating with more significant disease) are those treated with erythropoietin, leading to the association of erythropoietin use and disease progression. Although subjects with anemia had an associated faster rate of progression, we could not detect a difference in the rate of progression with those treated with erythropoietin, when we modeled the relationship with an interaction term. Additionally, we did see that those with anemia who were not treated with erythropoietin had an increased risk of disease progression in the univariate analysis, suggesting that it is the anemia and not the use of erythropoietin that contributes to disease progression.

Furthermore, growth hormone as a surrogate measure for short stature was associated with a higher risk for renal progression independent of other factors in the analysis. Short stature in the pediatric CKD population is associated with a lower quality of life, increased rate of hospitalization, and death. Although the reported association between the use of growth hormone and renal progression is intriguing, a further analysis of the association with height was beyond the scope of our analysis but deserves further study.

We feel it important to acknowledge the limitations of our study. First, the NAPRTCS database, while being the largest database of its kind, is a voluntary registry. Thus, there may be a significant number of pediatric CKD patients who are not enrolled. Additionally, there is known to be a significant amount of missing data, which led to the exclusion of numerous patients in the multivariate analysis. Moreover, the available data are limited to information that is routinely collected in the database at 6-months intervals, not allowing for more complete or detailed information. Most importantly, it did not allow for the assessment of an association between chronic inflammatory state or degree of proteinuria and risk of disease progression, both areas of significant interest of late (19).

In these data, there is evidence of survivorship bias with evidence of a small but significant difference in progression rates between cohort years. Those with less severe disease and therefore slower progression may remain in the CKD cohort for longer and contribute more time at risk, leading the older cohort of patients to seem to have a lower risk of progression. Adjusting the analysis for cohort year will address this bias. However, as with any observational study, there exists the possibility of other sources of unmeasured bias that we were not able to address.

The eGFRs (and therefore CKD stages) were calculated using the original Schwartz equation (14). Our data analysis predated the revision of the recently published pediatric GFR estimating equation (20). The revised estimating equation for GFR was used for serum creatinine concentrations by enzymatic methods, whereas the original Schwartz formula is appropriate for serum creatinine concentrations performed by the Jaffe method (21). We acknowledge that having no indication of type of

creatinine assay is a limitation of the database. We applied the original Schwartz formula to estimate GFRs for this analysis because of concern that applying the updated estimating equation would tend to exaggerate the rate of progression and overestimate the strength of association, especially for those in earlier cohort years when the Jaffe method for creatinine determination was more commonly used.

It is important to emphasize that this study showed only association between identifiable risk factors and disease progression and did not show evidence of cause and effect. Although we controlled for many potentially confounding variables, it is possible that identified risk factors may be acting as surrogate markers for other conditions that were not collected as part of the NAPRTCS database. The ongoing prospective cohort study of CKD in children (22) addresses many of the limitations of this study and will provide an appropriate platform to replicate the findings from our retrospective cohort study.

Conclusions

Our retrospective cohort study of >4000 pediatric patients with CKD identified multiple risk factors associated with CKD progression. Our findings underline the importance of early detection and management of pediatric CKD in an attempt to delay CKD progression. Although not modifiable, the CKD risk factors of primary cause of CKD, CKD stage, and age allow identification of high-risk groups for intensive monitoring and attentive management. We were able to identify several clinical risk factors associated with renal progression in children, including anemia, hyperphosphatemia, hypocalcemia, hypertension, and short stature. These may represent potential targets for improved management of pediatric CKD patients that have the potential to impact the rates of disease progression. Given the limitations of our study design, our findings need to be confirmed by ongoing prospective studies of pediatric CKD before recommending definitive guidelines or interventions.

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Disclosures

None.

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