Aortic root dilatation in essential hypertension: prevalence according to new reference values

Title: Aortic root dilatation in essential hypertension: prevalence according to new reference values.

Short Title: Prevalence of Aortic root dilatation

Authors: Alberto MILAN (a), MD PhD, Eleonora AVENATTI(a), MD, Francesco TOSELLO(a), MD, Andrea IANNACCONE(a), MD, Dario LEONE (a), MD, Corrado MAGNINO(a), MD, Franco VEGLIO(a), MD

(a) Department of Medical Sciences, Division of Internal Medicine, Hypertension Unit, University Hospital 'S. Giovanni Battista', University of Torino, Italy.

Conflict of interest: None disclaimers

Total words count (including references, but not tables and legends): 3261

Number of tables: 3

Number of figures: ~~3~~ 4

Corresponding author: Alberto Milan, MD, PhD.

*Department of Medical Sciences, Division of Internal Medicine, Hypertension Unit, San Giovanni Battista Hospital, University of Torino, Torino, Italy.

Phone/Fax + 39 – 011 633 69; 52

e.mail: alberto.milan@unito.it

Abstract

Background Aortic root dilatation (ARD) and arterial hypertension represent two important risk factors for aortic dissection: prevalence of observed ARD is increasing – up to 12% in the latest available reports. Recently, published work was tested on a substantial number of healthy subjects for new reference ranges for aortic root dimension, suggesting new reference values for each patient considering age, gender, height or Body Surface Area (BSA).

Aim of the study was to evaluate the prevalence of ARD in hypertensives using various criteria.

Methods A total of 1076 untreated and treated essential hypertensive patients (mean age, 52.5±2 years) were considered for this analysis. We measured proximal aortic diameters using ultrasound imaging (echocardiography). ARD was defined when the observed aortic diameter was larger than predicted for age, gender and BSA (pBSA), or height (pHeight). Finally, we considered the Aortic diameter to BSA ratio (ASi) ≥ 2.1 cm/m^2 as third criterion to define ARD.

Results A total of 237 patients (22% of the study population) showed at least one among the three different criteria defining aortic dilatation. Prevalence of ARD, considering singularly each one of the criteria, varied between 12.8% (pBSA) and 16.9% (pHeight).

Conclusions Our study demonstrated a prevalence of ARD higher than previously reported. Our data suggest therefore the necessity of a correct choice of the diagnostic criterion that has to be applied in the single patient for definition of aortic root dilatation. In particular, using the criterion pHeight in obese subjects we may avoid underdiagnosis of this condition.

Key words: Aortic root dilatation; arterial hypertension; prevalence; echocardiography

Introduction

Aortic root dilatation represents an important risk factor for aortic dissection [1]. In the hypertensive population, presence of ARD is related to left ventricular hypertrophy, implying the burden of a greater cardiac organ damage [2]. Management of patients presenting such a feature is of emerging interest [3]: prevalence of observed ARD is increasing [4] – up to 12% in the latest available reports. Data in literature regarding ARD prevalence bear nevertheless some important limits: they often refer to M-Mode measures [4], with the intrinsic limit of the possible and constant under-estimation of real aortic dimension [5]. Moreover, due to the imperfect alignment of the ultrasound beam, it is also possible overestimation of aortic diameter. ~~Moreover~~ Finally, often only absolute values have been often considered and reported on (eg. 3.7 cm /3.9 cm for female and male respectively)[4], without considering important anthropometric factors that greatly influence aortic dimensions (e.g. body surface – BSA -)[6].

To overcome such limits latest guidelines [5] have proposed the use of a simple, clinically feasible correction of the absolute value for BSA, defining the ASi (aortic size index): an ASi> 2.1 cm/m2 would be considered a good marker of ARD. A recent European Society Hypertension (ESH) newsletter [3] underlined the importance of such an indexation. Meanwhile, a recently published work[6] tested on a substantial good number of healthy subjects supplies new reference ranges for aortic root dimension, considering corrections for age, gender, height (pHeight) or BSA (pBSA).

Aim of the present study has been to evaluate the prevalence of Sinus of Valsalva dilatation in a population of essential hypertensives using these recently published criteria [3, 4] and to test their limits and advantages.

Methods

Echocardiographic exams of essential hypertensive patients were retrospectively evaluated for the present study; all the exam were performed in the EchoLab of the Hypertension Unit of the Turin University between 2003 and 2012. All patients were referred for hypertension related organ damage evaluation; all of them had a full medical examination with height and weight measured by standardized methods the day of the echo evaluation. All blood pressure measurements were performed according to the ESH/ESC [7] recommendations and 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. Clinical and echocardiographic features were examined for exclusion or confounding criteria: age less than 18 or more than 80 years, 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. This lead to a total of 1076 echocardiographic exam available for the analysis.

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[8]. ~~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[9] 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/m2.7 in men[10].

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

~~BSA=0.20247 [weight$_{Kg}$ $^{0.425}$ x (height$_{cm}$/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 maximum distance between the two leading edges of the anterior and posterior aortic root walls at end diastole[5].

Echocardiograms were preliminarily read by a first reader and then re-evaluated by highly experienced reader (AM), blinded to subjects' clinical data and first report.

Our Institutional Review Committee approved the study and all subjects provided their written informed consent (CEI/330).

Aortic dilatation definitions

In our evaluation the nomograms recently proposed by Devereux et al.[6] for the definition of normal aortic dimensions were firstly considered

Predicted – BSA (pBSA)= 2.423+Age*0.009+BSA*0.461-0.267*Gender+0.261*1.96

Predicted – height (pHeight)= 1.519+Age*0.01+Height*0.01-0.247*Gender+0.215*1.96

with Gender defined as: Male=1, Female=2.

Afterwards, the definition derived from latest ESH indication [3, 6] (i.e. ASi criteria) were analyzed:

Aortic diameter /BSA<2.1 cm/m2

We defined the presence of aortic dilatation in every patients that presented at least one among the three following criteria [3, 6]

Aortic observed diameter larger than pBSA

Aortic observed diameter larger than pHeight

Aortic diameter /BSA>2.1 cm/m2

Statistical analysis was conducted using SAS V9.2 software (SAS Institute Inc. – Cary, NC, USA). The parametric distribution of the variables was analyzed 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.

Statistical significance was assumed if the null hypothesis could be rejected at $p<0.05$.

Results

Clinical characteristics of the study population are summarized in table 1.

A total of 237 patients (22% of the study population) showed at least one from the three criteria defining aortic dilatation. Prevalence of ARD, considering singularly each one of the criteria, varied between 12.8% (n=138, using the predicted BSA - pBSA - criterion) and 16.9% (n= 182, using predicted Height, pHeight - criterion). Use of ASi>2.1 cm/m2 proposed cut off, which considers BSA as well, would lead to a prevalence of 13.6%.

Subsequently, agreement rate in ARD diagnosis using different criteria was analysed (figure 1). A complete agreement was observed in the 38% of cases (n.92) defined as affected by ARD. ~~19.4% of patients showed two criteria for the diagnosis of ARD (pBSA and pHeight); the remaining met only one of the three criteria, and in particular definition of ARD was reached in 18.6% of the patients by the pHeight criterion and 23% by the ASi>2.1 criterion.~~

The sample population was then divided into the three subgroup depending on the presence of a strict (3/3 criteria), mild (2/3) or low agreement (1/3), in order to trace different features characterizing the three groups, compared to essential hypertensive patients free from ARD - data shown in table 2.

Briefly, patients meeting all three criteria for ARD diagnosis were older, with longer hypertension duration and were using a greater number of anti hypertensive drugs. Indexed left ventricular mass and atrial dimensions were significantly higher in this group when compared to patients free from aortic root dilatation – therefore meeting none of the proposed criteria.

Relative wall thickness and LV geometric patterns were not significantly different among groups.

Patients with a less strict agreement had slightly different clinical features. Patients with a mild agreement (2/3 criteria for ARD diagnosis, i.e. pBSA and pHeight) were younger (48±8.9 years), and with a greater BMI (27.9±3.2 kg/m^2) as compared to the other groups.

In order to clarify the peculiarity each criterion would underline in the studied patients, we considered separately subjects meeting one single criterion; patients meeting pBSA criterion for ARD diagnosis (48% of the entire population with aortic enlargment) were considered as the control group, due to the wide overlapping with positivity for other criteria. Results from this analysis are showed in table 3.

Patients meeting only the pHeight criterion for diagnosis were slightly younger (53 ± 12.5years) and with higher BMI (30 ± 3.3Kg/m^2). On the other hand, patients having an increased ASi were only were older (62.7±10.57 years) and with significantly lower BMI (22.7±2.18 Kg/m^2); in the latter group, prevalence of female gender was higher (44.4%).

Analysis by age decades is shown in figure 2. Basing diagnosis on pBSA criterion, prevalence of ARD in the first seven decades progressively increases from 10% (4^{th} decade) to 20% (7^{th} decade); the pHeight criterion maintains a greater sensitivity (between +2 and +5%) in all age groups compared to the pBSA. Last, the ASi>2.1 criterion, which takes into account BSA, but not age nor gender, defines as affected by ARD a significantly lower proportion of patients in the lower age groups (i.e. until 60 years of age), with a marked increase of diagnosis in the last two decades. This ASi>2.1 criterion would lead to a prevalence of ARD ranging from 25 to 40% in patients aged 70 and over, against an estimated prevalence of 15% and 25% using the pBSA and pHeight criterion respectively.

Finally, we analyzed the effect of BMI on the prevalence of dilation, depending on the different used criteria (Figure 3).

In subjects with normal weight, the use of the Asi criterion led to a prevalence of dilatation that was double compared to the one obatined with the pBSA (9.9%) and pHeight (10.6%) criterion (9,9% and 10.6% respectively). On the other hand, considering the pBSA criterion a lower proportion of dilatation was observed (p 0.03) in the normal weight patients compared to overweight (15.7%) and obese (13%) individuals.

In the subgroups of overweight and obese patients we observed a progressive and significant increase in the prevalence of aortic dilatation as defined by pHeight criterion (21% and 25%, respectively, $p < 0.0001$). On the contrary, the use of ASi led to a progressive and significant decrease of patients classified as dilated in the same subgroups (11.8% and 8.2%, $p < 0.0001$).

Discussion

Aortic root dilatation [11] and arterial hypertension [1] represent two of the main risk factors for aortic dissection. Furthermore, increased aortic dimensions are frequently associated with left ventricular hypertrophy [2].

For the first time, prevalence of aortic root dilatation in essential hypertensive patients was assessed using a 2D echocardiographic approach and newly proposed diagnostic criteria, which that take into account important correction factors like age, gender, BSA and height. With such an approach, prevalence of proximal aortic segment (Sinus of Valsalva) dilatation in the study population was as high as 17%. The use of cut offs based on Aortic diameter to BSA ratio (ASi>2.1 criterion) even if clinically easier, may lead to over diagnosis as well as under diagnosis in specific subgroups of patients (elderly or female patients and obese patients respectively).

Many published studies [2, 4, 12-15] have approached the topic of ARD prevalence in arterial hypertension. Available data in literature indicate for such a condition prevalence ranging from 4 [12, 14] to 11.8% [4], while the prevalence we observed (up to 17%) is notably higher.

A possible bias influencing our results is due to patient selection: patients undergoing echocardiography in our EchoLab belong to a population of hypertensives referring to a high specialty, European excellence center. This may result in the presence of a higher percentage of subjects at high cardiovascular risk, or affected by resistant hypertension. However, the only mild prevalence (14%) of left ventricular hypertrophy registered in the population reasonably rules out this hypothesis of selection bias.

Aortic root dimension evaluation has always been part of a standard echocardiographic exam. However, many of the available data in literature are derived from MMode measures [4, 13], and it is now recognized [16] that this approach leads to a mild but constant underestimation (by 2 mm) of aortic diameters when compared to 2D measurements and is biased by translational movement of the aortic root. Recommendations in recent guidelines [5, 16] favor therefore the 2D evaluation. Since we used this latter one, this could have assisted in giving our study a particularly high sensitivity for ARD detection.

Traditional cut off values for definition of aortic root dilatation were validated on a very small population of healthy adults, and by the use of nomograms[17]. In order to simplify the approach to this pathological feature, it has been suggested to define aortic root dilatation by the use of absolute dimensions, using as cut off values derived from dimension distribution in healthy subjects (i.e. > 37mm for women and >39 mm for men) [2]. This strategy, which has the undoubted advantage of simplicity in clinical practice, presents some limits in the lack of acknowledgements of the natural history of aortic root dilatation[18]. In the present study, the use of the previously cited cut offs would have led to a nevertheless high prevalence (20%), carrying the same important limitations. First of all, it is generally recognized that aortic dimension are strictly related to patients' age [6, 17, 19, 20]. Use of absolute cut offs that do not consider the ageing process may lead to an important under-diagnosis of these pathological features in relatively young adults. On the other hand, an over-diagnosis may occur in the older age groups, as confirmed in our data as well.

Moreover, aortic dimensions are generally strictly related to body surface [6, 17, 19, 20]. For this reason, it has been proposed, and recently remarked [3] on the opportunity of an indexation for body surface is a good method for identifying patients with aortic dilatation, considering the high prognostic value of such a diagnosis in the respect of the risk of dissection[21].

Current Guidelines suggest hence the use of BSA indexation in evaluating aortic root dimensions. This recommendation nevertheless carries the potential risk of an under-diagnosis in obese patients, which represents, however, a substantial percentage of hypertensive subjects, and of an over diagnosis in the subgroup with lower BSA (e.g. women).

The present study compared the three newest proposed definitions for aortic root dilatation. In the meantime potential different clinical and morphological features of subgroups of patients which meet each single criterion were analyzed. Presence of only 1 or 2 criteria for diagnosis of aortic dilatation did not identify peculiar clinical phenotype. A low concordance in the diagnostic criteria does not necessarily imply milder involvement in the pathological evolution of aortic dilatation, as supported by the finding that patients with a low agreement (1 to 3 criteria) had, however, a significantly greater LVH prevalence compared with non-dilated individuals.

Use of proposed nomograms offer the advantage of a more accurate ARD diagnosis, taking into account all the major confoundants. In younger patients or in obese subjects, use of pHeight criterion, against the standard BSA indexation (ASi>2.1 criterion) would lead to a greater sensitivity, thus potentially identifying patients at a higher risk of complication, both in terms of aortic rupture, and of cardiovascular complications related to hypertension. Moreover, defining aortic root dilatation with use of such nomograms would avoid the risk of over-diagnosis in the population of patients aged 60 and over.

Having analyzed different limits of the criteria, our study cannot actually identify an univocally preferred one for clinical use. Further longitudinal studies will be required in order to clarify the prognostic value of every criterion in hypertensive patients.

Figure 4 shows the proposed flow chart for the diagnosis of aortic dilatation and simplified management of patients free from specific risk factors, based on our experience and preliminar data. It is our opinion, based on the here exposed data and on our personal clinical records, that aortic root dilatation diagnosis may be made on the basis of a pBSA criterion in the general population, saving the pHeight criterion for obese patients. Once diagnosis has thus been made, in the specific subgroup of patients showing low BSA, the ASi criterion may be of help for further risk stratification. Such individuals, with increased aortic dimensions, but still under the suggested cut off of 55 mm for cardio-surgical evaluation, may have their risk better evaluated with the ASi, as demonstrated by other authors [21].

Conclusions

Our study evaluates the prevalence of aortic root dilatation in essential hypertensive patients with the use of recently proposed nomograms; prevalence is higher than previously reported, and as high as 12.8% considering pBSA and 16.9% considering pHeight. Use of the widely applied ASi criterion (ASi>2.1 criterion) even if clinically easier, may lead to overdiagnosis (elderly and female patients) as well as underdiagnosis (obese patients). Our data suggest therefore the usefulness of a correct choice of the diagnostic criterion which has to be applied to the single patient for definition of aortic root dilatation.

References

1. Pape, L.A., T.T. Tsai, E.M. Isselbacher, J.K. Oh, T. O'Gara P, A. Evangelista, et al., Aortic diameter >or = 5.5 cm is not a good predictor of type A aortic dissection: observations from the International Registry of Acute Aortic Dissection (IRAD). Circulation, 2007. 116(10): p. 1120-7.
2. Cuspidi, C., S. Meani, V. Fusi, C. Valerio, C. Sala, and A. Zanchetti, Prevalence and correlates of aortic root dilatation in patients with essential hypertension: relationship with cardiac and extracardiac target organ damage. J Hypertens, 2006. 24(3): p. 573-80.
3. Baguet, J.P., O. Chavanon, C. Sessa, F. Thony, P. Lantelme, G. Barone-Rochette, and J.M. Mallion, European Society of Hypertension scientific newsletter: hypertension and aortic diseases. J Hypertens, 2012. 30(2): p. 440-3.
4. Cuspidi, C., F. Negri, M. Salvetti, L. Lonati, C. Sala, A. Capra, et al., Aortic root dilatation in hypertensive patients: a multicenter survey in echocardiographic practice. Blood Press, 2011. 20(5): p. 267-73.
5. Evangelista, A., F.A. Flachskampf, R. Erbel, F. Antonini-Canterin, C. Vlachopoulos, G. Rocchi, et al., Echocardiography in aortic diseases: EAE recommendations for clinical practice. European Journal of Echocardiography, 2010. 11(8): p. 645-658.
6. Devereux, R.B., G. de Simone, D.K. Arnett, L.G. Best, E. Boerwinkle, B.V. Howard, et al., Normal limits in relation to age, body size and gender of two-dimensional echocardiographic aortic root dimensions in persons >/=15 years of age. Am J Cardiol, 2012. 110(8): p. 1189-94.

7. Mancia, G., S. Laurent, E. Agabiti-Rosei, E. Ambrosioni, M. Burnier, M.J. Caulfield, et al., Reappraisal of European guidelines on hypertension management: a European Society of Hypertension Task Force document. J Hypertens, 2009.
8. Milan, A., M.A. Caserta, S. Del Colle, A. Dematteis, F. Morello, F. Rabbia, et al., Baroreflex sensitivity correlates with left ventricular morphology and diastolic function in essential hypertension. J Hypertens, 2007. 25(8): p. 1655-64.
9. Devereux, R.B., D.R. Alonso, E.M. Lutas, G.J. Gottlieb, E. Campo, I. Sachs, and N. Reichek, Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. Am J Cardiol, 1986. 57(6): p. 450-8.
10. de Simone, G., R. Izzo, M. Chinali, M. De Marco, G. Casalnuovo, F. Rozza, et al., Does information on systolic and diastolic function improve prediction of a cardiovascular event by left ventricular hypertrophy in arterial hypertension? Hypertension, 2010. 56(1): p. 99-104.
11. Parish, L.M., J.H. Gorman, 3rd, S. Kahn, T. Plappert, M.G. St John-Sutton, J.E. Bavaria, and R.C. Gorman, Aortic size in acute type A dissection: implications for preventive ascending aortic replacement. Eur J Cardiothorac Surg, 2009. 35(6): p. 941-5; discussion 945-6.
12. Palmieri, V., J.N. Bella, D.K. Arnett, M.J. Roman, A. Oberman, D.W. Kitzman, et al., Aortic root dilatation at sinuses of valsalva and aortic regurgitation in hypertensive and normotensive subjects: The Hypertension Genetic Epidemiology Network Study. Hypertension, 2001. 37(5): p. 1229-35.
13. Bella, J.N., K. Wachtell, K. Boman, V. Palmieri, V. Papademetriou, E. Gerdts, et al., Relation of left ventricular geometry and function to aortic root dilatation in patients with systemic hypertension and left ventricular hypertrophy (the LIFE study). Am J Cardiol, 2002. 89(3): p. 337-41.
14. Cuspidi, C., S. Meani, C. Valerio, A. Esposito, C. Sala, M. Maisaidi, et al., Ambulatory blood pressure, target organ damage and aortic root size in never-treated essential hypertensive patients. J Hum Hypertens, 2007. 21(7): p. 531-8.
15. Cipolli, J.A.A., F.A.S. Souza, M.C.S. Ferreira-Sae, J.A. Pio-Magalhaes, E.S. Figueiredo, V.G. Vidotti, et al., Sex-specific hemodynamic and non-hemodynamic determinants of aortic root size in hypertensive subjects with left ventricular hypertrophy. Hypertens Res, 2009. 32(11): p. 956-961.
16. Lang, R.M., M. Bierig, R.B. Devereux, F.A. Flachskampf, E. Foster, P.A. Pellikka, et al., Recommendations for chamber quantification. Eur J Echocardiogr, 2006. 7(2): p. 79-108.
17. Roman, M.J., R.B. Devereux, R. Kramer-Fox, and J. O'Loughlin, Two-dimensional echocardiographic aortic root dimensions in normal children and adults. Am J Cardiol, 1989. 64(8): p. 507-12.
18. Elefteriades, J.A. and E.A. Farkas, Thoracic Aortic Aneurysm Clinically Pertinent Controversies and Uncertainties. J Am Coll Cardiol, 2010. 55(9): p. 841-857.
19. Milan, A., F. Tosello, S. Abram, A. Fabbri, A. Vairo, D. Leone, and F. Veglio, Arterial Hypertension and aortic root dilatation: an unsolved mystery. Italian Journal of Medicine, 2010.
20. Milan, A., F. Tosello, M. Caserta, D. Naso, E. Puglisi, C. Magnino, et al., Aortic size index enlargement is associated with central hemodynamics in essential hypertension. Hypertens Res, 2011. 34(1): p. 126-32.
21. Davies, R.R., A. Gallo, M.A. Coady, G. Tellides, D.M. Botta, B. Burke, et al., Novel measurement of relative aortic size predicts rupture of thoracic aortic aneurysms. Ann Thorac Surg, 2006. 81(1): p. 169-77.
22. Hiratzka, L.F., G.L. Bakris, J.A. Beckman, R.M. Bersin, V.F. Carr, D.E. Casey, Jr., et al., 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the Diagnosis and Management of Patients With Thoracic Aortic Disease. A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and

Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. Circulation, 2010. 121(13): p. e266-369.

Figure Legends

Figure 1. Patients with aortic dilatation: proportion of the various subjects in accordance with the different criteria used

Figure 2. Prevalence of aortic dilatation according to different criteria, stratified by decade of age. We observe an average increase in the prevalence of dilatation with different criteria, with exponential increase in prevalence using the only criterion ASi. (pBSA the predicted Aortic Root based on BSA; pHeight Aortic Root predicted based on height; ASi Aortic Size Index)

Figure 3.

Prevalence of aortic dilatation according to different criteria, stratified normal weight, overweight and obese subjects. * $p<0.001$ vs. BMI < 25 Kg/m^2; # $p<0.05$ vs BMI 25-30 Kg/m^2

Figure 4.

Proposed flow chart for proximal thoracic Aorta evaluation in hypertensive subjects. ASi>2.75 cm/m^2 should be considered in this case as prognostic marker[21] for aortic dissection (see the text). (SoV: sinus of Valsalva; pBSA: the predicted Aortic Root based on BSA; pHeight: Aortic Root predicted based on height; ASi: Aortic Size Index; MRI: magnetic resonance imaging; CT computed tomography; risk factors for aortic dissection following AHA recommendation [22])

Table 1. Clinical characteristics of the patients

Variable	Mean±Standard deviation
N	1076
Age (years)	52.56±12.44
Male prevalence (%)	69%
Body Mass Index (BMI)(Kg/m2)	26.55±4.11
Systolic blood pressure (mmHg)	140.04±18.12
Diastolic blood pressure (mmHg)	84.45±11.12
Heart rate (bpm)	71.16±11.19
Current smokers (%)	20%
Overweight (BMI>25 Kg/m^2)	42.6%
Obesity (BMI>30 Kg/m^2)	17%
Normal-high Blood Pressure/Grade 1 Hypertension	81.5%
Grade 2-3 Hypertension	18.4%
Isolated systolic hypertension	18%
SoV dilatation	
Predicted BSA	12.8%
Predicted height	17.6%
Aortic Size index>2.1 cm/m^2	14.8%
At least 1 criteria	22.8%

BSA: Body Surface Area; Aortic Size index=Sinus of Valsalva/BSA

Table 2. Clinical and echocardiographic characteristics of the patients according to the presence/absence of the aortic root dilatation

	Dilated	**Not dilated**	P		
	Strict evidence (3/3 criteria)	Intermediate evidence (2/3 criteria)	Weak evidence (1/3 criteria)		
Clinical features					
N	92	46	99	800	
Age (years)	59.3±10.60¶#	48±8.9	58±12.43¶#	51.03±12.28	<0.0001
Sex (male%)	73.9%	93.5%	69.4%	65%	0.0007
BMI (Kg/m^2)	25.9±3.5#	27.9±3.2	26±4.6	26.6±4.2	0.03
SBP/DBP (mmHg)	139.8±17 / 84.±11	144±23 / 88±15	141±16 / 83±10.2	140±18 / 84±11	0.61 / 0.10
PP (mmHg)	26±3.5#	27.9±3.2*	26±4.6	26.6±4.2	0.03
Hypertension duration (months)	84[30-192]	79[35-156]	60[13-139]	60[12-120]	0.02
Number of hypertensive drugs/patient	2[1-3]	2[0-2]	1[0-2]	1[0-2]	0.02
Echocardiographic features					
~~LVM/BSA (g/m^2)~~	~~100±24.8¶~~	~~94.3±21.8~~	~~92.9±20.5~~	~~87.6±20.7~~	~~<0.0001~~
LVM/height $^{2.7}$ ($g/m^{2.7}$)	44.6±12.7¶	40.46±10.4	41.7±9.8	39.3±10.4	<0.0001
RWT	0.43±0.08	0.43±0.11	0.41±0.08	0.41±0.08	0.15
LAVi (cc/m^2)	34.12±11.7¶	30.11±8.36	33.2±9	30±9.1	0.0001
LVH%	28.6%	15.2%	23.5%	16.5%	0.01
SoV (cm)	4.3±0.4†¶	4.2±0.15†¶	3.8±0.3‡	3.4±0.37‡	<0.0001
Ascending aorta (cm)	3.97±0.4†¶	3.97±0.4¶	3.7±0.5‡	3.35±0.5‡	<0.0001

* vs High; # vs intermediate; † vs. low; ¶vs normal; ‡ vs. all

BMI: body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; PP: pulse pressure; LVM: left ventricular mass; BSA= body mass index; RWT: relative wall thickness; LAVi= Left atrial volume/BSA; LVH: left ventricular hypertrophy; SoV: sinus of Valsalva.

Table 3. Clinical and echocardiographic characteristics of the patients according to the aortic root dilatation criterion

	Dilated	p		
	pBSA[1]	pHeight	ASi>2.1 cm/m^2	
Clinical features				
N	138	44	55	
Age (years)	55.6±11.32	52.7±12.46	62.7±10.57[‡]	<0.0001
Sex (male%)	80%	86.4%	55.6%	0.003
SBP/DBP (mmHg)	141±19 /86±13	137±14 / 84±9	143.1±17 / 82±10.9	0.36 / 0.19
PP (mmHg)	54.9±11.48	53.3±9.01	60.7±16.1[‡]	0.01
BMI (Kg/m^2)	26.6±3.56[‡]	30.1±3.36[‡]	22.7±2.18[‡]	<0.0001
Hypertension duration (months)	84[35-175]	47[12-120]	60[22-180]	0.10
Number of hypertensive drugs/patient	2[1-3]	1[0-2]	1[1-2]	0.3
Echocardiographic features				
~~LVM/BSA (g/m^2)~~	~~98.1±23.9~~	~~97±18.2~~	~~89.6±21.7~~	~~0.06~~
LVM/height $^{2.7}$ (g/$m^{2.7}$)	43.2±12.1	44.8±9.1[†]	39.2±9.6[#]	0.02
RWT	0.43±0.09	0.42±0.07	0.40±0.08	0.15
LAVi (cc/m^2)	32.8±10.9	32.5±8.9	33.7±10.1	0.83
LVH%	23.9%	32.6%	16.4%	0.07
SoV (cm)	4.27±0.3	3.99±0.2	3.67±0.3	<0.0001
Ascending aorta (cm)	3.97±0.4	3.82±0.6	3.71±0.5	0.02

[*] vs pBSA; [#] vs pHeight; [†] vs. Baguet; [‡] vs. all

[1] the pBSA includes the largest number of subjects with overlapping criteria for aortic dilatation

BMI: body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; PP: pulse pressure; LVM: left ventricular mass; BSA= body mass index; RWT: relative wall thickness; LAVi= Left atrial volume/BSA; LVH: left ventricular hypertrophy; SoV: sinus of Valsalva.