Blood Pressure

ISSN: 0803-7051 (Print) 1651-1999 (Online) Journal homepage: informahealthcare.com/journals/iblo20

Aortic root dilatation in hypertensive patients: A multicenter survey in echocardiographic practice

Cesare Cuspidi, Francesca Negri, Massimo Salvetti, Laura Lonati, Carla Sala, Anna Capra, Alberto Milan, Gian Battista Danzi, Alberto Morganti & The Working Group on Heart and Hypertension of the Italian Society of Hypertension

To cite this article: Cesare Cuspidi, Francesca Negri, Massimo Salvetti, Laura Lonati, Carla Sala, Anna Capra, Alberto Milan, Gian Battista Danzi, Alberto Morganti & The Working Group on Heart and Hypertension of the Italian Society of Hypertension (2011) Aortic root dilatation in hypertensive patients: A multicenter survey in echocardiographic practice, Blood Pressure, 20:5, 267-273, DOI: 10.3109/08037051.2011.565556

To link to this article: https://doi.org/10.3109/08037051.2011.565556

Published online: 09 Mar 2011.

Blood Pressure, 2011; 20: 267–273

ORIGINAL ARTICLE

Aortic root dilatation in hypertensive patients: A multicenter survey in echocardiographic practice

CESARE CUSPIDI[1,2], FRANCESCA NEGRI[1,2], MASSIMO SALVETTI[3], LAURA LONATI[2], CARLA SALA[4], ANNA CAPRA[1], ALBERTO MILAN[5], GIAN BATTISTA DANZI[6] & ALBERTO MORGANTI[7] ON BEHALF OF THE WORKING GROUP ON HEART AND HYPERTENSION OF THE ITALIAN SOCIETY OF HYPERTENSION

[1]*Department of Clinical Medicine and Prevention, University of Milano-Bicocca, Milano,* [2]*Istituto Auxologico Italiano IRCCS, Milano,* [3]*Department of Medical and Surgical Sciences, Clinica Medica, University of Brescia, Brescia, Italy,* [4]*Heart and Lung Department, University of Milano and Fondazione Ospedale Maggiore Policlinico, Milano* [5]*Department of Medicine and Experimental Oncology, Division of Internal Medicine, University of Torino, Torino,* [6]*Division of Cardiology Fondazione Ca' Granda Policlinico IRCCS, Milano, Italy,* [7]*Chair of Internal Medicine and Hypertension Center, Ospedale S. Giuseppe, Italy*

Abstract

Background and aim. Aortic root dilatation (ARD) is a cardiovascular phenotype of adverse prognostic value; its prevalence has been mostly investigated in population-based samples and selected hypertensive cohorts. Data from clinical practice are rather scant. Thus, we examined the prevalence and correlates of ARD in a large sample of hypertensive patients referred by general practitioners for a routine echocardiographic examination. *Methods*. A total of 2229 untreated and treated hypertensive subjects (mean age 62 years) referred to 17 outpatient echocardiographic laboratories across Italy for detection of hypertensive subclinical cardiac damage were included in the study. ARD was defined by aortic diameter exceeding 3.7 cm in women and 3.9 cm in men. *Results*. ARD was found in 263 patients, with an overall prevalence of 11.8% (16.9% in men and 6.2% in women, $p < 0.05$). In multivariate regression analyses, body surface area (BSA), left ventricular (LV) mass and age were in ranking order the most important correlates of aortic root size in the whole population study as well as in men. In women, LV mass and its derivative indexes were the most important independent variables associated to aortic root size. *Conclusions*. This multicenter nationwide survey indicates that ARD is a frequent cardiovascular phenotype in hypertensives referred to echo-labs for detection of hypertensive organ damage. BSA, LV mass and age are the most important correlates of this phenotype. The hierarchical order of these factors differs between genders, LV mass being the strongest independent variable in women.

Key Words: *Aortic root dilatation, hypertension, left ventricular mass*

Introduction

Aortic root dimensions in human subjects are related to age, body size, gender, blood pressure (BP) levels and the degree of aortic regurgitation (1–4). Previous studies pointed towards hypertension as a major determinant of aortic root dilatation (ARD); this relationship, however, has been challenged by negative findings from other investigations (5–8).

These conflicting data may result from differences in study design, definition of the aortic phenotype and site of BP measurement. This last point has been elegantly addressed by Jondeau et al. (9) in a cross-sectional study showing that in patients with Marfan syndrome aortic diameter was related to central but not to brachial pressure.

Mounting evidence indicates that dilatation of the most proximal segment of the systemic arterial tree in hypertension may be regarded as a sign of organ damage paralleling other subclinical markers of established prognostic value such as left ventricular hypertrophy (LVH), carotid atherosclerosis and microalbuminuria (10–12). Furthermore,

Correspondence: Cesare Cuspidi, Istituto Auxologico Italiano, Clinical Research Unit, Viale della Resistenza 23, 20036 Meda, Italy. Tel: 0039- 0362/772433. Fax: 0039-0362/772416. E-mail: cesare.cuspidi@unimib.it

(Received 30 November 2010; accepted 16 February 2011)

ISSN 0803-7051 print/ISSN 1651-1999 online
DOI: 10.3109/08037051.2011.565556

the available evidence indicates that ARD is independently associated with abdominal obesity, metabolic syndrome and inflammatory markers (i.e. C-reactive protein), thus supporting a role of metabolic and low-grade inflammatory factors in the pathogenesis of large arteries alterations (13).

The prognostic value of ARD in the absence of aneurysmatic alterations remains to be fully elucidated. In a large biracial cohort of 3993 elderly surveyed in the Cardiovascular Health Study and free from overt cardiovascular diseases at baseline, aortic root dimensions were predictive of stroke and cardiovascular mortality in both genders as well as of congestive heart failure in males (14).

Prevalence rates and clinical correlates of ARD have been evaluated in population-based samples (5) and in hypertensive cohorts attending outpatient hypertension hospital clinics (15) or enrolled in clinical trials (10). To our knowledge, only scant observations have been generated from patients seen in current clinical practice.

Therefore, we sought to investigate this issue in a multicenter nationwide survey involving a large number of hypertensive patients referred from general practitioners to an echocardiographic laboratory for routine examination; our aim was to determine the prevalence and correlates of ARD.

Methods

For the present investigation, data derived from two Italian multicenter surveys performed by the Working Group on Heart and Hypertension of the Italian Society of Hypertension during the period 2008–2009, have been pooled.

The first study including 2646 patients enrolled from 14 centers and was designed to assess how frequently an echo examination is requested in current practice for detection of hypertensive subclinical cardiac damage (16). The second one, including 2513 patients enrolled from nine centers, was undertaken to investigate the difference between self-reported and measured weight and height in individuals referred to outpatient echo labs by general practitioners for a routine examination and the impact of the difference in these anthropometric parameters on the estimated prevalence of LVH (17).

In both studies, participating laboratories were requested to enroll at least 100 adult outpatients of either sex, consecutively referred by general practitioners, whose written prescription identified the clinical indications for the examination. No exclusion criteria were defined for the enrollment with the exception of patients in whom altered LV geometry made estimated LV unreliable. Patients' demographic data, medical history and medications were collected in a structured interview by attending physicians at echo-labs.

Measurements

Clinic BP was measured by mercury sphygmomanometer with appropriate-sized cuffs; measurements were performed in the echocardiographic laboratories after the subjects had been resting for 3–5 min in the sitting position. Three measurements were taken from the non-dominant arm at 1-min intervals and the average was used to define patient's representative values.

Echocardiographic procedures

Echo and Doppler examinations were performed in each participating centre according to a standardized protocol. In brief, M-mode, two-dimensional and Doppler echo examinations were carried out with commercially available instruments. In particular, end-diastolic (d) and end-systolic (s) LV internal diameters (LVID), interventricular septum thickness (IVST) and posterior wall thickness (PWt) were measured from two-dimensionally guided M-mode tracings recorded at a speed of 50–100 cm/s, during at least three consecutive cycles according to the Penn convention. Relative wall thickness (RWT) was defined by the ratio of PWT plus IVST to LVIDd; LV mass was estimated by Devereux's formula $\{1.04[(IVSTd + PWTd + LVIDd)^3 - LVIDd^3] - 13.6\}$ (18) and normalized to body surface area (BSA) or height$^{2.7}$ ($h^{2.7}$). LV ejection fraction was measured from the four-chamber apical projection by the product of area $\times$ ventricular length.

Aortic root size was measured at the level of Valsalva's sinuses by M-mode tracings, under two-dimensional control, as the maximal distance between the two leading edges of the anterior and posterior aortic root wall at end diastole (19).

Definition of cardiac phenotypes

Aortic root was considered dilated when its diameter exceeded 3.7 cm in women and 3.9 cm in men (12). LVH was defined by absolute LV mass and by normalized values according to the following gender specific thresholds: (i) LV mass index $\geq$ 116/96 g/m^2; (ii) LV mass index $\geq$ 49/45 g/h$^{2.7}$ in men and women, respectively (19).

Patterns of abnormal LV geometry were defined as follows: (i) LV concentric remodeling (normal LV mass index combined with RWT $\geq$ 0.43); (ii) eccentric LVH (increased LV mass index combined with RWT $<$ 0.43); and (iii) concentric LVH (increased LV mass index combined with RWT $\geq$ 0.43) (19).

Two files per patient have been e-mailed to the Clinical Research Center, Istituto Auxologico Italiano, University of Milano-Bicocca, acting as coordinating centre for the final analysis and included: (i) a questionnaire containing demographic and clinical data, (ii) echo diagnostic report.

The protocols of both studies have been approved by the Ethics Committee of the coordinating center (Istituto Auxologico Italiano and University of Milano-Bicocca). The study was conducted in accordance with Good Clinical Practice guidelines.

Statistical analysis

Statistical analysis was performed by the SAS System (version 6.12; SAS Institute Inc., Cary, North Carolina, USA) and was mostly descriptive; values were expressed as means ± SD or as percentages. Mean values have been compared by Student's *t*-test for independent samples and categorical data analyzed by the chi-square test or the Fischer's exact test when appropriate. The strength of correlation between variables was tested by linear correlation analysis and multiple regression analysis. The value of $p < 0.05$ was considered statistically significant.

Results

A total of 2299 out of 5222 individuals recruited in both surveys by 17 participating centers between February 2008 and June 2009 were hypertensives and fulfilled the inclusion criteria; seventy cases were excluded, because of unavailable or incomplete echocardiographic reports.

Thus, 2229 subjects (52.3% males) were eligible for the final analysis. Briefly, the mean age was 62 ± 13 years, mean BP 140 ± 17/83 ± 10 mmHg, 85% of the study sample was on antihypertensive drugs, 26% was obese according to the 1998 National Institutes of Health classification (i.e. body mass index, BMI ≥ 30 kg/m^2), 8% was affected by diabetes mellitus (fasting glucose ≥ 126 mg/dl or on glucose lowering medications or history of diabetes mellitus).

ARD, as defined by the cut-off values > 3.9 cm in men and > 3.7 cm in women, was found in 263 patients, with an overall prevalence of 11.8% (16.9% of men and 6.2% of women, $p < 0.05$).

As shown in Table IA, men with ARD were older and had higher BSA and BMI than their counterparts; no differences were found in clinic systolic and diastolic BP values, prevalence rate of diabetes mellitus, obesity and use of antihypertensive drugs. As reported in Table IB, at variance from men, women with ARD had similar body size indexes and were more frequently on antihypertensive treatment than their counterparts.

In both genders, end-diastolic LV diameter, LV absolute and relative wall thickness, LV mass and LV mass indexed both to BSA and h$^{2.7}$ were significantly greater in patients with ARD than in those with normal aortic root size (Tables IIA and IIB).

When echocardiographic data were analyzed as categories, i.e. presence or absence of altered LV structure and geometry, LVH prevalence in men with and without ARD was, respectively, 63.7% vs 51.0% by criterion A ($p < 0.001$) and 71.0% vs 60.7% by criterion B ($p = 0.003$).

The trend was even more significant in women: 90.9% vs 62.1% by criterion A ($p < 0.0001$) and 90.9% vs 66.0% by criterion B ($p < 0.0001$); all differences remained significant after controlling for age and diastolic BP.

LV ejection fraction was lower in men with ARD as compared with those with normal aortic size, whereas non-significant differences were seen in women. Mitral flow velocity E/A ratio tended to be lower and left atrium diameter greater in patients with ARD, regardless of gender.

Correlation analyses

Univariate correlation analyses between aortic root diameter as a continuous variable and several clinical/echocardiographic parameters in the whole population as well as in both genders are given in Table III. In the total study sample aortic root diameter showed positive correlations with body size measures, LV mass (and its normalized indexes), left atrium diameter, and to a lesser extent with age and clinic systolic BP.

Table IA. Clinical characteristic in hypertensive men with and without aortic root dilatation at echocardiography.

	Aortic root dilatation		
	Yes (n = 197)	No (n = 970)	p
Age (years)	62.2 ± 11.3	59.3 ± 13.0	0.02
Clinic BP (mmHg)	136 ± 16/82 ± 10	139 ± 17/84 ± 11	NS
Heart rate (beats/min)	70 ± 12	71 ± 11	NS
Weight (kg)	86.1 ± 14.9	82.0 ± 13.3	<0.0001
Height (cm)	174 ± 7	172 ± 8	<0.001
BSA (m^2)	2.0 ± 0.18	1.95 ± 0.17	<0.001
BMI (kg/m^2)	28.5 ± 4.7	27.4 ± 4.1	0.02
Obesity (%)	30.1	23.9	NS
Diabetes mellitus (%)	9.1	7.4	NS
Elderly (>65 years) (%)	44.4	37.8	<0.01
Treatment (%)	87.2	82.3	NS

Data are shown as means ± SD or percent. BP, blood pressure; BSA, body surface area; BMI, body mass index.

Table IB. Clinical characteristics in hypertensive women with and without aortic root dilatation at echocardiography.

	Aortic root dilatation		
	Yes (n = 66)	No (n = 996)	p
Age (years)	70.3 ± 9.9	63.9 ± 13.3	0.0002
Clinic BP (mmHg)	140 ± 18/81 ± 10	141 ± 18/82 ± 10	NS
Heart rate (beats/min)	71 ± 10	72 ± 11	NS
Weight (kg)	72.7 ± 16.4	68.5 ± 13.4	NS
Height (cm)	160 ± 8	158 ± 7	NS
BSA (m^2)	1.75 ± 0.20	1.70 ± 0.16	NS
BMI (kg/m^2)	28.6 ± 6.3	27.4 ± 5.3	NS
Obesity (%)	36.6	27.3	NS
Diabetes mellitus (%)	5.5	8.9	NS
Elderly (>65 years) (%)	80.3	54.3	<0.0001
Treatment (%)	95.5	85.3	0.02

Data are shown as means ± SD or percent. BP, blood pressure; BSA, body surface area; BMI, body mass index.

A significant inverse relationship was found between aortic root diameter and LV ejection fraction as well as E/A ratio. In a gender-based analysis LV mass persisted as the most important variable associated to aortic root size in both genders, whereas systolic BP and LV ejection fraction lost their statistical significance.

Multiple regression models were constructed to evaluate the independent contribution of different factors on aortic root size (Table IV): BSA, LV mass and age were in ranking order the most important correlates of aortic root size in the whole population and in men. When the first model was run again by replacing LV mass with LV mass/$h^{2.7}$, similar findings were obtained. In a third model, which included BMI and LV mass/BSA, the latter, followed by left atrium diameter and age, was the most important determinant of aortic root diameter. In women, LV mass, LV mass/BSA and LV mass/$h^{2.7}$, turned out to be the strongest variables associated to aortic diameter in all models.

Discussion

The present study provides the first comprehensive evaluation of ARD prevalence and correlations of this aortic phenotype with clinical and echocardiographic variables in a large group of hypertensive patients referred to outpatient echo-labs for a routine assessment of hypertension-related subclinical cardiac damage. In contrast to previous studies carried out in patients selected according to pre-defined epidemiological and research protocols, our series included patients referred to echo-labs by their practitioners and more likely represent hypertensive subjects managed in the primary care setting, in particular the fraction of patients routinely referred to echocardiographic examination for the evaluation of hypertensive cardiac damage on the basis of the physicians' clinical judgment.

Our study shows that ARD at Valsava's sinuses was present in a relevant fraction of the population (i.e. 10%), with a frequency threefold higher in men than in women. Demographic variables such as BSA,

Table IIA. Echocardiographic variables in hypertensive men with and without aortic root dilatation.

	Aortic root dilatation		
	Yes (n = 197)	No (n = 970)	p
LVIDd (mm)	51.8 ± 5.2	50.5 ± 5.1	0.002
IVSTd (mm)	11.4 ± 1.6	10.8 ± 1.5	<0.0001
PWTd (mm)	10.2 ± 1.6	9.8 ± 1.4	0.0002
LV RWT	0.42 ± 0.06	0.41 ± 0.07	<0.05
Aortic root (mm)	42.2 ± 3.8	34.5 ± 3.1	<0.0001
Left atrium (mm)	40.3 ± 6.1	39.5 ± 5.5	NS
LVEF (%)	63.5 ± 7.8	65.3 ± 8.0	0.007
E/A ratio	0.93 ± 0.37	1.00 ± 0.37	NS
LV mass (g)	258.3 ± 69.7	230.3 ± 61.9	<0.0001
LV mass/BSA (g/m^2)	129.4 ± 35.1	118.6 ± 30.1	<0.0001
LV mass/h ($g/m^{2.7}$)	58.5 ± 16.9	53.8 ± 15.4	<0.0001

Data are shown as means ± SD or percent. LVIDd, diastolic LV internal diameter; IVSTd, diastolic interventricular septum thickness; PWTd, diastolic posterior wall thickness; LV, left ventricular; RWT, relative wall thickness; LVEF, left ventricular ejection fraction; BSA, body surface area.

Table IIB. Echocardiographic variables in hypertensive women with and without aortic root dilatation.

	Aortic root dilatation		
	Yes (n = 66)	No (n = 996)	p
LVIDd (mm)	48.8 ± 4.1	46.6 ± 4.5	0.002
IVSTd (mm)	11.1 ± 1.7	10.1 ± 1.7	0.0003
PWTd (mm)	9.8 ± 1.3	9.1 ± 1.4	<0.0001
LV RWT	0.43 ± 0.07	0.41 ± 0.07	<0.05
Aortic root (mm)	40.3 ± 5.1	30.9 ± 3.2	<0.0001
Left atrium (mm)	38.7 ± 6.2	36.9 ± 5.9	<0.01
LVEF (%)	63.7 ± 6.8	66.0 ± 7.1	NS
E/A ratio	0.88 ± 0.42	0.94 ± 0.34	NS
LV mass (g)	220.4 ± 48.5	180.3 ± 52.8	<0.0001
LV mass/BSA (g/m^2)	127.4 ± 31.2	106.2 ± 29.3	<0.0001
LVmass/h2.7 ($g/m^{2.7}$)	63.3 ± 16.9	52.5 ± 16.3	<0.0001

Data are shown as means ± SD or percent. LVIDd, diastolic LV internal diameter; IVSTd, diastolic interventricular septum thickness; PWTd, diastolic posterior wall thickness; LV, left ventricular; RWT, relative wall thickness; LVEF, left ventricular ejection fraction; BSA, body surface area.

Table III. Univariate correlation analysis between aortic root diameter and clinical/echocardiographic parameters in the study population as a whole and in both genders.

	All (n = 2229)		Men (n = 1167)		Women (n = 1062)	
	r	p-value	r	p-value	r	p-value
Age (years)	0.07	0.001	0.11	0.0002	0.22	<0.0001
Clinic SBP (mmHg)	0.06	0.008	0.04	NS	0.01	NS
Clinic DBP (mmHg)	0.04	NS	0.02	NS	0.02	NS
Weight (kg)	0.34	<0.0001	0.17	<0.0001	0.16	<0.0001
Height (cm)	0.40	<0.0001	0.15	<0.0001	0.11	<0.0001
BSA (m^2)	0.40	<0.0001	0.19	<0.0001	0.17	<0.0001
BMI (kg/m^2)	0.11	<0.0001	0.10	0.0007	0.11	0.0004
LV mass (g)	0.38	<0.0001	0.20	<0.0001	0.29	<0.0001
EF (%)	−0.08	0.001	0.05	NS	0.05	NS
LV RWT	0.03	NS	0.01	NS	0.08	0.01
Left atrium (mm)	0.19	<0.0001	0.08	0.01	0.14	<0.0001
E/A ratio	−0.07	0.005	−0.11	0.002	−0.15	<0.0001

SBP, systolic blood pressure; DBP, blood pressure; BSA, body surface area; BMI, body mass index; LV, left ventricular; EF, ejection fraction; RWT, relative wall thickness.

age and absolute LV mass were the most important predictors of aortic root size in the whole study sample as well as in men. In women, LV mass was the most important factor related to the aortic phenotype.

These findings deserve the following comments.

Estimates of ARD depend on the clinical characteristics of subjects under investigation as well as on criteria defining this cardiac phenotype. Our estimates, based on cut-off points representing the 97th percentile of a small group of apparently normal, normotensive adults (12), should be interpreted in the light of this limitation. Normal reference values and methods for normalizing aortic diameter to body size remain a matter of debate. The intersociety Lang's report (19) suggests different reference values specific for sex, age (for each decade, starting from the third one) and body size, all derived from a large random sample of normotensive adults in the general Framingham population (1). Such a complex indication is hardly implementable in clinical as in research settings.

Table IV. Multiple linear regression analyses between aortic and clinical/echocardiographic variables in the study population as a whole and in both genders.

Independent variable	β	p
4A All hypertensive patients (n = 2229) (Model 1)		
BSA (m^2)	0.368	<0.0001
LV mass (g)	0.283	<0.0001
Age (years)	0.100	0.0004
E/A ratio	−0.073	0.002
Systolic BP (mmHg)	−0.071	0.002
Left atrium diameter (mm)	−0.065	0.02
LVEF (%)	0.039	NS
4B Hypertensive men (n = 1167) (Model 1)		
BSA (m^2)	0.236	<0.0001
LV mass (g)	0.223	<0.0001
Age (years)	0.131	0.001
E/A ratio	−0.093	0.01
Left atrium diameter (mm)	−0.064	NS
4C Hypertensive women (n = 1062) (Model 1)		
LV mass (g)	0.262	<0.0001
Age (years)	0.148	0.001
BSA (m^2)	0.097	0.02
LV relative wall thickness	−0.064	NS
E/A ratio	−0.061	NS
Left atrium diameter (mm)	−0.044	NS

BSA, body surface area; LV, left ventricular; BP, blood pressure; EF, ejection fraction.

Aortic root diameter normalized to BSA has been regarded as a reliable parameter accounting for differences in body size. Nonetheless, echocardiographic guidelines (19) do not provide detailed reference intervals as also this approach has the major limitation of relying on the geometric difference between two variables, namely the linear dimension of aortic root diameter and the quadratic dimension of BSA (20).

Our observed prevalence of ARD at Valsalva's sinuses was similar to that found by Bella et al. (10%) in 947 patients with moderate to severe hypertension and electrocardiographic signs of LVH (10) and by Cipolli et al. (10.5%) in 438 hypertensives with echocardiographic LVH (i.e. LV mass > 51 $g/h^{2.7}$) (13). Overall, these values were higher than that reported by Palmieri et al. (4.2%) in 2096 hypertensive patients included in the Hypertension Genetic Network study (5) and by ourselves (6.1%) in a large cohort of 3366 uncomplicated hypertensives attending an outpatient hypertension clinic (12). Thus, in hypertensive patients referred for evaluation of subclinical cardiac damage in current practice, ARD prevalence is relevant and comparable with that documented in hypertensive patients with LVH. This finding may be explained by the fact that our patients had a similar age and prevalence of echocardiographic LVH as the participants in the LIFE sub-study (10) and were older than patients examined by Cipolli et al. (13).

Our results extend previous findings by showing that determinants of the aortic phenotype are gender-related. In men, indeed, BSA, LV mass and age were, in ranking order the most important correlates of aortic root diameter in two multivariable regression models. At difference, in women LV structure parameters (i.e. absolute LV mass, LV mass/BSA and LV mass/$h^{2.7}$) were the most important determinants of aortic root size in multivariable models. This finding supports the existence of a robust association between LVH and aortic root dimensions independently of covariates and refines this notion by showing that LVH in the female gender is the strongest factor related to the aortic phenotype. It is of interest to note that less than 10% of hypertensive women with ARD exhibited a normal LV mass.

ARD associated with systemic hypertension is the result of multiple mechanisms acting in parallel on LV structure; in particular, chronic pressure overload may be a determinant of both aortic dilatation and altered LV structure and geometry (6). Growth factors involved in the pathogenesis of LVH (e.g. angiotensin II, endothelin I, catecholamines, aldosterone, fibroblast growth factor, insulin-like growth factor, etc.) are also invoked in ARD (21).

The link between LV diastolic dysfunction and ARD merits to be commented. We found a significant, inverse relationship between mitral E/A ratio, an index of diastolic function of proven prognostic value (22), and aortic root size in the total population as in men in all multivariable regression models; this was not the case in woman, probably because of the dominant effect of LVH in this gender. Recently, an independent association between a new integrated index of diastolic function, namely deceleration time/peak E velocity ratio, and aortic root size has been shown in a population-based sample (23) and in a hypertensive cohort (24). Altogether, these findings suggest a common pathways in the pathogenesis of ARD and LV diastolic dysfunction. This link was further supported by the independent relation between left atrial diameter, a valid surrogate of left atrial volume (25) reflecting LV relaxation/filling, and aortic root size observed in the whole study population.

Some limitations of our study need to be acknowledged. First, as aortic root measurements were performed at a single level, we cannot exclude that measurements at multiple levels (i.e. annulus, supraortic ridge and ascending aorta) may have yielded different results. It should be pointed out that available evidence is mostly based on aortic measurements at a single level (i.e. Valsava's sinuses) (5,7,10,12). Second, the lack of association between BP and aortic root size may be explained by the fact that the majority of patients (85%) was on antihypertensive treatment, in line with a previous study conducted in treated hypertensives (10,12). Third, since patients with moderate-severe aortic regurgitation were excluded from the study, no information on the relationship between aortic root and valve insufficiency could be obtained.

In conclusion, our study shows that dilatation of the most proximal segment of the arterial tree, is a frequent cardiovascular phenotype, in particular in the male gender, in the setting of patients referred to echo-labs for detection of subclinical hypertensive organ damage. BSA, LV mass and age are the most important correlates of this phenotype in both genders. The hierarchical order of these factors, however, differs between genders, being LV mass the strongest independent variable in women. Altogether, these findings suggest that ARD, in human hypertension, is driven by different sex-related pathophysiological mechanisms. The clinical and prognostic value of these observations remains to be investigated in future studies.

Conflict of interest: None. The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

1. Vasan RS, Larson MG, Benjamin EJ, Levy D. Ecocardiographic reference value for aortic root size: The Framingham Heart Study. J Am Soc Echocardiogr. 1995;8:793–800.
2. Lakatta EG, Levy D. Arterial and cardiac aging: Major shareholders in cardiovascular disease enterprises: Part I: Aging arteries: A "set up" for cardiovascular disease. Circulation. 2003;107:139–146.
3. Kim M, Roman MJ, Cavallini C, Schwartz JE, Pickering TG, Devereux RB. Effect of hypertension on aortic root size and prevalence of aortic regurgitation. Hypertension. 1996; 28:47–52.
4. Lam CSP, Xanthakis V, Sullivan ML, Lieb W, Aragam J, Redfield MM, et al. Aortic root remodeling over the adult life course. Longitudinal data from the Framingham Heart Study. Circulation. 2010;122:884–890.
5. Palmieri V, Bella JN, Arnett DK, Roman MJ, Oberman A, Kitzman DW, 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;37:1229–1235.
6. O'Rourke MF, Nichols WW. Aortic diameter, aortic stiffness, and wave reflection increase with age and isolated systolic hypertension. Hypertension. 2005;45:652–658.
7. Farasat SM, Morrell CH, Scuteri A, Ting CT, Yin FCP, Spurgeon HA, et al. Do hypertensive individuals have enlarged aortic root diameters? Insights from studying the various subtypes of hypertension. Am J Hypertens. 2008;21: 558–563.
8. Meuleman C, Boccara, F, Nguyen XL, Di Angelantonio E, Ederhy S, Janower S, et al. Is the aortic root dilated in obstructive sleep apnoea syndrome? Arch Cardiovasc Dis. 2008;101:391–397.
9. Jondeau G, Boutourye P, Lacolley P, Laloux B, Dubourg O, Bourdarias JP, Laurent S. Central pulse pressure is a major determinant of ascending aorta dilatation. Circulation 1999; 99:2677–2681.
10. Bella JN, Wachtell K, Boman K, Palmieri V, Papademetriou V, Gerdts E, 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;89:337–341.

11. Rayner BL, Goodman H, Opie LH. The chest radiograph. A useful investigation in the evaluation of hypertensive patients. Am J Hypertens. 2004;17:507–510.
12. Cuspidi C, Meani S, Fusi V, Valerio C, Sala C, Zanchetti A. Prevalence and correlates of aortic root dilatation in patients with essential hypertension: Relationship with cardiac and extra-cardiac organ damage. J Hypertens. 2006;24:573–580.
13. Cipolli JAA, Souza FAS, Ferreira-Sae MCS, Magalhaes JAP, Figueiredo ES, Vidotti VG, et al. Sex-specific hemodynamic and non-hemodynamic determinants of aortic root size in hypertensive subjects with left ventricular hypertrophy. Hypertens Res. 2009;32:956–961.
14. Gardin JM, Arnold AM, Polak J, Jackson S, Smith V, Gottdiener J. Usefulness of aortic root dimension in persons >65 years of age in predicting heart failure, stroke, cardiovascular mortality, all-cause mortality and acute myocardial infarction (from the Cardiovascular Health Study). Am J Cardiol. 2006;97:270–275.
15. Cuspidi C, Meani S, Valerio C, Esposito A, Sala C, Masaidi M, et al. Ambulatory blood pressure, target organ damage, and aortic size in never treated essential hypertensive patients. J Hum Hypertens. 2007;21:573–50.
16. Cuspidi C, Negri F, Giudici V, Capra A, Muiesan ML, Agabiti-Rosei E, et al. Echocardiography in clinical practice: The burden of arterial hypertension. A multicenter Italian Survey. J Hum Hypertens. 2010;24:395–402.
17. Cuspidi C, Negri F, Giudici V, Muiesan ML, Grandi AM, Ganau A, et al. Self reported weight and height: Implications for left ventricular hypertrophy detection: An Italian multicenter study. Clin Exp Hypertens. 2011 in press.
18. Devereux RB, Reickek N. Echocardiographic determination of left ventricular mass in man. Anatomic validation of the method. Circulation. 1977;55:613–618.
19. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Chamber Quantification Writing Group; American Society of Echocardiography's Guidelines and Standards Committee; European Association of Echocardiography. Recommendations for chamber quantification: A report from the American Society of Echocardiography's Guidelines and Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr. 2005;18:1440–1463.
20. de Simone G, Chinali M. Aortic root dimension and hypertension: A chicken-egg dilemma. Am J Hypertens. 2008;21: 489–490.
21. Schmieder RE. The role of non-haemodynamic factors in the genesis of LVH. Nephron Dial Transplant. 2005;20: 2610–2612.
22. Bella JN, Palmieri V, Roman MJ, Liu JE, Welty TK, Lee ET, et al. Mitral ratio of peak early to late diastolic filling velocity as a predictor of mortality in middle-aged and elderly adults. The Strong Heart Study. Circulation. 2002;105:1928–1933.
23. Mishra RK, Galloway JM, Lee ET, Best LG, Russell M, Roman MJ, Devereux RB. The ratio of mitral deceleration time to E-wave velocity and mitral deceleration slope outperform deceleration time alone in predicting cardiovascular outcomes: The Strong Heart Study. J Am Soc Echocardiogr. 2007;20:1300–1306.
24. Chinali M, Aurigemma GP, de Simone G, Mishra RK, Gerdts E, Wachtell K, et al. Mitral E wave deceleration time to peak E velocity ratio and cardiovascular outcome in hypertensive patients during antihypertensive treatment (from the LIFE Echo-Substudy). Am J Cardiol. 2009;104: 1098–1104.
25. Kizer JR, Bella JN, Palmieri V, Liu JE, Best LG, Lee ET, et al. Left atrial diameter as an independent predictor of first cardiovascular events in middle-aged and elderly adults: The Strong Heart Study (SHS). Am Heart J. 2006;151: 412–418.

Appendix: List of investigators

Bonanomi C, Settimi E, Danzi GB, Division of Cardiology, Fondazione Ospedale Maggiore Policlinico, Milano; **Capra A, Scanziani E, Giannattasio C, Trocino G, Casati A,** Department of Clinical Medicine and Prevention, Clinica Medica, University of Milano-Bicocca, Milan, and Division of Cardiology, Ospedale San Gerardo, Monza, Italy; **Chiappa L, Paggi A, Morganti A,** Chair of Internal Medicine and Hypertension Center, Ospedale S. Giuseppe, Italy; **Degli Esposti D, Bacchelli S,** Department of Internal Medicine, Aging and Kidney diseases, University Hospital of Bologna, Bologna, Italy; **Ganau A, Oppo A,** Cattedra di Malattie dell'Apparato Cardiovascolari, Università di Sassari, Italy; **Grandi AM, Nicolini E, Mongiardi C,** Department of Clinical Medicine, University of Insubria, Varese, Italy; **Lonati L, Branzi G, Parati G,** Division of Cardiology, Istituto Auxologico Italiano IRCCS Milan, Italy; **Longo M, Valerio C, Marconi M,** Centro Trasfusionale e di Immunoematologia Fondazione Ospedale Maggiore Policlinico Mangiagalli e Regina Elena, IRCCS Milano; **Macca G,** Division of Clinical Cardiology San Carlo Hospital, Paderno Dugnano, Italy; **Milan A, Avenatti E, Veglio F,** Department of Medicine and Experimental Oncology, Division of Internal Medicine, University of Torino, Torino, Italy; **Muiesan ML, Salvetti M, Paini A, Galbassini G, Monteduro C,** Department of Medical and Surgical Sciences, Clinica Medica, University of Brescia, Brescia, Italy; **Negri F, Giudici V, Valerio C, Re A, Cuspidi C,** Department of Clinical Medicine and Prevention, University of Milano-Bicocca, Milan, and Clinical Research Unit, Istituto Auxologico Italiano, Meda, Italy; **Pellizzoli S, Robustelli F,** Division of Cardiology, Hospital of Morbegno, Italy; **Rao MAE, Iovino GL, Arcucci O, De Luca N,** Department of Clinical Medicine and Cardiovascolar Sciences, Università degli Studi "Federico II", Napoli, Italy; **Tocci G, Ciavarella M, Volpe M,** Division of Cardiology, II Faculty of Medicine, University of Rome La Sapienza, Sant' Andrea Hospital, Rome; **Vaccarella A,** Servizio di Cardiologia-Presidio Operativo e di Ricerca di Casatenovo I.N.R.C.A-IRCCS, Italy; **Veglia MG,** Division of Cardiology, Hospital Madonna delle Grazie, Matera, Italy.