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Original Article

Evaluation of arterial stiffness in elderly with prehypertension

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Abstract

Arterial stiffness is an independent marker of cardiovascular (CV) risk that increases with age. Hypertension is known to augment the age-related arterial stiffness. The influence of prehypertension on arterial stiffness in elderly is least studied. The present study was aimed to assess the age-associated arterial stiffness in the elderly subjects with prehypertension. A cross sectional study was conducted on elderly subjects aged 60-80 years with prehypertension (n=25) and age-matched normotensives (n=20). The arterial stiffness was assessed by measuring: (1) Pulse wave velocity between carotid-femoral (c-f PWV) and brachial-ankle (baPWV) (2) Augmentation index (AIx) and (3) Arterial stiffness index (ASI) at brachial (bASI) and tibial artery (aASI). We found a significant increase in c-f PWV ($p<0.001$), baPWV ($p<0.001$) and AIx@75 ($p<0.001$) in prehypertensives than normotensive elderly individuals. There was no significant difference in the ASI at brachial and tibial arteries. The significant predictor of c-f PWV and AIx@75 was SBP ($\beta=0.584$, $p=0.04$; $\beta=0.700$, $p=0.019$ respectively), and aASI was PP ($\beta=0.493$, $p=0.049$). These findings show an augmentation of age-related arterial stiffness in elderly with prehypertension.

Introduction

A meta analysis of data from 61 observational studies involving more than one million individuals indicated that the cardiovascular (CV) risks associated with high blood pressure (BP) begin from the level of 115/75 mmHg and each increment of 20 mmHg systolic and 10 mmHg diastolic BP is associated with two-fold increase in mortality from both ischemic heart disease and stroke (1). Based on these evidences, the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure in its 7th Report (JNC 7) introduced a prehypertension (pre-HT) category with a systolic blood pressure (SBP) of 120 to 139 mmHg and diastolic blood pressure (DBP) of 80 to 89 mmHg, requiring attention and intervention at an early stage (2). An association of pre-HT and increased risk of major CV events has been documented (3, 4).

The arterial stiffness is an independent marker of CV risk (5) that increases with age and elevation of BP (6). Systolic BP and pulse pressure (PP) are related to the physical properties of elastic arteries. Pulse wave velocity (PWV), augmentation index (AIx) and arterial stiffness index (ASI) are markers of arterial stiffness which are widely accepted and recommended for measure of arterial stiffness (7, 8). PWV is a measure of regional arterial stiffness. An elevation in PWV indicates an increase in arterial stiffness or decrease in vascular compliance. AIx is

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a measure of wave reflection. An increase in AIx reflects an elevation in arterial stiffness. ASI is a measure of local arterial stiffness. Measurement of PWV and wave reflection have now recognized as an important prognostic indicator than BP to assess the CV risk. Carotid-femoral PWV (c-f PWV) is a gold standard measure of aortic stiffness (7). Brachial-ankle PWV (baPWV) is also an index of arterial stiffness and is strongly correlated with c-f PWV (9). It reflects the function of central elastic artery and peripheral muscular arteries. It is a simple measure of arterial stiffness and an independent predictor of carotid atherosclerosis in the elderly (10).

Hypertension is known to elevate the arterial stiffness (6). Impaired aortic elastic properties in young and middle-aged subjects with pre-HT have been reported (11, 12). As per our knowledge one study evaluated the influence of pre-HT on central large arterial function by measuring PWV and AIx but that too was restricted to middle-aged subjects (13). Though the elderly subjects are at greater CV risk with respect to arterial stiffness, arterial function in prehypertensive subjects were least studied. Therefore, the present study was aimed to evaluate the age-associated arterial stiffness in the elderly subjects with pre-HT.

Methods

A cross sectional study was conducted in elderly male subjects aged 60-80 years (14) with pre-HT (n=25) and age-matched normotensives (n=20). Subjects on any medications, subjects with diabetes mellitus, CV diseases or suffering from any acute or chronic diseases were excluded from the study. Informed consent was obtained for participation in the study. The study was approved by the institutional ethical committee of Sri B.M. Patil Medical College, Hospital and Research Centre, BLDE University, India as per the guidelines (2006) of Indian Council of Medical Research. Declaration of Helsinki has been followed during the entire study. All the recordings were done in the morning between 8 am to 11 am at room temperature following supine rest for 10 minutes.

I. Measurement of blood pressure and diagnosis of prehypertension

Brachial artery BP was measured thrice at an interval of one minute in sitting posture using mercury sphygmomanometer. The average of three recordings was considered. Subjects with SBP between 120 and 139 mmHg or DBP between 80 and 89 mmHg were diagnosed as pre-HT as per JNC 7 report (2). Subjects with systolic BP < 120 mmHg and a diastolic BP < 80 mmHg were considered as normotensives. Pulse pressure was calculated as the difference between SBP and DBP, and mean arterial pressure (MAP) as one third of PP plus DBP.

II. Assessment of arterial stiffness

Vascular function was assessed by Oscillometric method using a non-invasive automatic device (Periscope, Genesis Medical Systems, India). Periscope is a validated 8-channel real time PC-based simultaneous acquisition and analysis system (15). The acquisition rate was 200 samples per second. This device uses four BP cuffs and two-channel ECG leads to record arterial pressure waveforms and ECG simultaneously. The recordings were made in supine position. ECG electrodes were placed on ventral surface of both wrists and medial side of ankles, and BP cuffs were wrapped on both upper arm and above ankles. The BP cuffs were connected to an oscillometric pressure sensor that measures BP volume waveforms and to a plethysmographic sensor that determines volume pulse form from the brachial and tibial arteries. The data obtained in 10 seconds was stored in the computer for further analysis. As the device is fully automated and does not require any operator for handling any probe to record the waveforms, it is devoid of any operator bias. Periscope is fully automatic, so once the test is started, the recording completes itself by displaying the results directly. It calculates PWV, AIx and ASI as follows:

i. Calculation of pulse wave velocity

   a. Brachial-ankle PWV: Periscope estimates baPWV (reflects stiffness of central elastic artery & peripheral semi-muscular arteries)

using arterial pressure waveforms (Brachial and Tibial artery) and ECG recordings (Lead I & II). Pulse transit time (PTT) in seconds elapsed between brachium and respective ankle was taken as the time difference between the R-wave of ECG and foot of respective pulse wave. The distance between the sampling points of baPWV was calculated automatically by the device according to the height of the subject. The baPWV was calculated by dividing the distance by PTT.

$$\text{brachial - ankle PWV} = \frac{\text{Lba}}{\text{PTTba}}$$

Where Lba = Distance between respective brachium and ankle

PTTba = PTT between brachium and respective ankle was calculated as the time difference between the feet of respective pulse wave originated from R-wave (QRS complex) of ECG.

b. The carotid-femoral PWV, a measure of aortic stiffness was calculated by the composite baPWV found out by averaging left and right baPWV. Periscope estimates the c-f PWV on the basis of equation (0.8333* Avg. baPWV-233.33) derived by regression analysis between baPWV and c-f PWV from the studies conducted elsewhere (9).

ii. Calculation of arterial stiffness index.

ASI reflects local arterial stiffness. Periscope calculates ASI using oscillometric envelopes. ASI at brachial artery as brachial ASI (bASI) and tibial artery as ankle ASI (aASI) was calculated by quantifying the oscillometric envelopes derived from the oscillations in the respective artery.

ASI = (Systolic side value of cuff pressure at 80% of maximal oscillation amplitude of cuff) - (Diastolic side value of cuff pressure at 80% of maximal oscillation amplitude of cuff).

iii. Estimation of aortic augmentation index

Aortic pressure was measured by Oscillometric PWV method. Periscope uses brachial BP and c-f PWV to determine the aortic root pressure. It was based on the mathematical analysis of invasive aortic pressure values (Fluid-filled catheter method) with respect to the brachial BP and PWV found non-invasively. Aortic root pressure values were directly proportional to a combination of both the brachial pressure value and c-f PWV. A significant correlation was found in these parameters value when multivariate regression analysis was carried out. Equation relating aortic pressure, brachial pressure and c-f PWV values with respective coefficients was derived and added in the Periscope to determine equivalent aortic pressure.

The rise in the systolic pressure is called an augmentation pressure. Augmentation index is the ratio of augmentation pressure to the aortic PP and is expressed in percentage. This Oscillometric PWV method used for estimation of aortic AIx by periscope has been validated (16). As it was reported that AIx is influenced by heart rate, an index normalized for a heart rate at 75 bpm (AIx@75) was used in this study (17).

III. Statistical analysis:

The obtained data was expressed in mean and standard deviation. To determine the statistical significance between the two groups, an Unpaired t test was used for normally distributed data and Mann-Whitney U test for non-normally distributed data. The Pearson's correlation coefficient (normal data) and Spearman's correlation coefficient (non-normal data) was used to determine an association between arterial stiffness and BP parameters. The predictors of arterial stiffness were determined by multiple linear regression analysis. Statistical significance was established at $p< 0.05$. Data was analyzed using SPSS software version 20.

Results

I. Baseline characteristics

The baseline characteristics of elderly prehypertensive and normotensive subjects were given in Table I. There was no significant difference in age, BMI, plasma glucose, total cholesterol and serum triglyceride between two groups. As expected SBP ($p<0.001$) was significantly high in pre-HT subjects as compared to normotensives. PP ($p<0.001$) and MAP ($p<0.001$) were also significantly increased in pre-HT subjects than normotensives. There was no significant difference in DBP between the two groups.

II. Vascular function analysis

There was a significant increase in c-f PWV ($p<0.001$), baPWV ($p<0.001$) and AIx@75 ($p<0.001$) in prehypertensives than normotensive subjects. We could not find any significant difference in the peripheral arterial stiffness parameters between the two groups (Table II).

III. Association between arterial stiffness and blood pressure parameters.

The bivariate correlations between arterial stiffness variables and BP variables of the entire study population (n=45) is shown in Table 3. Carotid-femoral PWV was significantly correlated with SBP ($p<0.001$), PP ($p=0.006$) and MAP ($p<0.001$). Brachial-ankle PWV was significantly correlated with SBP ($p<0.001$), PP ($p<0.001$) and MAP ($p<0.001$); and AIx@75 with SBP ($p<0.001$) and PP ($p<0.005$). Among the peripheral arterial stiffness parameters, bASI was significantly correlated with SBP ($p=0.044$) and PP ($p=0.012$); aASI with SBP ($p=0.005$), PP ($p=0.002$) and MAP ($p=0.014$).

In a multiple regression analysis of the entire cohort (n=45), the significant determinant of c-f PWV and AIx@75 was SBP ($\beta=0.584$, $p=0.042$; and $\beta=0.700$, $p=0.019$ respectively) and aASI was PP ($\beta=0.493$, $p=0.049$).

TABLE I: Baseline characteristics of elderly subjects with prehypertension (n=25) and normal blood pressure (n=20).

Variable	*Prehypertensive*	*Normotensive*	*t value*	*p value*
Age (years)	69.60±5.362	67.50±4.46	1.404	0.168
BMI (kg/m^2)	23.52±4.03	21.83±3.71	1.452	1.154
SBP (mmHg)	134.80±3.416	115.5±2.12	22.081	0.000***
DBP (mmHg)	73.56±4.71	71.35±4.94	1.529	0.134
Pulse pressure (mmHg)	61.24±6.13	47.70±7.24	6.86	0.000***
MAP (mmHg)	94.56±3.74	87.55±4.39	5.05	0.000***
Plasma Glucose (mg/dL)	90.29±10.16	90.56±11.44	–0.083	0.937
Total Cholesterol (mg/dL)	178.51±27.68	172.50±24.3	0.766	0.449
Serum Triglyceride (mg/dL)	97.96±22.65	91.31±16.11	1.162	0.252

BMI - Body mass index, SBP - systolic blood pressure, DBP - Diastolic blood pressure, MAP-Mean arterial pressure. Values are mean±SD; *p<0.05, **p<0.01, ***p<0.001

TABLE II: Arterial stiffness parameters in elderly prehypertensive and normotensive individuals.

Variable	*Prehypertensive*	*Normotensive*	*95% confidence interval*		*t-value*	*P value*
			Lower	*Upper*		
c-f PWV (m/s)	12.63±2.21	9.75±1.47	1.718	4.045	4.995	0.000***
baPWV (m/s)	19.16±4.01	14.24±2.02	2.929	6.903	4.989	0.000***
AIx@75 (%)	33.84±6.66	24.15±4.40	6.193	13.186	5.59	0.000***
bASI	31.44±6.66	28.05±6.81	–0.683	7.463	1.678	0.101
aASI	47.48±9.35	42.20±9.77	–0.491	11.051	1.845	0.072

Values are mean±SD; *p<0.05, **p<0.01, ***p<0.001.

TABLE III: Bivariate correlations between arterial stiffness and blood pressure parameters (n=45).

Variables	*c-f PWV (m/s)*	*baPWV (m/s)*	*AIx@75*	*bASI*	*aASI*
SBP (mmHg)	0.556***	0.619***	0.504***	0.302*	0.412**
DBP (mmHg)	0.156	0.226	–0.096	–0.260	0.149
PP (mmHg)	0.405**	0.493***	0.416**	0.373**	0.452**
MAP (mmHg)	0.456**	0.541***	0.230	–0.27	0.365*

Values are correlation coefficients (r); *p<0.05, **p<0.01, ***p<0.001

Discussion

Age-related arterial stiffness is implicated in the development of hypertension especially in elderly people. Aortic stiffness is an independent predictor of all cause CV morbidity and mortality in hypertensive patients (18) and in elderly populations (7). Even in well-functioning elderly individuals also, an elevated c-f PWV is associated with CV events (19). Therefore arterial stiffness has become an important biomarker in the evaluation of CV risk.

In the present study, the central and peripheral arterial function was evaluated in elderly subjects with pre-HT. We found a significant increase in c-f PWV by 22.80% (p<0.001), baPWV by 25.67% (p<0.001) and AIx@75 by 28.63% (p<0.001) in prehypertensive subjects than normotensives. These findings indicate an increase in central arterial stiffness in prehypertensives than normotensives. Tomiyama H et al. assessed arterial stiffness in elderly subjects at various degrees of hypertension by measuring baPWV only. They demonstrated that age-related arterial stiffness is augmented in phases according to the severity of hypertension (20). Aortic PWV <12 m/s is a strong predictor of CV risk (21). In this study, the mean c-f PWV in subjects with pre-HT was 12.63 m/s. This high PWV in elderly with pre-HT shows that they are at CV risk. There was an increase in mean bASI and aASI, an index of brachial and tibial artery stiffness respectively, in prehypertensives than normotensives but were not statistically significant. These findings demonstrate an augmentation in age-related arterial stiffness in elderly with pre-HT.

The age-related structural change in the media of aorta include fracture of elastin, increase in collagen and calcium deposits. These changes in media are associated with increased expression of matrix metalloproteinases (MMP). The factors those determine the stiffness of arteries and its ability to expand and recoil are structural proteins and pressure exerted by blood on their wall (22). The acceleration in age-associated arterial stiffness in prehypertensive subjects may be attributed to increase in BP. In the present study, SBP was the significant determinant of aortic PWV and wave reflection.

However, the relation between arterial stiffness and high BP remains unclear. Dernellis et al. in a longitudinal study in middle-aged and elderly subjects have shown that arterial stiffness increases before the development of hypertension (23). Liao D et al showed that the risk of development of hypertension increases by 15% with an increase in arterial stiffness by 1% standard deviation independent of established risk factors and level of BP in middle-aged subjects (24). In contrast, other studies showed that hypertension accelerates the rate of arterial stiffness (20, 25). These studies imply the bidirectional relationship between the arterial stiffness and BP (26).

Aortic stiffness is shown as an independent predictor of progression to hypertension in normotensive subjects (23). Individuals with pre-HT were found at greater risk to develop hypertension and the rate of progression was higher in elderly (27, 28). This progression of pre-HT to hypertension in elderly can be attributed to elevation in arterial stiffness.

In the elderly an age-related increase in arterial stiffness increases SBP and decreases DBP, thus causing the widening of PP (29). This high PP creates greater pulsatile stress on the arterial system

and may result in vascular damage (30). PP was shown as a strong predictor of coronary artery disease and CV mortality in older persons (31, 32). Moreover, it is also more closely associated to CV events than SBP or DBP alone (31). Pulse pressure is a best tool for measuring vascular aging. We found a significant increase in PP ($p<0.001$) in prehypertensives and it was positively correlated with c-f PWV ($p=0.006$), baPWV ($p<0.001$), AIx ($p<0.001$), bASI ($p=0.012$) and aASI ($p=0.002$). However in normotensives PP was within the normal range.

Conclusion

We found a significant increase in arterial stiffness in elderly subjects with pre-HT as compared to normotensives. A significant correlation between arterial stiffness and SBP has been noticed. Pulse pressure was also found significantly high in prehypertensives than normotensive subjects. It can be concluded from the present study that elderly individuals are at CV risk with respect to arterial stiffness even at prehypertensive stage.

Limitations of the study

Though CV risks in males are equal to females after menopause, only males have participated in the present study, which is the major limitation of the study. The sample size may be less to derive the definite conclusion. Therefore, future studies should evaluate arterial stiffness in elderly with pre-HT of both genders with large sample size.

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Conflict of interest

The authors declare that there is no conflict of interests.

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