

Blood Pressure Control and Left Ventricular Mass in Children with Chronic Kidney Disease

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Summary

Background and objectives Heart disease is a major cause of death in young adults with chronic kidney disease (CKD). Left ventricular hypertrophy (LVH) is common and is associated with hypertension. The aims of this study were to evaluate whether there is a relationship between LVH and BP in children with CKD and whether current targets for BP control are appropriate.

Design, setting, participants, & measurements In this single-center cross-sectional study, 49 nonhypertensive children, (12.6 ± 3.0 years, mean GFR 26.1 ± 12.9 ml/min per 1.73 m²) underwent echocardiographic evaluation and clinic and 24-hour ambulatory BP monitoring. LVH was defined using age-specific reference intervals for left ventricular mass index (LVMI). Biochemical data and clinic BP for 18 months preceding study entry were also analyzed.

Results The mean LVMI was 37.8 ± 9.1 g/m^{2.7}, with 24 children (49%) exhibiting LVH. Clinic BP values were stable over the 18 months preceding echocardiography. Patients with LVH had consistently higher BP values than those without, although none were overtly hypertensive (>95th percentile). Multiple linear regression demonstrated a strong relationship between systolic BP and LVMI. Clinic systolic BP showed a stronger relationship than ambulatory measures. Of the confounders evaluated, only elemental calcium intake yielded a consistent, positive relationship with LVMI.

Conclusions LVMI was associated with systolic BP in the absence of overt hypertension, suggesting that current targets for BP control should be re-evaluated. The association of LVMI with elemental calcium intake questions the appropriateness of calcium-based phosphate binders in this population.

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Introduction

Left ventricular hypertrophy (LVH) is a known risk factor for premature death in hypertensive adults (1,2). Systemic arterial hypertension and LVH are frequently observed in adults with chronic kidney disease (CKD). The cardiovascular death rates in young adults with CKD is reported to be between 30 and 700 times that of the normal population (3,4). Conversely, better cardiovascular outcome is seen in CKD patients with lower BP levels (5,6).

In those with childhood-onset CKD, it is likely that cardiovascular pathology also develops in childhood (7). Understanding the relationship between BP and LVH in children with CKD is therefore critical if a rational approach to antihypertensive therapy is to be developed. To date, evidence for this relationship remains controversial, despite two large multicenter observational reports, one from Europe (8,9) and the other from the United States (10). Adult studies suggest a continuous relationship between BP and cardiovascular morbidity and mortality. This relationship is more pronounced in those with CKD, leading

to recommendations for more stringent BP targets in this group (11,12). In contrast, “normal” or “safer” BP levels in children with CKD have not been established from clinical evidence of end-organ damage.

Most children in the largest pediatric study in CKD demonstrating a relationship between LVH and BP were hypertensive (10). Our aims after adjustment for confounders were to evaluate whether there is a relationship between LVH and BP in children with CKD who are not hypertensive and whether current targets for BP control are appropriate.

Materials and Methods

Study Population

Fifty-two children attending the CKD clinic at Evelina Children’s Hospital in London were enrolled from March 2006 to August 2008. The point at which patients were recruited to the study was not at initial presentation and diagnosis of CKD, but rather during their follow-up in our tertiary center.

Renal function was determined by estimated GFR (eGFR) using the Schwartz formula (13), and CKD stage was defined according to published defini-

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tions (14). The inclusion criteria were (1) eGFR \leq 70 ml/min per 1.73 m² for at least 3 months, (2) age 5 to 18 years, and (3) height > 120 cm. The exclusion criteria were (1) failure to obtain good quality ambulatory BP monitoring (ABPM; details below); (2) peritoneal or hemodialysis; (3) structural cardiac abnormality; and (4) "uncontrolled hypertension," defined as clinic BP measurements greater than the 95th percentile on three consecutive clinic visits immediately preceding the day of study. The institutional ethics committee approved the study protocol. Informed consent was obtained from parents and/or patients for participation in the study. Case records were reviewed for demographic data and relevant medications.

Investigations on Day of Study

The following were performed in study participants at the same clinic visit: (1) history and physical examination; (2) anthropometry, including height, weight, and body mass index (BMI); (3) clinic BP measurement of systolic BP (SBP) and diastolic BP (DBP) with calculation of pulse pressure and mean arterial pressure (MAP); (4) ABPM; (5) echocardiography; (6) laboratory investigations including hemoglobin, serum creatinine, albumin, bicarbonate, urea, corrected calcium (Ca), phosphorus (P), intact parathyroid hormone (iPTH), and nonfasting lipid profile; and (7) protein creatinine ratio on a random urine specimen.

Retrospective Data Set

Because LVH is likely to develop over a period of time, we retrospectively collected information from outpatient clinic visits 1 (pre-1m), 3 (pre-3m), 6 (pre-6m), 9 (pre-9m), 12 (pre-12m), and 18 (pre-18m) months before the day of study. "Time-averaged level," an average value for laboratory parameters, was calculated for the 18-month period before study entry.

Clinic BP and 24-Hour ABPM

Clinic BP was measured using a mercury sphygmomanometer until early 2008 and subsequently using a calibrated aneroid instrument. ABPM studies were performed using Spacelabs 90207 and Spacelabs 90217 oscillometric ambulatory BP devices (Spacelabs Inc., Redmond, WA). Ambulatory BP measurements were performed once every 30 minutes from 7:00 a.m. to 11:00 p.m. and hourly from 11:00 p.m. to 7:00 a.m. A single investigator (M.D.S.) analyzed ambulatory BP study data. An ABPM study was excluded if (1) there were >2 hours of interrupted recordings at any time during the 24-hour period, or (2) the duration of recording was inadequate (*i.e.*, <20 hours in total, <12 hours continuously, or did not include nighttime measurements).

Definition of Hypertension by Clinic BP and 24-Hour ABPM

Clinic BP normal values were defined using the Fourth Report Criteria of the National High Blood Pressure Education Program Working Group in the United States (15). All clinic BP measurements were analyzed as z-scores.

Hypertension was defined as SBP or DBP more than the 95th percentile for age, sex, and height (≥ 1.645 z-score).

All mean ABPM parameters were analyzed as z-scores using the normative limits as per the study by Wuhl *et al.* (16). Hypertension was defined at z-score values ≥ 1.645 .

Echocardiography

Left ventricular mass (LVM) was calculated using M-mode echocardiography using images obtained in parasternal long-axis or short-axis view of the left ventricle (LV), as recommended by the American Society of Echocardiography (17) and as reported previously (18). Echocardiographers were blinded to BP measurements and medical therapy. All studies were stored digitally and analyzed by one author (J.M.S.) who was also blinded as above. LVH was defined as left ventricular mass index (LVMI) greater than the 95th percentile using age-specific reference intervals for normal children (19). We also report LVM for height z-scores when appropriate (20). Relative wall thickness (RWT) was calculated as the average thickness of the posterior and septal wall divided by LV diastolic diameter (21). Patients with increased LVMI (≥ 95 th percentile) and elevated RWT (≥ 0.387) were defined as having concentric LVH, with increased LVMI (≥ 95 th percentile) and normal RWT (< 0.387) as having eccentric LVH, and those with normal LVMI (< 95 th percentile) and elevated RWT (≥ 0.387) as having concentric remodeling. Diastole was assessed by measurement of the maximal early (E wave) and late (A wave) diastolic flow velocities (E/A) obtained from pulsed-wave transmitral Doppler interrogation.

Laboratory Methods

Plasma creatinine was measured using a validated and National Institute of Standards and Technology-traceable stable isotope dilution electrospray liquid chromatography mass spectrometry method using an AB/Sciex API5000 instrument (Applied Biosystems, Warrington, United Kingdom) (22). The Schwartz formula with our previously described correction factor was used to calculate the eGFR (23). High-sensitivity C-reactive protein (hsCRP) was measured using immunonephelometric methods on a BN Prospec automated analyzer (Siemens Healthcare, Frimley, United Kingdom).

Statistical Analyses

Data are expressed as mean \pm SD, with two-group comparisons via the unpaired *t* test, χ^2 test, and Fishers exact test as appropriate. Multiple linear regression was used to assess the relationship between BP (independent variable) and LVMI (dependent variable). Separate models were assessed for each of the BP measures. All models included adjustment for confounders that were selected from the literature or were pathophysiologically relevant; namely, BMI, eGFR, current antihypertensive medication, time-averaged iPTH, time-averaged serum Ca values, and elemental Ca intake from Ca-based phosphate binders. Multicollinearity was quantified using the variance inflation factor (upper acceptable limit = 4). Goodness of fit was expressed as the adjusted *r*². Standardized residual plots were inspected for all models, and influence of individual obser-

valuations was examined using Cooks distance and dfit-beta values. Comparison of SBP and DBP over time was via a random coefficients mixed model. Statistical analyses were performed using Minitab version 15 and SPSS version 15.

Results

Of the 52 children who agreed to participate in the study, 3 (5.8%) were excluded because of poor-quality echocardiograms, leaving 49 study subjects. Nineteen of 49 (38.8%) children were under pediatric nephrology services since birth or infancy, and the median (interquartile range [IQR]) age of the remaining 30 subjects at the time of initial clinical diagnosis was 7.1 (5.4, 13.0) years. The median (IQR) follow-up with tertiary pediatric nephrology services was 7.2 (1.9, 11.0) years for all patients at the time of recruitment to the study. There was no significant difference between age at initial presentation between patients with and without LVH ($P = 0.66$).

Patient Characteristics

Patient demographics and details of antihypertensive medications and hydroxylated vitamin D3 are shown in Table 1. Thirty-eight (82.5%) were white Caucasian with no difference in racial mix between subjects with and without LVH ($P = 0.86$). Thirty-five children received Ca-based phosphate binders: The dose was significantly higher in the 17 subjects with LVH than in the 18 children with no LVH (1.61 ± 0.87 versus 0.98 ± 0.61 g/d of elemental Ca respectively; $P = 0.02$).

LVH, LVMI, and LV Geometry

LVH was found in 49% (24 of 49) of the subjects with a mean LVMI of 45.3 ± 5.0 g/m^{2.7} as compared with 30.6 ± 5.6 g/m^{2.7} in patients with no LVH ($P < 0.001$). LVH was eccentric in all patients. There were no significant differences in LV geometry between patients with and without LVH (for details, see Supplementary Appendix Table 1).

BP Findings

On day of study. Figure 1, a and b, demonstrate the relationship of clinic SBP z-score with LVMI ($P = 0.001$) and height-specific LVM z-score ($P = 0.001$). Table 2 shows the average clinic BP and 24-hour ambulatory BP values for patients with and without LVH. The analysis of daytime and nighttime periods gave similar results. Details of clinic BP and ambulatory BP values for all patients on the day of study along with results of ambulatory daytime and nighttime periods are shown in the Supplementary Appendix Tables 2 and 3. Masked hypertension was observed in 21 subjects (43%), 10 of which had isolated nocturnal hypertension. Thirteen subjects (61.9%) with masked hypertension had LVH, of which 5 with LVH had isolated nocturnal hypertension.

Analysis of BP before study entry. SBP and DBP z-scores are shown in Figure 2, a and b. Patients with LVH had significantly higher SBP and DBP values over the period of analysis (intercept $P < 0.001$ for SBP and $P = 0.03$ for DBP). SBP and DBP variables remained constant over time for both groups (slope was not different from zero; SBP and DBP $P > 0.3$), and the difference between the two groups remained constant (group-time interaction for SBP and DBP $P > 0.3$).

Biochemical Characteristics

Table 3 shows results of time-averaged analysis for studied biochemical parameters. The overall median (IQR) hsCRP level for these 49 subjects was 0.58 (0.17, 1.49) mg/L. Only three subjects had hsCRP levels >10 mg/L, and all three patients had LVH. Detailed results of all biochemical analyses are shown in Supplementary Appendix Table 4.

Determinants of LVMI and LVH

Table 4 shows the results for each of the models assessing the relationship between clinic BP measures and LVMI after adjustment for confounders. SBP was the only BP measure that maintained a consistent association with

Table 1. Patient demographics on the day of study

Demographics	All Patients (n = 49)	No LVH (n = 25)	LVH (n = 24)	P
Age (years)	12.6 ± 3.0	13.0 ± 3.0	12.3 ± 3.1	0.41
Male gender, n (%)	29 (59.2%)	13 (52%)	16 (66.7%)	0.39
Primary diagnosis structural disease, n (%)	38 (77.6%)	21 (84%)	17 (70.8%)	0.32
Height z-score	-0.65 ± 1.28	-0.69 ± 1.34	-0.62 ± 1.23	0.84
Weight z-score	0.03 ± 1.26	-0.25 ± 1.21	0.33 ± 1.27	0.10
BMI z-score	0.53 ± 1.29	0.18 ± 1.33	0.89 ± 1.17	0.05
Antihypertensive medications, n (%)	27 (55.1%)	13 (52%)	14 (58.3%)	0.78
ACEI ± ARB or combination with ACEI ± ARB, n	24	13	11	
CKD stage 3; stage 4; stage 5, n	19; 22; 8	11; 11; 3	8; 11; 5	0.64
Hydroxylated vitamin D3, n	35	16	19	0.61
Hydroxylated vitamin D3 dose, μg/d	0.41 ± 0.23	0.39 ± 0.22	0.43 ± 0.25	

Data shown as mean ± SD unless stated otherwise. LVH was defined using age-specific reference intervals for normal children (19). ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker.

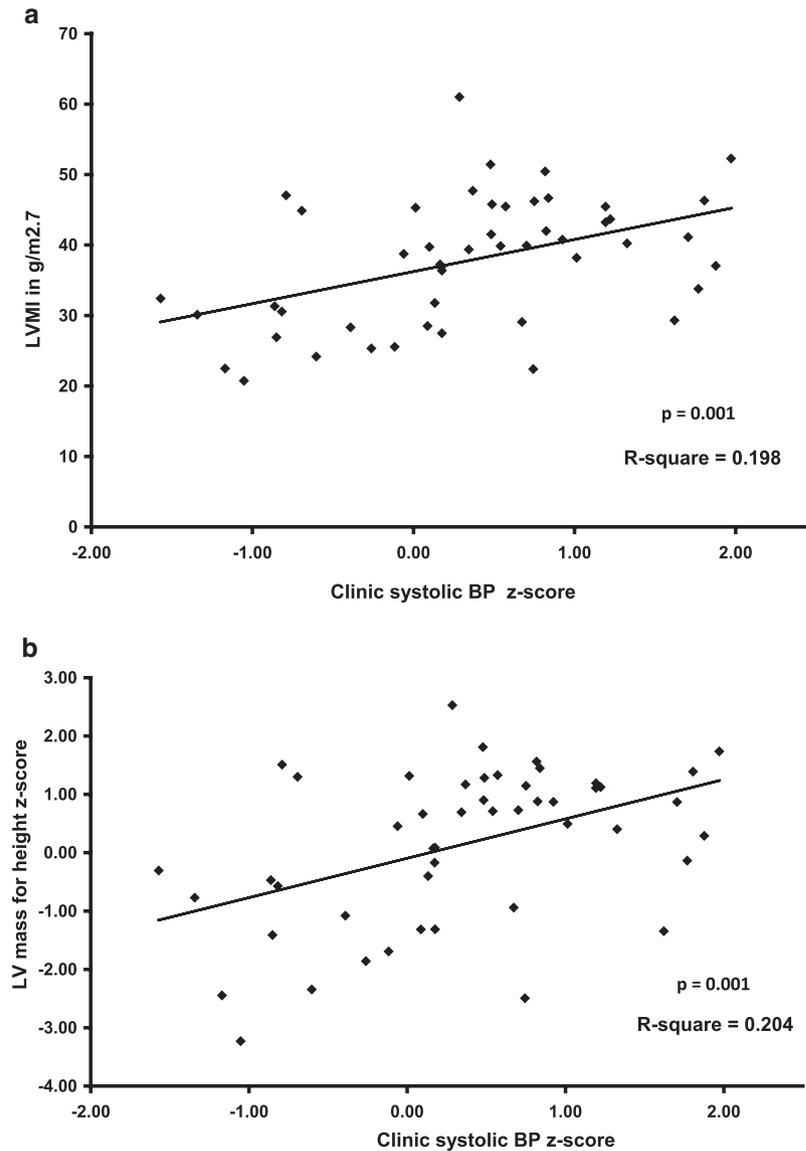


Figure 1. | (a) Relationship of clinic SBP z-score with indexed LVM in all patients. (b) Relationship of clinic SBP z-score with LVM for height-specific z-scores (20) in all patients.

BP Characteristics	24-Hour Ambulatory BP			Clinic BP		
	No LVH	LVH	<i>P</i>	No LVH	LVH	<i>P</i>
SBP (mmHg)	110 ± 11.7	117 ± 10.9	0.02	107 ± 10	112 ± 8.8	0.05
DBP (mmHg)	66 ± 7.7	71 ± 10.5	0.05	63 ± 12.6	67 ± 11.5	0.25
Pulse pressure (mmHg)	45 ± 8.1	45 ± 7.3	0.81	44 ± 9.2	45 ± 11.2	0.71
MAP (mmHg)	82 ± 8.6	88 ± 9.6	0.03	78 ± 11	82 ± 9.3	0.14
SBP (z-score)	-0.32 ± 1.43	0.90 ± 1.58	0.007	0.03 ± 0.95	0.67 ± 0.70	0.01
DBP (z-score)	-0.18 ± 1.49	0.80 ± 2.16	0.07	0.07 ± 1.10	0.47 ± 0.91	0.18
MAP (z-score)	0.22 ± 1.43	1.36 ± 1.91	0.02			

Data shown as mean ± SD unless stated otherwise. LVH was defined using age-specific reference intervals for normal children (19).

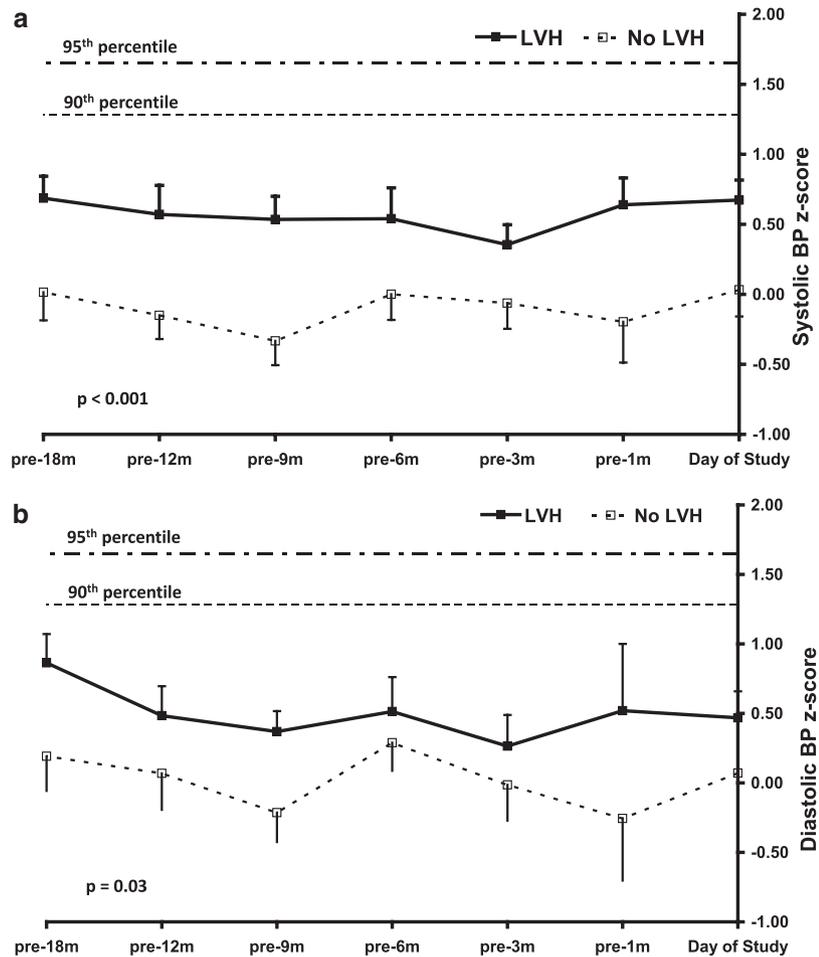


Figure 2. | Clinic SBP z-scores in children with CKD stage 3 to 5 with and without LVH. LVH was defined using age-specific reference intervals for normal children (19). Interrupted lines at the 90th and 95th percentile denote the clinical definition of prehypertension and hypertension, respectively (15). Data are shown as mean ± SEM. (b) Clinic DBP z-scores in CKD stage 3 to 5 patients with and without LVH. LVH was defined using age-specific reference intervals for normal children (19). Interrupted lines at the 90th and 95th percentile denote the clinical definition of prehypertension and hypertension, respectively (15). Data are shown as mean ± SEM.

Table 3. Biochemical parameters of all study patients				
Parameter	All Patients (n = 49)	No LVH (n = 25)	LVH (n = 24)	P
eGFR (ml/min per 1.73 m ²)	26.1 ± 12.95	28.6 ± 13.40	23.4 ± 12.18	0.17
Time-averaged hemoglobin (g/dl)	12.1 ± 1.46	12.4 ± 1.56	11.8 ± 1.31	0.15
Time-averaged serum Ca (mmol/L)	2.41 ± 0.08	2.38 ± 0.08	2.43 ± 0.07	0.05
Time-averaged serum phosphate (mmol/L)	1.47 ± 0.17	1.50 ± 0.13	1.44 ± 0.18	0.23
Time-averaged serum Ca-P product (mmol ² /L ²)	3.54 ± 0.39	3.56 ± 0.35	3.51 ± 0.44	0.62
Time-averaged serum iPTH (ng/L)	111.4 ± 112.7	99.5 ± 101.4	123.8 ± 124.4	0.46
hsCRP (mg/L), median (IQR)	0.58 (0.17, 1.49)	0.74 (0.39, 1.38)	0.57 (0.15, 1.49)	0.67
Urine protein/creatinine ratio (mg/mmol) (n = 37)	86.1 ± 111.4	81.9 ± 102.7 (n = 19)	90.5 ± 122.7 (n = 18)	0.82

The results of biochemical parameters collected retrospectively up to 18 months immediately before the day of study are shown as a "time-averaged" level. All data are shown as mean ± SD. LVH was defined using age-specific reference intervals for normal children (19).

Table 4. Quantification of the relationship between BP (independent variable) and LVMI (dependent variable) expressed in g/m^{2.7} via multiple linear regression

Variable	Model A, Clinic SBP z-Score		$r^2 = 0.40$, Adjusted $r^2 = 0.29$	
	Coefficient	SEM	P	Variance Inflation Factor
Clinic SBP z-score ^a	3.94	1.41	0.008	1.41
BMI	0.12	0.28	0.67	1.06
eGFR	-0.09	0.10	0.37	1.58
Antihypertensive medication	-0.65	2.22	0.77	1.13
Time-averaged log iPTH	-0.28	1.59	0.86	1.38
Time-averaged serum Ca	13.17	15.26	0.39	1.44
Elemental Ca intake	2.99	1.32	0.03	1.27

A separate model was constructed for each of the BP methods with adjustment for the same confounders throughout. Model A shows the results for the model using clinic SBP z-score; the coefficients for all confounders are also shown. Similar models (with confounders not shown) were constructed for clinic DBP z-score and clinic pulse pressure 24-hour and nocturnal BP readings (results in text and Supplementary Appendix Table 5). LVH was defined using age-specific reference intervals for normal children (19). "Time-averaged," time-averaged value over preceding 18 months; serum Ca, serum-corrected Ca levels; elemental Ca intake, elemental Ca intake in g/d from prescribed Ca-containing phosphate binders.

^aCoefficient interpretation is such that an increase in clinic SBP z-score of 1 unit is associated with an increase in LVMI of 3.94 g/m^{2.7}.

LVH; none of the measures of DBP or pulse pressure were significant. Results of each of the models for all other BP measures are shown in Supplementary Appendix Table 5. Of the three systolic methods, clinic SBP yielded a stronger association (model $r^2 = 0.40$) than 24-hour (model $r^2 = 0.34$) or nocturnal SBP (model $r^2 = 0.33$). Ca intake from Ca-based phosphate binders maintained a significant positive relationship with LVMI in all three systolic models ($P = 0.02$ to 0.04).

Discussion

Initial results from this prospective study demonstrate a significant association between BP and indexed LVM (Figure 1, a and b) in a group of children with CKD stages 3 to 5. Despite having BP measurements consistently below the 95th percentile (Figure 2, a and b), 49% of our subjects were found to have LVH (LVMI \geq 95th percentile) as defined by using recently published age-specific reference intervals. Thus, even for children who are not hypertensive, the level of BP would appear to be an important determinant of LVH. The extension of the relationship between BP and LVH to nonhypertensive children with CKD that we report here is novel and in keeping with adult observations that the relationship between BP and target organ damage is a continuum.

The Chronic Kidney Disease in Children (CKiD) study recently reported cross-sectional data in 198 patients who had a single clinic BP measurement performed together with echocardiography and 24-hour ABPM studies (10). They reported LVH in 34% of the 36 subjects with confirmed hypertension (clinic BP $>$ 95th percentile and ambulatory BP $>$ 95th percentile) and in 20% of the 75 subjects with elevated ambulatory BP but normal clinic BP ("masked" hypertension), but only in 8% of the 83 subjects with normal clinic and ambulatory BP. They found masked and confirmed hypertension to be significant independent predictors of LVH and concluded that casual BP alone was insufficient to predict

the presence of LVH in children with CKD. In our study, we found a strong correlation between SBP within the normal range and LVMI (Figure 1, a and b). Similar to the CKiD study (10), we found a high prevalence of LVH in subjects with masked hypertension, but in contrast with the CKiD study, clinic SBP proved to be the strongest predictor of LVM: Ambulatory BP did not add further predictive influence.

Our findings are at variance with the multicenter Effect of Strict Blood Pressure Control and ACE Inhibition on the Progression of CRF in Pediatric Patients (ESCAPE) study, which found no association between BP and LVH (8,9). The ESCAPE study documented a single clinic BP measurement and ABPM for 156 patients with ABPM z-scores (24-hour MAP, daytime MAP, and nighttime MAP) of 1.17 ± 1.75 , 0.88 ± 1.62 , and 1.34 ± 1.92 , respectively. These BP values are higher than those observed in our study (0.78 ± 1.76 , 0.57 ± 1.49 , and 1.22 ± 1.64 , respectively); however, the prevalence of LVH in the ESCAPE study was lower (33%) than in our study. We also did not observe an association with male gender, anemia, ponderosity, or hyperparathyroidism with LVH (8). The role of inflammation in this cohort may be important with previous evidence from the ESCAPE study suggesting elevated hsCRP to be associated with abnormal LV geometry and LVH (8). We report here no correlation of hsCRP with indexed LVM and LVH. This may be because of the relatively narrow range of LVMI in our subjects, but also because of the comparatively better levels of BP, anemia, and hyperparathyroidism control in our cohort.

It is interesting to discuss further the relationship of renal function with indexed LVM and LVH in light of our study results. The mean GFR in the ESCAPE and CKiD study cohorts was much higher at 49 and 43 ml/min per 1.73 m², respectively, than we report for our study cohort at 26.1 ml/min per 1.73 m². Because our prevalence rates of LVH are higher at 49% than the ESCAPE and CKiD studies, on first inspection, this may suggest that deteriorating

renal function is associated with increasing LVH. However, as shown clearly in Tables 1 and 4, we found no significant relationship of GFR with LVH or indexed LVM. In adult patients with CKD, it has been shown that LVM increases progressively as renal function deteriorates (24). Similarly, the ESCAPE study reported significantly higher mean LVMI in subjects with CKD stage 4 when compared with CKD stages 2 and 3 (8). In contrast, the CKiD study reported no significant influence of GFR on LVH and LVMI or of CKD stage with LVH (10). Our study results are similar to the CKiD data with no significant relationship of GFR with LVH or indexed LVM when analyzed for categorical and continuous relationship. One of the possible reasons for this conflicting data may be related to the methods used to measure GFR: The ESCAPE study used a modified Jaffe reaction to measure creatinine and used a nonmodified “old” Schwartz formula to measure GFR (8), whereas the CKiD and our study used more accurate methods to measure GFR.

The assessment of increased LVM in children is not straightforward. Different authors have indexed LVM for body weight (25), height (1,26,27), or body surface area (28). LVM for body size is higher in smaller, younger children than in older children (18,20). Thus, the relationship between LVM and body size is not constant in the pediatric age range (18,20). We have recently published data on the effect of different methods of indexation of LVM in childhood (18), demonstrating that this has a significant effect on the proportion of children who might be considered to have LVH. In this study, we have chosen to index LVM to height^{2.7} in keeping with most reports using age-specific reference intervals for normal children that have been published recently (19). The ESCAPE study used a cut of indexed LVM ≥ 38.6 g/m^{2.7} to define LVH (8). If that method had been used in our study, then 26 of 49 subjects (53.1%) would have had LVH. Thus, only two additional subjects would have been categorized with LVH compared with the age-specific reference intervals we used (19). LVMI decreases with increasing height in children to become relatively constant in children taller than 120 cm. To account for this, LVM for height z-scores have been published (20). Although attractive, the absolute values of LVM reported appear higher than those in most earlier reports (1,19,27). In our population, the use of these LVM for height z-scores resulted in only three children (6%) having LVH defined as a z-score >1.645 SD above the mean, but most importantly the relationship between BP and LVH remained (Figure 1, a and b).

The LV geometry we have observed in patients also differs from that reported in the ESCAPE and CKiD studies (8,10). We have only observed eccentric LVH in our patients, whereas in these studies (8,10) LVH was concentric in 6% to 12% of affected patients and a further 9% to 10% were demonstrated to have concentric remodeling. Eccentric hypertrophy has classically been associated with volume overload, but there was no clinical evidence to suggest that this is the explanation for the observed ventricular geometry in our patients. The absence of concentric hypertrophy (typically associated with hypertension) in our cohort may be related to their better BP control. The factors affecting LV geometry in

this patient group merit further longitudinal study as proposed by the CKiD group and us.

Of the other risk factors evaluated in this cohort, we found that prescribed elemental Ca intake from Ca-based phosphate binders added to the risk of developing LVH. Those children with a LVMI greater than the 95th percentile had significantly higher (although normal) time-averaged serum Ca values than those without LVH. There was no difference in time-averaged serum phosphate levels, Ca-P product, or iPTH between the two groups. The number of children taking calcium carbonate was similar in the two groups, but the mean prescribed dose was significantly higher in the 17 children with LVH than the 18 with normal LVM. Ca-based phosphate binders may lead to Ca overload and is incriminated in ectopic soft tissue calcification, coronary artery calcification, and increased carotid intima media thickness (29–33). Careful attention to Ca-P balance with the use of noncalcium-containing phosphate binders should further reduce cardiovascular risk.

Strengths of our study include presentation of data as z-scores and indexation of LVM to allow comparisons across the pediatric age and height range. Echocardiographic data were obtained by a single team and analyzed consistently. Limitations of this study include its cross-sectional nature and limited number of subjects. Although it is impossible to be certain, we believe there was no selection bias in the recruitment of patients to this study because we have included the first 49 consecutive subjects who agreed to participate and who had suitable study-related investigations. Our unit is the designated government-funded referral center for pediatric nephrology services for a defined geographical population from southeastern England. The ethnic and gender mix in our study patients is typical of the population of children with CKD in the United Kingdom (34). It is possible that this initial single-center, relatively smaller study cohort may not be representative of all CKD patients in the United Kingdom. A larger multi-center U.K.-wide study with more subjects whose range of renal dysfunction is spread across CKD stages may be more representative.

In adults with CKD, expert groups and international committees now recommend more stringent BP targets equivalent to the 50th to 75th percentile in the general population (11,12). In contrast, until recently, recommendations for children with CKD were to maintain BP below the 90th percentile for the child's age, gender, and height (15). On the basis of the findings of the ESCAPE study, the European Society of Hypertension now recommends maintaining BP below the 75th percentile primarily to retard progression of renal failure (35).

Our findings of a high prevalence of LVH in children with CKD and BP well below the 90th percentile, together with the experience in adults, add further to the argument for lowering BP targets. The optimum level of BP control to improve cardiovascular prognosis in children with CKD should ideally be addressed in a randomized controlled trial.

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Disclosures

None.

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