ORIGINAL ARTICLE

Relationship of Arterial Stiffness with Hypertension and its Management in a North-Indian Urban Population Free of Cardiovascular Disease

Ravi R Kasliwal, MD, DM, Manish Bansal, MD, DNB,
Rahul Mehrotra, MD, DNB, Naresh Trehan, MD, *Gurgaon, India*

ABSTRACT

Background: Arterial stiffness is an important prognostic marker for cardiovascular (CV) events in many patient subsets, especially in hypertensives. However, the relationship between hypertension and arterial stiffness has not been adequately studied among Indians.

Methods: One hundred forty-four individuals who were free of CV disease were included in the study and subjected to clinical examination, biochemical investigations, and arterial stiffness assessment. Right and left brachial-ankle pulse wave velocity (baPWV), carotid-femoral pulse wave velocity (cfPWV), and augmentation index (AIx), estimated using PeriScope® device, were used as measures of arterial stiffness.

Results: Mean age of the subjects was 45.7±11.6 years and 75.7% were males. Of the 144 subjects, 101 (70.1%) were found to have hypertension. All arterial stiffness parameters (cfPWV, right and left baPWV, and AIx) were significantly elevated in patients with hypertension (993.4 ± 382.6 cm/sec, 1430.7 ± 593.0 cm/sec, 1534.1 ± 347.4 cm/sec, and 20.0 ± 10.9% respectively in hypertensives and 799.5 ± 188.8 cm/sec, 1175.9 ± 277.7 cm/sec, 1331.1 ± 214.4 cm/sec, and 10.8 ± 10.7% respectively in nonhypertensives, p <0.01). Both systolic and diastolic blood pressure (BP) had significant correlation with cfPWV, right and left baPWV, and AIx. Although, the hypertensive patients with controlled BP (<140/90 mmHg) still had increased arterial stiffness as compared to non-hypertensives with normal BP, they had much less stiff arteries as compared to those with elevated BP levels , even if they were not previously known to be hypertensives.

Conclusions: The present study shows that in North-Indian subjects without known CV disease, arterial stiffness is significantly increased among hypertensives and is positively correlated with both systolic and diastolic BP. All measures of arterial stiffness improve with control of BP. Assessment of arterial stiffness may thus be helpful in tracking vasculoprotective effects of antihypertensive therapy in clinical practice. (J Clin Prev Cardiol 2012;1:1–8)

Key Words: Arterial stiffness; augmentation index; cardiovascular disease; hypertension; pulse wave velocity.

Introduction

Arterial stiffness is being increasingly recognized as an important contributor of cardiovascular (CV) morbidity and mortality in many patient subsets, particularly in the elderly, hypertensives, and those with end-stage renal disease (1–10). Increased arterial stiffness results in rapid reflection of arterial pulse waveform from periphery which results in augmentation of central aortic systolic blood pressure (BP). At the same time, stiffening of aorta causes loss of elastic recoil which, coupled with absence of reflected wave during diastole, results in fall in central aortic diastolic pressure. While the increase in aortic systolic pressure increases cardiac afterload, the fall in aortic diastolic BP compromises coronary perfusion. Together, these pathological alterations adversely affect myocardial oxygen demand–supply relationship, thereby increasing CV morbidity and mortality (11).

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Recent technical advancements have made noninvasive measurement of arterial stiffness feasible in clinical practice. Segmental pulse wave velocity (PWV), central aortic pressure, and augmentation index (AIx) are some of the measures of arterial stiffness which can be easily and reproducibly computed using the newer, noninvasive techniques (1). Several clinical trials have demonstrated utility of these parameters in CV risk stratification as well as in guiding antihypertensive therapy (1, 10, 12). Acknowledging the available evidence base, European Society of Cardiology has recommended assessment of

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Corresponding Author: Ravi R Kasliwal
Chairman, Clinical and Preventive Cardiology,
9, 3rd Floor OPD Block, Medanta–The Medicity,
Sector 38, Gurgaon, Haryana-122001, INDIA.
Ph: +91-124-4141414 | Fax: +91-124-4834111
Email: rrkasliwal@hotmail.com

arterial stiffness as an integral component of evaluation of any individual with hypertension (HT) (12).

Given the rapidly increasing burden of CV risk factors and CV disease in India, arterial stiffness measurement can be of great clinical value in Indians also. Unfortunately, the vast differences in CV disease epidemiology between Indians and the Western populations preclude direct extrapolation of results obtained in Western populations to Indians. Although a few trials have studied arterial stiffness in Indians also, the experience has been limited mainly to patients with known coronary artery disease (CAD) or diabetes mellitus (13–16). Since the greatest value of arterial stiffness assessment appears to be in hypertensive individuals, we sought this study to define the relationship of HT and its management with arterial stiffness in Indian subjects.

Methods

One hundred forty-four subjects who were free from any CV disease and who had presented to our out-patient department with one or more CV risk factors were included in the study. Absence of CV disease was confirmed by lack of symptoms suggestive of the same and a negative exercise stress test. Informed consent was obtained from all participants prior to their enrolment in the study.

Once enrolled, all subjects underwent clinical evaluation, biochemical investigations, and assessment of arterial stiffness. Clinical evaluation included detailed history regarding the presence or absence of CV risk factors, duration of CV risk factors, and use of antihypertensive medications, and general physical examination which included height, weight, and BP measurement and the examination of CV system. BP was measured in the right arm in supine position, using a standard sphygmomanometer. Biochemical investigations included fasting and 2-hour post-prandial blood glucose estimation and fasting lipid profile.

Arterial stiffness assessment (Fig. 1)

Assessment of arterial stiffness was performed using the PeriScope® device (Genesis Medical Systems Pvt Ltd, Hyderabad, India) which has been shown to have high degree of reproducibility for this purpose (17). This device is based on oscillometric method and records arterial pressure waveforms noninvasively. ECG-gated pressure waveforms are recorded simultaneously from both arms and both ankles. From these pressure waveforms, in-built software automatically calculates PWV for different vascular segments—brachial-ankle PWV (baPWV), carotid-femoral PWV (cfPWV), etc. Central aortic pressure and AIx are derived from brachial pressure waveforms, using a previously validated transfer function (1).

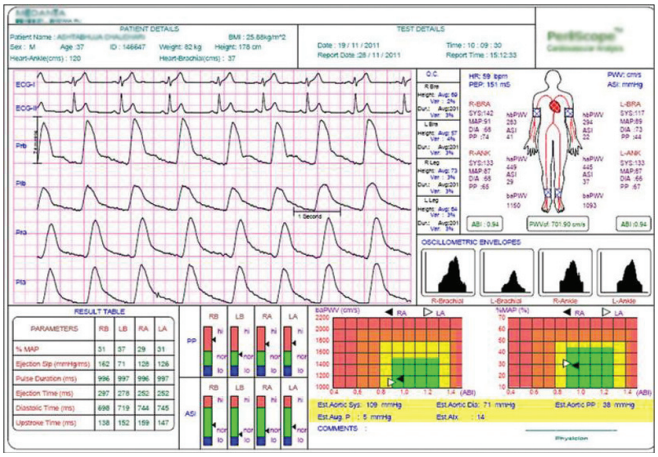

Figure 1. PeriScope® result sheet showing oscillometric pressure waveforms from different arteries and the various arterial stiffness parameters derived from these pressure waveforms.

Assessment of arterial stiffness was performed in the morning, after 10 hours overnight fast. Participants were asked to refrain from smoking for at least 4 hours before the procedure. Ongoing medications were not discontinued but the morning dose was delayed until completion of the test. The procedure was performed in supine position. After 10 minutes of supine rest, four BP cuffs, which were connected to the PeriScope® device, were tied around both arms and both ankles. These BP cuffs carried oscillometric sensors to record pressure waveforms from the underlying arteries. ECG electrodes were applied on wrists and ankles to record ECG simultaneously. The machine then automatically inflated and deflated all the cuffs simultaneously while recording pressure waveforms from all the four sites. From these pressure waveforms, right and left baPWV, cfPWV, central aortic systolic and diastolic BP, and AIx were calculated by the system as mentioned above.

Although the absolute values of different arterial stiffness parameters were used for analysis, they were also compared with age-and gender-specific normal values already stored in the database of the system. This nomogram was based on the data derived from 988 healthy Indian subjects, free from major CV risk factors and CV disease (13).

Definition of CV risk factors

For the purpose of the present study, HT was defined according to Joint National Committee (JNC) 7 guidelines as systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg or previous history of HT or self-reported use of antihypertensive medications (18). Diabetes mellitus was defined as fasting blood glucose ≥ 126 mg/dl or 2-hour postprandial blood glucose ≥ 200 mg/dl or pharmacological treatment for diabetes or previous history of diabetes mellitus. Dyslipidemia was defined as high total cholesterol (TC, ≥200 mg/dl) or low high density lipoprotein-cholesterol (HDL-C, <40 mg/dl in men and <50 mg/dl in women) or history of dyslipidemia. Family history was considered positive if a coronary event had occurred in a male first-degree relative before the age of 55 years or a female first-degree relative before the age of 65 years. Smoking or tobacco use in any form during the preceding month was also considered to be a CV risk factor.

The study was approved by an independent ethics committee.

Statistical Analysis

The data was managed on Microsoft excel spreadsheet (version 2007, Microsoft Corp, Seattle, Washington). Values were expressed as mean ± standard deviation or as percentages. Comparisons between the groups were carried out using Student's unpaired *t* test, one-way analysis of variance, or chi-square test as appropriate. Correlations among different arterial stiffness measurements were assessed using Pearson's correlation coefficients. A *p* value <0.05 was considered statistically significant. All statistical analyses were done using SPSS for Windows (release 15.0, SPSS Inc, Chicago, IL, USA).

Results

Clinical characteristics of the study population are described in Table 1. Mean age of the subjects was 45.7 years and three-forth were males.

Of all the subjects, 70.1% had HT, 15.3% had diabetes mellitus, 22.9% were current smokers, 75.7% had dyslipidemia, and 41.7% had family history of premature CAD. Majority (83%) were overweight (body-mass index >23.0 kg/m^2) with overall mean body-mass index 27.3 kg/m^2. More than half (55.0%) had high TC and 41.0% had low levels of HDL cholesterol.

Table 1.
Clinical and Biochemical Characteristics of the Study Population

Parameter	Value*
Age (years)	45.7 ± 11.6
Male gender	109 (75.7%)
Hypertension	101 (70.1%)
Diabetes mellitus	22 (15.3%)
Current smoking	33 (22.9%)
Family history of premature CAD	60 (41.7%)
Dyslipidemia	106/140 (75.7%)
Total cholesterol (mg/dl)	200.9 ± 48.1
High total cholesterol†	77/140 (55.0%)
HDL cholesterol (mg/dl)	40.3 ± 10.1
Low HDL cholesterol†	57/139 (41.0%)
LDL cholesterol (mg/dl)	130.4 ± 45.3
Body mass index (kg/m2)	27.3 ± 4.8
Systolic blood pressure (mmHg)	133.6 ± 16.5
Diastolic blood pressure (mmHg)	79.0 ± 11.0
Fasting blood glucose (mg/dl)	101.8 ± 34.9
2-hr PP blood glucose (mg/dl)	116.5 ± 57.2

*All values are in mean ± S.D. for continuous variables and actual value with percentage in parentheses for categorical variables.
†See text for definitions.
CAD, coronary artery disease; HDL, high density lipoprotein; LDL, low density lipoprotein; PP, postprandial.

Arterial stiffness parameters (Table 2)

Mean cfPWV was 935.5 ± 29.0 cm/sec in the overall study population. Mean right baPWV was 1354.6 ± 44.3 cm/sec and mean left baPWV was 1473.5 ± 326.4 cm/sec. When compared with the reference population, 57.6% had elevated cfPWV, 51.4% had elevated right baPWV, and 70.8% had elevated left baPWV.

Mean central aortic systolic BP was 115.1 ± 16.6 mmHg which was 18.5 mmHg lower than the brachial systolic BP (p <0.001). Mean central aortic diastolic BP was 79.3 ± 10.1 mmHg which was similar to brachial diastolic BP (79.4 ± 11.0, p >0.05). Average augmentation pressure was 6.9 mmHg with mean AIx 17.2 ± 11.6 mmHg.

Blood pressure control and relationship with arterial stiffness parameters

Of the 144 subjects, 101 were found to have HT. Fifty-four of the 101 hypertensive subjects (53.5%) had their

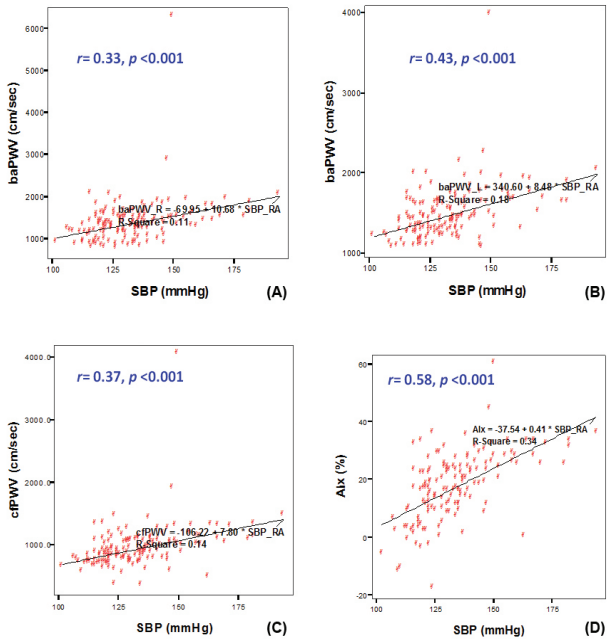

Figure 2. Relationship between systolic blood pressures. (A) Right brachial-ankle pulse wave velocity, (B) left brachial-ankle pulse wave velocity, (C) carotid-femoral pulse wave velocity, (D) augmentation index. (r, Pearson's correlation coefficient)

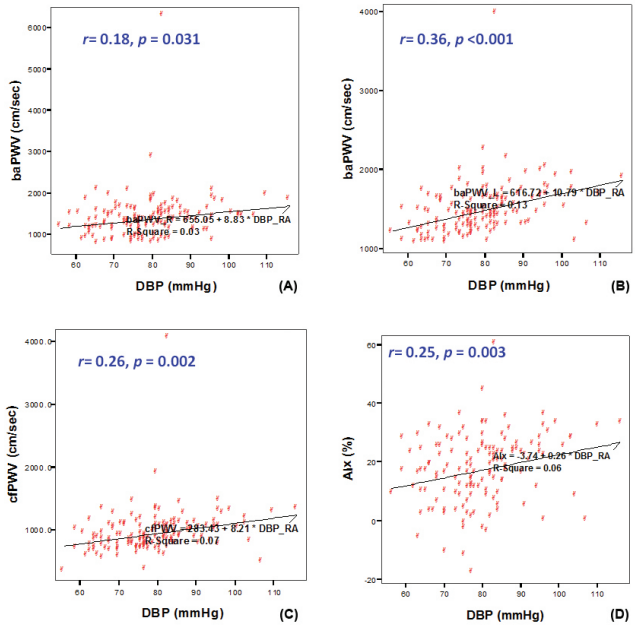

Figure 3. Relationship between diastolic blood pressures. (A) Right brachial-ankle pulse wave velocity, (B) left brachial-ankle pulse wave velocity, (C) carotid-femoral pulse wave velocity, (D) augmentation index. (*r*, Pearson's correlation coefficient)

BP controlled (systolic BP <140 mmHg and diastolic BP <90 mmHg). Of the remaining 47 subjects, 34 (72.3%) had BP in the range of stage 1 HT and 13 (27.7%) in the range of stage 2 HT as defined by the JNC 7 guidelines on HT (18). Among the patients with controlled BP, two-third were on antihypertensive medications, whereas one-third were on life style measures alone. Overall, 49 patients (48.5% of hypertensives) were on medications and 75.0% of them had their BP controlled below 140/90 mmHg level.

All arterial stiffness parameters (cfPWV, right and left baPWV and AIx) were significantly elevated in patients with HT (993.4 ± 382.6 cm/sec, 1430.7 ± 593.0 cm/sec, 1534.1 ± 347.4 cm/sec, and 20.0 ± 10.9%, respectively, in hypertensives and 799.5 ± 188.8 cm/sec, 1175.9 ± 277.7 cm/sec, 1331.1 ± 214.4 cm/sec, and 10.8 ± 10.7%, respectively, in non-hypertensives, p <0.01). Both, systolic and diastolic BP had significant correlation with cfPWV, right and left baPWV, and AIx (Figs. 2 and 3) with the strongest correlation obtained between systolic BP and AIx (Pearson's correlation coefficient 0.58, p <0.001).

Table 2.

Arterial Stiffness Parameters in the Study Population

Parameter	Value*
Carotid-femoral pulse wave velocity (cm/sec)	935.5 ± 29.0
Elevated carotid-femoral pulse wave velocity†	83 (57.6%)
Right brachial-ankle pulse wave velocity (cm/sec)	1354.6 ± 44.3
Elevated right brachial-ankle pulse wave velocity†	74 (51.4%)
Left brachial-ankle pulse wave velocity (cm/sec)	1473.5 ± 326.4
Elevated left brachial-ankle pulse wave velocity†	102 (70.8%)
Brachial systolic blood pressure (mmHg)	133.6 ± 16.5
Central aortic systolic blood pressure (mmHg)	115.1 ± 16.6
Brachial diastolic blood pressure (mmHg)	79.4 ± 11.0
Central aortic diastolic blood pressure (mmHg)	79.3 ± 10.1
Augmentation pressure (mmHg)	6.9 ± 6.1
Augmentation index (%)	17.2 ± 11.6

*All values are in mean ± S.D. for continuous variables and actual value with percentage in parentheses for categorical variables.

†Compared with age- and gender-specific normal values derived from a reference population.

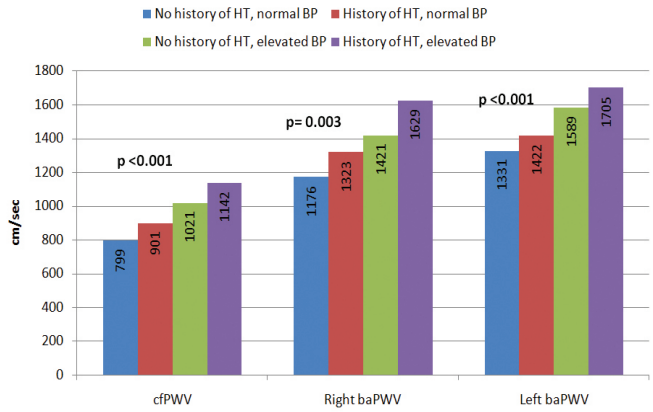

Figure 4. Arterial stiffness in different vascular segments in hypertensive and nonhypertensive subjects according to control of blood pressure. BP, blood pressure; baPWV, brachial-ankle pulse wave velocity; cfPWV, Carotid-femoral pulse wave velocity; HT, hypertension.

We divided all patients into four groups according to history of HT and level of BP control—group 0 (no history of HT and BP also normal, <140/90 mmHg), group 1 (history of HT but BP controlled), group 2 (no history of HT but elevated BP), and group 3 (history of HT and elevated BP). Although there was no significant difference in systolic BP between group 0 and 1 (123.6 ± 8.5 mmHg and 126.4 ± 8.3 mmHg respectively, p=NS) and between group 2 and 3 (152.1 ± 16.7 mmHg and 152.1 ± 14.0 mmHg, respectively, p=NS), there was progressive increase in cfPWV, right baPWV, and left baPWV from group 0 to 3 (p <0.01, Fig. 4). This suggested that effective control of BP could result in improvement in arterial stiffness in known hypertensives. However, arterial stiffness in these individuals still remained elevated as compared to non-hypertensives with normal BP.

Relationship of arterial stiffness parameters with other CV risk factors (Table 3)

There was no difference in cfPWV, right and left baPWV, and AIx in patients with or without diabetes mellitus, smoking, and family history of premature CAD and dyslipidemia (except increased right baPWV in patients without dyslipidemia; 1540.4 ± 880.5 vs 1288.0 ± 350.2 cm/sec, p = 0.02). In addition, there was no correlation between any of the above arterial stiffness parameters and fasting blood glucose, TC, and HDL-cholesterol.

Discussion

Our study, which assessed arterial stiffness in North-Indian subjects who were free of CV disease, showed that (1) hypertensive patients have significantly

Table 3.
Selected Arterial Stiffness Parameters in Relation to Cardiovascular Risk Factors.

Risk factor		cfPWV (cm/sec)	Right baPWV (cm/sec)	Left baPWV (cm/sec)	Augmentation index (%)
Hypertension	No (43)	799.5 ± 188.8	1175.9 ± 277.7	1331.1 ± 214.4	10.8 ± 10.7
	Yes (101)	993.4 ± 382.6	1430.7 ± 593.0	1534.1 ± 347.4	20.0 ± 10.9
	P	0.002	0.008	0.001	<0.001
Diabetes mellitus	No (122)	931.0 ± 366.6	1361.1 ± 563.0	1460.2 ± 333.5	16.9 ± 11.8
	Yes (22)	960.6 ± 217.0	1318.7 ± 309.2	1547.4 ± 279.5	19.2 ± 10.0
	P	0.71	0.73	0.25	0.38
Current smoking	No (111)	933.2 ± 382.1	1342.2 ± 586.9	1476.3 ± 356.6	16.7 ± 12.3
	Yes (33)	943.3 ± 193.9	1396.6 ± 274.1	1464.3 ± 197.5	19.2 ± 8.5
	P	0.88	0.61	0.86	0.27
Family history of premature CAD	No (84)	930.2 ± 235.1	1350.6 ± 315.6	1466.2 ± 258.7	18.4 ± 10.9
	Yes (60)	942.9 ± 463.4	1360.3 ± 737.6	1483.8 ± 404.9	15.6 ± 12.4
	P	0.83	0.91	0.75	0.16
Dyslipidemia	No (34)	1013.9 ± 584.2	1540.4 ± 880.5	1514.1 ± 492.4	17.9 ± 14.7
	Yes (106)	901.8 ± 226.3	1288.0 ± 350.2	1448.0 ± 249.1	16.6 ± 10.4
	P	0.10	0.02	0.30	0.56

CAD, coronary artery disease; cfPWV, carotid-femoral pulse wave velocity; baPWV, brachial-ankle pulse wave velocity.

increased arterial stiffness, (2) arterial stiffness increases progressively as BP increases, and (3) arterial stiffness can be improved with effective control of BP, though it still remains elevated as compared to non-hypertensives with normal BP.

HT is one of the most important determinants of arterial stiffness. A number of studies in Western populations have shown that arterial stiffness is significantly related to BP and is an independent predictor of CV events in hypertensives (1, 4–6, 10). Owing to its significant prognostic value, assessment of arterial stiffness has been recommended as a routine tool, wherever available, in the evaluation of hypertensive individuals (12). In addition, assessment of arterial stiffness may also be helpful in guiding antihyhpertensive therapy (1, 19). Various pharmacological and nonpharmacological interventions aimed at control of BP have been shown to improve arterial stiffness also, though not to the same extent (19–27). There is evidence to suggest that such improvement in arterial stiffness may be an important determinant of benefits achieved with antihypertensive therapy. In a study on patients with end-stage renal disease, Guerin et al. (28) found that lack of attenuation of arterial stiffness in spite of reduction in BP was an independent predictor of all-cause mortality. In addition, use of angiotensin-converting enzyme inhibitors was associated with better survival, an effect which was independent of BP reduction (28). In the Regression of Arterial Stiffness in a Controlled Double-Blind (REASON) trial, a combination of perindopril and indapamide produced much greater reduction in systolic BP and pulse pressure (both indirect measures of arterial stiffness) than atenolol, despite similar reduction in diastolic BP (29). The greater effect of perindopril/ indapamide combination on systolic BP and pulse pressure was associated with greater reduction in left ventricular mass also (30). The clinical value of such effects was evaluated further in the Conduit Artery Function Evaluation (CAFÉ) study (19), which was a substudy of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) (31). Despite a similar impact on brachial BP, amlodipine/perindopril based therapy resulted in substantially greater effect on central aortic pressure than atenolol-based regimen. Importantly, the greater effect of amlodipine/perindopril therapy on central aortic pressure was associated with reduced incidence of CV events and of renal impairment (19).

Several studies have measured arterial stiffness in Indian subjects also but none has adequately reported its relationship with HT. In a study on almost 4000 individuals, which included 988 healthy controls, Sridhar et al. found significantly elevated PWV in patients with diabetes, CAD, end-stage renal disease, or rheumatoid arthritis but effect of BP on PWV was not reported (13). Similarly, Kasliwal et al. measured baPWV in patients with and without CAD and found significantly elevated baPWV among those with CAD but its relationship with HT or BP was not studied (14). In the Chennai Rural Urban Epidemiologic Study, Mohan et al. studied 1985 subjects without known diabetes. Arterial stiffness, measured as AIx, increased with increasing risk of diabetes as estimated by Indian Diabetes Risk Score. An additional finding of the study was weak but statistically significant correlation between AIx and both systolic and diastolic BP (15). In another study, PWV in different arterial segments was found to correlate with systolic and diastolic BP but once again, no further information was available on its relationship with HT (16). In a study comparing 90 healthy South Asians living in Britain with 62 matched white Europeans, arterial stiffness was found to be significantly increased in South Asians. Interestingly, mean arterial pressure was found to be an independent predictor of arterial stiffness only in South Asians and not in white Europeans (32). Our study is therefore the first one to report effect of HT and BP control on arterial stiffness in Indian subjects

Limitations

The main limitation of our study was small sample size which precluded assessment of relative impact of different BP-lowering therapies (life style measures, drugs belonging to different classes) on arterial stiffness. Small sample size was also the likely reason responsible for lack of association between arterial stiffness and other CV risk factors such as diabetes. In addition, we did not employ ambulatory BP monitoring to determine consistency of BP control. It is therefore difficult to determine whether relatively lower values of arterial stiffness parameters seen in hypertensive subjects with "controlled BP" (group 1) were merely reflective of lower BP values at the time of arterial stiffness assessment or if they actually reflected improvement in arterial stiffness. However, as mentioned above, it is noteworthy that the values of arterial stiffness parameters were much higher in hypertensive patients with "controlled BP"(group 1) than in non-hypertensive subjects with normal BP (group 0) in spite of almost similar average BP values in the two groups. Similarly, known hypertensives with

elevated BP (group 3) had stiffer arteries than group 2 patients who had almost similar BP but were not previously known to be hypertensives. This suggests that BP at the time of arterial stiffness assessment alone was not the primary determinant of arterial stiffness and the lower values of arterial stiffness parameters seen in group 1 subjects were indeed result of improved arterial compliance.

Conclusions

Our study showed that in North-Indian adult subjects, free of CV disease, arterial stiffness is significantly increased among hypertensives and the degree of arterial stiffness increases progressively with increase in BP. More importantly, control of BP can bring about significant improvement in arterial stiffness as well. This makes assessment of arterial stiffness a potentially useful tool for tracking vasculoprotective effects of antihypertensive therapy in clinical practice. However, a larger study is needed to address prognostic implications of these findings and also to determine differential effect of various BP-lowering therapies on arterial stiffness in Indian subjects.

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Conflict of Interest

None

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