

Forty-four-hour interdialytic ambulatory blood pressure monitoring and cardiovascular risk in pediatric hemodialysis patients

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Abstract

Background. Children undergoing chronic hemodialysis are at risk of cardiovascular disease and often develop left ventricular hypertrophy (LVH). Twenty-four-hour ambulatory blood pressure monitoring (ABPM) is known to better predict cardiovascular morbidity than casual blood pressure (BP) measurement. Given the BP variability attributed to interdialytic fluid overload, 44-h ABPM should better delineate cardiovascular morbidity in pediatric hemodialysis patients.

Methods. In this cross-sectional study, 17 children (16.7 ± 2.9 years) on chronic hemodialysis underwent 44-h interdialytic ABPM and routine echocardiogram. Left ventricular mass index (LVMI) was calculated by height-based equation; LVH was defined as an LVMI in the ≥ 95 th percentile for height-age and gender. Hypertension was defined by the recommendations of the Fourth Report of the National High Blood Pressure Education Program for casual measurements, and by those of the American Heart Association for ABPM.

Results. Twenty-four percentage of patients were hypertensive by casual post-dialytic systolic BP, whereas 59% were hypertensive by ABPM. Eighty-eight percentage of patients had abnormal cardiac geometry: 53% had LVH. Thirty-five percentage (6 of 17) had masked hypertension, including four with abnormal cardiac geometry, of which, three had LVH. LVMI correlated with ABPM, but not with casual measurements. Strongest correlations with an increased LVMI were with 44-h diastolic BP: at night ($r = 0.53$, $P = 0.03$) and total load ($r = 0.57$, $P = 0.02$). LVH was similarly associated with 44-h nighttime BP: systolic ($P = 0.02$), diastolic ($P = 0.01$) and mean arterial ($P = 0.01$).

Conclusions. Casual BP measurement underestimates hypertension in pediatric hemodialysis patients and does not correlate well with indicators of cardiovascular morbidity. In contrast, 44-h interdialytic ABPM better characterizes hypertension, with nighttime parameters most strongly predicting increased LVMI and LVH.

Keywords: blood pressure; children; hemodialysis; hypertension; left ventricular hypertrophy

Introduction

Cardiovascular disease is the most common cause of mortality in patients with end-stage renal disease (ESRD) [1]. Children undergoing chronic hemodialysis often exhibit left ventricular hypertrophy (LVH) and/or diastolic dysfunction, as well as other parameters of ventricular pathology [1]. In many cases, these changes are due to hypertension [2]. Blood pressure (BP) can be assessed in a number of ways, including traditional readings by auscultation or an oscillometric device in the clinical setting, readings by an oscillometric device at home or ambulatory BP monitoring (ABPM). ABPM has recently been shown to provide more predictive information than casual BP (CBP) measurements with respect to cardiovascular disease in pediatric dialysis patients [3]. Furthermore, it allows the study of additional parameters, including nocturnal dipping: the absence of

physiologic dipping is an independent predictor of increased left ventricular mass index (LVMI) [3, 4], a surrogate marker of cardiac disease in children receiving long-term dialysis [5].

Patients on chronic, intermittent hemodialysis represent an important subset of patients, whose progressive interdialytic weight gain contributes to their BP variability and hypertension [6]. Therefore, for the accurate diagnosis of hypertension in the adult patient, 44-h interdialytic ABPM [7], as opposed to the standard 24-h assessment, is recommended. While ABPM has not always identified a difference between first-day and second-day parameters, it has been shown in adult hemodialysis patients that some may be normotensive in the first 22-h period after dialysis, yet hypertensive in the second 22-h period [8]. In fact, in a small group of pediatric hemodialysis patients who were admitted in order to control intake for research

purposes, interdialytic weight gain was related to BP over a 44-h period [4]. The purpose of the current investigation was to delineate patterns of ABP during a complete 44-h interdialytic period and to examine their correlation with surrogate markers of cardiovascular disease in children undergoing chronic hemodialysis.

Subjects and methods

Study population and design

This was a cross-sectional, single-center study of 17 children on chronic hemodialysis, approved by the Institutional Review Board. Included patients were at least 6 years old and without severe developmental delay, to ensure tolerance of the ABP monitor. They were of a height of ≥ 120 cm, due to the available normative data for pediatric ABPM, and clinically stable on hemodialysis for at least 1 month prior to entry. Patients with congenital heart disease or primary cardiomyopathy were excluded.

During the 6-month study period, clinical data (height, weight, body mass index and interdialytic weight gain) were collected monthly and averaged. Routine laboratory data (urea reduction ratio, hemoglobin, ferritin, serum albumin/calcium/phosphorus and alkaline phosphatase) were similarly averaged. Intact parathyroid hormone was checked every 3 months, whereas 25-hydroxy vitamin D was checked once. Biomarkers specific to cardiovascular risk [9], including cardiac C-reactive protein and pro-brain natriuretic peptide, and routine echocardiogram were assessed once during the study period. Medications, including the number of antihypertensives prescribed, were recorded and averaged over the 6-month period.

Blood pressure measurement

CBP was measured before and after hemodialysis, by an oscillometric device, using an appropriately sized arm cuff, in the standing position. Monthly values were averaged and classified according to the Fourth Report of the National High Blood Pressure Education Program [10]. Hypertension by CBP measurement was defined as >95 th percentile for age, gender and height percentile. While the Fourth Report is based on a seated position, standing measurement is common practice in dialysis units and may be more comparable with measures obtained by ABPM.

ABPM was performed using the SpaceLabs 90217[®] oscillometric monitors (SpaceLabs Healthcare, Issaquah, WA, USA) once during the 6-month period. Cuff size was selected based on measured arm circumference. BP was recorded every 20 min during wake hours, and every 30 min during sleep hours. Wake and sleep hours were programmed based on the patient's self-report of typical sleep pattern. The monitor was worn mid-week for 44 h, from the completion of one hemodialysis session to the initiation of the next, avoiding the long interdialytic period. During this time, a diary was kept to note true wake and sleep hours, as well as times of anti-hypertensive medication administration, if prescribed. Hypertension by ABPM was defined according to the American Heart Association recommendations [11], using normative data adapted from Wühl *et al.* [12]. ABP was indexed for gender and height.

CBP was classified as normotensive, prehypertensive or hypertensive: normotension CBP <90 th percentile, prehypertension CBP >90 th percentile and hypertension CBP

>95 th percentile. Subsequently accounting for ABP, BP reflected either true normotension, white coat hypertension, masked hypertension or sustained hypertension [13, 14]. True normotension was defined as CBP and mean ABP <95 th percentile plus BP load $<25\%$. White coat hypertension was CBP >95 th percentile, but mean ABP <95 th percentile plus BP load $<25\%$. Masked hypertension was CBP <95 th percentile, but mean ABP >95 th percentile plus BP load $>25\%$. Sustained hypertension was defined as CBP and mean ABP >95 th percentile plus BP load $>25\%$ [15]. Load is the percentage of readings in a given time period that exceed the 95th percentile. Nocturnal dipping is the physiologic decrease in BP at night, by at least 10%. Blunted dipping is a decline of $<10\%$.

Echocardiography and cardiac geometry

Two-dimensional, M-mode echocardiograms were performed as part of the routine evaluation of chronic hemodialysis patients, using standard techniques. They were interpreted by an experienced pediatric cardiologist. Left ventricular mass was calculated by the Devereux formula: the measurements required for the formula were obtained offline by a different pediatric cardiologist blinded to the BP values. LVMI was determined by dividing the mass by the patient's height (m)^{2.7}, minimizing the effects of age, gender and weight. LVH was defined as LVMI ≥ 95 th percentile for height-age and gender, according to the normative data of Khoury *et al.* [16], as it is clinically applicable in pediatrics [5]. Height-age, rather than chronological age, was used to minimize overestimation of cardiac burden, since children with end-stage renal failure are often of short stature. Left ventricular geometry was determined by the relative wall thickness (RWT), which was measured as the total wall thickness and age-adjusted as described by de Simone *et al.* [17]. A concentric geometric pattern was evident when RWT was ≥ 95 th percentile at 0.375 or 0.430, for patients aged 1–17 years or over 18 years, respectively. Therefore, the four geometric patterns included: (i) normal geometry with LVMI and RWT <95 th percentile, (ii) concentric remodeling with LVMI <95 th percentile but RWT ≥ 95 th percentile, (iii) eccentric hypertrophy with LVMI ≥ 95 th percentile but RWT <95 th percentile and (iv) concentric hypertrophy with LVMI and RWT ≥ 95 th percentile.

Statistical analysis

Standard deviation (Z) scores were calculated for demographic and BP parameters using the available corresponding normative data [10, 11, 18], with 1.383 for the 90th percentile and 1.645 for the 95th percentile. Descriptive data are presented as median and interquartile range, with percentages for categorical variables. Categorical variables were compared by Fisher's exact test. Univariate analysis for paired comparisons was performed using the Wilcoxon *t*-test for unequally distributed variables. The Mann-Whitney test was used to compare the mean ranks of various parameters relative to LVH. Univariate and multiple regression analyses were used to evaluate the relationship between biochemical and BP parameters, interdialytic weight gain and LVMI, and to determine the independent factors linked to LVH and LVMI. Independent predictive variables affecting LVH and LVMI were selected for the analysis based on clinical judgment and included hemoglobin, interdialytic weight gain, serum phosphorus and BP parameters. A *P*-value of <0.05 was

considered significant. All graphs and statistical analyses were performed using GraphPad Prism® for Windows, Version 5.03 (La Jolla, CA, USA).

Results

Patient characteristics

From a cohort of 30 pediatric hemodialysis patients, 10 were excluded based on the above criteria and 3 refused ABPM. Of the 17 patients included, the average age was 16.7 ± 2.9 years; 41% were male. The majority of patients were African American (82%), and the remaining 18% were Hispanic. The predominant primary renal disorder was focal segmental glomerular sclerosis, in accordance with the racial distribution of our patients. On average, patients were of short stature and underweight. Nine of the 17 patients (53%) were prescribed anti-hypertensive treatment. Eight of the patients had a history of renal allograft failure. The median time on renal replacement therapy was 14.5 (range 1–76) months. Typical interdialytic weight gain was 3.3–5.5% of estimated dry weight, in a 44-h period. The baseline characteristics, including biochemical and medication parameters, are summarized in Table 1.

Blood pressure measures

CBP measurements were taken in the hospital-based, pediatric dialysis unit, both before and after a given hemodialysis session. A median Z-score with interquartile range for pre-dialytic systolic BP (SBP) was 2.33 (–0.19–3.30), and that for post-dialytic SBP was 0.73 (–0.29–1.60). The median Z-score with interquartile range for pre-dialytic diastolic BP (DBP) was 1.64 (0.60–2.59), and that for post-dialytic DBP was 1.13 (0.73–1.65). Using CBP measurement alone, the prevalences of pre-dialytic systolic and diastolic hypertension were 59 and 47%, respectively. The post-dialytic prevalences were 24 and 29%. With fluid removal throughout a typical 3-h session, the mean post-dialytic systolic and diastolic BPs were significantly lower than the pre-dialytic measures ($P < 0.001$ and $P = 0.004$). Due to evolving clinical practice toward control of BP to the 90th percentile in patients with ESRD, Table 2 compares prevalence rates of hypertension based on the standard of care and evolving practice.

ABPM was performed for an average of 43 ± 2 h, capturing 98 ± 15 readings ($75\% \pm 16$ successful readings), per participant. Weight gain during the 44-h ambulatory monitoring period of 4.5% of dry weight (3.2–5.9) was similar to that during an average interdialytic period (Table 1). The median Z-scores for each ABP parameter are graphed over time in Figure 1. All nocturnal pressures were noted to be higher than daytime recordings. The difference between CBP and ABP identified masked systolic hypertension in 35% (6 of 17) of patients (Figure 2). Of these six participants, four were hypertensive on interdialytic Day 1, and all were hypertensive on interdialytic Day 2. Masked diastolic hypertension was unveiled in 18% (3 of 17) of patients, of which two were hypertensive on Day 1, and all were hypertensive on Day 2. In total, there were 6 (35%) patients with either systolic masked hypertension or both systolic and diastolic masked hypertension. No patients were identified to have white coat hypertension.

There were substantial rates of abnormal load and blunted nocturnal dipping in this study population. Fifty-nine percentage (10 of 17) of patients had abnormal systolic and diastolic loads above 25% over the 44-h monitoring period. Of note, when analyzing the difference between SBP load on Day 1 when compared with Day 2, there was an additional patient with abnormal load on Day 2 only, though total 44-h load was within the normal range. This participant was also confirmed to have abnormal cardiac geometry, concentric remodeling. With respect to physiologic dipping, 76% (13 of 17) of children exhibited nocturnal blunting of either SBP or DBP. Interestingly, 3 of 17 patients displayed improvement in SBP dipping, from abnormal to normal range, throughout the 44-h period. Similarly, 4 of 17 patients showed improved DBP dipping.

In comparing CBP measures with ABP measures, it appears that casual pre-dialytic systolic and diastolic pressures were the highest and more closely approximated interdialytic Day 2 ambulatory values, as expected. Casual post-dialytic systolic pressures were the lowest measured pressures, even in comparison with interdialytic Day 1 values.

Cardiac geometry

Overall, 88% of patients had an abnormal geometric pattern, while only 2 of 17 patients had normal cardiac geometry. Echocardiography revealed elevated LVMI among the

Table 1. Patient characteristics^a

Clinical		Biochemical	SI units	Conventional units
Age (years)	16.7 ± 2.9^b	Urea reduction ratio (%)	72 (67, 76)	
Gender	M: 7 (41%)/F: 10 (59%)	Hemoglobin	(mmol/L) 6.7 (6.6, 6.9)	(g/dL) 10.8 (10.7, 11.1)
Race/ethnicity	AA: 14 (82%)/H: 3 (18%)	Ferritin	(pmol/L) 1097 (546, 1357)	(ng/mL) 488 (243, 604)
Height (Z-score)	–1.28 (–1.98, –0.63)	Serum albumin	(g/L) 38 (36, 40)	(g/dL) 3.8 (3.6, 4)
Weight (Z-score)	–0.98 (–1.44, –0.27)	Serum calcium	(mmol/L) 2.3 (2.1, 2.5)	(mg/dL) 9.3 (8.5, 9.8)
Body mass index (Z-score)	–0.05 (–0.62, 1.37)	Serum phosphorus	(mmol/L) 2.1 (1.8, 2.4)	(mg/dL) 6.4 (5.7, 7.5)
Interdialytic weight gain (%)	4.4 (3.3, 5.5)	Alkaline phosphatase	(Unit/L) 108 (88, 180)	
Time on dialysis (months)	14 (11, 23)	Intact PTH	(ng/L) 462 (244, 579)	(pg/mL) 462 (244, 579)
Medications		25-OH Vitamin D	(nmol/L) 87 (55, 107)	(ng/mL) 35 (22, 43)
Anti-hypertensive (n)	1 (0, 3)	Pro-BNP	(ng/L) 2297 (412, 3851)	(pg/mL) 2297 (412, 3851)
		Cardiac CRP	(mg/L) 1.4 (0.6, 4.1)	

M, male; F, female; AA, African American; H, Hispanic; SI, International System of Units; PTH, parathyroid hormone; D, vitamin D; OH, hydroxyl; BNP, brain natriuretic peptide; CRP, C-reactive protein.

^aData presented as median (interquartile range)—except for age, see below.

^bMean \pm standard deviation.

participants, with a median Z-score of 1.79 (1.00–3.39, interquartile range). Fifty-three percentage of patients had an LVMI of the ≥ 95 th percentile, and therefore, a diagnosis of LVH. Similarly abnormal, 65% of patients had an RWT of the ≥ 95 th percentile, and therefore, a diagnosis of concentric cardiac geometry. Six exhibited concentric remodeling; four had eccentric LVH, and five had concentric LVH. Of the six patients with masked hypertension, two had normal cardiac geometry, one had concentric remodeling and three had LVH (one eccentric and two concentric).

In associating BP indices with LVMI by linear regression, ambulatory diastolic and mean arterial parameters showed the greatest correlation with an increased LVMI (Table 3). Overall, 44-h diastolic BP and load correlated with LVMI, with nighttime DBP particularly significant (Figure 3). Mean arterial and diastolic load were uniformly correlated with an increased LVMI, while systolic load was not. CBP showed no correlation with LVMI (data not shown).

Duration on dialysis, interdialytic weight gain and biochemical markers were not significantly associated with LVMI by linear regression, nor with the presence of LVH by *t*-test (Supplementary Table S1). Only BMI Z-scores and serum phosphorus tended to be directly related ($P=0.11$ and 0.12 , respectively), and hemoglobin tended to be inversely related to LVMI ($P=0.14$). Multiple regression analysis using these potential determinant variables confirmed that DBP load was the only significant determinant of LVMI (β coefficient = 0.04 ; *t*-ratio = 2.4 ; $P=0.035$).

Table 2. Comparison of hypertension definitions

CBP	Prevalence ^a		Association with LVH ^b	
	≥ 90 th Percentile (%)	≥ 95 th Percentile (%)	≥ 90 th Percentile	≥ 95 th Percentile
Pre-dialytic SBP	59	59	0.64	0.64
Pre-dialytic DBP	65	47	0.33	0.64
Post-dialytic SBP	29	24	0.03	0.08
Post-dialytic DBP	35	29	0.03	0.03

Italics indicate that the value is not statistically significant.

^aPrevalence of study patients with BP parameter \geq the 90th or 95th percentiles for age, gender and height.

^bFisher's exact test of association of elevated BP and the presence of LVH, with elevated BP defined as \geq the 90th or 95th percentiles for age, gender and height; results expressed as *P*-values.

Mann-Whitney *t*-test comparison between ABPM indices and LVH also showed slightly more significant relationships between overall, 44-h parameters than 22-h measures. Figure 4 highlights the significance of hypertensive systolic, diastolic and mean arterial BP in association with the presence of LVH. CBP was variably associated with LVH (Table 2). The BP dipping pattern did not correlate with LVMI or the presence of LVH.

Discussion

In our cross-sectional analysis of pediatric hemodialysis patients, we confirm a high prevalence of hypertension employing 44-h interdialytic ABP recordings, and we identified a strong predictive relationship of the diastolic load and nighttime diastolic BP on left ventricular mass and cardiac remodeling. Cardiovascular disease remains prevalent in pediatric ESRD patients and is the leading cause of morbidity and mortality in adult patients with childhood-onset chronic kidney disease [19]. Increased arterial aging is characteristic of ESRD populations [20], and chronic, undiagnosed hypertension may explain at least part of this cardiac burden. Assessment in intermittently hemodialyzed patients has been challenging, due to interdialytic weight gain, the inability to test both arms due to vascular access, and the potential for white coat effect, which may be as high as 40% in general pediatric patients [7, 14]. Therefore, accurate diagnosis of hypertension in children on hemodialysis requires ABPM, which is the only method of determining circadian variation with nocturnal BP, BP load, blunted nocturnal dipping and masked hypertension [7], all of which carry a worse prognosis when compared with normotension [21].

While mortality rates in chronically hemodialyzed adults are more strongly associated with the long interdialytic interval, implicating the negative impact of progressive hypervolemia [22], using a similar endpoint for the systematic study in pediatrics is not possible due to the low prevalence of ESRD and cardiac deaths [1]. Therefore, we must rely on LVH as the most reliable surrogate marker of cardiac disease in children with end-stage kidney failure. Early studies show greater correlation of ABPM than CBP to LVH in adults and children on dialysis [3, 23, 24].

In this study, pre-dialytic CBP values were significantly higher than post-dialytic values, as expected. However, when compared with ABP data, pre-dialytic CBP overestimated

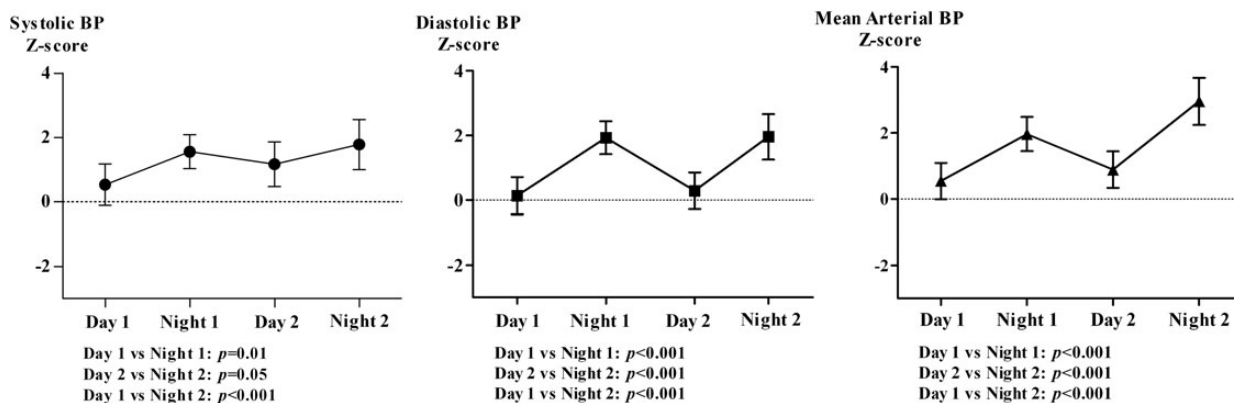


Fig. 1. Forty-four-hour trends in blood pressure. Systolic, diastolic and mean arterial BP median Z-scores are trended over time. Significance of difference between median Z-scores from different time periods is detailed below each graph; *p*, *P*-value.

the degree of hypertension, in agreement with the adult data reported by Mitra *et al.* [25]. Post-dialytic SBP, the most frequently used measure to diagnose hypertension in dialysis patients, actually underestimated the true degree of hypertension in our patients. This contradicts the results from Chaudhuri *et al.* [3], where no difference was identified. Furthermore, in our study, no measure of CBP had a linear relationship with LVMI. Interestingly, association with LVH was appreciated only for post-dialytic CBP. Historically, it is debated whether pre- or post-dialytic CBP is the more relevant practical measure of BP in the dialysis unit. In this study, predialytic CBP overestimated hypertension and did not correlate with LVMI or LVH. Post-dialytic CBP underestimated hypertension, but did correlate with the presence of LVH, possibly reflecting sustained severe hypertension.

Forty-four-hour ABPM clearly identified the progressive development and/or worsening of hypertension during the entire interdialytic period. Most notable is the degree of nocturnal hypertension, such that all nighttime pressures were greater than daytime ones. Up to 59% of patients were hypertensive by ABPM, an elevated rate consistent with the expectation that ambulatory hypertension is more common in African Americans with chronic kidney disease [26]. Second interdialytic day median

Z-scores tended to be greater than first-day scores. This finding in children echoes the suggestion made by Martin *et al.* [8] in adult hemodialysis patients also assessed over 44 h and underscores the usefulness of this more prolonged ABPM. Masked hypertension was identified in 35% of patients by SBP and in 18% by DBP, when compared with previous rates of 12% in children on dialysis [3] or 35% in those with chronic kidney disease [26]. Furthermore, more masked hypertension was identified with prolonged monitoring, than with 24-h ABPM. White coat hypertension was not seen, concurring with its rarity in this particular pediatric population [3, 26].

Nocturnal, circadian BP dipping was quite abnormal, with up to 53% of patients having nocturnal hypertension, and up to 76% having blunted dipping. Overall, nocturnal hypertension was more profound than daytime hypertension, a trend that exists in children with chronic kidney disease [26]. While it is still unclear whether elevated nocturnal BP is a mediator or consequence of cardiovascular disease [21], it is a predictor of both increased LVMI and LVH in hemodialysis patients, both in this study and previous reports [3,8]. In addition, it may be seen as early as Day 1 after a given session of hemodialysis. Therefore, greater attention must be paid to the control of nocturnal hypertension, through evening dosing of anti-hypertensive medication [27], whose effect may only be determined by ABPM.

Abnormal cardiac geometry was prevalent in 88% of patients, including the majority of patients identified as having masked hypertension, emphasizing the poor prognosis of this entity. Eccentric LVH, seen in 24% of our patients, has not been consistently shown in children undergoing daily peritoneal dialysis [28, 29], pointing toward the differential effect of larger shifts in volume during hemodialysis. Overall, nocturnal pressures and BP load were clearly more predictive of abnormal cardiac geometry than casual or daytime pressures, confirming the fundamental need for ABPM in pediatric dialysis patients. Furthermore, 44-h parameters were slightly more predictive than those of the first 22 h. Therefore, in answering the question of whether 44-h (versus 24-h) ABPM is warranted in children who are intermittently hemodialyzed, one can surmise that the trend in this study would indicate

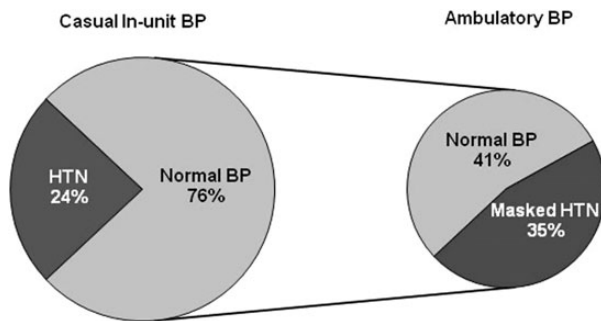


Fig. 2. Masked hypertension identified by ABPM. In-unit, casual, oscillometric BP measurement post-dialysis identified 76% of patients with normal range BP. ABPM on this 76% of patients identified masked hypertension in 35% of the total study group, yielding a true hypertension prevalence of 59% of patients.

Table 3. Linear regression BP correlation with LVMI^a

	SBP				DBP				MAP ^b			
	r	P	Change	95% CI	r	P	Change	95% CI	r	P	Change	95% CI
Casual												
Pre-dialysis	0.23	0.38	0.23	-0.31-0.77	0.25	0.34	0.18	-0.21-0.57				
Post-dialysis	0.27	0.30	0.19	-0.19-0.58	0.19	0.46	0.08	-0.15-0.31				
Ambulatory												
44 h Total	0.38	0.14	0.61	-0.22-1.44	0.49	0.046	0.68	0.02-1.35	0.47	0.06	0.67	-0.03-1.36
22 h Daytime ^c	0.36	0.16	0.56	-0.25-1.38	0.40	0.11	0.55	-0.15-1.25	0.40	0.12	0.55	-0.15-1.24
44 h Daytime ^d	0.33	0.19	0.54	-0.30-1.37	0.42	0.09	0.56	-0.10-1.23	0.40	0.11	0.54	-0.14-1.23
22 h Nighttime ^c	0.41	0.10	0.54	-0.11-1.19	0.51	0.04	0.64	0.05-1.22	0.46	0.06	0.60	-0.04-1.23
44 h Nighttime ^d	0.41	0.10	0.61	-0.13-1.34	0.53	0.03	0.66	0.08-1.25	0.47	0.06	0.65	-0.02-1.32
Load												
44 h Total	0.46	0.06	10.90	-0.66-22.4	0.57	0.02	11.90	2.55-21.3	0.51	0.04	11.57	0.86-22.3
22 h Daytime ^c	0.36	0.15	8.34	-3.52-20.2	0.52	0.03	10.34	0.90-19.8	0.51	0.04	10.66	0.67-20.7
22 h Nighttime ^c	0.55	0.02	14.28	2.39-26.2	0.54	0.03	13.31	1.82-24.8	0.51	0.04	13.09	0.98-25.2

Statistically significant values are in bold.

r, correlation coefficient; P, P-value; CI, confidence interval; h, hour.

^aBP parameters are analyzed from Z-score raw data.

^bMAP, mean arterial pressure—only measured values were reported and analyzed (not calculated values).

^cCorresponding BP parameter within the first 22-h period.

^dCorresponding BP parameter within the total 44-h period.

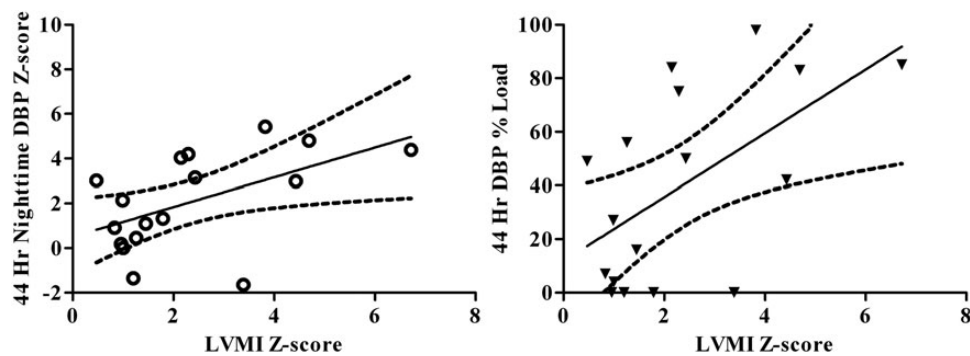


Fig. 3. Graphical correlation of 44-h diastolic BP and load with LVMI. Left panel shows the linear regression correlation between nighttime DBP over the 44-h interdialytic period and LVMI, P 0.03, r 0.53, CI 0.08–1.25. Right panel shows the linear regression correlation between diastolic load over the 44-h interdialytic period and LVMI, P 0.02, r 0.57, CI 2.55–21.3.

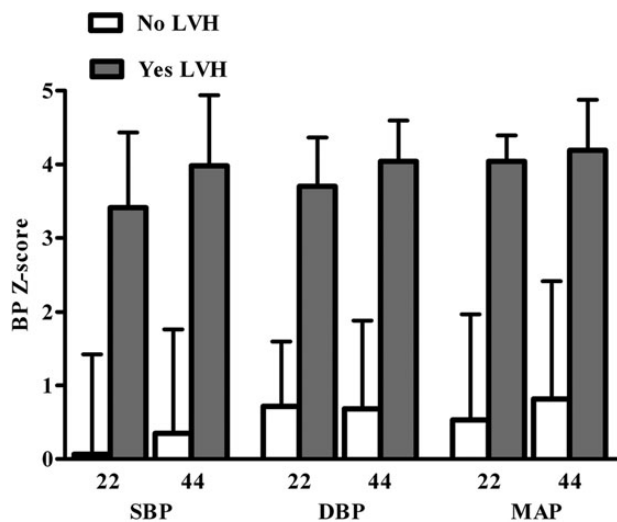


Fig. 4. Nighttime BP parameter Z-scores between patients with LVH and without LVH. Median Z-scores with interquartile ranges for nighttime BP parameter during the first 22-h period versus the entire 44-h; P values for SBP 22 and 44 h were 0.03 and 0.02, respectively; P values for DBP 22 and 44 h were 0.02 and 0.01, respectively; P values for MAP 22 and 44 h were 0.02 and 0.01, respectively.

stronger correlations from prolonged monitoring, which may be further supported by studies in larger cohorts. Although limited, 24-h ABPM provides clinically significant information, due to the increased mortality associated with the long interdialytic interval in adults [22], our study supports 44-h ABPM in children undergoing maintenance hemodialysis.

Limitations of this study include the dependence on normative data not entirely comparable with the study population. The Wühl *et al.* tables are based on a population of predominantly European and Caucasian children that lacks both racial and ethnic diversity [12, 19]. Our study population, reflecting the urban center in South Florida, did not include a single Caucasian patient. Knowing that African Americans tend to have higher nocturnal BP with decreased physiologic dipping, our mean values and prevalence rates may be higher than anticipated simply due to trends in racial differences. The normative ABP data also show a marked lack of variability in DBP, which may result in underestimation of hypertension in shorter children, such as those with ESRD. In an effort to address this risk in calculating LVMI, chronologic age

was adjusted to height-age. Finally, it has been noted that the ideal normative data for ABP should be based on mean arterial pressure, as this is what is actually measured by the portable oscillometric device [13]. Interestingly, in the present study, mean arterial pressure values mirrored the 44-h trends of SBP and DBP, and correlated well with increased LVMI and the presence of LVH.

In conclusion, 44-h ABPM is the most informative and comprehensive means of assessing hypertension in pediatric hemodialysis patients. Appropriately performed, ABPM is capable not only of identifying increased BP load, masked hypertension and nocturnal hypertension, but also of predicting cardiac burden.

Supplementary data

Supplementary data is available online at <http://ndt.oxfordjournals.org>.

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Conflict of interest statement. None declared.

References

- Lilien MR, Groothoff JW. Cardiovascular disease in children with CKD or ESRD. *Nat Rev Nephrol* 2009; 5: 229–235
- Gruppen MP, Groothoff JW, Prins M *et al.* Cardiac disease in young adult patients with end-stage renal disease since childhood: a Dutch cohort study. *Kidney Int* 2003; 63: 1058–1065
- Chaudhuri A, Sutherland SM, Begin B *et al.* Role of twenty-four-hour ambulatory blood pressure monitoring in children on dialysis. *Clin J Am Soc Nephrol* 2011; 6: 870–876
- Sorof JM, Brewer ED, Portman RJ. Ambulatory blood pressure monitoring and interdialytic weight gain in children receiving chronic hemodialysis. *Am J Kidney Dis* 1999; 33: 667–674
- Shamszad P, Slesnick TC, Smith EO *et al.* Association between left ventricular mass index and cardiac function in pediatric dialysis patients. *Pediatr Nephrol* 2012; 27: 835–841
- Agarwal R. Interdialytic hypertension—an update. *Adv Chronic Kidney Dis* 2011; 18: 11–16
- Agarwal R. Assessment of blood pressure in hemodialysis patients. *Semin Dial* 2002; 15: 299–304

8. Martin LC, Franco RJS, Gavras I *et al.* Is 44-hour better than 24-hour ambulatory blood pressure monitoring in hemodialysis? *Kidney Blood Press Res* 2006; 29: 273–279
9. Fliser D, Wiecek A, Suleymanlar G *et al.* European REnal and Cardiovascular Medicine working group of the European Renal Association-European Dialysis and Transplant Association (ERA-EDTA): the dysfunctional endothelium in CKD and in cardiovascular disease: mapping the origin(s) of cardiovascular problems in CKD and of kidney disease in cardiovascular conditions for a research agenda. *Kidney Int Suppl* 2011; 1: 6–9
10. National High Blood Pressure Education Program Working Group on Hypertension Control in Children and Adolescents: The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. *Pediatrics* 2004; 114: 555–576
11. Urbina E, Alpert B, Flynn J *et al.* Ambulatory blood pressure monitoring in children and adolescents: recommendations for standard assessment: A Scientific Statement from the American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee of the Council on Cardiovascular Disease in the Young and the Council for High Blood Pressure Research. *Hypertension* 2008; 52: 433–451
12. Wühl E, Witte K, Soergel M *et al.* Distribution of 24-h ambulatory blood pressure in children: normalized reference values and role of body dimensions. *J Hypertens* 2001; 20: 1995–2007
13. Flynn JT, Urbina EM. Pediatric ambulatory blood pressure monitoring: indications and interpretations. *J Clin Hypertens* 2012; 14: 372–382
14. Redwine KM, Daniels SR. Prehypertension in adolescents: risk and progression. *J Clin Hypertens* 2012; 14: 360–364
15. Agarwal R, Sinha AD, Light RP. Toward a definition of masked hypertension and white-coat hypertension among hemodialysis patients. *Clin J Am Soc Nephrol* 2011; 6: 2003–2008
16. Khoury PR, Mitsnefes M, Daniels SR *et al.* Age-specific reference intervals for indexed left ventricular mass in children. *J Am Soc Echocardiogr* 2009; 22: 709–714
17. de Simone G, Daniels SR, Kimball TR *et al.* Evaluation of concentric left ventricular geometry in humans: evidence for age-related systematic underestimation. *Hypertension* 2005; 45: 64–68
18. Kuczmarski RJ, Ogden CL, Guo SS *et al.* 2000 CDC growth charts for the United States: methods and development. *Vital Health Stat* 2002; 11: 1–190
19. Flynn JT. Ambulatory blood pressure monitoring in children: imperfect yet essential. *Pediatr Nephrol* 2011; 26: 2089–2094
20. London G, Covic A, Goldsmith D *et al.* European REnal and Cardiovascular Medicine working group of the European Renal Association-European Dialysis and Transplant Association (ERA-EDTA): arterial aging and arterial disease: interplay between central hemodynamics, cardiac work, and organ flow-implications for CKD and cardiovascular disease. *Kidney Int Suppl* 2011; 1: 10–12
21. Agarwal R, Martinez-Castelao A, Wiecek A *et al.* European REnal and Cardiovascular Medicine working group of the European Renal Association-European Dialysis and Transplant Association (ERA-EDTA): the lingering dilemma of arterial pressure in CKD: what do we know, where do we go? *Kidney Int Suppl* 2011; 1: 17–20
22. Foley RN, Gilbertson DT, Murray Tet *et al.* Long interdialytic interval and mortality among patients receiving hemodialysis. *N Engl J Med* 2011; 365: 1099–1107
23. Hopkins K, Bakris GL. Assessing blood pressure control in dialysis patients: finally a step forward. *Hypertension* 2009; 53: 448–449
24. Agarwal R. Volume-associated ambulatory BP patterns in hemodialysis patients. *Hypertension* 2009; 54: 241–247
25. Mitra S, Chandna SM, Farrington K. What is hypertension in chronic haemodialysis? The role of interdialytic blood pressure monitoring. *Nephrol Dial Transplant* 1999; 14: 2915–2921
26. Samuels J, Ng D, Flynn JT *et al.* Chronic kidney disease in children study group: ambulatory blood pressure patterns in children with chronic kidney disease. *Hypertension* 2012; 60: 43–50
27. Minutolo R, Gabbai FB, Borrelli S *et al.* Changing the timing of antihypertensive therapy to reduce nocturnal blood pressure in CKD: an 8-week uncontrolled trial. *Am J Kidney Dis* 2007; 50: 908–917
28. Bircan Z, Duzova A, Cakar N *et al.* Predictors of left ventricular hypertrophy in children on chronic peritoneal dialysis. *Pediatr Nephrol* 2010; 25: 1311–1318
29. Bakkaloglu SA, Borzych D, Ha IS *et al.* for the International Pediatric Peritoneal Dialysis Network. Cardiac geometry in children receiving chronic peritoneal dialysis: findings from the International Pediatric Peritoneal Dialysis Network (IPPN) Registry. *Clin J Am Soc Nephrol* 2011; 6: 1926–1933

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