Time to Initiation of Antihypertensive Therapy After Onset of Elevated Blood Pressure in Patients With Primary Proteinuric Kidney Disease

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Rationale & Objective: The objective of the study was to estimate the prevalence of hypertension in patients with proteinuric kidney disease and evaluate blood pressure (BP) control.

Study Design: Retrospective cohort study.

Setting & Participants: Data from adults and children with proteinuric kidney disease enrolled in the multicenter Kidney Research Network Registry were used for this study.

Exposure: Proteinuric kidney disease.

Outcomes: Hypertension and BP control.

Analytical Approach: Patients with white-coat hypertension were excluded. Patients were censored at end-stage kidney disease onset. Patients were defined as hypertensive either by hypertension diagnosis code, having 2 or more encounters with elevated BPs, or treatment with antihypertensive therapy excluding renin-angiotensin-aldosterone system blockade. Elevated BP was defined as greater than 95th percentile for children and >140/90 mm Hg in adults. Sustained BP control was defined as 2 or more consecutive encounters with BPs lower than 95th percentile for children and <140/90 mm Hg for adults. Kaplan-Meier and Cox proportional hazards analyses were used to evaluate the time to initiation of antihypertensive therapy.

Results: 842 patients, 69% adults and 31% children, with a total observation period of 6,722 patient-years were included in the analysis. 644 (76%) had hypertension during observation. There was no difference in the prevalence of hypertension between children and adults (74% vs 78%; P = 0.3). Hypertension was most common among those of African American race compared with other races (90% vs 72%-75%; P = 0.003). 504 (78%) patients with hypertension achieved BP control but only 51% achieved control within 1 year. 140 (22%) patients with hypertension never achieved BP control during a median of 41 (IQR, 24-73) months of observation.

Limitations: Differing BP control goals that may lead to overestimation of the controlled patient population.

Conclusions: Hypertension affects most patients with proteinuric kidney disease regardless of age. Time to BP control exceeded 1 year in 50% of patients with hypertension and 22% did not demonstrate control. This study highlights the need to address hypertension early and completely in disease management of patients with proteinuric kidney disease.

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Hypertension (HTN) is the second most common reported cause of end-stage kidney disease in the United States.[1] It is also clear that HTN commonly coexists with chronic kidney disease (CKD). Furthermore, uncontrolled HTN is associated with accelerated deterioration in kidney function and progression of cardiovascular disease (CVD) in patients with CKD. Despite these associations, inadequate blood pressure (BP) control has been documented in both adults and children with CKD. An analysis of the Fourth National Health and Nutrition Examination Survey (NHANES IV) revealed that only 37% of adult participants with CKD had BPs controlled to a goal of <130/ 80 mm Hg.[2] Similarly, Wong et al[3] demonstrated that patients with coexisting CKD and CVD had poor BP control rates when compared with those without cardiovascular comorbid conditions. More recent analysis demonstrated that up to one-third of patients with CKD stages 1 to 2 were unaware that they had elevated BPs and suggested that only 11% were treated appropriately.[4] Two longitudinal cohorts of children with CKD, the Chronic Kidney Disease in Children (CKiD) Study and North American Pediatric Renal Transplant Cooperative Study (NAPRTCS), demonstrated a prevalence of uncontrolled HTN in 37% and 48% of study participants, respectively.[5,6] Additionally, these studies found that 39% and 50% of patients, respectively, with elevated BPs were not receiving antihypertensive therapies.[5,6] Barriers to the recognition and treatment of HTN may include changing guidelines as to the definition of HTN and, for children, the need for detailed charts or calculations requiring sex, age, and height to derive the BP percentiles, and concern that intensive control of BP may cause adverse events in certain patient populations. However, there is consensus that BP control is crucial for slowing the progression of CKD and lowering CVD risk.[7,8]

The cited studies have evaluated cohorts of patients with the full spectrum of CKD causes. Because of the nature of

glomerular diseases, including a variety of disease courses such as progressive, relapsing and remitting, and resolving; management with therapies known to cause HTN; and affected populations in children and adults, we undertook this study to evaluate and characterize BP control and antihypertensive therapy management practices in a cohort of adult and pediatric patients with glomerular disease enrolled in a multicenter observational cohort study.

METHODS

Participants and Data Source

The Kidney Research Network (KRN) Registry is an ongoing study of patients with glomerular disease that began enrollment in November 2015 to improve the treatment options and health outcomes of patients with proteinuric kidney disease.[9] Patients enrolled in KRN from 7 participating internal medicine and pediatric nephrology practices in the United States provided consent to share both retrospective and prospective data from their electronic health records, including demographics, diagnosis, kidney biopsy report, laboratory results, vital signs, and medications from ambulatory and hospitalization encounters. Patients were consented to join the registry at any point in their disease course, but retrospective data were collected from the earliest existing health record data point.

The diagnosis was confirmed by the patient's primary nephrologist at the time of registry consent. Kidney diagnoses were grouped into focal segmental glomerulosclerosis, membranous nephropathy (membranous), minimal change disease, nephrotic syndrome–not biopsied (allowable for children only), and other (including immunoglobulin A [IgA] nephropathy, Alport syndrome, systemic lupus erythematosus World Health Organization class V, C3 glomerulopathy, IgM nephropathy, C1Q nephropathy, and fibrillary glomerulonephritis). The study protocol was reviewed and approved by the University of Michigan Institutional Review Board (HUM00099659).

For this analysis, we excluded patients with evidence of end-stage kidney disease before their first record in the KRN data registry (n = 212) and patients with a diagnosis of white-coat HTN (n = 58; Fig 1). Analyses were censored at the last electronic health record extraction (March 2018). Estimated glomerular filtration rate was calculated using the modified CKiD formula in children and CKD-EPI (CKD Epidemiology Collaboration) in adults.[10,11]

HTN Definitions

When encounters had more than 1 BP recorded, the average measurement of the encounter was used in the analysis. Elevated BP was defined using contemporary guidelines in place at the time of patient care delivery, specifically as readings greater than 95th percentile for age, sex, and height for those aged 1 to 17 years, >140/90 mm Hg for those aged 18 to 65 years, and >150/90 mm Hg for those older than 65 years.[12,13] Patients were defined as hypertensive either using *International Classification of Diseases, Ninth (Tenth) Revision (ICD-9[10])* diagnosis code (codes available in Table S1), having 2 or more consecutive encounters with elevated BPs, or a record of antihypertensive therapy: β-blockers, calcium channel blockers, central agonists, α-blockers, and vasodilators. Renin-angiotensin-aldosterone system blockade therapy or diuretics was not used as an indicator for HTN in this population because those therapies may have been prescribed to treat proteinuria or edema in the absence of HTN. Patients with white-coat HTN, identified by *ICD-9* code 796.2 or *ICD-10* code R03.0, were excluded from analysis. Sustained BP control was defined as 2 or more consecutive non-elevated BP measurements: 95th or lower percentile in patients aged 1 to 17 years, ≤140/90 mm Hg in patients aged 18 to 65 years, and ≤150/90 mm Hg in patients older than 65 years.

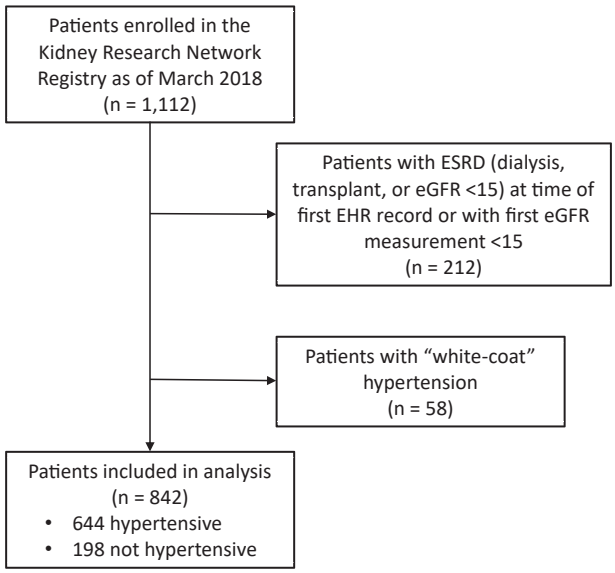

Figure 1. Flow diagram of included patients. Abbreviations: eGFR, estimated glomerular filtration rate; EHR, electronic health record; ESRD, end-stage renal disease.

Statistical Analysis

Descriptive analyses were conducted on the full analysis sample and for patients with and without HTN separately using frequency and percentage for categorical variables and median and interquartile range (IQR) for continuous variables, respectively. Categorical comparisons were made using χ^2 test, and continuous comparisons, using Kruskal-Wallis test. First, this comparison was made between patients with and without HTN. We subdivided the HTN group into those able and unable to reach BP control. Additionally, in patients with HTN, Kaplan-Meier and Cox proportional hazards models were used to analyze the time from the first qualifying HTN criterion to sustained BP control, and we reported the proportion of patients able to control by 1, 2, and 3 years after the onset of HTN. In 29 patients, we were unable to define an initial HTN diagnosis date and these were

Table 1. Demographics and Clinical Characteristics of Patients With and Without HTN

	Overall (n = 842)	Hypertensive (n = 644)	Not Hypertensive (n = 198)	*P*
No. of patients	842 (100%)	644 (77%)	198 (24%)	—
Age, y	34 [13-51]	37 [13-53]	23 [14-42]	0.002
Adults	578 (69%)	448 (70%)	130 (66%)	
Children	264 (31%)	196 (30%)	68 (34%)	
Sex				0.42
Female	366 (43%)	275 (43%)	91 (46%)	
Male	476 (57%)	369 (57%)	107 (54%)	
Race				0.003
White	467 (55%)	350 (54%)	117 (59%)	
African American	117 (14%)	105 (16%)	12 (6%)	
Asian	109 (13%)	82 (13%)	27 (14%)	
Other	149 (18%)	107 (17%)	42 (21%)	
Ethnicity				0.24
Non-Hispanic	684 (81%)	531 (82%)	153 (77%)	
Hispanic	119 (14%)	86 (13%)	33 (17%)	
Unknown	39 (5%)	27 (4%)	12 (6%)	
Diagnosis				<0.001
FSGS	184 (22%)	154 (24%)	30 (15%)	
Membranous	100 (12%)	85 (13%)	15 (8%)	
Minimal change	124 (15%)	89 (14%)	35 (18%)	
NS, not biopsied	108 (13%)	67 (10%)	41 (21%)	
Other	326 (39%)	249 (39%)	77 (39%)	
CKD stage				<0.001
1	378 (45%)	258 (40%)	120 (61%)	
2	161 (19%)	134 (21%)	27 (14%)	
3	190 (23%)	26 (26%)	21 (11%)	
4	103 (12%)	79 (12%)	24 (12%)	
Missing	10 (1%)	4 (1%)	6 (3%)	
eGFR, mL/min/1.73 m^2	83 [43-116]	76 [42-112]	104 [67-126]	<0.001
UPCR, mg/mg	2.2 [0.6-6.3]	2.3 [0.7-6.6]	1.4 [0.4-5.1]	0.003
Systolic BP index	0.96 [0.90-1.03]	0.97 [0.92-1.04]	0.91 [0.85-0.99]	<0.001
Diastolic BP index	0.92 [0.85-1.00]	0.93 [0.86-1.01]	0.88 [0.81-0.95]	<0.001
Weight status				<0.001
Overweight	502 (64%)	420 (69%)	82 (48%)	
Not overweight	280 (36%)	192 (31%)	88 (52%)	
Treated with IST, ever				0.06
Treated	573 (68%)	449 (70%)	124 (63%)	
Not treated	269 (32%)	195 (30%)	74 (37%)	
Treated with BP medications, ever				<0.001
Qualifying HTN medications[a]	408 (48%)	408 (63%)	0 (0%)	
ACEi/ARB or diuretics only	192 (23%)	111 (17%)	81 (41%)	
None	242 (29%)	125 (19%)	117 (59%)	

Note: Categorical variables are shown as frequency and percentage, and *P* value comparisons use χ^2 test; continuous variables, as median [interquartile range], and *P* value comparisons use Kruskal-Wallis test.

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BP, blood pressure; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FSGS, focal segmental glomerulosclerosis; HTN, hypertension; IST, immunosuppressive therapy; NS, nephrotic syndrome; UPCR, urinary protein-creatinine ratio.

[a]Beta-blockers, calcium channel blockers, central agonists, α-blockers, and vasodilators.

excluded from the time-to-control analyses, leaving 615 patients.

Time from onset of HTN to onset of pharmacologic therapy was also examined. Among patients with HTN, frequencies and percentages of those treated with each therapy were reported, as well as the frequencies of patients who were treated with each therapy as their first antihypertensive therapy. When combination or multiple therapies were prescribed on the same day as initial antihypertensive therapy, all prescribed drugs were included, for example, combination diuretic–angiotensin-converting enzyme (ACE) inhibitor medication was reported as diuretic and ACE inhibitor therapies. Patients were censored at end-stage kidney disease onset. All analyses were conducted using Statistical Analysis System (SAS), version 9.4 (SAS Institute for Data Management).

Table 2. Demographic and Clinical Characteristics of Patients by BP Control

	1: Not Hypertensive (n = 198)	2: Hypertensive: Never Reached BP Control (n = 140)	3: Hypertensive: Reached BP Control (n = 504)	*P* (column 1 vs 2 vs 3)	*P* (column 2 vs 3)
Age, y	22 [11-42]	35 [10-50]	39 [14-55]	<0.001	0.02
Adults	119 (60%)	91 (65%)	362 (72%)		
Children	79 (40%)	49 (35%)	142 (28%)		
Sex				0.68	0.73
Female	91 (46%)	58 (41%)	217 (43%)		
Male	107 (54%)	82 (59%)	287 (57%)		
Race				<0.001	<0.001
White	117 (59%)	54 (39%)	296 (59%)		
African American	12 (6%)	28 (20%)	77 (15%)		
Asian	27 (14%)	21 (15%)	61 (12%)		
Other	42 (21%)	37 (26%)	70 (14%)		
Ethnicity				0.02	0.007
Non-Hispanic	153 (77%)	106 (76%)	425 (84%)		
Hispanic	33 (17%)	22 (16%)	64 (13%)		
Unknown	12 (6%)	12 (9%)	15 (3%)		
Diagnosis				<0.001	0.004
FSGS	30 (15%)	27 (19%)	127 (25%)		
Membranous	15 (8%)	10 (7%)	75 (15%)		
Minimal change	35 (18%)	23 (16%)	66 (13%)		
NS, not biopsied	41 (21%)	24 (17%)	43 (9%)		
Other	77 (39%)	56 (40%)	193 (38%)		
CKD stage				<0.001	0.70
1	120 (61%)	57 (41%)	201 (40%)		
2	27 (14%)	29 (21%)	105 (21%)		
3	21 (11%)	34 (24%)	135 (27%)		
4	24 (12%)	18 (13%)	61 (12%)		
Missing	6 (3%)	2 (1%)	2 (1%)		
eGFR, mL/min/1.73 m^2	104 [67-126]	74 [40-116]	76 [43-110]	<0.001	0.91
UPCR, mg/mg	1.4 [0.4-5.1]	1.9 [0.5-6.6]	2.7 [0.8-6.5]	0.004	0.12
Systolic BP index	0.91 [0.85-0.99]	1.03 [0.95-1.11]	0.96 [0.91-1.02]	<0.001	<0.001
Diastolic BP index	0.88 [0.81-0.95]	1.03 [0.88-1.14]	0.92 [0.86-1.00]	<0.001	<0.001
Weight status				<0.001	0.13
Overweight	82 (48%)	95 (74%)	325 (67%)		
Not overweight	88 (52%)	33 (26%)	159 (33%)		
Treated with IST, ever				0.07	0.17
Treated	124 (63%)	91 (65%)	358 (71%)		
Not treated	74 (37%)	49 (35%)	146 (29%)		
Treated with BP medications, ever				<0.001	<0.001
Qualifying HTN medications[a]	—	49 (35%)	359 (71%)		
ACEi/ARB or diuretics only	81 (41%)	21 (15%)	90 (18%)		
None	117 (59%)	70 (50%)	55 (11%)		

Note: Categorical variables are shown as frequencies and percentages, and *P* value comparisons use χ^2 test; continuous variables as median [interquartile range], and *P* value comparisons use Kruskal-Wallis test.

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BP, blood pressure; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HTN, hypertension; FSGS, focal segmental glomerulosclerosis; IST, immunosuppressive therapy; NS, nephrotic syndrome; UPCR, urinary protein-creatinine ratio.

[a]β-Blockers, calcium channel blockers, central agonists, α-blockers, and vasodilators.

RESULTS

As of March 2018, there were 1,112 patients enrolled in the KRN Registry. These analyses are based on a total of 842 patients eligible for this analysis (Fig 1). Among the 842 patients, 644 (76%) had HTN at some point during their observation period. Characteristics of these patients are shown in Table 1. There was no difference in the prevalence of HTN between children and adults (74.2% vs 77.5%; P = 0.3), although the median age among those with HTN was significantly older than among those without HTN (median age, 37 vs 23 years; P = 0.002). Patients with HTN were more likely to be of African American race (P = 0.003), have focal segmental glomerulosclerosis or primary membranous (P < 0.001), and have a lower estimated glomerular

Table 3. Demographics and Clinical Characteristics of Patients With HTN: Undocumented Versus Documented HTN

	Undocumented HTN (n = 39)	Documented HTN[b] (n = 605)	*P*
Age, y	5 [4-13]	39 [15-53]	<0.001
Adults	5 (13%)	443 (73%)	
Children	34 (87%)	162 (27%)	
Sex			0.58
Female	15 (38%)	260 (43%)	
Male	24 (62%)	345 (57%)	
Race			0.45
White	26 (67%)	324 (54%)	
African American	5 (13%)	100 (17%)	
Asian	3 (8%)	79 (13%)	
Other	5 (13%)	102 (17%)	
Ethnicity			0.10
Non-Hispanic	37 (95%)	494 (82%)	
Hispanic	2 (5%)	84 (14%)	
Unknown	0 (0%)	27 (4%)	
Diagnosis			<0.001
FSGS	6 (15%)	148 (24%)	
Membranous	1 (3%)	84 (14%)	
Minimal change	11 (28%)	78 (13%)	
NS, not biopsied	13 (33%)	54 (9%)	
Other	8 (21%)	241 (40%)	
CKD stage			<0.001
1	33 (85%)	225 (37%)	
2	4 (10%)	130 (21%)	
3	1 (3%)	168 (28%)	
4	0 (0%)	79 (13%)	
Missing	1 (3%)	3 (0%)	
eGFR, mL/min/1.73 m^2	121 [97-165]	72 [41-108]	<0.001
UPCR, mg/mg	4.4 [0.9-9.7]	2.3 [0.7-6.4]	0.10
Systolic BP index	0.94 [0.90-0.97]	0.98 [0.92-1.05]	0.002
Diastolic BP index	0.90 [0.84-0.98]	0.94 [0.86-1.01]	0.19
Weight status			0.32
Overweight	24 (62%)	396 (69%)	
Not overweight	15 (38%)	117 (31%)	
Treated with IST, ever			0.31
Treated	30 (77%)	419 (69%)	
Not treated	9 (23%)	186 (31%)	
Treated with BP medications, ever			<0.001
Qualifying HTN medications[a]	19 (49%)	92 (15%)	
ACEi/ARB or diuretics only	20 (51%)	105 (17%)	
None	0 (0%)	408 (67%)	

Note: Categorical variables are shown as frequencies and percentages, and *P* value comparisons use χ^2 test; continuous variables as median [interquartile range], and *P* value comparisons use Kruskal-Wallis test.

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BP, blood pressure; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FSGS, focal segmental glomerulosclerosis; HTN, hypertension; IST, immunosuppressive therapy; NS, nephrotic syndrome; UPCR, urinary protein-creatinine ratio.

[a]β-Blockers, calcium channel blockers, central agonists, α-blockers, and vasodilators.

[b]Documented by diagnosis codes or medications.

filtration rate (76 [IQR, 42-112] vs 104 [IQR, 67-126] mL/min/1.73 m^2; $P < 0.001$) and higher urinary protein-creatinine excretion (2.3 [IQR, 0.7-6.6] vs 1.4 [IQR, 0.4-5.1] mg/mg; $P = 0.003$) than patients without HTN.

Of the 644 patients with HTN, 504 (78%) subsequently achieved BP control and 140 (22%) did not. Characteristics of these patients are described in Tables 2 and 3. Excluding the 29 patients for whom an initial HTN diagnosis was not available, 51% of 615 patients with HTN had BP controlled within 1 year after HTN onset; 64%, within 2 years; 73%, within 3 years; and 80%, within 4 years of HTN onset. There was no difference in time to BP control by age ($P = 0.7$; Fig 2).

Table 4 shows the frequency of antihypertensive therapy by drug class among all 644 patients with HTN. Among these patients, 80.6% were ever treated with an antihypertensive therapy. The most commonly used therapies were ACE inhibitor/angiotensin II receptor blockers (ARBs; 56.5%), diuretics (54.2%), and β-blockers (40.7%). Antihypertensive therapies by age and BP control status are also shown in Table 4. Overall, children were less likely to be treated with ACE inhibitor/ARBs, β-blockers, central agonists, and α-blockers than adults. Patients with controlled HTN were more likely to have received antihypertensive therapy ($P < 0.001$). Table 5 describes the first antihypertensive therapies used. Among the 519 patients with HTN ever treated with antihypertensive therapies, initial therapies were diuretics in 40%, ACE inhibitor/ARBs in 38%, β-blockers in 33%, and calcium channel blockers in 29%.

DISCUSSION

CKD is a global public health problem affecting an estimated 30 million American adults and an unknown number of children.[1] HTN, a known CKD comorbid condition, is associated with poorer kidney and cardiovascular outcomes. Recommendations for the management of HTN in this at-risk population can be found in practice guidelines proposed by the National Kidney Foundation Kidney Diseases Outcomes Quality Initiative (NKF/KDOQI) and Kidney Disease: Improving Global Outcomes (KDIGO), Eighth Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8), 4th Report Task Force, and more recently, American Academy of Pediatrics clinical practice guideline for screening and management of high BP in children and adolescents.[7,12-15]

The results of this study highlight the prevalence of HTN (~75%) in a cohort of patients with glomerular disease regardless of age. Despite evidence that intensification of BP control slows progression of kidney disease and decreases cardiovascular events and death,[16,17] the achievement of adequate and timely BP control in at-risk groups remains suboptimal. In patients with HTN in our study, BP control was achieved in only 51% and 64% of patients within 1 and 2 years of diagnosis, respectively. As expected given the proteinuric nature of this cohort, ACE inhibitor/ARB agents were the preferred antihypertensive

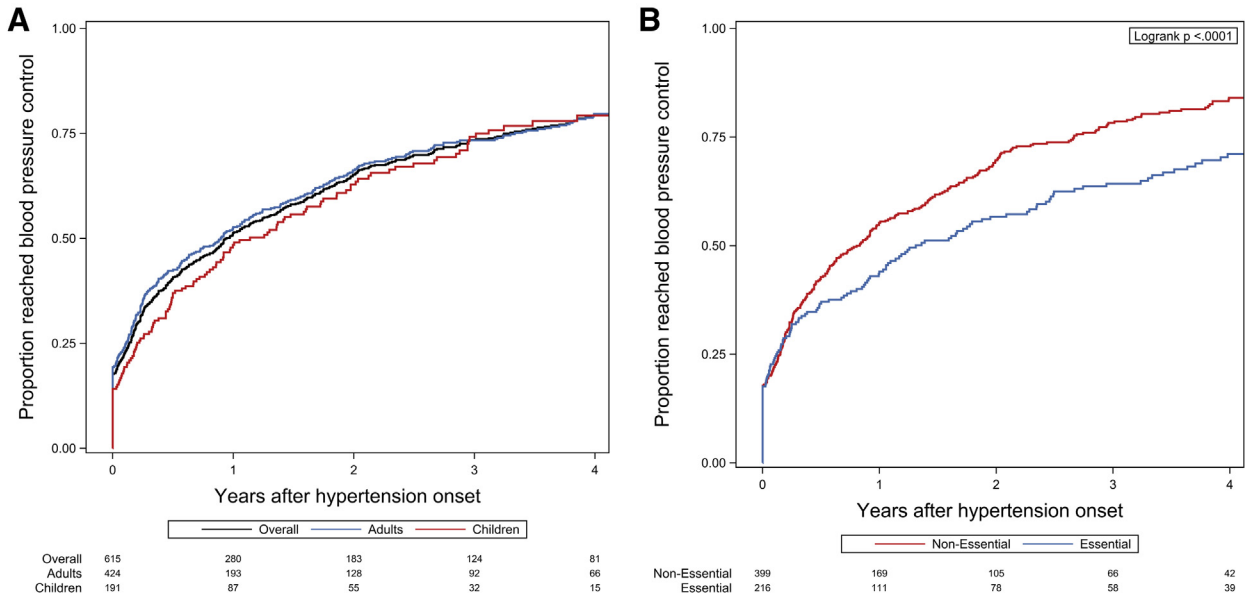

Figure 2. Time to sustained blood pressure (BP) control after hypertension onset in patients with hypertension (A) in adults, children, and overall and (B) by age group.*Log-rank *P* = 0.69. n = 615. Sustained BP control is defined as 2 or more BP measurements in a row less than 95th percentile in children or <140/90 mm Hg in adults.

Table 4. Summary of Antihypertensive Therapies Prescribed in Patients With Proteinuric Kidney Disease Overall, by Age and BP Control Status

	Hypertensive Patients (n = 644)	Adults (n = 448)	Children (n = 196)	*P*	Never Controlled (n = 140)	Controlled (n = 504)	*P*
Any	519 (80.6%)	366 (82%)	153 (78%)	0.28	70 (50%)	449 (89%)	<0.001
ACEi/ARB	364 (56.5%)	281 (63%)	83 (42%)	<0.001	29 (21%)	335 (67%)	<0.001
Diuretics	349 (54.2%)	234 (52%)	115 (59%)	0.13	43 (31%)	306 (61%)	<0.001
Loop	294 (45.7%)	181 (40%)	113 (58%)	<0.001	38 (27%)	256 (51%)	<0.001
Thiazide	149 (23.1%)	95 (21%)	54 (28%)	0.08	9 (6%)	140 (28%)	<0.001
Potassium sparing	109 (16.9%)	85 (19%)	24 (12%)	0.04	9 (6%)	100 (20%)	<0.001
β-Blockers	262 (40.7%)	204 (46%)	58 (30%)	<0.001	24 (17%)	238 (47%)	<0.001
CCB	246 (38.2%)	166 (37%)	80 (41%)	0.37	34 (24%)	212 (42%)	<0.001
Central agonist	119 (18.5%)	100 (22%)	19 (10%)	<0.001	5 (4%)	114 (23%)	<0.001
α-Blockers	117 (18.2%)	98 (22%)	19 (10%)	<0.001	14 (10%)	103 (20%)	0.005
Aldosterone inhibitors	109 (16.9%)	85 (19%)	24 (12%)	0.04	9 (6%)	100 (20%)	<0.001
Vasodilators	28 (4.3%)	24 (5%)	4 (2%)	0.06	0 (0%)	28 (6%)	0.004

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BP, blood pressure; CCB, calcium channel blocker.

agent followed by diuretics. A total of 140 of 842 (16.6%) patients in this study failed to achieve BP control during observation, and these individuals had fewer antihypertensive therapies prescribed.

The prevalence of HTN demonstrated in the current longitudinal analysis is consistent with prior cross-sectional reports in patients with CKD.[18-20] More importantly, the current study also confirmed the suboptimal control of HTN in this population, with only 51% reaching target values in the first year after diagnosis with HTN with gradual improvement during nephrology management with up to 80% control within 4 years from diagnosis.[18,19] In a previous publication from a cross-sectional analysis of adults with CKD managed by nephrologists, 85.7% of participants had HTN and 67.1% had BP controlled to <140/90 mm Hg.[20] Two cross-sectional analyses of children with CKD managed by pediatric nephrologists have reported that 75% and 74% of children had a well-controlled systolic BP, that is, less than the 90th percentile,[5] or controlled BP based on 24-hour ambulatory BP monitoring,[21] respectively. By comparison, cross-sectional analysis of adults with elevated serum creatinine levels and HTN enrolled in community-based studies that did not originate in nephrology programs reported that only 20% to 27% of adult participants had HTN control.[19,22-25]

In the current study, 80% of patients demonstrated BP control within 4 years of HTN onset. In contrast, time-to-control analyses in adults with HTN without CKD have shown much shorter intervals. In an examination of 223

Table 5. Frequency of First Treatment Class of Antihypertensive Therapies by Age and BP Control Status Among Those Treated With Any Antihypertensive Therapy

	Hypertensive Patients (n = 519)	Adults (n = 366)	Children (n = 153)	*P*	Never Controlled (n = 70)	Controlled (n = 449)	*P*
Diuretics	206 (40%)	119 (33%)	87 (57%)	<0.001	29 (41%)	177 (39%)	0.75
Loop	166 (32%)	82 (22%)	84 (55%)	<0.001	26 (37%)	140 (31%)	0.32
Thiazide	42 (8%)	32 (9%)	10 (7%)	0.40	2 (3%)	40 (9%)	0.08
Potassium sparing	32 (6%)	30 (8%)	2 (1%)	0.003	4 (6%)	28 (6%)	0.87
ACEi/ARB	195 (38%)	161 (44%)	34 (22%)	<0.001	19 (27%)	176 (39%)	0.05
β-Blockers	170 (33%)	144 (39%)	26 (17%)	<0.001	16 (23%)	154 (34%)	0.06
CCB	150 (29%)	101 (28%)	49 (32%)	0.31	24 (34%)	126 (28%)	0.29
α-Blockers	53 (10%)	48 (13%)	5 (3%)	<0.001	5 (7%)	48 (11%)	0.36
Central agonist	45 (9%)	38 (10%)	7 (5%)	0.03	2 (3%)	43 (10%)	0.06
Aldosterone inhibitors	33 (6%)	31 (8%)	2 (1%)	0.002	4 (6%)	29 (6%)	0.81
Vasodilators	7 (1%)	6 (2%)	1 (1%)	0.38	0 (0%)	7 (2%)	0.29

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BP, blood pressure; CCB, calcium channel blocker.

patients with HTN based on insurance claims data, the median number of months to BP goal was 3.3 (95% confidence interval, 2.5-4.8).[26] Similarly, the Avoiding Cardiovascular Events Through Combination Therapy in Patients Living With Systolic Hypertension (ACCOMPLISH) trial randomly assigned 11,500 with high-risk HTN to receive single-tablet combination therapy with ACE inhibitor/calcium channel blocker (benazepril/amlodipine) or ACE inhibitor/diuretic (benazepril/hydrochlorothiazide).[27] By study month 6, a total of 73% of patients had achieved a target BP of 140/90 mm Hg and maintained control at study month 12.[27] Time to BP control in patients without CKD has been reported to be related to encounter frequency.[28] Specifically, Morrison et al[28] found that median time to BP control of 130/85 mm Hg was 1.3 months in patients without CKD with HTN seen once every 1 to 2 weeks as compared to 14 months in patients with more extended encounter intervals of 3 to 6 months. Given these findings, increasing the encounter frequency with a nephrologist and targeted BP intervention may be strategies worthy of testing in patients with glomerular CKD.

This study has limitations. This study used a conservative threshold to define HTN. Clinical practice guidelines, national working groups, and clinical trials support differing BP control goals, and these goals have changed over time. Our conservative definitions used the goals that were prevailing during the majority of the visit encounters included in this registry. These may lead to overestimation of the controlled patient population. Casual BP measurements from clinical health records were used and ambulatory BP reports were not available. Use of casual BPs may lead to misclassification of BP control and measure-dependent HTN classification. In addition, adherence to the prescribed medications was unable to be assessed in this cohort. This is a persistent challenge to studies based on electronic health record data but is counterbalanced by having a large sample of patients and encounters consistent with typical management of patients with glomerular disease. The analytic sample was also representative with respect to age, geography, and academic versus community practice.

Overall, this study found that 75% of patients with glomerular disease had HTN. Control of BP was achieved in only half the patients within 1 year of HTN diagnosis and was not achieved in 16.6% over a 4-year period. With the goal of BP control to preserve kidney function and prevent CVD, this study suggests that systems-level interventions may be needed to support clinical practices to achieve more timely BP control on an individual and practice level.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1: ICD-9 and ICD-10 codes obligating hypertension.

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