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ARTICLE

24-h central pressure is a valuable predictor for left ventricular hypertrophy in non-dialysis patients with chronic kidney disease

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Abstract

The current research on the relationship between 24-h central pressure and 24-h brachial pressure with left ventricular hypertrophy (LVH) is characterised by limited sample size and inconsistent findings. Furthermore, the association has never been explored in chronic kidney disease (CKD). A multicentre, cross-sectional study among non-dialysis patients with CKD was conducted. All participants underwent brachial and central ambulatory blood pressure monitoring using MobilO-Graph PWA, while trained cardiologists performed echocardiography. In this study, 2117 non-dialysis patients with CKD were examined. 24-h central systolic blood pressure with c2 calibration (24-h c2SBP) demonstrated a stronger association with left ventricular mass index and LVH compared with 24-h brachial systolic blood pressure (24-h bSBP) in the univariate and multivariate regression analyses. The multivariate net reclassification index (NRI) analysis revealed that 24-h c2SBP exhibited greater discriminatory power over 24-h bSBP (NRI = 0.310, 95% CI [0.192–0.429], $P < 0.001$). Applying 130/135 mmHg as the threshold for 24-h bSBP/c2SBP to cross-classify, the patients were divided into concordant normotension (1509 individuals), isolated brachial hypertension (155 individuals), isolated central hypertension (11 individuals), and concordant hypertension (442 individuals). With concordant normotension as the reference, the multivariable-adjusted ORs were 0.954 (95% CI, 0.534–1.640; $P = 0.870$) for isolated brachial hypertension and 2.585 (95%CI, 1.841–3.633; $P < 0.001$) for concordant hypertension. Among non-dialysis patients with CKD, 24-h c2SBP exhibits greater efficacy in identifying the presence of LVH compared with 24-h bSBP. The presence of LVH was greater in cases of concordant hypertension compared with cases of isolated brachial hypertension and concordant normotension.

Keywords 24-h central pressure · 24-h brachial pressure · Chronic kidney disease · Left ventricular hypertrophy

Introduction

The global prevalence of chronic kidney disease (CKD) is estimated to be 9.1% in 2017 [1], while high systolic blood pressure (SBP) ranks as the leading cause of Level 2 risk factor for attributable deaths worldwide in 2019 [2]. Blood pressure (BP) is a modifiable risk factor, and the method of its measurement holds great significance. Ambulatory brachial BP measurement has demonstrated superiority over clinic BP readings [3], while the potential of ambulatory central pressure measurement holds promise as well. Although ambulatory central and brachial pressure measurements can be taken simultaneously and exhibit a strong correlation, central pressure is distinct from brachial pressure due to factors such as amplification effects [4], antihypertensive impacts [5], and circadian rhythms [6].

Left ventricular hypertrophy (LVH) is not solely a response of elevated BP [7] but also a significant indicator for adverse

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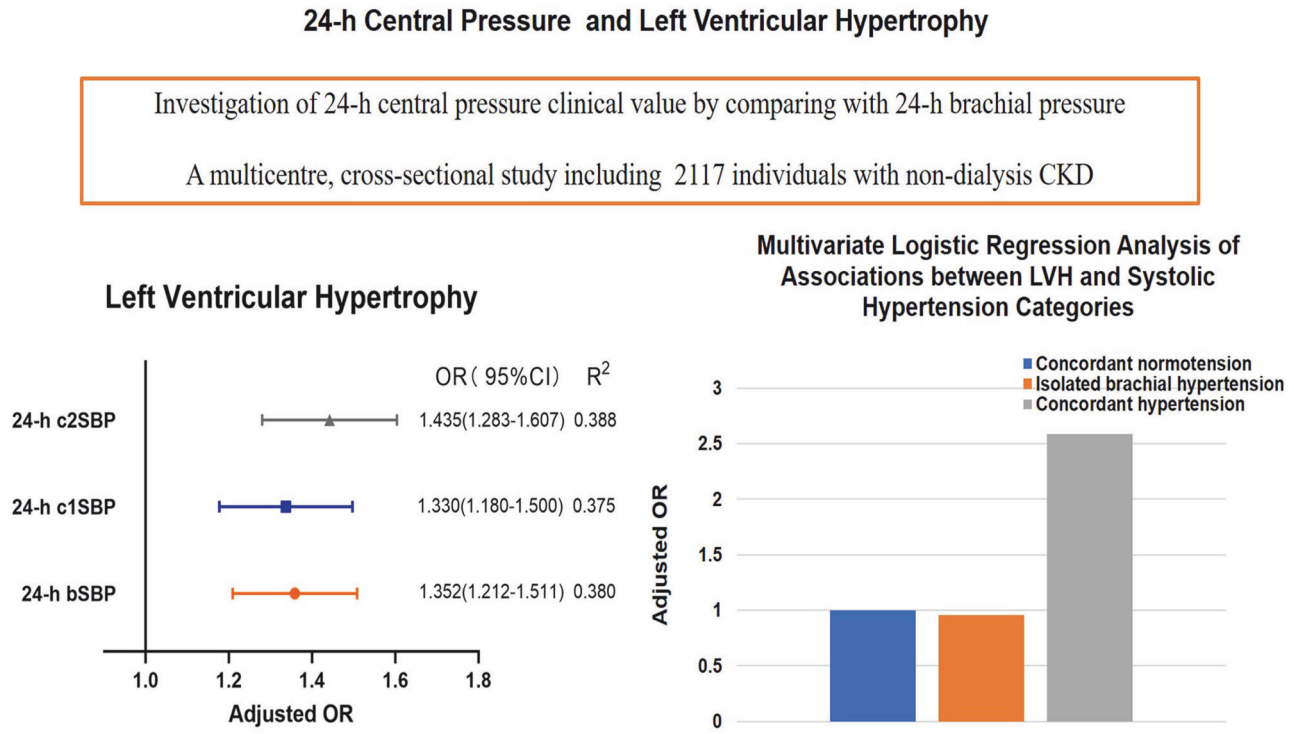
Graphical Abstract



cardiovascular disease outcomes [8–10]. Several studies have demonstrated that its regression with antihypertensive treatment enhances outcomes associated to hypertension [11–13]. The proximity of central pressure to LVH is likely closer than that of brachial pressure, as it represents the direct burden on the left ventricle during early systole. Despite this, there is limited research addressing the relationship between 24-h central pressure and 24-h brachial pressure concerning LVH. Three studies have suggested a stronger correlation between 24-h central pressure and LVH compared with 24-h brachial pressure [14–16], whereas two other studies reported contradictory findings [17, 18]. Perhaps the device-related discrepancies, the measurement setting (home, hospital) [19], the differences in study populations, and the calibration of central BP account for the inconsistent results.

Patients with CKD constitute a distinct population characterised by a high incidence of cardiovascular events, abnormal BP rhythm, and challenges in BP control [20, 21]. Surprisingly, the association between central pressure and LVH is yet to be investigated in this group. Furthermore, existing research on this topic has been constrained by relatively modest sample sizes ($n < 500$). Additionally, a study applied the cut-off values of clinic brachial SBP and central SBP to cross-classify and found that isolated high brachial SBP and isolated high central SBP had intermediate levels of arterial damage between concordant normotension and concordant hypertension [22]. However, to our knowledge, no study has explored the presence of target organ damages based on cross-classification of ambulatory central versus brachial blood pressure.

This study aimed to verify whether 24-h central pressure is superior to 24-h brachial pressure in terms of LVH in a large CKD population and to investigate the difference in the presence of LVH among different groups which were cross-classified based on the threshold of ambulatory brachial and central SBP [6, 7].

Methods

Study design and participants

This multicentre, cross-sectional study enroled patients who were admitted to the Department of Nephrology at our hospital and the Third Affiliated Hospital of Southern Medical University between April 2018 and June 2023. The inclusion criteria encompassed patients diagnosed with CKD, specific diagnostic criteria presented in the Supplemental Material; age of at least 18 years; and completed ambulatory blood pressure monitoring (ABPM) of valid quality. Exclusion criteria encompassed known non-hypertensive causes of LVH (e.g. hypertrophic cardiomyopathy, valvular heart disease), transplant or dialysis, arrhythmias (atrial fibrillation, atrial flutter, sick sinus syndrome, II or III degree of atrioventricular block),

ongoing treatment with medium to large amounts of glucocorticoids or immunosuppressants (cyclosporine or tacrolimus), pregnancy or breastfeeding, estimated glomerular filtration rate (eGFR) fluctuations exceeding 30% within the previous 3 months, cardiocerebrovascular disease within the previous 3 months, and an unstable clinical status, including recent severe infections or aggressive malignancies.

The study protocol was approved by the Ethics Committee and the Institutional Review Board of our hospitals. Written informed consent was obtained from all patients prior to data collection.

BP measurements

Clinic brachial BP was measured at the doctor's office in a seated position using a standard oscillometric device after a 5-min rest before the ABPM device was installed. The reported clinic BP values were the mean of three measurements taken at 1–2-min intervals. All patients underwent brachial and central ABPM using MobilO-Graph PWA (IEM, Stolberg, Germany), which has been validated on the criteria of the British Hypertension Society and the European Society of Hypertension for measurement of brachial pressure [23, 24]. The accuracy of the automated oscillometric device for measuring central pressure was verified against invasive fluid-filled or gold-standard high-fidelity microtip catheters and the non-invasive, Food and Drug Administration–approved, validated SphygmoCor device [25, 26]. Brachial and central BP were obtained simultaneously. Following the conventional brachial BP measurement, pulse waves were recorded at the diastolic BP (DBP) level for approximately 10 s. After digitalisation, a three-step algorithm was applied. As there is no consensus regarding the optimal calibration method, both the brachial SBP and DBP calibration method (c1 calibration) and the mean arterial pressure (MAP) and DBP calibration method (c2 calibration) were used in the current study. The monitor process entailed automated measurements programmed at 15-min intervals during the daytime (7:00 am to 10:00 pm) and 30-min intervals at night (10:00 pm to 7:00 am). Appropriate cuff size was chosen based on the arm circumference and placed on the non-dominant arm.

Echocardiography

Trained cardiologists conducted the echocardiography procedures. Linear measurements of the left ventricular internal diameter (LVID), interventricular septum (IVS), and posterior wall thickness (PWT) were assessed using M-mode tracings at the end of diastole, according to the recommendations of the American Society of Echocardiography and the European Association of Cardiovascular Imaging [27]. Left ventricular mass (LVM) was calculated using the formula, LVM $(g) = 0.8 \times (1.04 \times [(LVID + IVS + PWT)^3 — LVID^3] + 0.6)$, which is closely related to LVM at autopsy [28]. Based on recent guidelines, the left ventricular mass index (LVMI) standardises LVM to body surface area. LVH is defined as the LVMI exceeding 115 g/m^2 in males or 95 g/m^2 in females [29].

Collection of other data

The demographic characteristics were obtained at the initial study visit and from clinical records. Routine laboratory investigations were measured using a 7180 Biochemistry Auto-analyzer (Hitachi, Tokyo, Japan) in the central laboratory. The baseline laboratory value was defined within three days of performing ABPM. Diabetes was defined as fasting glucose of at least 7.0 mmol/L, non-fasting glucose of at least 11.1 mmol/L, use of glucose-lowering drugs, or self-reported diabetes. Hypertension was defined as a systolic blood pressure of at least 140 mm Hg, diastolic blood pressure of at least 90 mm Hg, or use of antihypertensive drugs for treatment of hypertension.

Statistics

Statistical analysis was performed using SPSS 25.0 (IBM, Chicago, Illinois, USA) and R Version 4.3.0. Statistical significance was set at $P < 0.05$. The Kolmogorov–Smirnov test was employed to determine the normal distribution of the continuous variables, which are presented as the mean ± SD or median (interquartile range) based on the normality of distribution. Categorical variables are presented as frequencies and percentages. The ANOVA or nonparametric test for continuous variables and the χ^2 test for categorical variables were utilized respectively between groups. Central SBP was divided into four groups based on quartile, *P*-values for multiple comparisons were corrected according to the Bonferroni method, and *P*-trend was calculated by the Chi-square trend test. Univariate and multivariate linear or logistic regression analyses were performed to calculate the association between BP indices and LVMI or LVH. These parameters were introduced separately into each model to mitigate collinearity issues between central and brachial BP. Receiver operator characteristic (ROC) analysis was employed to determine the discriminatory potential of BP parameters in relation to LVH, with area under the curve (AUC) values and their 95% CIs calculated. The Delong method was used to compare AUCs. The net reclassification index (NRI) and integrated discrimination increment (IDI) were assessed to reclassify individuals into groups with or without LVH. According to the ambulatory brachial and central SBP thresholds, participants were categorised into four groups. Multivariate logistic regression analyses were applied to compare the occurrence of LVH across these different groups.

Table 1 Characteristics of participants

Demographic parameters	Overall ($n = 2117$)	24-h c2SBP < 135 mmHg ($n = 1664$)	24-h c2SBP ≥135 mmHg ($n = 453$)	*P*
Age	47.82 ± 12.91	46.81 ± 12.96	51.52 ± 12.00	<0.001
Sex (male), N (%)	1126 (53.2)	863 (51.9)	263 (58.1)	0.019
Body mass index, kg/m^2	24.09 ± 3.84	23.90 ± 3.67	24.75 ± 4.35	<0.001
Smoking, N (%)	617 (29.1)	459 (27.6)	158 (34.9)	0.003
Alcohol consumption, N (%)	473 (22.3)	357 (21.5)	116 (25.6)	0.060
Diabetes mellitus, N (%)	445 (21.0)	307 (18.4)	138 (30.5)	<0.001
Hypertension, N (%)	1405 (66.4)	972 (58.4)	433 (95.6)	<0.001
Cardiovascular disease history, N (%)	218 (10.3)	140 (8.4)	78 (17.2)	<0.001
Antihypertensive medication, N (%)	1489 (70.3)	1076 (64.7)	413 (91.2)	<0.001
Proteinuria (mg/24 h)	2294.81 ± 3661.13	1973.51 ± 3482.14	3529.17 ± 4053.92	<0.001
ACR (mg/g)	462.48 (86.65, 1541.72)	338.74 (57.56, 1147.02)	1232.09 (462.48, 2803.53)	<0.001
Haemoglobin(g/L)	123.52 ± 25.93	126.59 ± 24.38	112.23 ± 28.24	<0.001
Glucose (mmol/L)	4.77 (4.30, 5.40)	4.73 (4.30, 5.30)	4.88 (4.37, 5.73)	0.003
Serum phosphate (mmol/L)	1.25 ± 2.54	1.23 ± 2.85	1.33 ± 0.47	0.475
iPTH (pmol/L)	5.54 (4.06, 8.04)	5.54 (3.86, 6.78)	7.36 (5.54, 17.68)	<0.001
BUN (mmol/L)	6.40 (4.60, 10.91)	5.90 (4.40, 9.02)	10.80 (6.52, 18.70)	<0.001
Creatinine (μmol/L)	108.60 (75.00, 206.00)	99.00 (70.80, 160.33)	209.00 (105.00, 453.00)	<0.001
eGFR (mL/min/ 1.73m^2)	62.00 (28.00, 98.00)	71.00 (40.00, 102.00)	30.00 (11.00, 60.00)	<0.001
LVMI (g/m^2)	84.11 ± 24.69	79.09 ± 20.01	102.52 ± 30.79	<0.001
LVH, N (%)	313 (14.8)	138 (8.3)	175 (38.6)	<0.001
Clinic SBP (mmHg)	134 ± 22	129 ± 20	154 ± 21	<0.001
24-h bSBP (mmHg)	122 ± 16	116 ± 10	145 ± 10	<0.001
24-h c1SBP (mmHg)	115 ± 14	109 ± 10	134 ± 9	<0.001
24-h c2SBP (mmHg)	124 ± 15	118 ± 10	146 ± 10	<0.001

ACR albumin-to-creatinine ratio, *iPTH* intact parathyroid hormone, *BUN* blood urea nitrogen, *eGFR* estimated glomerular filtration rate, *LVMI* left ventricular mass normalised to body surface area, *LVH* left ventricular hypertrophy, *24-h bSBP* 24-h brachial systolic blood pressure, *24-h c1SBP* 24-h central systolic blood pressure with c1 calibration, *24-h c2SBP* 24-h central systolic blood pressure with c2 calibration

Results

Characteristics of participants

A total of 2117 non-dialysis patients with CKD were included in this study. The mean age of the participants was 47.82 ± 12.91 years, and 1126 (53.2%) participants were males. More than half of the individuals were hypertensive, and 21.0% of the patients had diabetes mellitus. The mean LVMI was 84.11 ± 24.69 g/m^2, and 14.8% of the population had LVH. The average clinic SBP was 134 ± 22 mmHg, 24-h brachial systolic blood pressure (24-h bSBP) was 122 ± 16 mmHg, 24-h central systolic blood pressure with c1 calibration (24-h c1SBP) was 115 ± 14 mmHg and 24-h central systolic blood pressure with c2 calibration (24h-c2SBP) was 124 ± 15 mmHg. The data have been categorised both below and above the threshold for 24-h c2SBP [6] (Table 1). Further details are presented in Supplementary Table S1.

Association of central pressure and LVH

The percentage of LVH by 24-h c1SBP or 24-h c2SBP quartiles among all included participants is shown in Fig. 1. The percentage of LVH in the first, second, third, and fourth quartiles of 24-h c1SBP was 5.27%, 7.95%, 13.23%, and 32.7%, respectively. A linear trend was observed with

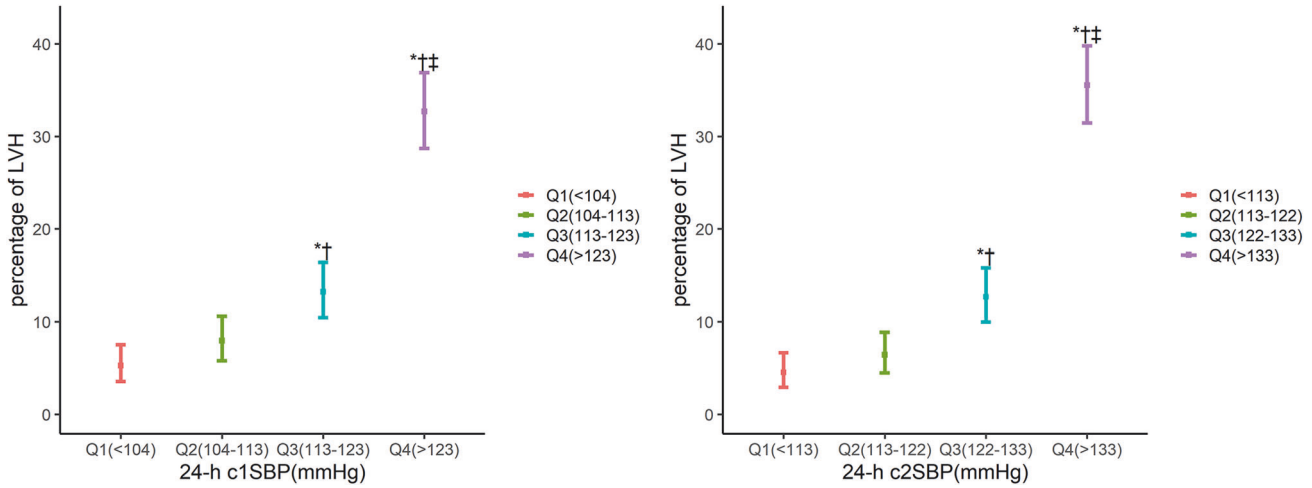


Fig. 1 Percentage of Left Ventricular Hypertrophy in Different Groups According to Quartiles of 24-h c1SBP or 24-h c2SBP. *$P < 0.05$ compared with Q1 (24-h c1SBP < 104 mmHg) or (24-h c2SBP < 113 mmHg). †$P < 0.05$ compared with Q2 (104–113 mmHg in 24-h c1SBP) or (113–122 mmHg in 24-h c1SBP). ‡$P < 0.05$ compared with Q3 (113–123 mmHg in 24-h c1SBP) or (123–133 mmHg in 24-h c1SBP). The I bar denotes the 95% confidence intervals. 24-h bSBP, 24-h brachial systolic blood pressure; 24-h c1SBP, 24-h central systolic blood pressure with c1 calibration; 24-h c2SBP, 24-h central systolic blood pressure with c2 calibration

respect to the prevalence of LVH across these groups (*P*-trend <0.001). Similarly, based on the 24-h c2SBP values, the percentage of LVH in the first, second, third, and fourth quartiles was 4.53%, 6.42%, 12.69%, and 35.54%, respectively. A linear trend was also observed in the distribution of LVH prevalence across the four groups (*P*-trend < 0.001).

Univariate and multivariate correlation of BP with LVMI and LVH

In univariate and multivariate linear regression analyses examining the associations between various BP indices and LVMI, 24-h c2SBP consistently demonstrated stronger relevance to LVMI than other indices across all models. This was evident through the largest β coefficient and the highest R-square values within the models that included 24-h c2SBP (Supplementary Table S2). Regarding univariate and multivariate logistic regression analyses aimed at exploring the associations between BP indices and LVH, clinic SBP, 24-h bSBP, 24-h c1SBP, and 24-h c2SBP were all significantly correlated with LVH. In model 4, a 10 mmHg change in 24-h bSBP, 24-h c1SBP, and 24-h c2SBP, the incidence of LVH increased by 35.2%, 33.0%, and 43.5%, respectively (Table 2). As presented in Table 2, 24-h c2SBP was more strongly associated with LVH than other induces in all models, reflected in the largest odds ratio and the highest R-square values inclusion of 24-h c2SBP in the models. Additional subanalyses were performed using multivariate logistic regression. The results remained consistent across subgroups defined by age (<45 years and >45 years), sex (female and male), CKD stage (stage 3–5), antihypertensive medication usage, and the absence of β-blocker medication. Within the subgroup of individuals aged <45 years, only 24-h c2SBP

Table 2 Univariate and multivariate logistic regression analyses of associations between BP indices and LVH (per 10 mmHg)

	BP indices	OR	95% CI		*P*	R^2
Model 1	Clinic SBP	1.433	1.354	1.518	<0.001	0.135
	24-h bSBP	1.846	1.700	2.009	<0.001	0.191
	24-h c1SBP	1.880	1.719	2.062	<0.001	0.167
	24-h c2SBP	1.944	1.784	2.125	<0.001	0.209
Model 2	Clinic SBP	1.421	1.341	1.508	<0.001	0.166
	24-h bSBP	1.875	1.722	2.046	<0.001	0.231
	24-h c1SBP	1.909	1.741	2.100	<0.001	0.208
	24-h c2SBP	1.967	1.800	2.156	<0.001	0.244
Model 3	Clinic SBP	1.220	1.133	1.315	<0.001	0.361
	24-h bSBP	1.433	1.296	1.586	<0.001	0.376
	24-h c1SBP	1.426	1.277	1.594	<0.001	0.369
	24-h c2SBP	1.509	1.361	1.676	<0.001	0.384
Model 4	24-h bSBP	1.352	1.212	1.511	<0.001	0.380
	24-h c1SBP	1.330	1.180	1.500	<0.001	0.375
	24-h c2SBP	1.435	1.283	1.607	<0.001	0.388

24-h bSBP 24-h brachial systolic blood pressure, *24-h c1SBP* 24-h central systolic blood pressure with c1 calibration, *24-h c2SBP* 24-h central systolic blood pressure with c2 calibration

Model 1: univariate logistic regression analysis

Model 2: adjusted for age and sex

Model 3: adjusted for age, sex, body mass index, alcohol consumption, smoking, diabetes mellitus, cardiovascular disease history, presence of hypertension, antihypertensive medications, haemoglobin, eGFR, and iPTH

Model 4: adjusted for age, sex, body mass index, alcohol consumption, smoking, diabetes mellitus, cardiovascular disease history, presence of hypertension, antihypertensive medications, haemoglobin, eGFR, iPTH, and clinic SBP

independently exhibited an association with LVH (Supplementary Figure S1).

Analysis for discrimination of LVH

The ROC curve analysis revealed that all BP induces significantly discriminated LVH. The AUC values were 0.718, 0.755, 0.738, and 0.768 for clinic SBP, 24-h bSBP, 24-h c1SBP, and 24-h c2SBP, respectively (Fig. 2). The Delong method demonstrated that the predictive discrimination was comparable between the clinic SBP and 24-h c1SBP ($P = 0.184$). Meanwhile, 24-h bSBP displayed greater discriminatory ability than clinic SBP ($P = 0.013$) and 24-h c1SBP ($P < 0.001$). Notably, 24-h c2SBP demonstrated a significant discriminatory power compared with 24-h bSBP regard to LVH presence ($P < 0.001$) (Supplementary Table S3). Reclassification analysis revealed that 24-h bSBP presented significantly higher discriminatory abilities compared with clinic SBP and 24-h c1SBP in the univariate and multivariate analyses. However, 24-h c2SBP exhibited significantly greater discriminatory power over 24-h bSBP in the univariate analysis (NRI = 0.383, 95% CI [0.265–0.501], $P < 0.001$; IDI = 0.016, 95% CI [0.009–0.022], $P < 0.001$) and multivariate analysis (NRI = 0.310, 95% CI [0.192–0.429], $P < 0.001$; IDI = 0.008, 95% CI [0.005–0.011], $P < 0.001$) (Table 3).

Cross-classification of central and brachial systolic hypertension

Based on the 2023 European Society of Hypertension (ESH) threshold for 24-h bSBP (threshold, 130 mmHg) [7] and the threshold for 24-h c2SBP in accordance with a recent study from a global research consortium (threshold, 135 mmHg) [6], the study population was cross-classified into four groups, namely concordant normotension (1509 individuals), isolated brachial hypertension (155 individuals), isolated central hypertension (11 individuals), and concordant hypertension (442 individuals) (Supplementary Figure S2), the characteristics of participants according to cross-classification is shown in Supplementary Table S4. Due to the limited size of the isolated central hypertension group, the multivariate logistic regression analysis encompassed the other three groups. Within these groups, the prevalence of LVH was observed in 117 (7.8%), 21 (13.5%), and 172 (38.9%) participants with concordant normotension, isolated brachial hypertension, and concordant hypertension, respectively. With concordant normotension as the reference, the multivariable-adjusted ORs were 1.097 (95% CI, 0.619–1.867; $P = 0.742$) for isolated brachial hypertension and 3.138 (95% CI, 2.285–4.318; $P < 0.001$) for concordant hypertension. Furthermore, after adjusting for clinic SBP, the multivariable-adjusted ORs were 0.954 (95% CI, 0.534–1.640; $P = 0.870$) for isolated brachial hypertension and 2.585 (95%CI, 1.841–3.633; $P < 0.001$) for concordant hypertension (Table 4). A direct comparison between isolated brachial hypertension and concordant hypertension was performed, using isolated brachial hypertension as the reference. The multivariable-adjusted ORs, were 2.984 (95% CI, 1.733–5.338; $P < 0.001$) and 2.832 after additional adjustment for clinic SBP (95% CI, 1.637–5.087; $P < 0.001$) (Supplementary Table S5).

In this study, the association of 24-h central SBP and 24-h brachial SBP with renal abnormalities were also explored, which were assessed by urine albumin/creatinine ratio > 300 mg/g and eGFR <60 ml/min/1.73m^2. The 24-h central SBP and 24-h brachial SBP were comparable in the correlation of the renal abnormalities (Supplementary Table S6). Therefore, the primary focus of this article remained on the relationship with LVH.

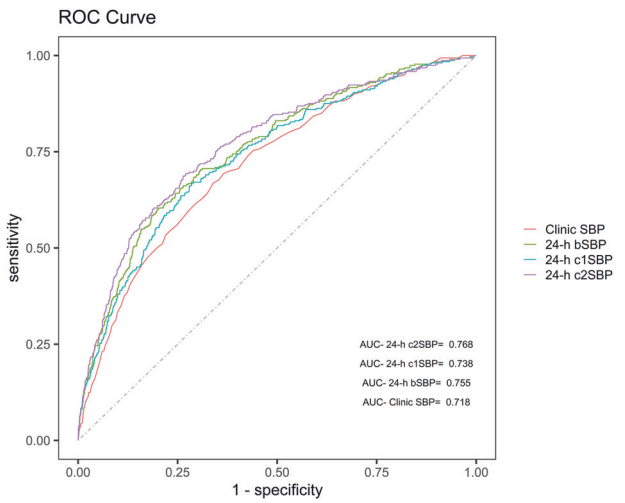


Fig. 2 Receiver operating characteristic (ROC) curve analysis assessing the BP Induces with the presence of LVH. AUC indicates the area under the curve. 24-h bSBP, 24-h brachial systolic blood pressure; 24-h c1SBP, 24-h central systolic blood pressure with c1 calibration; 24-h c2SBP, 24-h central systolic blood pressure with c2 calibration

Discussion

In this cross-sectional study, we firstly investigated whether 24-h central pressure is superior to 24-h brachial pressure on LVH in 2117 individuals with non-dialysis CKD and compared the presence of LVH between different groups according to cross-classification of the ambulatory central versus brachial hypertension. The LVH percentages showed a gradual increase with elevated central pressure, indicating a linear trend. Our findings demonstrated that 24-h c2SBP exhibited a stronger association with LVMI and LVH. Moreover, it exhibited enhanced discriminatory ability in

Table 3 Comparison of reclassification among BP Indices using the NRI and IDI regarding LVH

	BP indices	NRI	95% CI	*P*	IDI	95% CI	*P*
Model 1	Clinic SBP vs. 24-h bSBP	0.318	0.199–0.437	<0.001	0.046	0.026–0.066	<0.001
	Clinic SBP vs. 24-h c1SBP	0.178	0.059–0.298	0.004	0.028	0.009–0.047	0.004
	Clinic SBP vs. 24-h c2SBP	0.379	0.260–0.497	<0.001	0.062	0.040–0.083	<0.001
	24-h bSBP vs. 24-h c1SBP	−0.638	−0.727–−0.481	<0.001	−0.018	−0.022–−0.014	<0.001
	24-h bSBP vs. 24-h c2SBP	0.383	0.265–0.501	<0.001	0.016	0.009–0.022	<0.001
	24-h c1SBP vs.24-h c2SBP	0.622	0.506–0.739	<0.001	0.034	0.026–0.041	<0.001
Model 2	24-h bSBP vs. 24-h c1SBP	−0.343	−0.461–−0.224	<0.001	−0.005	−0.007–−0.003	<0.001
	24-h bSBP vs. 24-h c2SBP	0.310	0.192–0.429	<0.001	0.008	0.005–0.011	<0.001
	24-h c1SBP vs. 24-h c2SBP	0.320	0.202–0.439	<0.001	0.013	0.008–0.017	<0.001

24-h bSBP 24-h brachial systolic blood pressure, *24-h c1SBP* 24-h central systolic blood pressure with c1 calibration, *24-h c2SBP* 24-h central systolic blood pressure with c2 calibration

Model 1, univariate NRI or IDI analysis

Model 2, adjusted for age, sex, body mass index, alcohol consumption, smoking, diabetes mellitus, cardiovascular disease history, presence of hypertension, antihypertensive medications, haemoglobin, eGFR, iPTH, and clinic SBP

Table 4 Multivariate logistic regression analysis of associations between LVH and systolic hypertension categories

	Group	OR	95% CI		*P*
Model 1	Concordant normotension	Reference			
	Isolated brachial hypertension	1.097	0.619	1.867	0.742
	Concordant hypertension	3.138	2.285	4.318	<0.001
Model 2	Concordant normotension	Reference			
	Isolated brachial hypertension	0.954	0.534	1.640	0.870
	Concordant hypertension	2.585	1.841	3.633	<0.001

Concordant normotension: 24-h bSBP <130 mmHg, 24-h c2SBP < 135 mmHg; Isolated brachial hypertension: 24-h bSBP > 30 mmHg, 24-h c2SBP < 135 mmHg; Concordant hypertension: 24-h bSBP >130 mmHg, 24-h c2SBP > 135 mmHg

Model 1: adjusted for age, sex, body mass index, alcohol consumption, smoking, diabetes mellitus, cardiovascular disease history, presence of hypertension, antihypertensive medications, haemoglobin, eGFR, and iPTH

Model 2: adjusted for age, sex, body mass index, alcohol consumption, smoking, diabetes mellitus, cardiovascular disease history, presence of hypertension, antihypertensive medications, haemoglobin, eGFR, iPTH, and clinic SBP

predicting the presence of LVH, surpassing the predictive power of 24-h bSBP. The cross-classification of ambulatory brachial hypertension versus central hypertension revealed that the presence of LVH was greater in concordant hypertension compared with isolated brachial hypertension and concordant normotension, with no difference between the latter two groups.

LVH caused by hypertension is a marker and predictor of cardiovascular morbidity and mortality within hypertensive populations [30, 31], including those with CKD [32]. Moreover, LVH is associated with higher renal risk [10]. A prospective multicentre study by Weber et al. suggested that despite 24-h c2SBP displaying superior statistical predictiveness for LVH, the association between 24-h c2SBP and LVM demonstrated a numerical, albeit not statistically significant, advantage over that between 24-h bSBP and LVM [14]. Our study was consistent with the findings reported by Protogerou et al., wherein 24-h c2SBP was better associated with LVMI and LVH than 24-h bSBP in patients with hypertension [15]. Furthermore, another study, using the BPLab device for measuring central pressure, similarly suggested a greater correlation between 24-h central pressure and LVH over that between 24-h bSBP and LVH [16]. However, the findings of two studies, featuring sample sizes of less than 300, were inconsistent with those of our study. Hu et al. reported that the correlation coefficient between 24-h bSBP and LVMI was marginally higher than 24-h central SBP and LVMI (0.281 *vs.* 0.252), while the test was not used to compare the two different correlation coefficients, and the calibration for central pressure was not specified in the study [18]. Another study by Blanch et al. demonstrated that the 24-h central SBP did not exhibit

superiority over 24-h brachial pressure in relation to LVMI or LVH and the LVH presence discrimination among hypertensives [17].

Waveform calibration is a crucial factor since the optimal method for detecting the accuracy of central pressure remains debatable. In an invasive study, the mean difference between invasive central SBP and noninvasive central SBP with c1 calibration was −14.4 mm Hg, which was systematically higher than the mean difference of −3.0 mmHg between invasive central SBP and noninvasive central SBP with c2 calibration [26]. Furthermore, a meta-analysis suggested that the estimation error for central SBP was −1.83 mmHg and −7.78 mmHg when c2 calibration and c1 calibration were used, respectively [33]. This is likely attributed to the widely acknowledged underestimation of invasive bSBP by noninvasive cuff-based measurement [34]. In contrast, the MAP, assessing as the oscillations are maximal during cuff deflation, demonstrates significant accuracy compared with the invasive method [35]. In the current study, it was observed that 24-h c2SBP but not 24-h c1SBP was closely associated with LVH and exhibited superior discriminatory ability in predicting LVH presence compared with 24-h bSBP. A study by Argyris et al. suggested the superiority of 24-h c2SBP over 24-h bSBP in terms of assessing carotid arterial damage [36].

As reported by Weber et al., the correlation between 24-h bSBP and 24-h c1SBP was stronger compared with that between 24-h bSBP and 24-h c2SBP. Pearson's coefficient of 24-h c2SBP and 24-h bSBP within the group of individuals with 24-h bSBP ranging between 121 and 130 mmHg was as low as 0.35, indicating that 24-h c2SBP offers additional valuable information [6]. Furthermore, research has demonstrated that categorising individuals based on their clinic brachial SBP levels resulted in substantial overlap in clinic central SBP values. For instance, approximately 70% of participants with high-normal clinic brachial SBP exhibited clinic central SBP levels comparable to those with stage 1 clinic brachial hypertension [4]. Taken together, these findings suggest that the non-invasive 24-h central ABPM is a method that could improve LVH risk assessment beyond the already presented method of the 24-h brachial ABPM.

Using the cross-classification approach to distinguish ambulatory brachial hypertension versus ambulatory central hypertension by c2 calibration, our findings indicate that the presence of LVH was higher in cases of concordant hypertension compared with cases of isolated brachial hypertension and concordant normotension. However, no significant difference was observed between the latter two groups, distinctly bringing additional clinic value from 24-h c2SBP. In the subgroup where antihypertensive medications are administered to individuals with isolated brachial hypertension, there is a further reduction in the original normal central BP. This is attributed to the fact that antihypertensive drugs inevitably lower both brachial and central BP [37]. Given that BP plays a pivotal role in driving proper organ perfusion, which is critical for optimal organ function [38], it is imperative to carefully consider the treatment strategy for this subgroup. Participants with concordant hypertension might be at a higher risk of developing LVH and cardiovascular disease. Therefore, more attention should be paid to this subgroup.

As is well known that DBP is relatively constant in conduit arteries [39] and can play a role in cardiac damage [40]. To exclude the impact of DBP and allow the models to be comparable, all models were further adjusted for 24-h brachial DBP. The results were also consistent (Supplementary Table S7-9), indicating that the superiority of 24-h c2SBP in terms of LVH was independent of DBP. Certain limitations of this study warrant acknowledgement. First, the study cohort primarily comprised Chinese inpatients with CKD, making direct extrapolation of findings to other subject groups a matter of caution. However, there is a significant need for further research in this group, considering the prevalence of CKD in China is 10.8% [41], and cardiovascular events are widely perceived as the leading cause of death in this population [42]. Second, given the cross-sectional design of this study, only associations can be inferred, and cause-and-effect relationships need to be explored in prospective studies. Lastly, it is important to exercise prudence when extending the findings to other measurement devices, as the brachial and central ambulatory BP assessments were conducted using the MobilO-Graph PWA. MobilO-Graph PWA is the most widely used device for measuring ambulatory central BP, and the feasibility and reproducibility of the device to assess central haemodynamics at rest and during daily ambulatory monitoring have been validated [43, 44], including in Chinese [45].

In conclusion, our findings suggest a stronger association between 24-h c2SBP and LVH and a greater discriminatory ability for identifying the presence of LVH in non-dialysis patients with CKD compared with 24-h bSBP. Despite the close interrelation between central and brachial BP, central BP yields valuable clinical value. The presence of LVH in isolated brachial hypertension did not significantly differ from that in concordant normotension, accentuating the need for a thoughtful treatment strategy in this subgroup. Furthermore, the focus should be on addressing concordant hypertension in clinical practice to prevent adverse clinical outcomes. More prospective studies are needed to investigate the effects of antihypertensive drugs on 24-h central BP, the threshold of 24-h central BP, and its possible superiority over 24-h brachial pressure in terms of target organ damages, and cardiovascular events and death before recommending its routine use.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

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