Association of central arterial blood pressure and left ventricular hypertrophy in patients with chronic kidney disease

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Research Article

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Abstract

Aims: In the general population, central arterial blood pressure has proved to be more closely related to left ventricular hypertrophy than brachial arterial blood pressure. We aimed to investigate whether this relationship was true in patients with chronic kidney disease.

Methods: In this retrospective study, we reviewed the medical records of 289 adult patients with chronic kidney disease from the Zhejiang Provincial People's Hospital in Zhejiang, China. Demographic, echocardiographic, and brachial and central blood pressure parameters were retrieved from medical records. Central blood pressure was measured using the SphygmoCor® CvMS (AtCor, Australia) device and its corresponding software. Multivariate logistic regression analyses were performed to identify independent predictors of left ventricular hypertrophy. Receiver operating characteristic curves were used to determine the ability of central and brachial blood pressure to predict left ventricular hypertrophy.

Results: The left ventricular mass index was positively associated with both central and brachial blood pressures. However, multiple logistic regression analysis demonstrated that a central pulse pressure ≥ 58 mm Hg was an independent risk factor for left ventricular hypertrophy (OR=5.597, 95%CI 2.363-13.259, P <0.001). Brachial pulse pressure is not superior to central pulse pressure in predicting left ventricular hypertrophy (AUC = 0.695, 95%CI 0.634-0.756, P < 0.001 vs. AUC = 0.687, 95%CI: 0.626 to 0.748, P < 0.001, respectively; P = 0.4824).

Conclusions: Our results suggested that, similarly to the general population, central pulse pressure is a better parameter for predicting the occurrence of left ventricular hypertrophy in patients with chronic kidney disease.

1. Introduction

Chronic kidney disease (CKD) and its related complications are an important public health problem worldwide, and China is not an exception. According to a cross-sectional survey, the prevalence of CKD in this country is 10.8%.[1] KDIGO guideline divided CKD into five stages: stage 1 (GFR ≥ 90 ml / min / 1.73 m^2), stage2 (GFR 60–89 ml / min / 1.73 m^2), stage 3a (GFR 45–59 ml / min / 1.73 m^2), stage 3b (GFR 30–44 ml / min / 1.73 m^2), stage 4 (GFR 15–29 ml / min / 1.73 m^2), stage 5 (GFR < 15 ml / min / 1.73 m^2).[2] Cardiovascular mortality is considered the main cause of death in patients with CKD and is 2.6 times higher in such patients than in the general population.[3] In this regard, the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) CKD Cardiovascular disease (CVD) Working Group has issued a report emphasizing that CVD is a high-risk factor for death in CKD patients, and identified left ventricular hypertrophy (LVH) as the main intervention target.[4] LVH is an abnormal increase in left ventricular myocardial mass resulting from an increased afterload or diastolic overload[5] and it represents an independent predictor of cardiovascular events and mortality.[6]

It is widely accepted that blood pressure, traditionally measured with a sphygmomanometer in the brachial artery [brachial arterial blood pressure (BABP)], is directly associated with CVD and LVH. However, current evidence has shown that central arterial blood pressure (CABP) may be a more accurate predictor of cardiovascular events[7, 8] and LVH[9–11] than BABP in the general population. To our knowledge, there is no study focused on the relation between CABP and LVH in patients with CKD. The aim of this study is twofold: first, to investigate whether the CABP is a better predictor of LVH than BABP in this population, and second, to explore the risk factors for LVH.

2. Methods

2.1 Study design and participants

In this cross-sectional study, we reviewed the medical records of the Zhejiang Provincial People's Hospital in Zhejiang, China and identified 586 adults (>18 years old) with a diagnosis of CKD who had underwent CABP measurements between January 2017 and May 2019. CKD is defined as abnormalities of kidney structure or function, present for > 3 months, with implications for health. Patients with a history of general or local vasospasm (such as that following hypothermia in cardiopulmonary

bypass surgery, or of Raynaud's phenomenon), aortic stenosis (gradient > 60 mmHg), or a SphygmoCor system operation index ≤ 80 were excluded from the study. Finally, 289 patients were eligible for analysis.

This study was approved by the Medical Ethics Committee of Zhejiang Provincial People's Hospital, and was conducted in accordance with the Declaration of Helsinki (as revised in Brazil 2013). Written informed consent was obtained from each participant prior to inclusion.

2.2 Data collection

Demographic data such as age, gender, weight, height, history of smoking and drinking, duration of diabetes and hypertension, previous medical history, and current antihypertensive medication usage were collected. Whole blood samples (5–10 mL) were collected from each participant after 12–14 h of fasting to perform comprehensive blood analyses including albumin, glucose, blood urea nitrogen, creatinine, estimated glomerular filtration rate (eGFR), uric acid, potassium, sodium, calcium, magnesium, phosphate, total cholesterol, triglyceride, low-density lipoprotein cholesterol, haemoglobin, and platelet count. Regarding physical examination, the heart rate, BABP, height, and weight were measured by two clinicians in a quiet environment.

The eGFR was estimated according to the modified Modification of Diet in Renal Disease (MDRD) formula:

$eGFR$ (mL/min/1.73m^2) = $175 \times Scr^{-1.234} \times Age^{-0.179}$ (×0.79, if female)

in which Scr is the serum creatinine.[12] The body mass index (BMI) was calculated by dividing the body weight (in kilograms) by the square of the height (in meters).

2.3 Echocardiography

All echocardiographic examinations were performed by trained ultrasound physicians, in accordance with the American Society of Echocardiography guidelines.[13] The left ventricular mass (LVM) was calculated using the formula:

$$8 \times \{1.04 \times [(LVDd + LVPWd + IVSd)^3 - (LVDd)^3]\} + 0.6$$

in which *LVDd* is the left ventricular internal dimension at end-diastole, *LVPWd* the left ventricular posterior wall thickness at end-diastole, and *IVSd* the interventricular septum thickness at end-diastole.[14, 15] The left ventricular mass index (LVMI) was calculated using the formula: LVM/BSA, in which *BSA* is the body surface area. The formula used to calculate BSA was: $0.0061 \times \text{height (cm)} + 0.0128 \times \text{weight (kg)} - 0.1529$.

LVH was defined as a LVMI > 95 g/m^2 in women and >115 g/m^2 in men.[16]

2.4 Blood pressure measurement

2.4.1 CABP measurement

CABP measurements were obtained in the supine position after 10 minutes of rest, using the SphygmoCor® CvMS (AtCor, Australia, 2013) device and software. The Sphygmocor® operates through a tonometer placed on the right radial artery and is calibrated by standard cuff blood pressure. The Sphygmocor® CvMS CABP analysis option provides a derived ascending aorta waveform and a series of central artery indexes. The generalized transfer function of the SphygmoCor® software was used to estimate the CABP profile. Central systolic blood pressure (CSBP), central diastolic blood pressure (CDBP), central pulse pressure (CPP), augmentation pressure (AP), pulse wave velocity (PWV), augmentation index (AIx) and augmentation index

adjusted for 75 beats per minute of heart rate (AIx@75) were registered for analysis. To ensure consistency between measurements, recordings were discarded if the operator index was < 80%.

2.4.2 BABP measurements

BABP, including brachial systolic and diastolic blood pressure (BSBP and BDBP, respectively) was measured using the standardized American Heart Association protocol. Trained staff obtained three manual readings in the seated position after at least 10 minutes of rest.

2.5 Statistical analysis

We categorized patients into two groups according to the presence or absence of LVH and investigated the association of CABP and BABP with LVH. Summary statistics for normally distributed quantitative variables were expressed as means and standard deviations. For non-normally distributed variables, we used median and interquartile ranges; categorical data were summarized by ratios and percentages. Differences between the LVH and control groups regarding continuous variables with normal distribution were compared using the independent Student's t-test, while abnormally distributed continuous variables were compared using the Mann–Whitney unpaired test. Differences between groups were tested by chi-square statistics for proportions. Participants were categorized in quartiles according to blood pressure measurements, setting the first quartile as the reference group. The analysis of variance (ANOVA) or chi-squared tests were used to compare the covariates of CABP quartiles. Correlations between continuous variables were assessed using the Spearman correlation coefficient. Multivariate logistic regression analysis was used to identify predictors of LVH and their corresponding odds ratio (OR) and 95% confidence intervals (95% CI). Receiver operating characteristic (ROC) curves were used to evaluate the accuracy of CABP and BABP to predict LVH. Statistical significance was defined as $P < 0.05$ for all tests; all P-values were two-sided. Statistical analyses were performed using the Statistical Package for the Social Sciences (IBM Corp, Released 2016, IBM SPSS Statistics for Windows, version 24.0, Armonk, NY: IBM Corp, USA) , Prism® (version 8.0, GraphPad, San Diego, CA, USA) and MedCalc (version 19.1, MedCalc Software, Ostend, Belgium).

3. Results

3.1 General characteristics

Clinical and biochemical characteristics are shown in Table 1, while echocardiographic and blood pressure measurements are displayed in Table 2. Overall, 164 (56.7%) patients had LVH, and 125(43.3%) a normal LVMI ($P = 0.0013$, $\chi^2 = 10.361$). The mean age was 57 years old; male participants accounted for 65.7% of the population ($P = 0.003$, $\chi^2 = 8.746$). Half of participants were stage 5 CKD patients ($P < 0.001$, $\chi^2 = 61.213$) ; 29.4% underwent haemodialysis, and 15.2% peritoneal dialysis ($P < 0.001$, $\chi^2 = 33.497$).

Table 1
Baseline patient characteristics.

Variables		ALL (n = 289)	Non LVH group (n = 125)	LVH group (n = 164)	t / Z / χ^2 / F	P-Value
Age, yr		57(45,69)	54(39.5,68.5)	60(46,69)	-2.061	0.039
Sex	Men, n(%)	190(65.7%)	94(75.2%)	96(58.5%)	8.746	0.003
	Women, n(%)	99(34.3%)	31(24.8%)	68(41.5%)		
BMI, kg/m^2		23.07(20.65,25.73)	23.65(20.76,26.11)	22.79(20.50,25.18)	-1.669	0.095
CKD stages	1	39(13.5%)	30(24.0%)	9(5.5%)	61.213	< 0.001
	2	28(9.7%)	21(16.8%)	7(4.3%)		
	3	32(11.1%)	20(16.0%)	12(7.3%)		
	4	37(12.8%)	19(15.2%)	18(11.0%)		
	5	153(52.9%)	35(28.0%)	118(72.0%)		
Dialysis mode	HD	85(29.4%)	24(19.2%)	61(37.2%)	33.497	< 0.001
	PD	44(15.2%)	8(6.4%)	36(22.0%)		
	Non-dialysis	160(55.4%)	93(74.4%)	67(40.9%)		
Duration of dialysis, month	HD	29(16.5,80.5)	25.5(15.25,69)	31(17,89)	-0.747	0.455
	PD	34.5(20.25,67.75)	32.5(21,59)	34.5(19.5,71.75)	-0.38	0.709
History of smoking, n(%)	NO	210(72.7%)	87(69.6%)	123(75.0%)	1.041	0.308
	YES	79(27.3%)	38(30.4%)	41(25.0%)		
History of drinking, n(%)	NO	245(83.8%)	106(84.8%)	139(84.8%)	< 0.001	0.992
	YES	44(15.2%)	19(15.2%)	25(15.2%)		
Diabetes, n(%)	NO	209(72.3%)	97(77.6%)	112(68.3%)	3.069	0.08
	YES	80(27.7%)	28(22.4%)	52(31.7%)		
Hypertension, n(%)	NO	100(34.6%)	63(50.4%)	37(22.6%)	24.294	< 0.001
	YES	189(65.4%)	62(49.6%)	127(77.4%)		
History of cardiovascular disease, n(%)	NO	226(78.2%)	108(86.4%)	118(72.0%)	8.687	0.003
	YES	63(21.8%)	17(13.6%)	46(28.0%)		
History of cerebrovascular disease, n(%)	NO	253(87.5%)	110(88.0%)	143(87.2%)	0.042	0.837
	YES	36(12.5%)	15(12.0%)	21(12.8%)		

LVH, left ventricular hypertrophy; BMI, body mass index; CKD, chronic kidney disease; Alb, albumin, FBG, fasting blood glucose; BUN, blood urea nitrogen; Cr, creatinine; eGFR, estimated glomerular filtration rate; UA, uric acid; K, potassium; Na, sodium; Ca, calcium; Mg, magnesium; P, phosphate; TC, total cholesterol; TG, triglycerides; LDL-C, low density lipoprotein cholesterol; Hb, haemoglobin; PLT, platelet count.

The results are presented as number, percent, mean ± SD, median, 25-th and 75-th percentiles, 50-th and 75-th percentiles, or as appropriate.

Variables		ALL (n = 289)	Non LVH group (n = 125)	LVH group (n = 164)	t / Z / χ^2 / F	P-Value
Any hypertension medications, n(%)	NO	171(59.2%)	43(34.4%)	14(8.5%)	29.968	< 0.001
	YES	118(40.8%)	82(65.6%)	150(91.5%)		
Alb, g/L		35(29.6,38.95)	36.70(30.50,41.30)	34.15(29.40,37.30)	-2.775	0.006
FBG, mmol/L		4.83(4.31,5.53)	4.84(4.30,5.40)	4.82(4.32,5.65)	-0.434	0.664
BUN, mmol/L		15.9(7.81,22.37)	9.64(5.82,17.01)	18.72(12.62,23.94)	-6.777	< 0.001
Cr, μmol/L		378.4(121.95,810.05)	159.30(84.35,432.75)	534.80(297.35,896.33)	-6.795	< 0.001
eGFR, ml/min per 1.73 m^2		13.13(5.36,55.28)	40.52(12.00,86.30)	7.83(4.62,17.58)	-7.274	< 0.001
UA, μmol/L		408(340,482.5)	421.97 ± 129.18	407.77 ± 111.43	-1.001	0.318
K, mmol/L		4.2(3.85,4.78)	4.00(3.80,4.51)	4.33(3.92,5.01)	-3.843	< 0.001
Na, mmol/L		140.7(138.9,142.55)	140.70 ± 2.53	140.93 ± 3.09	0.897	0.37
Ca, mmol/L		2.2(2.04,2.34)	2.20 ± 0.25	2.18 ± 0.23	0.951	0.342
Mg, mmol/L		0.89(0.8,0.99)	0.87(0.79,0.95)	0.90(0.81,1.02)	-2.489	0.013
P, mmol/L		1.4(1.18,1.91)	1.29(1.07,1.52)	1.55(1.31,2.18)	-5.715	< 0.001
TC, mmol/L		4.46(3.5,5.65)	4.56(3.60,6.19)	4.34(3.44,5.17)	-2.294	0.022
TG, mmol/L		1.37(0.99,1.96)	1.53(1.10,2.40)	1.21(0.93,1.72)	-3.325	0.001
LDL-C, mmol/L		2.47(1.79,3.31)	2.51(1.84,3.69)	2.43(1.77,3.13)	-1.362	0.173
Hb, g/L		107.89 ± 27.14	122(102,137)	96(82.25,113)	-7.031	< 0.001
PLT, $x10^9$/L		199(157.5,241.5)	205(163,239.5)	193.50(147.50,245.25)	-1.244	0.214

LVH, left ventricular hypertrophy; BMI, body mass index; CKD, chronic kidney disease; Alb, albumin, FBG, fasting blood glucose; BUN, blood urea nitrogen; Cr, creatinine; eGFR, estimated glomerular filtration rate; UA, uric acid; K, potassium; Na, sodium; Ca, calcium; Mg, magnesium; P, phosphate; TC, total cholesterol; TG, triglycerides; LDL-C, low density lipoprotein cholesterol; Hb, haemoglobin; PLT, platelet count.

The results are presented as number, percent, mean ± SD, median, 25-th and 75-th percentiles, 50-th and 75-th percentiles, or as appropriate.

Table 2
Baseline echocardiographic and blood pressure parameters.

Variables	ALL (n = 289)	Non LVH group (n = 125)	LVH group (n = 164)	t / Z	P-Value
AO(mm)	31(28,34)	31(28,33)	31(28,34)	-0.675	0.5
LA(mm)	37(33.5,41)	35(32,38)	39.5(35,43.75)	-6.669	< 0.001
LVEF(%)	64(60,68)	65(61.5,69)	63(59,66.75)	-3.945	< 0.001
LVDd(mm)	49(46,53)	47(43,50)	52(48,55)	-8.019	< 0.001
LVDs(mm)	32(29,35)	30(27,33)	33(31,37)	-7.497	< 0.001
IVST(mm)	10(9,12)	9(9,10)	11(10,13)	-10.126	< 0.001
PWT(mm)	10(9,12)	9(8.5,10)	11(10,13)	-9.598	< 0.001
LVM(g)	194.16(147.97,241.60)	147.78(127.81,170.05)	227.73(194.21,272.18)	-12.234	< 0.001
LVMI(g/m^2)	116(90.38,146.68)	88.37(79.54,99.80)	144.21(122.93,166.48)	-14.048	< 0.001
BSBP, mm Hg	145(130,157)	140(120,150)	150(140,160)	-5.361	< 0.001
BDBP, mm Hg	80(75,90)	80(75,90)	80.5(75,92)	-0.710	0.478
BPP, mm Hg	59(48,71.5)	52(44.5,60)	65(50,79.75)	-5.444	< 0.001
Aix, %	28(19.5,34)	25(15.5,33)	30(22,35)	-3.019	0.003
Aix@75, %	27(18.5,33)	24(14,31)	29(21,34)	-3.520	< 0.001
AP, mmHg	13(7,19)	10(5,15)	15.5(9,22)	-4.831	< 0.001
HR, beats/min	71(65,81)	71(64,79)	72(65,82)	-0.711	0.477
CSBP, mm Hg	132(118,142.5)	124(112,136.5)	135.5(126,148)	-5.412	< 0.001
CDBP, mm Hg	83(75,92)	82(75.5,91)	83(75,94)	-0.676	0.499
CPP, mm Hg	45(35,58)	40(30,48)	52(37.25,63)	-5.683	< 0.001
PWV, m/s	10.6(8.4,13.95)	9.70(7.90,13.20)	11.55(8.75,14.48)	-3.198	0.001

AO, aortic diameter; LA, left atrium; LVEF, left ventricular ejection fraction; LVDd, left ventricular internal dimension in diastole; LVDs, left ventricular end-systolic diameter; IVST, interventricular septum thickness in diastole; PWT, left ventricular posterior wall thickness in diastole; LVM, left ventricular mass; LVMI, left ventricular mass index; BSBP, brachial systolic blood pressure; BDBP, brachial diastolic blood pressure; BPP, brachial pulse pressure; Aix, augmentation index; Aix@75, augmentation index adjusted for a 75 bpm heart rate; AP, augmentation pressure; HR, heart rate; CSBP, central systolic blood pressure; CDBP, central diastolic blood pressure; CPP, central pulse pressure; PWV, pulse wave velocity.

The results are presented as number, percent, mean ± SD, median, 25-th and 75-th percentiles, 50-th and 75-th percentiles, or as appropriate.

3.2 Differences between participants with and without LVH

Regarding blood pressure measurements, CSBP, CPP, BSBP, BPP, AIx, AIx@75, AP, and PWV were all significantly elevated in patients with LVH in comparison to patients with normal LVMI (Table 2). Other variables such as the BMI, fasting blood glucose, BDBP, and CDBP were not significantly different between groups.

3.3 Correlation between LVH and blood pressure measurements

As central and brachial blood pressure increased, the incidence of LVH did so proportionately. The incidence of LVH in the highest quartile was approximately 50% higher than in the lowest quartile (Fig. 1-A). Similarly, a direct relation between pulse

pressure (both CPP and BPP) and LVH was noticed (Fig. 1-B).

3.4 Multivariate logistic regression analysis

Multivariate regression analysis revealed that a CPP ≥ 58 mm Hg constituted an independent risk factor for LVH (OR = 5.597; 95% CI: 2.363 −13.259, P < 0.001 compared to the lowest quartile) (Table 3). The multivariate logistic regression model was constructed using forward method. The full model (-2 log likelihood = 293.099), model chi-squares (df = 8) = 5.146, p = 0.742. Additionally, phosphate and haemoglobin levels remained significantly associated with LVH after adjustment for several variables.

Table 3
Multivariate logistic regression analysis to identify predictors of LVH

Variable and Level, mmHg	Model1					
	OR(95%CI)	P-Value	overall P-Value	B	S.E.	Wald
Quartile group of central pulse pressure, mm Hg						
<35			< 0.001			31.801
35 to < 45	0.549(0.248–1.215)	0.139		-0.600	0.406	2.190
45 to < 58	2.191(1.011–4.750)	0.047		0.784	0.395	3.947
≥58	5.597(2.363–13.259)	< 0.001		1.722	0.440	15.318
P, mmol/L	3.212(1.784–5.786)	< 0.001		1.167	0.300	15.125
Hb, g/L	0.973(0.961–0.985)	< 0.001		-0.027	0.006	20.143
Adjusted for age, weight, height, blood urea nitrogen, creatinine, estimated glomerular filtration rate, potassium, magnesium, phosphate, total cholesterol, triglycerides,						
haemoglobin, haemodialysis, peritoneal dialysis, hypertension, history of cardiovascular disease, use of any antihypertensive medication. LVH, left ventricular hypertrophy;						
P, phosphate, Hb, haemoglobin. B, Bst coefficient. S.E., St. error. The results are presented as number, percent, mean ± SD, median, 25-th and 75-th percentiles,						
50-th and 75-th percentiles, or as appropriate.						

3.5 ROC curves

ROC curves were used to compare the ability of central and brachial pulse pressures to predict LVH. The area under the curve (AUC) for CPP and BBP was 0.695 (95%CI: 0.634–0.756; P < 0.001) and 0.687 (95%CI: 0.626 to 0.748; P < 0.001), respectively. When the cut-off of CPP is 45.5, the sensitivity was 64.60% and the specificity was 70.40%, with the value of sensitivity + specificity considered to be maximal. When the cut-off of BPP is 62.5, the sensitivity was 52.4% and the specificity was 77.60%, with the value of sensitivity + specificity considered to be maximal. Z-statistics for ROC is 0.702 (Fig. 2). Likewise, the ROC curve analysis was also conducted on pair-wise comparison between BPP and CPP. Pairwise comparison of ROC curves showed P = 0.4824, difference between area = 0.00846, standard error (DeLong et al.) = 0.0120, 95% CI = -0.0152 to 0.0321, z statistics = 0.702. Therefore, we found that BPP is not superior to CPP in the diagnosis of LVH.

4. Discussion

In summary, our study found that CPP has a strong association with LVH in CKD patients. LVH is a sign of subclinical organ damage, and is closely associated with an increase in cardiovascular morbidity and mortality in CKD patients. Although

brachial measurement is the preferred method for assessing blood pressure due to its simplicity and universal applicability, many simple, non-invasive methods for measuring CABP are available as well. These include pulse recording through arteries (carotid artery, brachial artery, radial artery), pulse acquisition technology (pressure measurement, echo tracking), pulse wave calibration, and mathematical analysis (transfer function, wave analysis).[17, 18] Summarize the studies with CABP on several clinical outcomes (Supplementary Table S1). Due to the pulse wave amplification effect, the peripheral arterial pressure is always greater than the corresponding aortic pressure. However, these are not strictly and proportionately related, so a normal peripheral arterial blood pressure can coexist with an increased CABP. It has been found that the latter is more closely related to LVH pathophysiology than peripheral blood pressure.[19]

Although non-invasive CABP measurement is widely used to predict cardiovascular outcomes in patients with coronary heart disease and hypertension, few studies including CKD patients were available to date.[20] In our study, non-invasive CPP (r = 0.288, P < 0.001) and BPP (r = 0.312, P < 0.001) have a strong relationship with LVMI. We found that BPP is not superior to CPP in predicting LVH [AUCs : CPP 0.695 (95%CI: 0.634–0.756, P < 0.001) vs BPP 0.687 (95%CI : 0.626–0.708, P < 0.001) P = 0.4824]. However, our study found that CPP is an independent risk factor for LVH (OR = 5.597, 95%CI : 2.363–13.259, P < 0.001). Previous studies[9, 21] and a meta-analysis[22] suggested that CABP is a stronger predictor of LVH than peripheral blood pressure. However, a study conducted by Rahman et al[23] in CKD patients (eGFR between 20 and 70 ml/min per 1.73 m^2), found that CABP was not superior to BABP in predicting cardiovascular events. Our study differs in that we included patients with an eGFR < 20 ml/min per 1.73 m^2. Because the lower the eGFR of the patient, the worse the kidney function, the greater the risk of cardiovascular death. Therefore, we believe that the cardiovascular accidents of these patients deserve our attention.

We found that after adjusting for confounding factors, CPP remained independently associated with LVH (OR = 5.597, 95%CI : 2.363–13.259, P < 0.001). Clinical studies have shown that pulse pressure is an independent predictor of cardiovascular and all-cause mortality in the general population[24, 25] and in patients with CKD.[26, 27] CABP pressure wave includes two parts: a forward wave produced by ventricular ejection and a reflected wave resulting from peripheral blood vessels stiffness. When the pressure wave travels from the elastic aorta to a hardened brachial artery, the upper part of the pressure wave becomes narrower, the systolic peak becomes more prominent, the systolic and pulse pressure increases, and the left ventricular afterload raises. This process leads to LVH, left ventricular diastolic dysfunction, and impaired coronary perfusion.[28] As the diameter of peripheral arteries decreases progressively, the stiffness increases; this changes the sum of wave reflections at specific points in the arterial tree, leading to an augmentation of pulse pressure and making the CPP lower than the BPP.

Notably, haemoglobin (OR = 0.973, 95%CI : 0.961–0.985, P < 0.001) and phosphate (OR = 3.212, 95%CI = 1.784–5.786, P < 0.001) levels also revealed to be independent predictors of LVH. Anaemia is a common clinical manifestation of CKD, mainly due to insufficient secretion of erythropoietin. Previous studies have shown that long-term flow/volume overload can lead to increased cardiac work in patients with chronic anaemia, leading to progressive heart enlargement and LVH.[29] Decreased Hb levels trigger left ventricular remodelling and increase ejection fraction and peak oxygen consumption in exercise tests[30]. Park et al[31] found that a decrease in Hb was significantly associated to LVH; this association was also present in non-anaemic participants. Their conclusions are consistent with the conclusions of our research.

Finally, some studies have reported that elevated serum phosphate levels are independently associated with LVH and an increased risk of CVD in CKD patients.[32] This is consistent with our conclusion. Elevated phosphate levels may stimulate the transformation of vascular smooth muscle cells into cells with an osteoblast phenotype, increase intracellular calcium levels, and induce arterial calcification.[33, 34] Furthermore, hyperphosphatemia can increase the levels of circulating fibroblast growth factor-23, which may contribute to the development of LVH.[33, 34]

All in all, our research confirmed that CABP and BABP are strongly related to LVH in patients with CKD. Furthermore, we have found that the measurement of BPP may be not superior valuable than CPP for assessing the risk of LVH in this CKD population. Anaemia and high levels of serum phosphate could lead to the development of left ventricular hypertrophy in CKD patients.

Our research has some limitations. First, our study is a single-center, cross-sectional observational study, and a causal relationship between blood pressure and clinical outcomes cannot be proven. Despite this limitation, our study is the first to propose a relation between CPP and LVH in CKD patients; future prospective cohort studies addressing the same clinical problem may confirm our results. Second, as we restricted our analysis to patients with CKD, our results cannot be generalized to other populations. Finally, in our study, half of the subjects received antihypertensive drugs which may affect CABP measurements. Although we adjusted our analysis for the usage of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, calcium channel blockers, and β-blockers, the effect of antihypertensive therapy on CABP deserves further investigation.

5. Conclusion

In summary, our study found that an increased CPP and phosphate levels, and decreased haemoglobin levels are independent risk factors for LVH in CKD patients. In this population, the measurement of BPP may be not superior valuable than CPP for assessing the risk of LVH.

Furthermore, in light of the current evidence, we speculate that CABP measurement in CKD patients might prove to be advantageous over BABP in terms of predicting hard outcomes such as CVD and mortality, and we make a call for further research in this area. Finally, proper treatment of elevated CPP and optimization of phosphate and haemoglobin levels may minimize the risk of LVH in CKD patients.

Declarations

Ethics approval and consent to participate

This study was approved through the local ethics committee of Zhejiang Provincial People's Hospital (Approval Number: 2021QT017). The study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. All participants have given their written informed consent.

Consent for publication

Not applicable.

Availability of data and material

The datasets used and/or analysed in this study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Authors' contributions

All authors conceived and designed the experiments. QH planned and coordinated the study and designed the protocol. RYC, LNS, YFZ, and JSZ collected the data. RYC, LNS and YML carried out the statistical analysis. RYC drafted the manuscript. All authors revised the manuscript and read and approved the final version. All authors contributed to the interpretation of results and act as guarantors for the integrity of the data and the accuracy of the data analysis.

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Figures

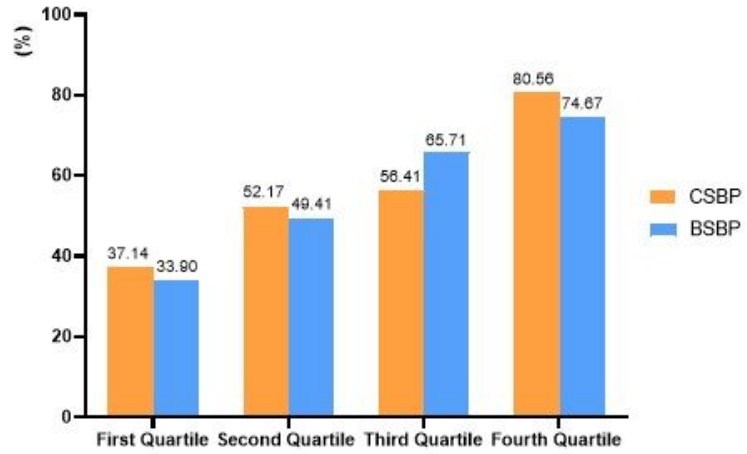


Figure1-A

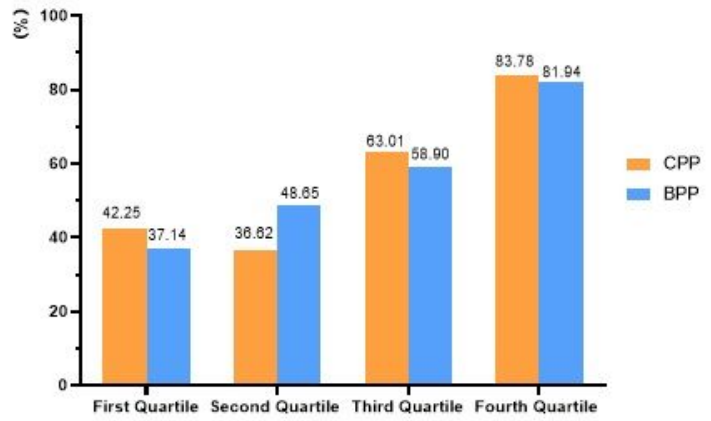
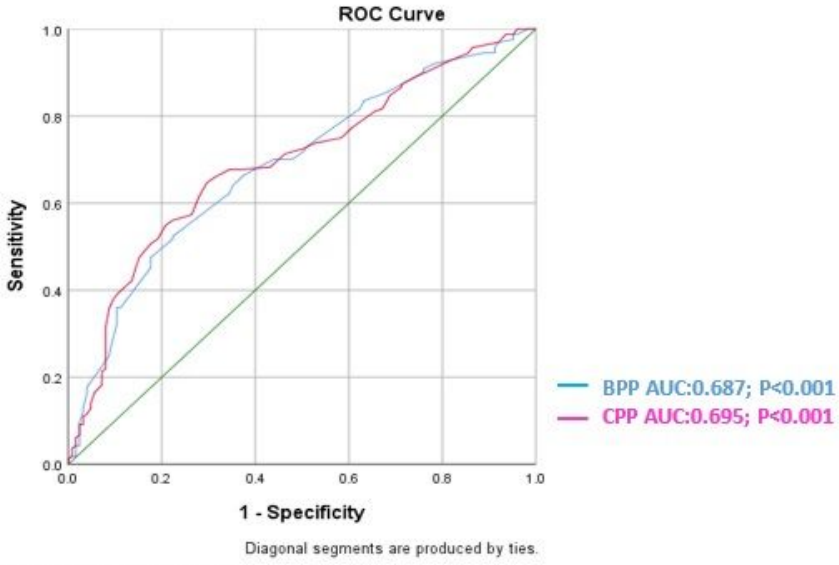


Figure 1-B

Figure 1

Incidence of left ventricular hypertrophy according to central and brachial systolic blood pressure (A) and pulse pressure (B) quartiles.



BPP, brachial pulse pressure; CPP, central pulse pressure;

Figure 2

Receiver operating characteristic curves for central and brachial pulse pressures for the prediction of LVH.

Supplementary Files

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- SupplementaryTableS1.docx