Ascending aortic dilatation, arterial stiffness and cardiac organ damage in essential hypertension

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Title:

Ascending aortic dilatation, arterial stiffness and cardiac organ damage in essential hypertension.

Running Title: Ascending aortic dilatation and target organ damage

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Abstract. [words 235]

Aims of this study were to evaluate the prevalence of proximal ascending aortic (pAA) dilatation in essential hypertensives and the association between pAA, arterial stiffness and cardiac organ damage.
Background. Few data are available regarding patients with pAA dilatation in arterial hypertension. It is not known whether pAA dilatation may be related to increased cardiac organ damage and what the relation with central hemodynamics and arterial stiffness would be.
Methods. A total of 345 untreated and treated essential hypertensive patients (mean age, 54.3±11 years) were considered for this analysis. We measured pulsatile hemodynamic parameters and the proximal aortic diameters directly using tonometry, ultrasound imaging (echocardiography) and Doppler.
Results. Prevalence of pAA dilatation was 17%. Peripheral haemodynamic parameters were similar in patients with and without ascending aorta dilatation. We observed a slightly increase of central systolic (129.81±15.4 vs. 125.02±14.7 p 0.02) and pulse pressure (45.02±10.4 vs. 42±9.54; p 0.02) in patients with pAA dilatation. Pulse wave velocity was significantly greater (9.26±2.33 vs. 7.70±1.69 p<0.0001), as well as the augmentation index (25.86±10.2 vs. 19.41±9.52; p<0.0001) in patients with pAA dilatation. Finally left ventricular hypertrophy was thrice as frequent (32.8% vs. 13.4% p<0.0001) compared to hypertensive patients without aortic dilatation.
Conclusions. This study Shows a high prevalence (17%) of ascending aorta dilatation in patients affected by essential hypertension, without further complications. Dilatation of the ascending aorta is associated both to an increased cardiac organ damage and arterial stiffness.

Keywords: Ascending aorta dilatation; Hypertension; Left ventricular hypertrophy; Pulse Wave Velocity; Central blood pressure

Aortic root dilatation is a common clinical feature in hypertensive patients (10%) [1]. The vast majority of data in literature[1, 2] refers to the first aortic segment, known as Sinus of Valsalva (SoV), that is routinely evaluated during a standard echocardiographic exam. SoV dilatation has been shown to be related to hypertension induced organ damage, and in particular to cardiac damage (i.e. left ventricular hypertrophy). Moreover, SoV dimensions, especially when increased, are associated to increased values parameters describing central hemodynamic [3, 4], but not to increased arterial stiffness as expressed by pulse wave velocity (PWV).

The second tract of the aortic root, the proximal Ascending Aorta (pAA), can undergo dilatation as well. Nevertheless, even if this tract can be evaluated through echocardiography, few data have been published evaluating patients with this specific phenotype. Roman et al.[5] observed the association between age and aortic dimensions to be stronger when considering ascending aorta instead of SoV and it has been reported [6] a faster growth progression of the ascending aneurysm in younger subjects.

It is not known whether pAA dilatation may be related to an increased cardiac organ damage and what the relation with central hemodynamics and arterial stiffness would be.

Aims of the present study were then firstly to evaluate pAA dilatation prevalence in essential hypertensive free from other associated clinical condition and describe such a phenotype in terms of central and peripheral hemodynamic, arterial stiffness and cardiac organ damage; secondly, to evaluate possible differences between such patients and the better studied ones showing SoV dilatation.

Methods

We evaluated 345 adult outpatients with consecutive essential hypertension who were referred to the echo lab of the Hypertension Unit, University of Turin for evaluation of target organ damage.

For recruitment, all individuals underwent a full medical examination. All BP measurements were performed according to the ESH/ESC[7] recommendations. Hypertension was defined by systolic blood pressure (SBP) $\geq$ 140 and/or diastolic blood pressure (DBP) $\geq$ 90 on 3 consecutive occasions or by the assumption of antihypertensive medications.

Exclusion criteria were: age less than 18 or more than 70 years, BMI $\geq$40, secondary hypertension, non hypertensive cardiovascular disease, any valvulopathy more than mild, bicuspid aortic valve, diabetes, presence of associated clinical conditions as defined by the ESH/ESC[7] guidelines, family history of aortic rupture, clinical characteristics suggesting a genetic predisposition to Aortic Disease such as Marfan syndrome. The study was approved by our Institutional Review Committee and all subjects provided their written informed consent.

Arterial Stiffness and Wave Reflection Measurements.

BP and heart rate were measured three times, at 2 min intervals, using a validated automatic oscillometric device (Omron Matsusaka Co., Ltd., Japan M5-I). The mean value from these three measurements was used for further analysis. Pulse Wave Velocity (PWV), a classic index of arterial stiffness was measured along the descending thoraco-abdominal aorta by the foot-to-foot velocity method, as previously published and validated[8]. Briefly, waveforms were obtained transcutaneously over the common carotid artery and the femoral artery and the time delay (t) was measured between the feet of the 2 waveforms. The distance (D) covered by the waves was assimilated to the distance measured between the 2 recording sites. PWV was calculated as PWV=D (meters)/t (seconds) using the Sphygmocor system (AtCor Medical, Sydney, Australia) on the day of the echocardiography assessment and after an overnight fast.

Augmentation Index and 'central' blood pressure parameters.

Radial artery waveforms were obtained with a high-fidelity micromanometer (SPC-301; Millar Instruments) from the wrist and a corresponding central waveform was generated with a validated transfer function (Sphygmocor) as previously described in detail and validated[9, 10]. Calibration of the radial arterial waveform obtained by applanation tonometry was carried out with SBP and DBP values recorded non invasively. DBP and mean arterial pressures (MAP) were assumed to remain constant throughout the arterial tree.

Augmentation pressure was the height of the late systolic peak above the inflection. The aortic or central augmentation index (AIx) was calculated as the ratio of the pressure difference between the "shoulder" of the pressure wave and "peak" systolic pressure (*P*)[11] and the PP according to the formula: AIx = (*P*/PP) X100. Values were considered as positive if the "shoulder" occurred before the peak pressure and as negative if the shoulder occurred after the pressure peak.

Central pulse pressure (cPP) was calculated as the difference between the estimated aortic systolic and diastolic pressures[10]. PP amplification ratio (PPamp) was calculated as the ratio of peripheral to central PP.

Echocardiography.

A two-dimensional echocardiogram was performed at rest in the left lateral decubitus position with commercially available ultrasound systems (ATL 5000; Bothell, Washington, USA). Multiple-frequency phased array transducers (2–4MHz) were used.

Technical details have been reported previously[12]. Briefly, the left ventricular mass (LVM) was estimated from the end-diastolic left ventricular internal diameter (LVIDd), interventricular septum (IVS) and inferolateral wall thickness (ILW) by Devereux's formula [13] and was normalized to height $^{2.7}$. Relative wall thickness (RWT) was calculated as (2*ILW)/LVIDd. Patterns of left ventricular geometry were defined according to ESH/ESC[7] recommendations. Left ventricular hypertrophy was defined as left ventricular mass indexed for height$^{2.7}$ > 46.7 g/m$^{2.7}$ in women or > 49.2 g/m$^{2.7}$ in men[14].

Body surface area (BSA) was calculated using the Dubois and Dubois formula:

$BSA=0.20247\ [weight^{0.425} \times (height/100)^{0.725}]$

Aortic size was measured using 2-dimensional echocardiography; images of the proximal aortic root were obtained from a parasternal long axis view, as the maximal distance between the two leading edges of the anterior and posterior aortic root walls at end diastole[15]. Two sites of the proximal aorta were considered: the Sinus of Valsalva, usually called aortic root , and the ascending aorta at its maximum size. All aortic diameters have been normalized to the BSA for the analysis, as above described.

Considering current literature[16] aortic dilatation was defined as aortic dimension indexed for BSA more then 2.1 cm/m^2. We considered two major group, according to the status of the ascending aorta. Secondly, we evaluated patient with or without dilatation of the Sinus of Valsalva in order to evaluate similarities and differences of this group compared to patients having pAA dilatation.

Statistical analysis.

Statistical analysis was conducted using SAS V8 software (SAS Institute Inc. – Cary, NC, USA). The parametric distribution of the variables was analysed using the Kolmogorov Smirnov test and residual analysis. Data are expressed as mean ± Standard Deviation (SD) or as median and interquartile difference if appropriate. Differences between means were examined using a *t* test or ANOVA for normal distributed variables. Kruskal Wallis or non parametric ANOVA were used for non normal distributed variables. Multiple regression analyses were used to assess the independent determinants of Aortic dimensions. Independent variables were selected based on their known or expected association with Aortic dimensions. Statistical significance was assumed if the null hypothesis could be rejected at $p<0.05$.

Results.

Table 1 shows clinical features of patients with ascending aorta dilatation compared with normal pAA. Prevalence of pAA dilatation was 17%.

Absolute aortic dimensions were significantly related to age (r 0.42 $p<0.0001$), BMI (r 0.28 $p<0.0001$), diastolic pressure (r 0.13 p 0.01). After correction for BSA, the correlation with BMI was no longer detectable, but the one with age was shown to be even stronger (r 0.54 $p<0.0001$). Peripheral haemodynamic parameters (table 1) were similar in patients with and without pAA dilatation.

Patients having pAA dilatation were an average ten years older and dilatation was more often seen in female (prevalence 24% vs 16%; $p<0.05$).

We observed a greater prevalence of active drug treatment (100% vs. 79.2%; p 0.01) and a greater number of antihypertensive drugs (1.45±1 vs. 2±0.97 p 0.007) used in patients with ascending aorta dilatation: similar in the two groups was, nevertheless, prevalence of different classes of drugs used.

Considering central hemodynamic parameters (table 2), we observed a significant increased of systolic and pulse pressure, while diastolic pressure, and, as expected, mean pressure, were similar.
Pulse wave velocity was significantly greater (9.26±2.3 vs. 7.7±1.7 p<0.0001), as well as the augmentation index , both when considering absolute (30±10.5 vs. 22.7±10; p<0.0001) and indexed for heart rate (25.9±10 vs. 19.4±9; p<0.0001) values. The PPamp ratio was significantly lower in the group of patients with aortic dilatation (124±11 vs. 134.5±15; p<0.0001), suggesting a greater arterial stiffness in such hypertensives. Considering echocardiographic variables (table 2) patients with pAA dilatation showed a significant increase of left ventricular mass (p <0.0001) compared to patients with normal aorta.
Left ventricular hypertrophy was thrice as frequent compared to hypertensive patients free from aortic dilatation; significantly increased was as well the relative wall thickness (0.43±0.10 vs. 0.40±0.07; p 0.01).
Patients with pAA dilatation showed significantly increased dimensions of SoV compared to the control group (39.09±5.11 vs. 36.86±4.75 p<0.0001)

Taken together, these data suggest a strong association between pAA dimensions (in particular when indexed for BSA) and hypertension related organ damage, in terms of both increased left ventricular mass and arterial stiffness.

Male-female differences

As described, the study population comprehended mainly male subjects (75%) but the prevalence of pAA dilatation was significantly greater in the female sex (24% vs 16% p<0.05).
Male and female patients had similar age and mean pressure. Male subjects had, in average, a greater systolic (133.6±16.7 vs. 139.0±15.0 p 0.01) and pulse pressure (52.7±11.7 vs. 56.6±10.6; p 0.005). Echocardiographic features such as left ventricular mass indexed for BSA and atrial dimension were similar. Considering parameters of central hemodynamic we observed similar pulse wave velocity and central pressure (systolic, diastolic and pulse pressure), but a clear and statistically significant increase of Augmentation Index in the female population (29.5±8.6 vs. 18.1±8.8 p<0.0001), together with a lower PPAmp Index (122.3±10.1 vs. 135.4±15.1; p<0.0001).

Considering only patients with pAA, the two subgroups (male vs female) had similar characteristics with the only exception, again, of the augmentation index (34.78±10.74 vs.22.13±7.31 p<0.0001), significantly greater in female, and the PPAmp Index (117.6±6.74 vs.126.76±11.33 p<0.0001), greater in the male population.

Ascending Aorta vs Sinus of Valsalva dilatation

The second part of the study focused on highlighting differences between dilatation involving ascending aorta and Sinus of Valsalva. Patients were then divided in four subgroups: normal aortic dimensions (group

A), SoV dilatation alone (group B), pAA dilatation alone (group C) and dilatation of both segments (group D). Clinical features are summarized in table 3.
Dilation of SoV alone was present in 15.9% of patients, while subjects with pAA dilatation were 11%, and 6.7% of the subjects showed a dilatation involving both segments. Patients with isolated dilatation of SoV (group B) and patients with normal aortic dimensions had very similar clinical features .
Hypertensive patients with lone pAA dilatation were averagely older, with a significant prevalence of female sex, like patients in group D with combined dilatation of SoV and pAA. Other features were substantially similar to those of other groups.
As for cardiac organ damage, left ventricular hypertrophy had a prevalence of 14% both in the group with SoV dilatation and in the group of patients with normal aortic dimensions while the prevalence was significantly higher in the subgroup of patients with pAA dilatation – with (39%) or without (28%) associated dilatation of SoV-.

In the evaluation of arterial stiffness parameters emerged that the subgroup of patients with pAA dilatation showed significantly increased Pulse Wave Velocity values (e.g. 9.0±1.7 vs. 7.7±2.1; $p<0.0001$) compared to patients without pAA enlargement. These data were confirmed even after correction for possible confounding variables such as age (data not shown).
Considering central hemodynamic parameters, a significant increase of central pulse pressure and augmentation index was detectable. Patients with isolated pAA dilatation had a significant increase of AIx and a similarly significant decrease of PPamp Ratio, when compared to other groups, and the difference was statistically relevant even when comparison was made with patients affected by dilatation of both SoV and pAA (table 4) .
Focusing our attention on the SoV dilatation group only, we observed that patients had central pressure values comparable to the ones of hypertensive patients free from aortic dilatation, but a significant increase of PPamp Ratio compared to all groups.

Lastly, we evaluated possible independent predictors of aortic dimensions. The performed multiple regression analysis (table 5) included clinical (age, sex, BMI), hemodynamic (pPP, cPP) and echocardiographic (LVMi) parameters, as well as parameters describing arterial stiffness (PWV, AIx, PPAmpIndex). We tested apart the different aortic segments (pAA and SoV) considering both absolute and indexed values. Results show that age and left ventricular mass are significantly associated to absolute and indexed aortic root dimensions, both considering pAA and SoV.
Pulse wave velocity, a strong index of arterial stiffness, was significantly associated to dimensions of proximal ascending aorta, but not to SoV diameters.

Discussion

The main findings of this study are: first, ascending aorta dilatation is a common phenotype in hypertensive patients, being present in up to 17% of our study population. Second, ascending aorta dilatation is associated to significant cardiac organ damage and to a similar increase of arterial stiffness. Lastly, hypertensive patients with Sinus of Valsalva dilatation alone (16% of our population), i.e. without associated dilatation of ascending aorta, show benign features in terms of cardiac organ damage and arterial stiffness, similar to those of essential hypertensive with normal aortic dimensions. Taken together, these data suggest the dilatation of the ascending aorta as a key point in the identification of subjects with a significant increased of organ damage, and, likely, of cardiovascular risk.

Prevalence and Clinical features

Dilatation of proximal aorta (Sinus of Valsalva, ascending aorta or both), represents a clinical phenotype with high prevalence in our group of hypertensives studied. One third of the patients had at least mild dilatation in one of the considered sites (Sinus of Valsalva, ascending aorta or both).

To the our knowledge, no data were reported previously on the prevalence of dilatation of proximal aorta, in uncomplicated essential hypertensive.

In our population, 11% of patients showed dilatation of the ascending aorta, with normal Sinus of Valsalva. This finding suggests that ascending aorta evaluation should be routinely performed during a standard echocardiographic exam in the hypertensive patient.

On the other hand, prevalence of SoV dilatation has been studied in hypertensive patients with a prevalence ranging from 4.2%[2] and 11%[1]. Our data are in agreement with recent reports[1] describing the high prevalence of SoV dilatation in hypertensive patients. In our population SoV dilatation (alone or in combination with ascending aorta dilatation) was twice as common (22%). This result may be due to a referral bias, as patients with such a phenotype are frequently referred to our Unit; moreover, in defining dilatation we followed the current European recommendations[16], using a single cut off that considers BSA indexation (2.1 cm/m^2), without taking into account absolute values of aortic diameter, as frequently done in published works [17]. Such a difference, if confirmed, would indicate a potential under diagnosis of SoV dilatation due to the lack of adjustment for BSA in the specific subgroup of patients with low BSA and small linear dimensions.

Some anthropometric variables such as age, sex and BSA showed to be strictly related to aortic dimensions. Aortic aging is characterized by loss of elastic vassal properties, with fragmentation and thinning of the artery walls. Progressive reduction of elastin concentration and parallel increase of collagen cause a reduction of vascular elasticity that determines aortic remodelling and dilatation[18].

In our population patients showing aortic dilatation were in average 10 ears older than patients with normal aortic dimensions. Our data confirm[6, 19] the association between Sinus of Valsalva, age and body surface, already described in different patients population, affected or not by essential hypertension: as expected, such association remains present considering not only SoV, but ascending aorta diameters as well, a subset never before analysed in hypertensives. The thigh association with height and weight underlines the importance of regularly applying BSA indexation when analysing aortic dimensions.

We observed a high female prevalence (43%) in the group of patients with isolated dilatation of the ascending aorta. Few data are present in literature [6, 20] regarding thoracic aortic aneurysm: in such a contest, the more dramatic complication, aortic dissection, has a worst prognosis in female patients[21]. Our finding clarify the importance of early identification of female subjects with pAA dilatation, as potentially carrying a higher dissection risk.

Furthermore, the group of patients with dilatation of the ascending aorta showed a significant increased of central hemodynamic parameters. In particular, women with ascending aorta dilatation, when compared to men, had a significant increase of Augmentation Index, with a parallel, significant reduction of great vessel elasticity, as described by a reduced PPampRatio. Central arterial pressure waveform differs significantly in women and men: it is known that women have an inappropriately higher vascular loading condition and larger reflected waves [22]. It has been recently hypothesized that increased AIx in female patients could be associated to greater risk of developing normal ejection fraction heart failure[22]. Our data confirm the association between female gender and AIx: in particular, increased AIx in patients with enlarged ascending aorta could identify a greater susceptibility of such a subgroup in developing aortic diseases.

Ascending Aorta Dilatation, Left Ventricular hypertrophy and Arterial Stiffness

Ascending Aorta dilatation in our population was strictly associated to an increased cardiac (left ventricular hypertrophy) and vascular (arterial stiffness) organ damage.

In the past [1, 17, 23], a significant association has been observed between Sinus of Valsalva dilatation and left ventricular mass, and this has been confirmed in our study. However, we show that only when a dilatation of Sinus of Valsalva is accompanied by a similar dilatation of the ascending aorta, a significant increase in left ventricular mass is detectable. On the other hand, with a selective dilatation of Sinus of Valsalva prevalence of left ventricular hypertrophy is similar to the one observed in hypertensives with normal aortic dimensions. Dilatation of the Ascending aorta would then be a stronger marker of hypertension-induced damage. Confirmatory in this hypothesis is the association we found between Ascending aorta dimensions and Pulse Wave Velocity.

Pulse wave velocity is a well known marker of cardiovascular risk[24, 25], as a index of arterial tree aging [26]. Sugawara et al.[27], using MRI, showed that elongation of ascending, but not of descendent, aorta, was directly associated to PWV increase even in apparently healthy subjects. Our study suggests that, in

hypertensive patients, for an increase in ascending aorta dimensions might occur a parallel loss of the elastic properties of the vessel, as shown by a direct and independent increased of the measured PWV.

Perspectives

In summary the present results indicate a high prevalence of ascending aorta dilatation in essential hypertensive (uncomplicated) patients. On this basis the evaluation of ascending aortic tract should be part of the routine echocardiography exam for the hypertensive patient in order to avoid a missed diagnosis of aortic dilatation.

Further the dilatation of the ascending aorta is associated to an increased cardiac organ damage and, similarly, to an increased arterial stiffness.

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Table 1. Clinical characteristics of the patients

Variable	**Normal Ascending Aorta**	**Dilated Ascending aorta**	P
N	284	61	
Age (years)	52.3±11.8	62.6±8.6	<0.0001
Male prevalence (%)	79.8%	70.5%	0.10
Body Mass Index (Kg/m2)	27.2±3.9	26.8±3	0.46
pSBP (mmHg)	137.6±15.5	139±15.2	0.5
pDBP (mmHg)	81.8±9.8	83.6±9.6	0.17
pMBP (mmHg)	101.3±11.2	103.7±11.4	0.12
pPP (mmHg)	55.8±10.9	55.4±10.9	0.77
HR (bpm)	68.2±10	65.8±9	0.08
Current smokers (%)	16.5%	11.5%	0.61
Duration of Hypertension (months)	60 [18-130]	120[48-240]	0.01
Overweight (BMI>25 Kg/m^2)	50.35%	50.82%	0.73
Obesity (BMI>30 Kg/m^2)	18.66%	14.75%	0.73
Blood Pressure <140/90	57.6%	46.3%	0.12
Grade 1	31.8	43.1	0.2
Grade ≥2 (≥160/100)	10.6	12.1	0.22
Isolated Systolic Hypertension	24.1%	25.8%	0.78
Active antihypertensive drugs (%)	79.2%	100%	0.01

ARB	73.7%	78.6%	0.52
ACE-I	18%	12%	0.43
CCB	46.3%	54.7%	0.32
Thiazydes	28.4%	40%	0.14
Beta Blockers	25.7%	35%	0.24
Number of Hypertensive drugs/pts	1.45±1.18	2±0.97	0.007

pSBP peripheral systolic blood pressure; pDBP peripheral diastolic blood pressure; pMBP peripheral mean blood pressure; pPP peripheral pulse pressure; BMI: body mass index; HR: heart rate; ARB: angiotensin II receptor Blockers; ACE-I Angiotensinogen Converting Enzyme Inhibitors.

Table 2. Pulse Wave Velocity, Central hemodynamic end Echocardiographic parameters

Variable	**Normal Ascending Aorta**	**Dilated Ascending aorta**	P
Pulse Wave Velocity (m/s)	7.70±1.69	9.26±2.33	<0.0001
Central Haemodynamics			
cSBP (mmHg)	125.02±14.7	129.81±15.43	0.02
cDBP (mmHg)	83.02±9.83	84.79±9.72	0.20
cMBP (mmHg)	101.31±11.17	103.71±11.43	0.12
cPP (mmHg)	41.99±9.54	45.02±10.37	0.02
Augmentation Index (%)	22.69±10.42	30.27±10.48	<0.0001
Augmentation Index HR75 (%)	19.41±9.52	25.86±10.20	<0.0001
PPamp ratio	134.5±15.3	124.1±11	<0.0001
Echocardiographic parameters			
LV morphology			
LVM (g)	170.2±45.5	181.96±52.3	0.07
LVMi ($g/m^{2.7}$)	38.3±9.3	44.9±12.3	<0.0001
RWT	0.40±0.07	0.43±0.1	0.01
Left ventricular hypertrophy (%)	13.4%	32.8%	0.002
Left Atrium			
LA diameter (mm)	37.3±5.1	38.55±5.8	0.09

LAV (cc)	58.8±19.2	59.41±13.2	0.83
LAVi (cc/m^2)	29.9±9.4	32.11±6.4	0.12
Aortic diameter (mm)			
Sinus of Valsalva	36.86±4.7	39.09±5.1	0.001
Ascending Aorta	34.67±4.7	41.59±3.8	<0.0001

cSBP central systolic blood pressure; cDBP central diastolic blood pressure; cMBP central mean blood pressure; cPP central pulse pressure; pPP peripheral pulse pressure; PPamp: Pulse Pressure amplification ratio (pPP/cPP); LVM: left ventricular Mass; LVMi: left ventricular Mass indexed height 2.7; RWT: relative wall thickness; LA: Left atrium; LAV: Left atrial volume; LAVi: Left atrial volume indexed for Body Surface Area

Table 3. Clinical and peripheral hemodynamic parameters according to the site of aortic dilatation

Variable	**Group A**	**Group B**	**Group C**	**Group D**	p
Sinus of Valsalva	Normal	Dilated	Normal	Dilated	
Ascending Aorta	Normal	Normal	Dilated	Dilated	
N (%)	229 (66.4%)	55 (15.9%)	38 (11%)	23 (6.67%)	
Age (years)	51.8±11.0*	54.3±14.5	62.7±8.8	62.4±8.5	<0.0001
Male prevalence (%)	78%	87%	57%	91%	0.002
Body Mass Index (Kg/m2)	27.2±3.7	27.6±4.7	26.4±2.4	27.5±3.	0.51
pSBP (mmHg)	137.6±15.4	137.2±16.3	137.4±16.1	141.7±13.5	0.66
pDBP (mmHg)	81.6±9.4	82.3±11.2	83.4±10.1	84.1±9.0	0.54
pMBP (mmHg)	101.4±10.9	101.0±12.3	103.2±12.2	104.5±10.3	0.46
pPP (mmHg)	56.0±10.8	54.9±11.6	54.0±11.4	57.6±9.8	0.55
HR (bpm)	67.7±9.7	70.2±11.3	65.0±10.2	67.1±6.6	0.08

Current smokers (%)	17%	12%	15.8%	4%	0.008
Duration of Hypertension (months)	60 [20-120]	96[15-168]	120[7-240]	104[54-188]	0.01
Antihypertensive drugs (%)	76%	81.8%	90%	100%	0.01

* $p<0.0001$ vs Group C and D

pSBP peripheral systolic blood pressure; pDBP peripheral diastolic blood pressure; pMBP peripheral mean blood pressure; pPP peripheral pulse pressure; BMI: body mass index; HR: heart rate;

Table 4. Pulse Wave Velocity, Central haemodynamics end Echocardiographic parameters according to the site of aortic dilatation

Variable	**Group A**	**Group B**	**Group C**	**Group D**	
Sinus of Valsalva	Normal	***Dilated***	Normal	***Dilated***	
Ascending Aorta	Normal	Normal	***Dilated***	***Dilated***	
Pulse Wave Velocity (m/s)	7.7±1.6 $^{\S\,\dagger}$	7.7±2.1 $^{\S\,\dagger}$	9.0±1.7$^{*\,\#}$	9.7±3.1 $^{*\,\#}$	<0.0001
cSBP (mmHg)	125.3±14.7	123.8±14.6	129.4±16.3	130.5±14.3	0.12
cDBP (mmHg)	82.9±9.4	83.6±11.4	84.4±10.2	85.4±9.1	0.57
cMBP (mmHg)	101.4±10.9	101.0±12.3	103.2±12.2	104.5±10.3	0.46
cPP (mmHg)	42.4±9.5	40.2±9.4	44.9±10.6 $^{\#}$	45.2±10.2$^{\#}$	0.06
Augmentation Index %	23.2±10.2§	20.7±11.3§	33.3±9.7* #	25.3±10.1§	<0.0001
Augmentation Index % HR75	19.6±9.3§	18.5±10.3§	28.4±9.5¶	21.6±10.1§	<0.0001
PPamp ratio	133.5±14.6$^{*\,\#}$	138.6±17.4¶	121.0±9.8¶	129.1±11.2$^{\#\,\S}$	<0.0001
					P
LV morphology					
LVM (g)	166.8±46.6	184.5±37.5*	175.5±55.7	192.6±45.3*	0.01
LVMi ($g/m^{2.7}$)	37.9±9.5§†	39.8±8.5†	43.8±12.4	46.7±12.1	<0.0001
RWT	0.41±0.08	0.40±0.06	0.44±0.11*$^{\#}$	0.42±0.1	0.07
Left Atrium					
LA diameter (mm)	37.0±4.92	38.46±5.83	39.54±5.92 *	36.9±5.4	0.02
LAV (cc)	57.5±19.3	63.78±18.59*	58.42±14.12	60.7±12.1	0.18
LAVi (cc/m^2)	29.5±9.3	31.80±9.72	32.21±6.77	32±6.1	0.16

Left ventricular hypertrophy (%)	13%	14%	28%	39%	0.002
Aortic diameter (mm)					
Sinus of Valsalva (mm)	35.5±4	42.66±2.96*	36.05±3.35# †	44.11±3.15*	<0.0001
Ascending Aorta (mm)	33.8±4.3	38.32±4.47	41.11±3.99	42.39±3.45	<0.0001

* p 0.001 vs Group A; # p< 0.05 vs. group B; § p<0.001 vs group C; † p 0.001 vs group D; ¶ p<0.0001 vs others

cSBP central systolic blood pressure; cDBP central diastolic blood pressure; cMBP central mean blood pressure; cPP central pulse pressure; pPP peripheral pulse pressure; PPamp ratio: Pulse Pressure amplification ratio (pPP/cPP); LVM: left ventricular Mass; LVMi: left ventricular Mass indexed height 2.7; RWT: relative wall thickness; LA: Left atrium; LAV: Left atrial volume; LAVi: Left atrial volume indexed for Body Surface Area

Table 5. Multiple Regression analysis

ng	Sinus of Valsalva						
te er	**Absolute diameter /BSA**	**Absolute diameter**	**Absolute diameter /BSA**				
0.44		0.43		0.37		0.27	
±SE	p	±SE	P	±SE	p	±SE	P
0.02	<0.0001	0.09±0.01	<.0001	0.15±0.02	<.0001	0.08±0.01	<.0001
0.09	0.7370	-0.09±0.03	0.0159	-0.23±0.09	0.0122	-0.22±0.03	<.0001
0.85	0.7327	0.60±0.36	0.0958	-2.31±0.82	0.0055	-0.34±0.36	0.3447
2.14	<0.0001	-	-	11.85±2.08	<.0001	--	--
0.16	0.0572	-0.17±0.08	0.0476	-0.42±0.16	0.0093	-0.22±0.08	0.0096
0.21	0.2764	0.12±0.11	0.2431	0.43±0.20	0.0355	0.23±0.11	0.04
0.02	<0.0001	0.06±0.01	<0.0001	0.08±0.02	0.0007	0.05±0.01	<.0001
0.14	0.0005	0.24±0.07	0.0015	-0.11±0.14	0.4045	-0.08±0.07	0.25
0.05	0.6271	0.02±0.02	0.3286	0.04±0.05	0.4493	0.03±0.02	0.19
0.07	0.2890	0.04±0.03	0.1767	0.21±0.06	0.0024	0.11±0.03	0.0016

BMI: body mass index; M: male; F: female; BSA: body surface area; pPP peripheral pulse pressure; cPP central pulse pressure; LVMi: left ventricular Mass indexed height 2.7; PWV: pulse wave velocity; AIx: Augmentation Index; PPamp: Pulse Pressure amplification ratio (pPP/cPP);