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Central Pulse Pressure in Chronic Kidney Disease: A CRIC Ancillary Study

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Abstract

Central pulse pressure can be non-invasively derived using the radial artery tonometric methods. Knowledge of central pressure profiles has predicted cardiovascular morbidity and mortality in several populations of patients, particularly those with known coronary artery disease and those receiving dialysis. Few data exist characterizing central pressure profiles in patients with mild-moderate chronic kidney disease who are not on dialysis. We measured central pulse pressure cross-sectionally in 2531 participants in the Chronic Renal Insufficiency Cohort study to determine correlates of the magnitude of central pulse pressure in the setting of chronic kidney disease. Tertiles of central pulse pressure (CPP) were < 36 mmHg, 36–51 mmHg and > 51 mmHg with an overall mean (± S.D.) of 46 ± 19 mmHg. Multivariable regression identified the following independent

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correlates of central pulse pressure: age, gender, diabetes mellitus, heart rate (negatively correlated), glycosylated hemoglobin, hemoglobin, glucose and PTH concentrations. Additional adjustment for brachial mean arterial pressure and brachial pulse pressure showed associations for age, gender, diabetes, weight and heart rate. Discrete intervals of brachial pulse pressure stratification showed substantial overlap within the associated central pulse pressure values. The large size of this unique chronic kidney disease cohort provides an ideal situation to study the role of brachial and central pressure measurements in kidney disease progression and cardiovascular disease incidence.

Keywords

Elasticity; epidemiology; diabetic nephropathies; hemodynamics; gender

Introduction

Chronic kidney disease (CKD) confers a substantial risk of cardiovascular target organ damage, especially when kidney function falls below 60 mL/min/1.73m^2 corresponding to National Kidney Foundation stages 3, 4 and 5 1 2 that appears inadequately explained by traditional cardiovascular risk factors 3. One goal of the Chronic Renal Insufficiency Cohort (CRIC) study is to examine traditional and novel risk factors for cardiovascular target organ damage and for progressive loss of kidney function in a diverse population with CKD 4. High blood pressure is known to influence the course of kidney disease progression 5. In recent years some data suggest that the pulse pressure (the difference of systolic and diastolic blood pressure) as derived from the standard brachial blood pressure measurement is better correlated than traditional blood pressure measures (systolic, diastolic) to the rate at which estimated glomerular filtration rates (eGFR) decline in CKD 6.

Measurements of central pulse pressure have been used for more than two decades in an attempt to improve further upon the predictive value of standard brachial blood pressure measurements 7. Studies have shown that there is substantial variability in the level of blood pressure in the aorta between people with similar brachial blood pressure measurements that is difficult to estimate without performing either an invasive or a non-invasive assessment of aortic pressure 8. The increasing use of validated non-invasive devices that estimate central blood pressure profiles based on radial artery tonometry has facilitated the incorporation of these measurements into prospective cohort studies such as the Anglo-Cardiff Collaborative Trial 9, the Strong Heart Study [10] and CRIC (which included measurements of central (aortic) pulse pressure using radial artery tonometry as an ancillary study beginning in 2005).

Aging has a marked effect upon the relationship between central and brachial pulse pressure, as does female gender [11]. However, little is known about the determinants of central aortic pressure pulse in the setting of CKD. Thus we aimed to determine clinical factors independently associated with central pulse pressure in CKD, and to evaluate how well brachial pulse pressure correlates with central pulse pressure in a large, ethnically diverse population of men and women with CKD.

Methods

Participants

Enrollment characteristics of the CRIC study have been previously described in detail [12]. Central aortic pulse pressure measurements were adopted into the CRIC protocol beginning at the second annual follow-up visit and all participants enrolled in the CRIC study were invited to become part of this ancillary protocol. The procedures were approved by the Institutional Review Boards at the 7 clinical centers and all participants provided written informed consent.

Procedures

Central pulse pressure measurements were performed supine after at least 5 minutes of rest using the Sphygmocor PVx System (AtCor Medical, West Ryde, Australia) via the right radial artery at all CRIC sites. All personnel were trained and certified to take blood pressure measurements in the dominant arm with a Tyco aneroid sphygmomanometer using American Heart Association standards and to perform the central pressure measurements using radial artery tonometry [13] 14. The operator captured 10 seconds of stable radial artery waveform. Pulse pressure was defined as the difference between the systolic and the diastolic blood pressure in mmHg. When this data was derived from standard blood pressure measurement it was brachial PP; when derived by algorithm from the radial artery waveform it was CPP.

Laboratory measures

Hemoglobin values were measured directly at the laboratories of each of the centers. Standard laboratory testing (e.g. serum creatinine, glucose, uric acid, calcium and phosphorous, etc.) was performed at the CRIC central laboratory in the University of Pennsylvania. The estimated glomerular filtration rate (eGFR) was determined according to the abbreviated MDRD formula using creatinine values calibrated to the Cleveland Clinic Laboratory [15]. Some laboratory results were only available at the baseline visit and are noted in Table 1.

Race

Race was classified as American Indian/Alaskan Native, Asian/Asian American, Black/African American, Native Hawaiian/Other Pacific Islander or White/Caucasian based on participant self-report.

Central Pulse Pressure Data

The data reported here represent central aortic pulse pressure measures obtained on participants whose second annual follow up visit occurred on or before March 31, 2009. The augmentation index is a ratio that reflects the portion of the central pulse pressure derived from pulse wave reflection.

Statistical Analyses

Continuous data are presented as mean ± standard deviation (S.D.). Categorical variables are expressed as proportions. Independent variables were pre-specified for analyses based on previous studies showing a relation to central pulse pressure (such as age, systolic blood pressure) or because they may affect pulse pressure and are known to be affected by kidney disease (such as calcium, hemoglobin). A plot of central pulse pressure in our population showed a substantial rightward skew and analyses were performed on both raw CPP data and natural-log-transformed data. Univariable regression models for central pulse pressure were used to assess the relationship between CPP and the selected variable. We performed multivariable linear regression to examine the associations between variables of interest and central pulse pressure [16]. All parameters significant at a $p \leq 0.20$ level in univariable regression were entered into both forward and backward selection algorithms. Where variables were known to be strongly correlated with each other (e.g. serum creatinine and eGFR) only the one with the stronger association was entered. Variables significant at the $p \leq 0.05$ level in the multivariable model were retained in the final model.

We considered two multivariable regression models: one with LnCPP as the outcome, ***without*** measures of brachial blood pressure as predictor; and one with LnCPP as the outcome, ***including*** measures of natural log-transformed brachial pulse pressure and brachial mean arterial pressure as predictors. All multivariable models were adjusted for clinical site. Analyses were executed in SAS 9.1 (SAS Institute, Cary, NC).

Results

Demographic characteristics of all participants eligible for central pulse pressure measurement at the year 2 follow up visit of the CRIC cohort are shown in Table 1, overall and stratified by those who did or did not have a successful central pulse pressure measurement. We anticipated data loss on approximately 20% of participants (due to arrhythmia and other difficulties with waveform capture) and we were unable to obtain or use measurements on 746 of 3277 eligible participants (22.7%).

Figure 1 shows the frequency distribution of central pulse pressure determinations in the overall sample and stratified by diabetes status. The tertiles of the central pulse pressure were < 36 mmHg, 36–51 mmHg and > 51 mmHg with an overall mean value of 46 ± 19 (S.D.).

Figure 2 presents mean central pulse pressure values for the cohort by strata of renal function that correspond to CKD stages. Given the large number of participants in CKD stage 3 (30–59.9 mL/min/1.73m^2 we divided this stage into stage 3A (45–59.9 mL/min/1.73m^2) and 3B (30–44.9 mL/min/1.73m^2). Each 10 mL/min/1.73m^2 decrement in eGFR was associated with an increase in central pulse pressure of about 2.5 mmHg (Table 2). A central pulse pressure of 50 mmHg was recently shown to be a significant independent predictor of cardiovascular outcomes in the Strong Heart Study where it represented the lower boundary of the highest quartile [17]. Figure 2 shows the increasing proportion (%) of those within each declining eGFR strata in CRIC that had a central pulse pressure ≥ 50 mmHg.

Table 2 displays the results of univariable regression of demographic, hemodynamic and laboratory data of our participants on central pulse pressure. The strongest univariable associations with central pulse pressure were presence of diabetes, brachial pulse pressure and brachial systolic blood pressure, decade of age, female gender, non-white ethnicity, serum calcium, the number of antihypertensive medications taken regularly and lower eGFR level.

Multivariable analyses are described in Table 3a–3c. In the absence of an adjustment for brachial blood pressure (Table 3a), there were independent contributions to the natural log-transformed central pulse pressure (LnCPP) that included age (10 years), gender, diabetes, heart rate, glycosylated hemoglobin (HbA_1C), hemoglobin, glucose and serum PTH concentration at baseline. When brachial pulse pressure and brachial mean arterial pressure were incorporated into the model (Table 3b) gender was the strongest non-blood pressure predictor term for LnCPP followed by age (10 years), diabetes, weight (per 10 kg) and heart rate. Weight and heart rate had negative influences on LnCPP. Glucose, glycosylated hemoglobin, hemoglobin and PTH concentrations were no longer independently associated with LnCPP. Table 3c shows that most of the variability in the multivariable model predicting LnCPP is explained from the natural log-transformed brachial pulse pressure. In the supplemental Table (online) we expanded our multivariable regression incorporating the time to central wave reflection (Tr) and augmentation index into the model to pursue these avenues as possible mechanisms by which these clinical factors might influence CPP, demonstrating that addition of augmentation index may mediate the effect of several clinical predictors of CPP, while aortic Tr was not a predictor of CPP in univariate or multivariable analysis. We refer the reader to the supplemental data section available at http://hyper.ahajournals.org for further details.

When discrete intervals of brachial pulse pressure were plotted against their corresponding levels of central pulse pressure there was a substantial overlap within the associated central pulse pressure values (Figure 3).

Discussion

We performed central aortic pressure measurements on a population of 2531 participants recruited specifically with impaired kidney function but not on dialysis, of whom approximately half were diabetic. Our results indicate that that central pulse pressure values are positively and independently correlated with increasing brachial pulse pressure, older age, female gender and the presence of diabetes in a population of participants with CKD. In addition we found a significant, though weaker, negative correlation between weight and heart rate, as noted in some other studies of central blood pressure [18]. Our results confirm a substantial overlap in central pulse pressures when participants are stratified by discrete levels of brachial-derived pulse pressures (Figure 3). This report adds to the literature because it examined a uniquely large cohort with a spectrum of kidney dysfunction at high cardiovascular risk, a population infrequently studied using central pressure measures. Reproducibility of central blood pressure measurements has been shown by others in non-CKD populations [19 20]. In addition our prior work in this CKD population as well as that of others[21 22] shows good reproducibility supporting the validity of these findings.

Central pressure measurements offer the opportunity to estimate the pulse pressure that the left ventricle and aorta actually "see" [7]. As the pressure wave travels from the elastic central vessels into the muscular arterial conduits there is a varying degree of increase ('amplification') in the systolic pressure whereas there is little change in diastolic or mean arterial pressure in the circulation. This rise in blood pressure is often expressed as an amplification ratio (defined as the pulse pressure in the brachial artery divided by the central aortic pulse pressure) [8]. As shown in our study and by others knowledge of the brachial blood pressure is an imperfect estimate of central blood pressure levels 8 (Figure 3).

Studies comparing brachial pulse pressure compared with central pulse pressure using outcomes such as left ventricular mass, or the occurrence of cardiovascular target organ damage (carotid intima-media thickness, or death) have shown independent predictive value for central pulse pressure measurements [23] 24 25 10 [26]. On the other hand, a recent meta-analysis of cardiovascular outcomes in longitudinal studies in which central hemodynamic measures were incorporated showed that whereas both central pulse pressure and the AIX predicted cardiovascular events and mortality, only the AIX did so independently of the brachial blood pressure [27]. The kidney is particularly vulnerable to increased pulsatile stress as reviewed recently by Loutzenhiser [28].

Patients with CKD [1 29] and end stage renal disease have substantial cardiovascular risk [30 31]. In a study of 349 subjects with CKD stages 4/5 a brachial pulse pressure of > 80 mmHg was an independent predictor of cardiovascular death or progression to ESRD requiring dialysis [32]. In a non-CKD population, the Strong Heart Study, central pulse pressure measures were superior to brachial pulse pressure in predicting carotid intima-media thickness and cardiovascular outcomes [10]. A second analysis of the Strong Heart Study data, including additional follow up time, derived a central pulse pressure of 50 mmHg or higher as a clinical meaningful threshold for increased cardiovascular target organ damage [17]. For that reason we chose to show the proportion of our populations, stratified by kidney function, with a central pulse pressure above 50 mmHg recognizing our study is observational while the Strong Heart Study data were longitudinal (Figure 2). The recognition that reduced kidney function in CKD is related strongly to cardiovascular disease morbidity and mortality has stimulated an ongoing search for biologic markers beyond traditional Framingham risk factors since these explain some but not all of the extra cardiovascular burden in CKD [1 33].

Our study had several limitations. We were unable to successfully capture radial pulse waveforms in about 23% of our CKD participants and there were differences in patient

characteristics between those with versus without successful waveforms. Importantly, though, the brachial pulse pressure was identical in both groups. Some laboratory values are only available at the baseline visit which occurred about 2 years before the first central pulse pressure measurement and these may have changed between baseline and the second year follow up visit. This caveat applies especially to glycosylated hemoglobin and serum PTH concentrations. Lastly, our participants take a number of antihypertensive medications which may affect CPP, although we did not find an independent effect of the number of antihypertensive agent classes taken.

Our findings in this large, diverse and unique CKD population show associations of age, gender, diabetes, heart rate, brachial systolic and pulse pressure with central pulse pressure. These are important associations in a group with such exceptional cardiovascular disease burden and are imperfectly represented by standard brachial pulse pressure determinations. The low resistance nature of the renal circulation predisposes the kidney to pressure-mediated damage [34]. Brachial pulse pressure measures have been shown to predict both the development of CKD and the rate of loss of kidney function when CKD is already present. Knowledge of brachial pulse pressure is an imperfect predictor of central pulse pressures, thus, measures of central pulse pressure may be useful in patients with CKD to quantify their risk of cardiovascular disease and CKD progression. The role of central pulse pressure in predicting progressive kidney function loss as well as incident cardiovascular disease in established mild-to moderate CKD remains to be seen.

Perspectives

Our findings in this large, diverse and unique CKD population show associations of age, gender, diabetes, heart rate, brachial systolic and pulse pressure with central pulse pressure. These are important associations in a group with such exceptional cardiovascular disease burden and are imperfectly represented by standard brachial pulse pressure determinations. The low resistance nature of the renal circulation predisposes the kidney to pressure-mediated damage. Brachial pulse pressure measures have been shown to predict both the development of CKD and the rate of loss of kidney function when CKD is already present. Knowledge of brachial pulse pressure is an imperfect predictor of central pulse pressures, thus, measures of central pulse pressure may be useful in patients with CKD to quantify their risk of cardiovascular disease and CKD progression. The role of central pulse pressure in predicting progressive kidney function loss as well as incident cardiovascular disease in established mild-to moderate CKD remains to be seen. Longitudinal data from CRIC and other studies pursuing the value of central blood pressure measures will clarify further this important issue.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Marshall Joffe, MD, had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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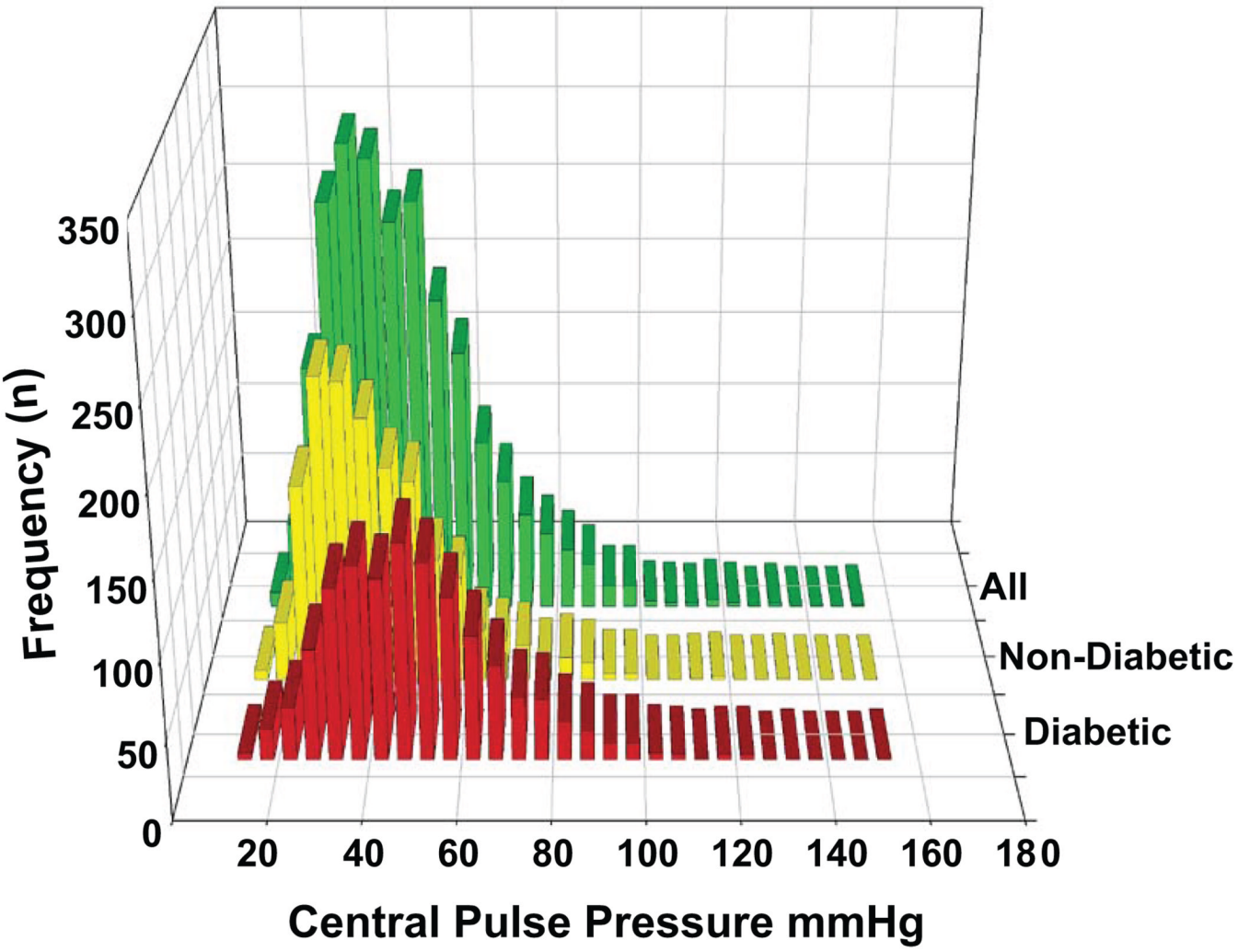

Figure 1.
Plot of Central Pulse Pressure in 5 mmHg increments along X-axis and number of participants in that increment on Y-axis. Green bars are all CRIC participants (n=2531). Yellow bars are those ***without*** (n=1343) and Ochre bars are those ***with*** (n=1188) diabetes.

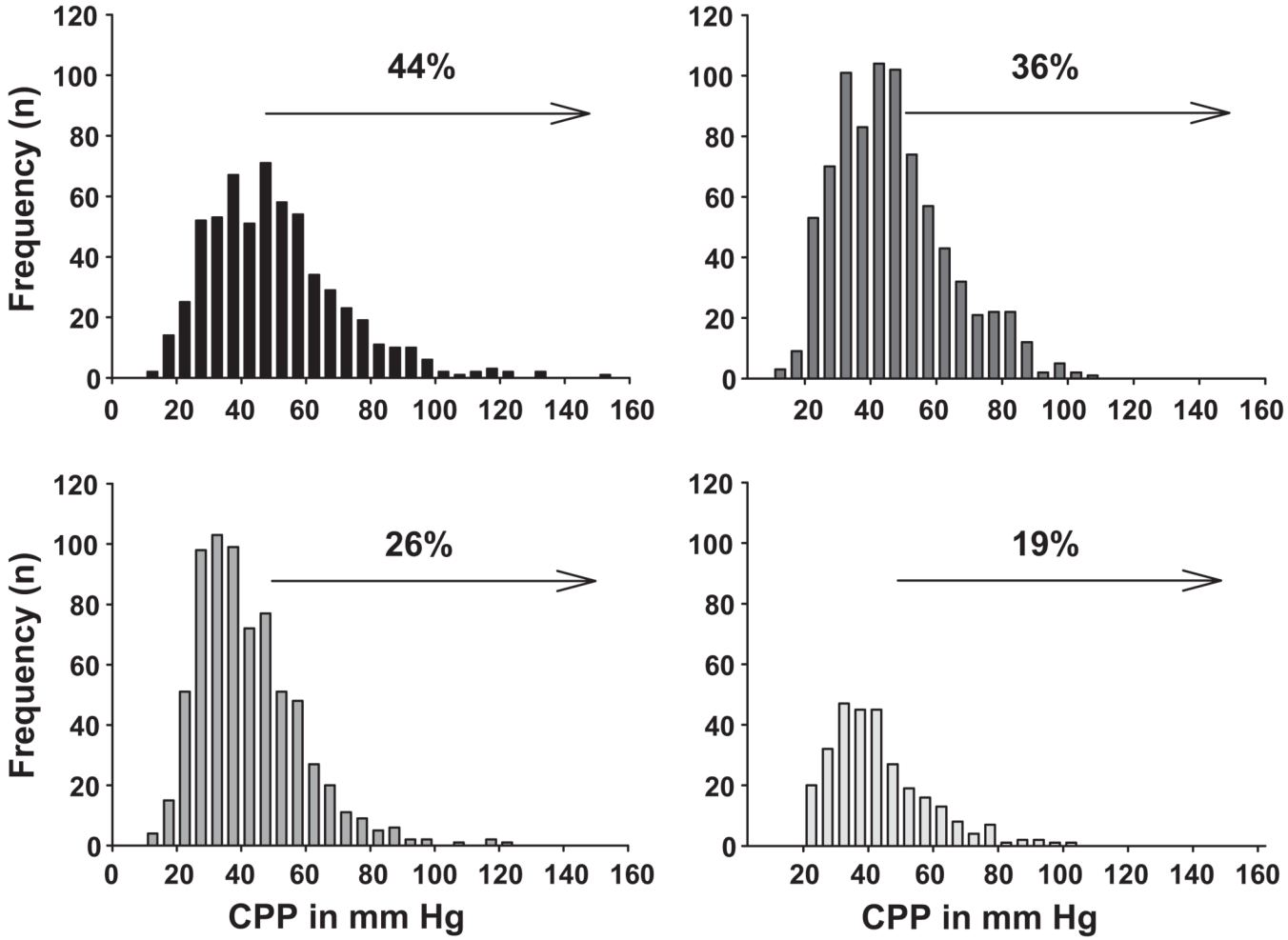

Figure 2.

Upper Left panel plots central pulse pressure in 10 mmHg increments among those with eGFR < 30 mL/min/1.73m2. Upper Right plots those with eGFR 30–44.9, Lower Left plots those with eGFR of 45–59.9 and the Lower Right panel depicts those with an eGFR > 60. Arrow onset marks Central Pulse Pressure (CPP) of 50 mmHg and percent (%) indicates the portion of participants within that eGFR range with a CPP > 50 mmHg.

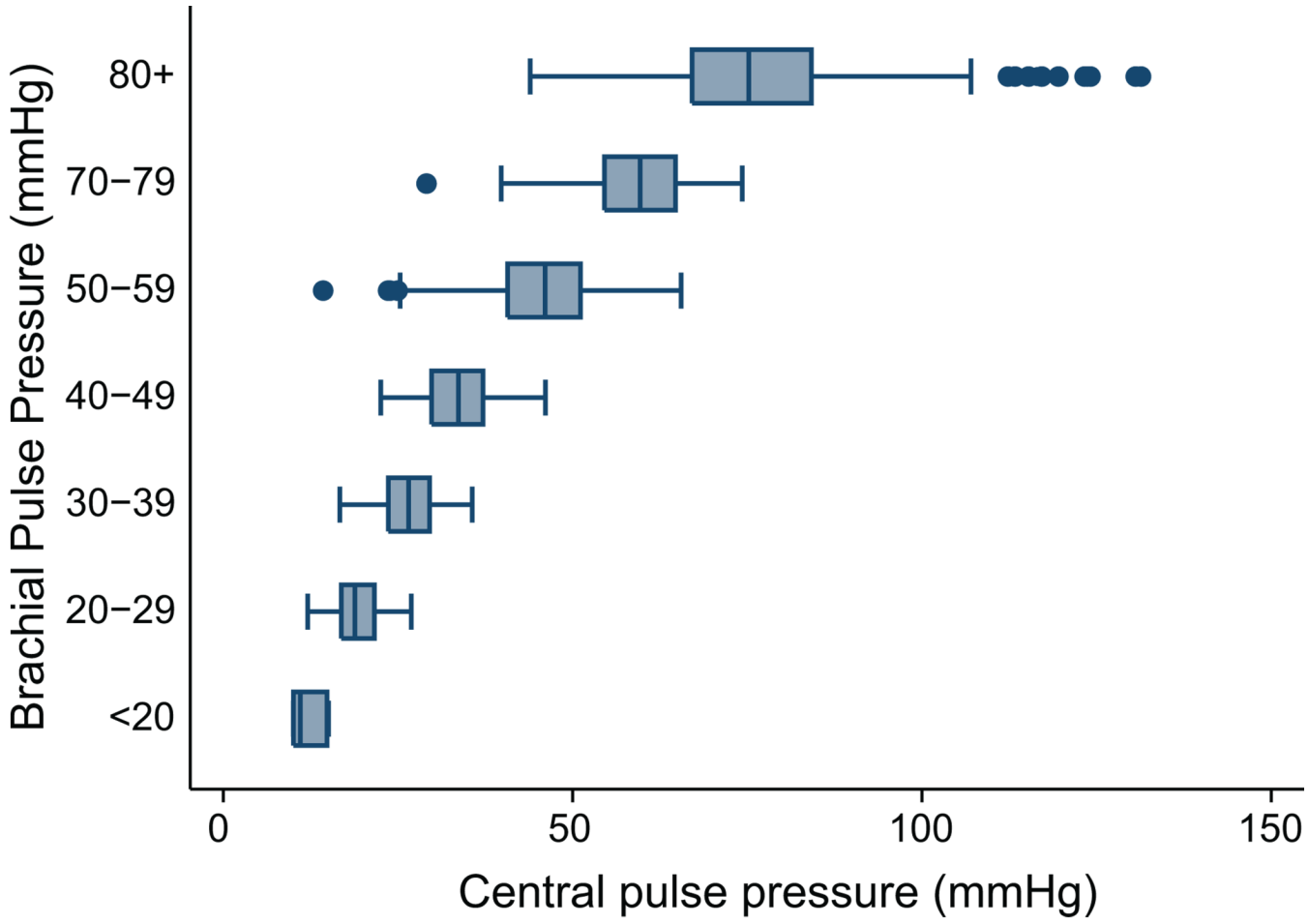

Figure 3.
shows discrete intervals of brachial pulse pressure in 10 mmHg increments on Y-axis and corresponding range of central pulse pressure measured on the X-axis. Box represents 25–75 percentile, whiskers indicate 95th percentile, line inside box is median value.

Table 1

Characteristics of CRIC participants

Variable	All Eligible N = 3277	Central Pulse Pressure available		
		No N=746	Yes N=2531	*P value*
Male	1796 (55.0%)	360 (48.3%)	1436 (57.1%)	<.0001
White	1601 (49.1%)	339 (45.4%)	1262 (50.1%)	<.0001
Black	1367 (41.9%)	364 (48.8%)	1003 (39.8%)	<.0001
Other	295 (9.04%)	43 (5.8%)	252 (10%)	<.0001
Diabetes (Yes)	1592 (48.8%)	404 (54.2%)	1188 (47.2%)	0.0008
Age, years	59.71 (10.82)	58.26 (10.47)	60.14 (10.88)	<.0001
*eGFR, mL/min/1.73m^2	41.32 (15.34)	41.22 (12.87)	41.34 (16)	0.8534
Weight, kg	91.23 (23.02)	98.85 (27.09)	88.97 (21.14)	<.0001
Systolic BP, mmHg	127.38 (22.11)	128.36 (21.5)	127.09 (22.29)	0.1677
Diastolic BP, mmHg	70.16 (12.87)	71.34 (12.92)	69.82 (12.83)	0.0047
Pulse Pressure, mmHg	57.22 (19.47)	57.05 (19.06)	57.27 (19.59)	0.7800
Augmentation Index, % (M(SD)/F(SD))	---	---	25(12)/31(11)	---
Amplification Ratio (M(SD)/F(SD))	---	---	1.33(0.23)/1.25(0.19)	---
Seated Heart Rate, beats/min	67.99 (11.35)	68.97 (11.41)	67.7 (11.32)	0.0072
Hemoglobin, g/dL	12.7 (1.78)	12.47 (1.84)	12.77 (1.75)	<.0001
Creatinine, mg/dL	1.95 (1.17)	1.77 (0.55)	2 (1.3)	<.0001
Triglycerides, mg/dL	152.87 (116.19)	162.01 (121.96)	149.95 (114.16)	0.0138
Calcium, mg/dL	9.28 (0.51)	9.2 (0.52)	9.3 (0.5)	<.0001
Phosphate, mg/dL	3.7 (0.66)	3.81 (0.67)	3.67 (0.65)	<.0001
Ca*Phosphate product	33.95 (6.24)	34.99 (6.22)	33.64 (6.21)	<.0001
†PTH, pg/mL	73.11 (67.64)	80.97 (77.37)	70.76 (64.27)	0.0004
†Urine Protein, g/24H	0.94 (2.09)	1.19 (2.63)	0.85 (1.86)	0.0002
†Hemoglobin A_1C, %	6.61 (1.54)	6.76 (1.64)	6.56 (1.51)	0.0032
†Uric Acid, mg/dL	7.37 (1.9)	7.72 (1.91)	7.27 (1.89)	<.0001
Medication: ACE-inhibitor	1601 (49.2%)	388 (52.2%)	1213 (48.3%)	0.0629
Medication: ARB	851 (26.1%)	204 (27.4%)	647 (25.7%)	0.3615
Medication: Calcium Antagonist	1310 (40.2%)	340 (45.7%)	970 (38.6%)	0.0005
Medication: Beta-blocker	1569 (48.2%)	422 (56.7%)	1147 (45.6%)	<.0001
Medication: Diuretic	1921 (59.0%)	523 (70.3%)	1398 (55.6%)	<.0001
Medication: Other BP Med	614 (18.9%)	174 (23.4%)	440 (17.5%)	0.0003

*Estimated Glomerular Filtration Rate;

†Available at Baseline only

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Table 2

Factors associated with Central Pulse Pressure

Variable		Central Pulse Pressure			*Ln Central Pulse Pressure		
		Est (StdErr)	R^2	p	Est (StdErr)	R^2	p
Female Sex		3.787 (0.75)	0.010	<.0001	0.089 (0.02)	0.012	<.0001
Race	Black	4.847 (0.79)	0.020	<.0001	0.106 (0.02)	0.020	<.0001
	Other	6.527 (1.28)	0.020	<.0001	0.128 (0.03)	0.020	<.0001
Ethnicity	Hispanic	4.700 (2.12)	0.025	<.0001	0.091 (0.04)	0.024	<.0001
Diabetes		10.449 (0.72)	0.076	<.0001	0.227 (0.02)	0.081	<.0001
Age (/10 years)		6.083 (0.33)	0.123	<.0001	0.147 (0.01)	0.162	<.0001
†eGFR (/10 mL/min/1.73m^2)		−2.483 (0.23)	0.045	<.0001	−0.053 (0.00)	0.046	<.0001
Weight (/10 Kg)		−0.769 (0.18)	0.008	<.0001	−0.015 (0.00)	0.006	<.0001
Waist (/10 cm)		0.262 (0.23)	0.001	0.2561	0.010 (0.00)	0.002	0.0356
‡MAP (/10 mmHg)		4.656 (0.26)	0.118	<.0001	0.093 (0.01)	0.106	<.0001
§SBP (/10 mmHg)		6.160 (0.12)	0.535	<.0001	0.127 (0.00)	0.512	<.0001
∥DBP (/10 mm Hg)		−1.200 (0.29)	0.007	<.0001	−0.030 (0.01)	0.009	<.0001
Heart Rate (/10 beats/min)		−3.187 (0.33)	0.037	<.0001	−0.073 (0.01)	0.043	<.0001
Brachial PP (/10 mmHg)		8.574 (0.09)	0.795	<.0001	0.179 (0.00)	0.778	<.0001
Hemoglobin (g/dL)		−3.098 (0.21)	0.083	<.0001	−0.069 (0.00)	0.094	<.0001
Glucose (/10 mg/dL)		0.575 (0.08)	0.021	<.0001	0.012 (0.00)	0.020	<.0001
Triglycerides (/10 mg/dL)		−0.060 (0.03)	0.001	0.0754	−0.002 (0.00)	0.003	0.0159
LDL-Cholesterol (/10 mg/dL)		−0.237 (0.11)	0.002	0.0374	−0.007 (0.00)	0.004	0.0045
Calcium (mg/dL)		−3.709 (0.75)	0.010	<.0001	−0.074 (0.02)	0.009	<.0001
#Phosphate (mg/dL)		1.979 (1.43)	0.005	0.1670	0.044 (0.03)	0.005	0.1608
#Calcium-Phosphate (product)		0.324 (0.06)	0.011	<.0001	0.007 (0.00)	0.013	<.0001
#Parathryoid Hormone (/10 pg/mL)		0.343 (0.06)	0.014	<.0001	0.008 (0.00)	0.016	<.0001

Variable	Central Pulse Pressure			*Ln Central Pulse Pressure		
	Est (StdErr)	R^2	p	Est (StdErr)	R^2	p
#Urine Protein (g/day)	1.439 (0.21)	0.021	<.0001	0.027 (0.00)	0.016	<.0001
#HemoglobinA$_1$C (%)	2.870 (0.24)	0.054	<.0001	0.063 (0.01)	0.058	<.0001
#Uric Acid (mg/dL)	0.848 (0.20)	0.007	<.0001	0.017 (0.00)	0.007	<.0001
Number of Antihypertensive Drugs	3.495 (0.24)	0.083	<.0001	0.078 (0.00)	0.093	<.0001

*Ln = Natural logarithm transformation of Central Pulse Pressure;

†eGFR=estimated Glomerular Filtration Rate;

‡MAP=Mean Arterial Pressure;

§SBP=Systolic Blood Pressure;

//DBP=Diastolic Blood Pressure;

¶Aortic Tr = Time to reflected wave in aortic pressure profile;

#Available at baseline visit only

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Table 3

a: Multivariable regression model for *LnCPP (no adjustment for brachial blood pressure)

Variable	Estimate (StdErr)	*p value*
Age (/10 years)	0.13 (0.01)	<.0001
Diabetes (Yes)	0.09 (0.02)	<.0001
Heart Rate (beats/minute)	−0.01 (0.00)	<.0001
Sex (Male)	−0.08 (0.01)	<.0001
HemoglobinA_1C (%)	0.03 (0.01)	<.0001
Hemoglobin (gm/dL)	−0.04 (0.00)	<.0001
Glucose (mg/dL)	0.00 (0.00)	0.0079
†PTH Baseline (pg/mL)	0.00 (0.00)	0.0019

b: Multivariable regression model for *LnCPP (adjusted for brachial pulse and mean arterial pressure)

Variable	Estimate (StdErr)	*p value*
†LnBPP (mmHg)	0.98 (0.01)	<.0001
Mean arterial pressure (mmHg)	0.00 (0.00)	<.0001
Age (/10 years)	0.03 (0.00)	<.0001
Sex (Male)	−0.06 (0.01)	<.0001
Diabetes (Yes)	0.02 (0.01)	0.0087
Heart Rate (beats/minute)	−0.01 (0.00)	<.0001
Weight (/10 kg)	−0.012 (00)	<.0001

c: Stepwise change in multivariable model R^2 (from Table 3b)

Variable	Model R^2
*LnBPP	0.8395081
LnBPP + †MAP	0.8396461
LnBPP + MAP + Age(/10yrs)	0.8444102
LnBPP + MAP + Age(/10yrs) + Diabetes (Y)	0.8447113
LnBPP + MAP + Age(/10yrs) + Diabetes (Y) + Heart Rate	0.8589313
LnBPP + MAP + Age(/10yrs) + Diabetes (Y) + Heart Rate + Sex	0.8668658
LnBPP + MAP + Age(/10yrs) + Diabetes (Y) + Heart Rate + Sex + Weight (/10 kg)	0.8705188

*Natural logarithm of Central Pulse Pressure;

†Available Baseline only

†Natural Logarithm of Brachial Pulse Pressure

*Natural Logarithm of Brachial Pulse Pressure;

†Mean Arterial Pressure in mmHg