

Original Article

Subclinical, hemodynamic, and echocardiographic abnormalities of high pulse pressure in hypertensive and non-hypertensive adults

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Abstract: Background: High pulse pressure (PP) is associated with cardiovascular events, but subclinical abnormalities in cardiac structure and function in relation to high pulse pressure are not well described. Methods and Results: 2225 hypertensive and 1380 non-hypertensive participants with adequate echocardiographic left ventricular measurements were evaluated. Non-hypertensives in the highest PP tertile (compared to the lower tertiles) were older (44 years vs. 40 years, $p < 0.009$), had higher systolic pressure [(SBP) 136 mmHg vs. 108 mmHg] and lower diastolic pressure [(DBP) 54 vs. 71 mmHg ($p = .0001$)], greater BMI (27 vs. 25 kg/m², $p < .001$) and more diabetes (4% vs. 2.25%, $p < .001$). In the hypertensive group, subjects in the highest PP tertile were older (52 vs 42 years), had higher SBP (157 vs. 116 mmHg) but lower DBP (65 vs. 83 mmHg). In the non-hypertensive group, higher PP (>60 mmHG) was associated with a higher frequency of echocardiographic structural and functional abnormalities, specifically, greater posterior and relative wall thickness, longer isovolumic relaxation time, and concentric left ventricular (LV) hypertrophy. Conclusion: In a population-based sample of hypertensive and non-hypertensive participants, higher PP was associated with subclinical abnormalities of cardiac structure and function, which exist even in the absence of hypertension and/or the use of antihypertensive treatment.

Keywords: Left ventricular hypertrophy, pulse pressure, hypertension, arterial stiffness, echocardiography

Introduction

Blood pressure (BP) rises significantly with age. Systolic BP continues to rise with increasing age while diastolic BP plateaus or even falls, resulting in a widening pulse pressure (PP) [1]. A widened PP measured at the brachial artery is associated with a stiffened aorta even though it is not an accurate measure of aortic PP [2, 3]. Such stiffening increases left ventricular pulsatile work, is associated with left ventricular hypertrophy, and requires greater coronary blood flow [4]. Aortic stiffness affects coronary blood flow response to percutaneous coronary intervention [4]. It is not surprising then that PP is associated with an increased risk of cardiovascular events (MI, CHF) and death [5-7].

Pulse pressure is determined by arterial stiff-

ness and stroke volume, but the relative contributions of each in unselected hypertensive subjects remains unclear [8]. The objective of this study is to assess the cross-sectional association of higher PP (adjusted for age and other covariates) and subclinical abnormalities of cardiovascular structure and function in a population-based sample of hypertensive and non-hypertensive adults.

Methods

Study population

The study population consisted of 2225 hypertensive patients and 1380 non-hypertensive subjects from the HyperGEN study who had adequate echocardiographic left ventricular mass measurements. Participants from the overall

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population were divided into tertiles of pulse pressure: <48 mmHg, 48-60 mmHg, and >60 mm Hg. We performed analyses separately for hypertensive and non-hypertensive individuals. The diagnosis of hypertension was defined as the use of one or more antihypertensive treatments or the average of three systolic blood pressures ≥ 140 or the average of three diastolic blood pressures ≥ 90 on two or more separate clinic visits (U.S. Department of Health and Human Services, National Institutes of Health, National Heart, Lung and Blood Institute, 2004).

This study is part of the Hypertension Genetic Epidemiologic Network (HyperGEN), in which genetic and environmental determinants of hypertension are being investigated in five geographical field centers: Forsyth County, NC; Minneapolis, MN; Framingham, MA; Salt Lake City, UT; and Birmingham, AL. Participants are hypertensive siblings ascertained through population-based cohorts (Atherosclerosis Risk in Communities Study, NHLBI Family Heart Study, Utah Family Tree Study, and the Framingham Heart Study) who met hypertension criteria previously described with onset by 60 years, and who did not have Type 1 diabetes or primary kidney disease. Non-hypertensive subjects were randomly selected from the computerized lists of registered motor vehicle operators in the field center catchment area (Birmingham, AL; Forsyth County, NC) or from the unrelated source cohorts that generated the hypertensive siblings.

Detailed information on study design and recruitment strategy is provided elsewhere [9, 10]. Institutional review boards at each of the participating institutions approved the research protocols, and all participants provided informed consent.

This report includes data from randomly selected subjects ($n = 1380$) and hypertensive siblings ($n = 2225$) with complete blood pressure measurements obtained from both arms using a standardized protocol and who had adequate left ventricular mass measurements.

Blood pressure measurements

Seated blood pressure was measured using an oscillometric blood pressure monitor (Dinamap 1846 SX/P, now manufactured by GE Healthcare Worldwide located in the United Kingdom) with the subject's elbow bent (cubital fossa)

positioned at the level of the heart. BP was measured by certified technicians who received centralized training, and the measurement process was regularly monitored to assure protocol adherence. Cuff size was chosen for each individual's right and left arm according to his or her mid-arm circumference, and the appropriate cuff size was used for each arm. Before BP measurements were acquired, subjects were seated alone in the room quietly for five minutes of rest. Six seated measurements were recorded and the last 5 (ie the first was dropped) were averaged.

In addition to the blood pressure examination, an interview was conducted to obtain information about demographics, writing handedness, family and personal history of cardiovascular disease, hypertensive medication use, and risk factors for cardiovascular disease. Methods used to ascertain body mass index (BMI) and current use of prescription medications have been described elsewhere [9-11].

Echocardiographic methods

2-dimensional (2D) and Doppler echocardiograms were performed and recorded utilizing protocols and methods adapted from those used in previously published studies [12-14] from the Weill Cornell Medical Center Echocardiography Laboratory (which served as the echocardiographic reading center for the HyperGEN study) [15].

Correct orientation of planes for 2D and Doppler echocardiographic imaging recordings was verified using standardized procedures [12]. Echocardiographic LV geometric measurements, including LV internal dimension and interventricular septal and posterior wall thicknesses, were measured on up to 3 echocardiographic cardiac cycles at end-diastole and end-systole (following the American Society of Echocardiography recommendation) [16, 17]. Segmental LV motion was graded using the 14-segment Mayo Clinic model [18], and scores for the motion of individual segments were summed to provide a geometry-independent estimate of LV ejection fraction as previously described [19].

Calculation of derived variables

Left ventricular mass was calculated by an anatomically validated formula ($r=0.90$) [20] with

good inter-study reproducibility ($r=0.93$) [21]. LV mass was normalized by body surface area and by height^{1.5}. LV hypertrophy was defined as LV mass index (LVMI) >104 g/m² in women and >116 g/m² in men, or LVMI > 47 g/m^{2.7} in women and 50 g/m^{2.7} in men when LV mass is indexed height [15, 21]. Relative wall thickness (RWT), an estimate of LV geometric concentricity, was calculated as LV posterior wall thickness divided by LV diastolic internal radius. Systolic cardiac functional indices were calculated by three different echocardiographic methods. These included LV ejection fraction (EF) calculated with end-diastolic and end-systolic LV volumes by the Teichholz method [22]. To assure that conclusions were not dependent on use of a specific geometric model to calculate LV volumes, EF was also calculated from stroke volume obtained by Doppler echocardiography which is the product of left ventricular outflow time-velocity integral and aortic annulus cross sectional area measured by 2D echocardiography [23]. Scores for the motion of individual LV segments were summed to provide another geometry-independent estimate of LV ejection fraction [19]. LV myocardial function was evaluated by LV mid-wall shortening and stress-corrected mid-wall shortening [24].

Statistical analysis

The data were transformed to normal distribution wherever necessary. We removed the effects of outliers ($<> 4SD$) by assigning them values of equal to $\pm 4SD$. Pulse pressure tertiles were calculated for the HyperGEN population overall. Since individuals in the study were related, we tested effects of pulse pressure tertiles on various outcomes using a linear mixed model, and in our mixed model accommodated correlated residuals of related individuals by modeling family ID as a random effect. We also tested if the means for the outcome variables for the middle and high tertile groups were different from the means of the lowest tertile group. The p-values were adjusted for multiple comparisons by estimating the number of independent hypotheses we analyzed using principal component analysis (Gao et al., 2008). Altogether we tested 35 hypotheses in each of hypertensive and non-hypertensive groups. The number of principal components that explained 99.5% variation was used as number of independent hypotheses. For each phenotype we tested pairwise comparisons. The p-values were

also adjusted for multiple pairwise comparisons using the Sheffe correction. In hypertensive samples, we also adjusted outcome variables for BP medications in addition to the other covariates (age, age², sex, race, center, SBP, BMI, BP medication, diabetes).

In the lowest PP tertile group, 61% were non-hypertensive and 28% hypertensive while in the highest PP tertile group hypertension prevalence was 11 and 40% respectively.

For the hypertensive sample, the first 24 principal components explained more than 99.5% of the variation; and, for the non-hypertensive sample, the first 25 components explained more than 99.5% of the variation. The Bonferroni thresholds for hypertensive and non-hypertensive samples are 0.00208 (0.05/24) and 0.002 (0.05/25) respectively.

Results

Clinical characteristics

The clinical characteristics by tertiles of PP in the hypertensive and non-hypertensive groups are shown in **Table 1**. Among the non-hypertensive participants (**Table 1A**), African Americans were over-represented in the highest tertile compared to either of the two lower tertiles; there were no significant ethnic differences across the PP tertiles in the hypertensive group. In the hypertensive group, women made up a higher percentage in the higher vs the lower PP tertiles, but this was not the case in the non-hypertensive group. Waist circumference and BMI increased as the PP rose in both the hypertensive and non-hypertensive groups. Diabetes was also more frequent as PP increased, particularly in the hypertensive group. Also, patients in the highest PP tertile had more prior myocardial infarctions (10 vs. 5.8%, $p<0.0001$) and revascularization procedures (11.2 vs. 6.9%, $p<0.006$), but not strokes (5.7 vs. 4.4%), or heart failure (2.6 vs. 2.3)-data not shown. The use of diuretics was the most frequent antihypertensive treatment overall, and was more commonly reported by participants in the highest PP tertile; however, the distribution of beta-blockers, ACE Inhibitors, and ARBs were about equal across PP tertiles. In those hypertensive patients receiving antihypertensive treatment calcium channel blocker therapy was more frequent in the highest tertile group (39 vs

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Table 1A. Clinical characteristics by tertiles of pulse pressure (non-hypertensive)

	N	<48 mmHg		≥48<60 mmHg		≥60 mmHg		ANOVA
		Mean	Mean	p-value (Scheffe)	Mean	p-value (Scheffe)	p-value	
Age, years ††	1365	39.82	39.48	0.9232	43.91	0.009	0.0009	
Women, %	1377	56.11	44.48	0.0006	48.08	0.1799	0.0003	
Black, %	1367	43.83	53.99	0.0045	60.90	0.0004	<0.0001	
BMI *	1365	25.53	27.10	0.0003	27.06	0.0545	0.0003	
Heart Rate †	1240	66.73	66.65	0.9944	64.22	0.1204	0.0643	
SBP, mmHg **	1365	108.39	120.63	<0.0001	136.4 3	<0.0001	<0.0001	
DBP, mmHg †	1365	71.07	62.14	<0.0001	53.95	<0.0001	<0.0001	
Diabetes, % †	1365	2.25	5.82	0.0198	3.97	0.7072	0.02	
Past or present smoker †	1364	29.80	30.67	0.9667	28.54	0.974	0.8836	
Waist Circumference*	1364	89.21	92.69	0.0037	92.33	0.1871	0.0037	

p-values for group mean comparisons are corrected using Scheffe adjustment; † controlled for age, age2, sex, race, center, SBP, BMI; †† controlled for sex, race, center, SBP, BMI; * controlled for age, age2, sex, race, center, SBP; ** controlled for age, age2, sex, race, center, BMI.

Table 1B. Clinical characteristics by tertiles of pulse pressure (hypertensive)

	N	<48 mmHg		≥48<60 mmHg		≥60 mmHg		ANOVA
		Mean	Mean	p-value (Scheffe)	Mean	p-value (Scheffe)	p-value	
Age, years ††	2202	42.40	45.48	< 0.0001	52	< 0.0001	< 0.0001	
Women, %	2220	57.23	56.32	0.9431	67.93	0.0001	< 0.0001	
Black, %	2208	64.27	60.35	0.3387	63.37	0.9378	0.2911	
BMI *	2202	26.00	27.56	< 0.0001	29.65	< 0.0001	< 0.0001	
Heart Rate †	2133	72.10	71.17	0.2144	69.79	0.0232	0.071	
SBP, mmHg **	2202	115.90	132.41	< 0.0001	157.20	< 0.0001	< 0.0001	
DBP, mmHg †	2202	82.79	73.66	< 0.0001	64.73	< 0.0001	< 0.0001	
Diabetes, % †	2202	6.70	10.41	0.3151	16.04	0.02	0.018	
Past or present smoker †	2183	35.91	33.10	0.6193	34.51	0.9378	0.5736	
Waist Circumference *	2194	89.89	93.37	0.0002	97.05	< 0.0001	< 0.0001	

p-values for group mean comparisons are corrected using Scheffe adjustment; † controlled for age, age2, sex, race, center, BP medication, SBP, BMI; †† controlled for sex, race, center, BP medication, SBP, BMI; * controlled for age, age2, sex, race, center, SBP; ** controlled for age, age2, sex, race, center, BMI.

31% p<.0009 – data not shown).

Echocardiographic assessments

Echocardiographic measures demonstrated that in non-hypertensive subjects, higher PP was associated with a greater prevalence of concentric LV hypertrophy (16.8 vs 10.8 p<.012) (Table 2A and B).

Hemodynamic assessments

In the hypertensive group, stroke volume and stroke index as well as total peripheral resistance and PP/stroke volume or stroke index,

were higher in the highest PP tertile group. In the non-hypertensive group isovolumic relaxation time was lowest in the highest tertile group and PP/stroke volume or stroke index were highest in the highest tertile group (Table 3A and B).

Laboratory findings

Fasting glucose and cholesterol rose with increasing tertiles of PP in both groups, but insulin levels rose with higher tertiles only in the non-hypertensive group (although the level of insulin was much higher in the hypertensive group, the difference between pulse pressure groups

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Table 2A. Left ventricular geometry by tertiles of pulse pressure (mmHg) (non-hypertensive)

	N	<48 mmHg	≥48<60 mmHg		≥60 mmHg		ANOVA
		Mean	Mean	p-value (Scheffe)	Mean	p-value (Scheffe)	p-value
Septal thickness, cm	1365	0.7778	0.7797	0.9565	0.7651	0.4866	0.2754
LVIDd, cm	1365	5.1223	5.1003	0.7284	5.1259	0.9964	0.6166
Posterior Wall thickness, cm	1365	0.7543	0.7584	0.8385	0.7396	0.4025	0.1309
LV Mass/BSA, g/m ²	1323	72.58	72.43	0.9888	71.21	0.7141	0.6786
LV mass, gm	1365	134.02	133.91	0.9984	131.82	0.7876	0.7412
Relative wall thickness	1365	0.2948	0.2976	0.6460	0.2888	0.4560	0.0841
End diastolic volume, ml	1365	124.97	123.73	0.7212	125.15	0.9977	0.615
LV Hypertrophy, %	1268	10.79	9.70	0.8173	16.79	0.0935	0.0122

p-values for group mean comparisons are corrected using Scheffe adjustment controlled for age, age2, sex, race, center, prior MI, revascularizaion, SBP, BMI.

Table 2B. Left ventricular geometry by tertiles of pulse pressure (mmHg) (hypertensive)

	N	<48 mmHg	≥48<60 mmHg		≥60 mmHg		ANOVA
		Mean	Mean	p-value (Scheffe)	Mean	p-value (Scheffe)	p-value
Septal thickness, cm	2202	0.8530	0.8519	0.9836	0.8553	0.9659	0.8612
LVIDd, cm	2202	5.29	5.33	0.3919	5.36	0.1862	0.1827
Posterior Wall thickness, cm	2202	0.7622	0.7564	0.5755	0.7627	0.9976	0.3385
LV Mass/BSA, g/m ²	2170	74.56	74.90	0.9396	76.81	0.2579	0.157
LV mass, gm	2202	151.79	152.83	0.8793	155.70	0.3803	0.3244
Relative wall thickness	2202	0.2899	0.2856	0.2689	0.2860	0.5558	0.2689
End diastolic volume, ml	2202	134.46	136.93	0.3875	139.00	0.187	0.183
LV Hypertrophy, %	2154	20.21	19.20	0.9284	23.96	0.5824	0.2049

p-values for group mean comparisons are corrected using Scheffe adjustment controlled for age, age2, sex, race, center, BP medication, prior MI, revascularizaion, SBP, BMI.

did not reach statistical significance) (**Table 4A** and **B**).

Contribution of hemodynamic variables

Table 5 presents the R squared values for SBP, DBP, and PP on the subclinical echocardiographic measures. The contributions of SBP and PP are almost equal in terms of their contributions to these subclinical echocardiographic measurements (**Table 5**).

Discussion

In this analysis of non-hypertensive and hypertensive subjects from the HyperGEN study, we analyzed clinical, hemodynamic, and echocardiographic cross-sectional associations of high PP. Our data suggests that higher PP (adjusted for age, race, diabetes mellitus, and CVD risk factors), is associated with subclinical abnormalities (in both hypertensive and non-

hypertensive subjects) such as increased LV mass and concentric LV geometry, and abnormal LV diastolic function; and, that PP is an almost equal contributor to these abnormalities when compared to SBP.

Blood pressure is a measure of both the conduit and cushioning functions of the large arteries. The conduit function is important in controlling the supply of blood flow to the periphery; while the cushioning function dampens the pressure oscillations that result from intermittent ventricular contraction. Ejection of blood into the aorta generates a forward propagating wave, which is then reflected primarily from the distal arteries. The collision of the forward propagating wave with the reflective waves (to a great degree dependent upon arterial stiffness - propagating waves travel faster in stiffer arteries) amplifies systolic pressure and creates a widening of the PP. Indeed, several studies have evaluated the clinical usefulness of as-

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Table 3A. Left ventricular systolic function and systemic hemodynamics by tertile of pulse pressure (non-hypertensive)

	N	<48 mmHg		≥48<60 mmHg		≥60 mmHg		ANOVA
		Mean	Mean	p-value (Scheffe)	Mean	p-value (Scheffe)	p-value	
LV EF, %	1364	60.81	61.42	0.3524	61.21	0.8478	0.3456	
Midwall shortening, %	1364	18.41	18.48	0.8624	18.63	0.5792	0.5792	
Stroke Volume, ml	1275	75.91	77.57	0.2957	77.14	0.7743	0.2937	
Stroke Index, ml/m ²	1235	40.41	41.33	0.1917	40.94	0.8126	0.1795	
IVRT, msec	1236	75.22	74.05	0.5228	70.92	0.0346	0.0336	
Cardiac Output	1234	5204.01	5240.65	0.906	5082.20	0.6513	0.3586	
Cardiac Index	1196	2735.31	2750.67	0.9367	2668.04	0.6093	0.3568	
Total peripheral resistance	1194	1453.46	1401.36	0.1174	1421.97	0.744	0.1098	
PP/Stroke Volume	1275	0.56	0.67	<0.0001	0.79	<0.0001	<0.0001	
PP/Stroke Index	1235	1.06	1.27	<0.0001	1.51	<0.0001	<0.0001	

p-values for group mean comparisons are corrected using Scheffe adjustment controlled for age, age2, sex, race, center, diabetes, SBP, BMI.

Table 3B. Left ventricular systolic function and systemic hemodynamics by tertile of pulse pressure (hypertensive)

	N	<48 mmHg		≥48<60 mmHg		≥60 mmHg		ANOVA
		Mean	Mean	p-value (Scheffe)	Mean	p-value (Scheffe)	p-value	
LV EF, %	2200	58.33	58.78	0.702	58.99	0.6706	0.6352	
Midwall shortening, %	2200	17.47	17.76	0.1207	17.82	0.2052	0.1039	
Stroke Volume, ml	2132	86.63	88.61	0.1691	91.33	0.0053	0.005	
Stroke Index, ml/m ²	2101	43.93	44.49	0.4869	45.82	0.0132	0.0078	
IVRT, msec	1982	77.36	75.88	0.3525	74.88	0.209	0.1963	
Cardiac Output	2088	6199.35	6248.52	0.8402	6317.63	0.5833	0.578	
Cardiac Index	2058	3122.53	3127.22	0.9936	3160.55	0.8042	0.7309	
Total peripheral resistance	2036	1164.45	1128.45	0.1029	1086.16	0.0025	0.0024	
PP/Stroke Volume	2132	0.53	0.63	<0.0001	0.72	<0.0001	<0.0001	
PP/Stroke Index	2225	1.08	1.28	<0.0001	1.45	<0.0001	<0.0001	

p-values for group mean comparisons are corrected using Scheffe adjustment controlled for age, age2, sex, race, center, BP medications, diabetes, SBP, BMI.

sessing the amplitude of this reflected wave [7, 25, 26]. A widened PP suggests an abnormality in vascular integrity (structure and/or function); and, therefore, a widened PP should be associated with vascular disease. A variety of studies have suggested this aforementioned association, but the HyperGEN study allows for an analysis of a fairly large population in order to explore the association of a large number of echocardiographic correlates of subclinical CVD.

A number of studies have addressed the relationship between PP and cardiac events, and between PP and LVH [27, 28]. In a large study with a follow-up of over 19 years, PP was associ-

ated with CV events after adjustment for age, cholesterol level, and tobacco use [27]. From the Strong Heart Study (a population based survey of the prevalence of CVD risk factors and incident CV morbidity and mortality in 13 American Indian communities) [29]. Palmieri evaluated the association of PP with CVD outcome and found it to be independent of LVH and systolic dysfunction and associated with higher CV mortality [30].

The strengths of this study include the relatively large sample size and the carefully performed measurements and centralized reading. Limitations beyond its cross sectional design are that

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Table 4A. Laboratory findings by tertiles of pulse pressure (non-hypertensive)

	N	<48 mmHg		≥48<60 mmHg		≥60 mmHg		ANOVA
		Mean	Mean	p-value (Scheffe)	Mean	p-value (Scheffe)	p-value	
Glucose, mg/dl	1364	99.30	98.91	0.8577	99.60	0.9535	0.674	
Total cholesterol, mg/dl	1364	166.85	165.73	0.9092	167.00	0.9994	0.8682	
HDL, mg/dl	1362	41.15	40.78	0.8736	39.83	0.517	0.5151	
LDL, mg/dl	1356	101.56	103.41	0.7797	103.82	0.8702	0.7657	
Triglycerides, mg/dl	1362	96.94	92.00	0.3657	96.26	0.9932	0.2835	
Insulin, mU/L	1363	6.27	6.63	0.371	6.15	0.9577	0.1833	
Creatinine, mg/dl	1364	0.8445	0.8430	0.9822	0.8620	0.4117	0.2439	

p-values for group mean comparisons are corrected using Scheffe adjustment controlled for age, age², sex, race, center, diabetes, SBP, BMI.

Table 4B. Laboratory findings by tertiles of pulse pressure (hypertensive)

	N	<48 mmHg		≥48<60 mmHg		≥60 mmHg		ANOVA
		Mean	Mean	p-value (Scheffe)	Mean	p-value (Scheffe)	p-value	
Glucose, mg/dl	2174	107.99	108.45	0.9138	109.03	0.7783	0.7768	
Total cholesterol, mg/dl	2201	177.22	176.45	0.9549	176.86	0.9946	0.9464	
HDL, mg/dl	2174	52.78	53.25	0.8444	54.92	0.1671	0.1105	
LDL, mg/dl	2157	100.34	97.05	0.3835	98.35	0.8299	0.3511	
Triglycerides, mg/dl	2175	87.44	89.14	0.8328	86.49	0.9683	0.5662	
Insulin, mU/L	2170	14.16	14.10	0.995	13.70	0.8075	0.7306	
Creatinine, mg/dl	2174	0.9038	0.8842	0.1676	0.8828	0.3358	0.1605	

p-values for group mean comparisons are corrected using Scheffe adjustment controlled for age, age², sex, race, center, BP medication, diabetes, SBP, BMI.

Table 5. R² Values for the various phenotypic variables

Phenotype	R ²		
	SBP	DBP	PP
Septal thickness, cm	0.1281	0.0622	0.0979
LVIDd, cm	0.0156	0.0027	0.0179
Posterior Wall thickness, cm	0.1227	0.0557	0.0984
LV Mass/BSA, g/m ²	0.1276	0.0469	0.1132
LV mass, gm	0.1184	0.0460	0.1021
Relative wall thickness	0.0451	0.0261	0.0307
End diastolic volume, ml	0.0157	0.0026	0.0180
LV Hypertrophy, %	0.0812	0.0281	0.0717

the participants were receiving a variety of anti-hypertensive agents, many of which have effects on LV hemodynamics and LVH. However, adjustment for BP medication did not change the relationship between PP and echocardiographic measures.

Finally, increased PP has been associated with increased heart failure and the types of subclinical

abnormalities that are observed here (increased LV mass, wall thickness, relative wall thickness (concentric LV remodeling) and reduced LV relaxation), are those that are also associated with diastolic heart failure (heart failure with preserved ejection fraction) [31, 32].

In summary, in a cross-sectional analysis of a

population-based sample, hypertensive patients with higher PP are: older, more likely to be white, independent of age, more likely to have diabetes, use more calcium channel blockers and diuretics, and have higher glucose and triglyceride levels. Furthermore, higher PP is associated with: higher LV mass and prevalence of LVH (both known to portend worse prognosis), prolonged isovolumic relaxation time, and higher stroke index. Higher PP reflects both higher stroke volume and arterial stiffness; and, when adjusted for age, race, gender, BMI, and prevalent CHD, higher PP is associated with higher LV mass, more LVH, and worse LV relaxation irrespective of the BP status.

Perspectives

The complications of long standing hypertension are well known and relate to arterial disease with clinical manifestations in the heart, brain and kidney. However, the paradigm of elevated blood pressure resulting in vasculopathy continues to be challenged. Rather than hypertension resulting in altered vascular structure and function, it appears that changes in vascular integrity (structure) precede, and may be causal, in the development of elevated blood pressure with resultant hypertension that ultimately leads to clinical events. The current data demonstrate that higher PP irrespective of BP status is associated with abnormalities of LV structure and function. The association of PP and the reported subclinical abnormalities (even in non-hypertensive subject's), and the suggestion that PP and SBP provide similar contributions to the echocardiographic variables, supports the above hypothesis.

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