Aortic Root Dilatation at Sinuses of Valsalva and Aortic Regurgitation in Hypertensive and Normotensive Subjects

The Hypertension Genetic Epidemiology Network Study


Abstract—The association of sinuses of Valsalva dilatation and aortic regurgitation with hypertension is disputed, and few data are available in population-based samples. We explored the relations of sinuses of Valsalva dilatation and aortic regurgitation to hypertension and additional clinical and echocardiographic data in 2096 hypertensive and 361 normotensive participants in the Hypertension Genetic Epidemiology Network study. Age and body surface area were used to predict aortic root diameter using published equations developed from a separated reference population. Aortic dilatation was defined as measured sinuses of Valsalva diameter exceeding the 97.5th percentile of the confidence interval of predicted diameter for age and body size. Aortic dilatation was present in 4.6% of the population. After adjustment for age and body surface area, mean aortic root diameter was larger in hypertensives with suboptimal blood pressure control than normotensives or hypertensives with optimal blood pressure control. In multivariate models, sinuses of Valsalva diameter was weakly positively related to diastolic blood pressure and to left ventricular mass independent of aortic regurgitation. Subjects with aortic dilatation were slightly older, were more frequently men, had higher left ventricular mass, and had lower left ventricular systolic chamber function independent of covariates. Sinuses of Valsalva dilatation was independently related to male gender, aortic valve fibrocalcification, and echocardiographic wall motion abnormalities but not to diastolic blood pressure (or history of hypertension in a separate model). The likelihood of aortic regurgitation increased with larger aortic root diameter, older age, female gender, presence of aortic valve fibrocalcification, and lower body mass index but not hypertension or diabetes. In a subsequent model, diastolic blood pressure was negatively related to aortic regurgitation independent of covariates. In a large population-based sample, sinuses of Valsalva diameter was only mildly larger in subjects with suboptimally controlled hypertension than in normotensives or well-controlled hypertensives, which did not result in differences in prevalence of aortic regurgitation among groups. Sinuses of Valsalva dilatation was associated with higher left ventricular mass and lower systolic function, which may contribute to higher cardiovascular risk in subjects with aortic root dilatation. (Hypertension. 2001;37:1229-1235.)

Key Words: aorta • heart valve diseases • hypertension, arterial • hypertrophy • echocardiography

Aortic root diameter at the sinuses of Valsalva is proportional to body size and increases with aging.1–3 Aortic root dilatation is a leading cause of aortic regurgitation.4–7 Aortic root dilatation at sinuses of Valsalva is diagnosed by relating actual diameter to the value predicted for a subject’s body surface area (BSA) and age.2 Results from the Framingham Heart Study suggest that blood pressure (BP) is positively related to sinuses of Valsalva diameter,1 although other studies have not found an association between sinuses of Valsalva diameter and hypertension.2,6,8,9 Little information is available on the relation between hypertension and aortic root diameter in population-based samples. Accordingly, the present study was undertaken to explore relations of arterial hypertension with dilatation at the sinuses of Valsalva and aortic regurgitation in a population-based sample controlling for common covariates.

Methods

Population

The Hypertension Genetic Epidemiology Network (HyperGEN) study is part of the National Heart, Lung, and Blood Institute (NHLBI) Family Blood Pressure Program designed to assess the genetic basis of hypertension in population-based samples. Onset of hypertension by age 60 and at least 1 additional hypertensive sibling willing to participate were required to be selected. Hypertension was
defined as systolic BP ≥140 or diastolic BP ≥90 mm Hg or by being treated for hypertension. Optimal BP control was defined by BP <140/90 mm Hg (n = 1342), whereas suboptimal BP control was defined by diastolic BP≥90 mm Hg (n=210). A random sample of individuals from the same source populations was also recruited without regard to their hypertension status. Individuals with type I diabetes mellitus were excluded. Four of 5 field centers in HyperGEN participated in the ancillary echocardiographic study. Study participants were recruited from previously defined and enumerated population-based samples, including the Atherosclerosis Risk in Communities study in Minneapolis and Forsyth County, North Carolina; the Minnesota Heart Study; and the Utah Health Family Tree Study. Selected participants from these parent studies previously participated in the NHLBI Family Heart Study, from which a large proportion of the hypertensive sibships was sampled for HyperGEN.

Of the 2534 adult participants with demographic, anthropometric, and clinical information regarding hypertension and diabetes status who also underwent echocardiography, those whose echocardiogram that did not yield technically satisfactory left ventricular (LV) (3%) or aortic root (0.7%) measurements or had more than mild aortic stenosis were excluded. The study population comprised 2452 subjects, 2096 hypertensive and 361 normotensive subjects, representing 97% of the HyperGEN cohort.

**Anthropometric Measurements, Clinical and Laboratory Data, Medical History**

Anthropometric measurements included body mass index, BSA, percent body fat mass calculated by bioelectric impedance according to published methods, and fat-free mass calculated as body weight – fat mass. Overweight was defined as body mass index ≥27.3 or ≥27.8 kg/m² in women or men. Fasting serum glucose, lipid, lipoprotein, and creatinine concentrations were obtained. Diabetes mellitus was diagnosed by American Diabetes Association criteria or use of hypoglycemic medication. History of myocardial infarction and use of antihypertensive medications were defined by participant self-reports. Duration of hypertension was defined as years from self-reported date of diagnosis or beginning of antihypertensive treatment or by reviewing medical documentation.

**Echocardiography**

Echocardiograms were performed following methods used in previous studies and centrally read at Cornell Medical Center. A standardized protocol was followed under which the parasternal acoustic long and short-axis views were used to record on videotape ≥10 consecutive beats of 2-dimensional M-mode recordings of the aortic root and left atrium and of the LV internal diameter and wall thicknesses at or just below the tip of the anterior mitral leaflet; color Doppler was used to search for mitral and aortic regurgitation. The apical window was used to record ≥10 cycles of 2-, 3-, 4-, and 5-chamber images and color Doppler recordings to assess LV wall motion and identify mitral and aortic regurgitation. Mitral anular calcification, aortic valve fibrocalkification, and bicuspid aortic valve were identified by visualization of the valves in long- and short-axis 2-dimensional views.

**Primary Echocardiographic Measures**

Correct orientation of planes for imaging and Doppler recordings was verified by standard procedures. LV internal dimension and septal and posterior wall thicknesses were measured at end-diastole and end-systole by American Society of Echocardiography recommendations, averaging up to 3 cardiac cycles. When optimal orientation of the LV M-mode could not be obtained, correctly oriented linear dimensions were measured from 2-dimensional imaging by the leading-edge American Society of Echocardiography convention. Wall motion was assessed in parasternal long- and short-axis views and in apical views, dividing the left ventricle in 5 segments at the base, 5 segments at the level of papillary muscles, and 4 segments at the apex. Echocardiograms were preliminarily read by a first reader and subsequently over-read by highly experienced readers who were blinded to subjects’ clinical data. The aortic annulus and sinuses of Valsalva diameters were evaluated at end-diastole in anatomically correctly oriented 2-dimensional parasternal views, procedures that maximize these dimensions. Annular diameter was measured from trailing edge to leading edge at the hinging points of the aortic cusps in parasternal 2-dimensional long-axis view, using color flow mapping to help delineate tissue-blood interfaces when necessary; sinuses of Valsalva diameter was measured by the leading-edge convention.

**Definition of Dilatation of Aortic Root at Sinuses of Valsalva**

As previously reported, BSA was used to predict sinuses of Valsalva diameter in 20 to 40 and ≥40 years age-strata by published equations. Dilatation at sinuses of Valsalva was diagnosed when measured diameter exceeded the 97.5 percentile of values predicted by subject’s BSA.

**Derived Measures of LV Structure**

End-diastolic LV dimensions were used to calculate LV mass by a formula yielding values closely related (r=0.90) to necropsy LV weight. Methods used for LV measurements have shown excellent reliability of LV mass (intraclass correlation coefficient=0.93) and good reliability of LV functional measurements used in this study (intraclass correlation coefficient=0.61 to 0.71). Relative wall thickness, a measure of concentricity of LV geometry, was calculated as 2×posterior wall thickness/internal dimension. End-diastolic and end-systolic LV volumes were calculated by the Teichholz method and validated by comparison with invasive and Doppler reference standards. Ejection fraction was calculated from diastolic and systolic LV volumes.

**Measures of LV Systolic Function**

The primary approach to assess myocardial contractile efficiency was evaluation of LV systolic midwall shortening in relation to end-systolic stress measured at the midwall at the level of the LV minor axis. Estimates of end-systolic stress by the described method are closely related to values calculated by substituting central diastolic notch BP that was estimated using planimetry for cuff BP (r=0.95). Midwall shortening and midwall shortening as a percent of the value predicted for observed end-systolic stress, termed stress-corrected midwall shortening, were calculated using previously reported methods. Stress-corrected LV chamber function was estimated by the ratio of end-systolic stress to end-systolic volume.

**Aortic Valve Function Assessment**

Aortic stenosis was identified by detection of moderately or severely reduced aortic cusps motion and assessment of valve area by the continuity equation using continuous wave recordings. Subjects with moderate or severe aortic stenosis (valve area <0.8 cm²/m²) were excluded. Color Doppler recordings from parasternal and apical windows were used to evaluate aortic and mitral regurgitation.

Aortic regurgitation was identified on the basis of the extent of diastolic turbulent flow (color variance signal) in the LV outflow tract, with mild (1+) aortic regurgitation when jets occupy <20% of aortic annular diameter at its origin and extending less than half way to the anterior mitral leaflet tip; 2+ regurgitation when jets fill 20% to 40% of annular diameter and extending up to the anterior mitral leaflet tip; 3+ regurgitation when jets occupy 40% to 60% of annular diameter, extending to or slightly beyond the anterior mitral leaflet tip; and 4+ regurgitation when jets occupy >60% of annular diameter extending to the posterior LV wall or more than half way to the LV apex. For jets that were oriented perpendicular to the aortic annular plane, priority was given to jet width criteria. Concomitant mitral regurgitation was assessed by color Doppler regurgitant jet area and depth criteria.
Statistical Analyses
Data are reported as mean±SD for continuous variables or proportions for categorical variables. For continuous variables, differences between hypertensives and normotensives and between participants with or without sinuses of Valsalva dilatation were assessed by t test for independent samples. Fisher’s exact test was used in 2×2 cross-tables with estimation of odds ratio (OR) and 95% confidence intervals (CI). χ² statistics were used for other cross-tables. ANCOVA was used to assess between-group differences in body size and composition, controlling for age and gender, and differences in LV structure and LV systolic function, controlling for age and BSA. Adjusted means and standard deviations are shown in tables. Multiple regression analysis was used to identify independent clinical and echocardiographic correlates of sinuses of Valsalva diameter. Logistic regression analysis was used to assess clinical and echocardiographic correlates (as reported in figures) of sinuses of Valsalva. Results concerning aortic regurgitation were confirmed controlling for an indicator for use of appetite suppressants in 33 individuals (1.4%) (results not shown). Two-tailed P<0.05 was considered statistically significant.

Results
Characteristics of Normotensive and Hypertensive Subjects
On average, hypertensives were older (55±11 versus 53±12 years) and predominantly female (61% versus 51%) compared with normotensives (P<0.001). Adjusting for age and gender, hypertensives had higher fat-free mass (54±9 versus 52±9 kg), BSA (1.98±0.23 versus 1.94±0.22 m²), body mass index (31.9±7.0 versus 28.7±5.9 kg/m²), adipose mass (35±14 versus 30±12 kg), and BP, partially by definition, (133/75±22/14 versus 115/66±16/11 mm Hg) (all P<0.001). After adjustment for age and BSA, mean sinuses of Valsalva diameter was marginally larger in normotensive adults than hypertensive adults (34.6 versus 34.1 mm, P=0.02); a further analysis revealed that hypertensives with suboptimal BP control had larger mean sinuses of Valsalva diameter than hypertensives with optimal BP control or normotensives (35.4 versus 33.9 and 34.6 mm, respectively, both P<0.05); hypertensives with optimal BP control had smaller sinuses of Valsalva diameter than normotensives (P<0.05).

In multiple regression analysis, sinuses of Valsalva diameter was positively related to age (β=0.26, P<0.001), male gender (β=0.38, P<0.001), BSA (β=0.25, P<0.001), presence of aortic regurgitation (β=0.26, P<0.001), and diastolic BP (β=0.08, P<0.001) (R=0.60, P<0.001), whereas diabetics did not enter the model. In a subsequent model, diastolic BP was substituted by 2 variables, one indicating normotension versus hypertension and the other indicating subjects with suboptimal BP control versus others: the model confirmed previous results and showed independent positive relation of sinuses of Valsalva diameter to suboptimal BP control (P<0.005) but not to hypertension (P=0.9) (R=0.62, P<0.001). When duration of hypertension replaced the variable indicating suboptimal BP control in the previous model, no independent relation of sinuses of Valsalva diameter to hypertension or its duration (both P≥0.4) was detected (R=0.61, P<0.001). An additional regression analysis showed sinuses of Valsalva diameter to be related to LV mass (β=0.16, P<0.001) independent of relations to age, gender, BSA, diastolic BP, diabetes, and aortic regurgitation (R=0.62, P<0.001).

Sinuses of Valsalva Dilatation and Aortic Regurgitation: Prevalences and Correlates
The prevalence of aortic root dilatation in the whole sample was 4.6% (Table 1), without differences between hypertensives and normotensives or between diabetics and nondiabetics. Sinuses of Valsalva dilatation were associated with male gender and absence of overweight but not smoking history. The prevalence of aortic regurgitation was 6.7% (Table 1) and was associated with absence of overweight, without relations to gender, hypertension, diabetes, or smoking. The prevalence of aortic regurgitation was similar in hypertensives with controlled or uncontrolled BP (6.5 versus 4.3%) (P>0.1).

### Table 1. Prevalence of Aortic Root Dilatation at Sinuses of Valsalva Within Subjects Divided According to Hypertension, Diabetes, Gender, Body Size, and Smoking Habit

<table>
<thead>
<tr>
<th>Categories</th>
<th>Aortic Root Dilatation</th>
<th>Aortic Regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study population</strong></td>
<td>4.6% (n=112)</td>
<td>6.7% (n=165)</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4.2%</td>
<td>5.8% P=NS</td>
</tr>
<tr>
<td>No</td>
<td>5.8%</td>
<td>6.6%</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4.2%</td>
<td>5.8% P=NS</td>
</tr>
<tr>
<td>No</td>
<td>4.6%</td>
<td>6.6%</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>2.0%</td>
<td>2.4%</td>
</tr>
<tr>
<td>Normal body weight</td>
<td>7.0%</td>
<td>7.0%</td>
</tr>
<tr>
<td>Overweight</td>
<td>3.4%</td>
<td>3.4% P=0.001</td>
</tr>
<tr>
<td>Smoker</td>
<td>5.3%</td>
<td>5.3%</td>
</tr>
<tr>
<td>Never smoked</td>
<td>3.8%</td>
<td>3.8% P=NS</td>
</tr>
</tbody>
</table>

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Clinical and Metabolic Findings in Subjects With or Without Sinuses of Valsalva Dilatation

Diastolic and mean BPs were higher in subjects with dilated sinuses of Valsalva, whereas age (56±14 versus 54±11 years, \(P<0.1\)), systolic BP, pulse pressure, and heart rate did not differ between groups (Table 2). Medication use and duration of hypertension did not differ between hypertensive subjects with or without aortic dilatation. Overall, body mass index, adipose mass, and fat-free mass were lower in subjects with dilated sinuses of Valsalva independent of age and gender. Glucose and creatinine levels and prevalence of self-reported myocardial infarction were comparable between groups. Total and HDL cholesterol were lower in subjects with dilated sinuses of Valsalva.

Sinuses of Valsalva Dilatation, Aortic and Mitral Annulus Fibrocalcification, and Regurgitation

Individuals with sinuses of Valsalva dilatation compared with those without sinuses of Valsalva dilatation had higher prevalence of mild (1+) (12.5 versus 3.9%) and moderate to severe (≥2+) (7.1 versus 2.1%, both \(P<0.001\)) aortic regurgitation, whereas the prevalence of mitral regurgitation did not differ between groups (25% versus 19%, \(P>0.1\)). Sinuses of Valsalva dilatation was associated with aortic valve fibrocalcification (21.4 versus 11.3%, \(P<0.001\); age- and gender-adjusted OR=1.8 and 95% CI, 1.1 to 2.9), but not mitral annular calcification (12% versus 14%, \(P>0.5\)) or mitral stenosis (3 subjects, all without aortic dilatation) (all \(P>0.1\)). Bicuspid aortic valve (n=3) and aortic stenosis (n=6) were detected in subjects with normal sinuses of Valsalva diameter.

LV Structure and Geometry in Subjects With or Without Sinuses of Valsalva Dilatation

After adjustment for age and BSA, sinuses of Valsalva dilatation was associated with larger aortic annular diameter and LV diameter, thicker LV walls, and higher LV mass, whereas relative wall thickness did not differ between groups (Table 3).

LV Systolic Function in Subjects With or Without Sinuses of Valsalva Dilatation

Participants with dilated sinuses of Valsalva had lower ejection fraction and midwall shortening and higher circumferential end-systolic stress and stroke volume (Table 3). The circumferential end-systolic stress/endo-systolic volume, afterload-corrected estimate of LV chamber function, and stress-corrected midwall shortening, estimate of myocardial contractility, were lower in subjects with sinuses of Valsalva dilatation. Echocardiographically detected segmental or global wall motion abnormalities were more than twice as common in individuals with aortic root dilatation (OR=2.5; 95% CI, 1.5 to 4.1).

To exclude potential confounding by ischemic heart disease, LV systolic function was reanalyzed in subjects without wall motion abnormalities or self-reported myocardial infarction (n=2117; 62% women, 4.1% with sinuses of Valsalva dilatation). In this subgroup, ejection fraction and circumferential end-systolic stress/endo-systolic volume were lower in subjects with dilated sinuses of Valsalva (both \(P<0.001\)), whereas circumferential end-systolic stress, midwall shortening, and stress-corrected midwall shortening showed trends parallel to those in the primary analysis.

### Table 2. Clinical Characteristics of Subjects With or Without Aortic Root Dilatation at Sinuses of Valsalva

<table>
<thead>
<tr>
<th>Clinical Variables</th>
<th>Dilated Aortic Root (n=112)</th>
<th>Normal Aortic Root Diameter (n=2343)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>133±24</td>
<td>130±22</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>77±13</td>
<td>73±12</td>
<td>0.002</td>
</tr>
<tr>
<td>Pulse pressure, mm Hg</td>
<td>56±16</td>
<td>57±16</td>
<td>NS</td>
</tr>
<tr>
<td>Mean blood pressure, mm Hg</td>
<td>96±16</td>
<td>92±14</td>
<td>0.001</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>68±12</td>
<td>69±11</td>
<td>NS</td>
</tr>
</tbody>
</table>

Within hypertensives

- Hypertensives treated, % | 82%   | 88%    | NS    |
- Duration of hypertension, y | 14±11 | 14±10  | NS    |
- Body mass index, kg/m² | 29.6±6.8 | 31.5±6.8 | <0.005* |
- Fat-free body mass, kg | 52±9 | 54±9    | <0.03* |
- Adipose mass, kg | 31±13 | 35±13   | <0.001* |
- Glucose, mmol/L | 6.11±2.55 | 6.11±2.44 | NS    |
- Creatinine, μmol/L | 92.8±23 | 89.3±38 | NS    |
- Total cholesterol, mmol/L | 3.05±0.85 | 5.20±1.01 | <0.001 |
- HDL cholesterol, mmol/L | 1.27±0.39 | 1.35±0.39 | <0.02 |

Self-reported history of heart attack, % | 7.2%  | 9.8%   | NS    |

*Mean and \(P\) values adjusted for age and gender by ANCOVA.
Correlates of Sinuses of Valsalva Dilatation

In a logistic regression analysis, sinuses of Valsalva dilatation was associated with male gender, aortic valve fibrocalcification, and echocardiographic LV wall motion abnormalities (all \(P<0.001\)) but not with diastolic BP or other variables considered (Figure 1).

Table 3. Left Ventricular Geometry, Systolic Function, and Arterial Stiffness in Hypertensive Subjects With or Without Aortic Root Dilatation at Sinus of Valsalva

<table>
<thead>
<tr>
<th>Echocardiographic Variables</th>
<th>Dilated Aortic Root</th>
<th>Normal Aortic Root Diameter</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Aortic anular diameter, cm</td>
<td>2.3±0.2</td>
<td>2.1±0.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV diastolic internal diameter, cm</td>
<td>5.4±0.5</td>
<td>5.2±0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Interventricular septum, cm</td>
<td>0.99±0.10</td>
<td>0.95±0.09</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV posterior wall, cm</td>
<td>0.93±0.10</td>
<td>0.89±0.10</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LV mass, g</td>
<td>204±41</td>
<td>175±41</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Relative wall thickness</td>
<td>0.34±0.05</td>
<td>0.35±0.05</td>
<td>NS</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>58±9</td>
<td>62±8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Midwall shortening, %</td>
<td>16.3±2.4</td>
<td>17.1±2.3</td>
<td>&lt;0.001</td>
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<tr>
<td>Circumferential end-systolic stress, Kdyne/cm²</td>
<td>179±44</td>
<td>163±42</td>
<td>&lt;0.001</td>
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<td>End-systolic stress/end-systolic volume, Kdyne/cm³</td>
<td>3.1±0.8</td>
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<td>Stress-corrected midwall shortening, %</td>
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*Mean and \(P\) values adjusted for age and BSA.

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Correlates of Aortic Regurgitation

As seen in Figure 2, aortic regurgitation was directly related to sinuses of Valsalva diameter, age, aortic valve fibrocalcification, and female gender (\(P<0.01\)) and negatively related to body mass index (\(P<0.01\)), whereas hypertension did not enter the model. In a subsequent model that included diastolic BP instead of the categorical variable for hypertension, aortic regurgitation was directly related to sinuses of Valsalva diameter, age, aortic valve fibrocalcification, and female gender (all \(P<0.001\)) and negatively related to diastolic BP (OR = 0.98/mm Hg; 95% CI, 0.97 to 0.998, \(P<0.05\)) and body mass index (\(P<0.005\)). After control for use of appetite suppressants, aortic regurgitation was directly related to age, aortic valve fibrocalcification, and female gender and negatively related to body mass index (\(P<0.005\)) but not to diastolic BP (\(P=0.08\)).

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</table>

*Mean and \(P\) values adjusted for age and BSA.

to body mass index (\(P<0.01\)), whereas hypertension did not enter the model. In a subsequent model that included diastolic BP instead of the categorical variable for hypertension, aortic regurgitation was directly related to sinuses of Valsalva diameter, age, aortic valve fibrocalcification, and female gender (all \(P<0.001\)) and negatively related to diastolic BP (OR = 0.98/mm Hg; 95% CI, 0.97 to 0.998, \(P<0.05\)) and body mass index (\(P<0.005\)). After control for use of appetite suppressants, aortic regurgitation was directly related to age, aortic valve fibrocalcification, and female gender and negatively related to body mass index (\(P<0.005\)) but not to diastolic BP (\(P=0.08\)).

Figure 1. Correlates of aortic root dilatation at sinuses of Valsalva. Adjusted OR and 95% CI, derived by multivariate logistic regression analysis, are reported for variables associated with aortic root dilatation at sinuses of Valsalva. Statistical significance is indicated by horizontal lines not crossing the vertical line.

Figure 2. Correlates of aortic regurgitation. Adjusted OR and 95% CI, derived by multivariate logistic regression analysis, are reported for variables associated with aortic regurgitation. Statistical significance is indicated by horizontal lines not crossing the vertical line.
Discussion

Hypertension and Sinuses of Valsalva Diameter and Aortic Regurgitation

Association of hypertension with aortic root dilatation is controversial.1,2,6,8 In our study in a population-based sample of hypertensives and randomly selected normotensives from the same source, hypertensives were, on average, older and had a higher body mass index and fat-free mass than normotensives. In multivariate models, neither hypertension nor duration of hypertension was significantly related to sinuses of Valsalva diameter. Diastolic BP showed a weak independent direct relation to sinuses of Valsalva diameter but not to the categorical variable indicating dilated sinuses of Valsalva. Sinuses of Valsalva diameter was strongly positively related to aortic regurgitation, which was in turn inversely related to diastolic BP. Therefore, the relation of diastolic BP to sinuses of Valsalva diameter may be mildly stronger than what we found. Moreover, most hypertensives were treated for hypertension, and those with optimal BP control had, on average, mildly smaller aortic root than normotensive subjects. Greater intra-aortic distending pressure in patients with uncontrolled hypertension was associated with larger sinuses of Valsalva, possibly related to dynamic stretch of the aorta caused by that organ’s elasticity. Although our study is cross-sectional, our findings suggest potential benefit of BP control to prevent aortic root enlargement in hypertension. However, the slightly greater sinuses of Valsalva diameter in participants with uncontrolled versus controlled hypertension did not yield more aortic regurgitation in the former group.

Aortic Root Dilatation, Aortic Regurgitation, and LV Structure and Function

As expected, sinuses of Valsalva dilatation and aortic regurgitation were strongly related, but hypertension was not associated with aortic regurgitation, which is consistent with other studies.7,8,27,28 However, sinuses of Valsalva diameter was positively related to LV mass, independent of covariates and aortic regurgitation, confirming independent relation of aortic root diameter to LV mass reported in population29 and clinical30 studies. The mechanism of the association between enlargement of the sinuses of Valsalva and LV mass independent of aortic regurgitation is uncertain and requires further investigation.

A new finding was that aortic root dilatation was independently associated with higher likelihood of LV wall motion abnormalities. This finding suggests a previously unrecognized association between aortic root dilatation and coronary heart disease, potentially parallel manifestations of atherosclerosis. In subjects with sinuses of Valsalva dilatation, LV enlargement without parallel increase in LV wall thickness was associated with increased end-systolic stress. Furthermore, the observed increased wall stress and LV mass necessitates increased coronary blood flow.31 However, sinuses of Valsalva dilatation was not significantly associated with self-reported myocardial infarction, suggesting that aortic dilatation may be related to clinically silent ischemic heart disease. Sinuses of Valsalva dilatation was related to lower myocardial contractility, estimated by stress-corrected LV systolic function. Further investigation is needed to verify whether the method used to calculate end-systolic stress may underestimate the “true” afterload in subjects with aortic dilatation, potentially yielding underestimation of stress-corrected LV systolic function in subjects with sinuses of Valsalva dilatation.

Aortic valve fibrocalcification has been found to be positively associated with aortic regurgitation.32 In the present report, we further demonstrate that aortic valve calcification was associated with aortic dilatation and aortic regurgitation independent of covariates including age.

Aortic Root Dilatation, Aortic Regurgitation, and Body Composition

Adipose mass and fat-free mass were lower in subjects with sinuses of Valsalva dilatation, independent of age and gender. Sinuses of Valsalva diameter, age, and aortic valve fibrocalcification were strong correlates of aortic regurgitation, and aortic regurgitation was independently negatively related to body mass index, confirming a recent report from the Strong Heart Study.32 In the Framingham Heart Study,28 a negative relation, albeit insignificant, between the degree of aortic regurgitation and body mass index was observed. Obesity may negatively affect echocardiographic study quality, potentially resulting in underestimation of aortic root diameter and aortic regurgitation. However, only 0.7% of subjects had nonmeasurable aortic root diameter. Prospective studies are needed to evaluate the temporal relation of hypertension and weight change to aortic dilatation and aortic regurgitation.

Gender and Aortic Regurgitation

In multivariate analyses, aortic regurgitation was more likely in women than in men, whereas sinuses of Valsalva dilatation was independently associated with male gender. In the Strong Heart Study, gender was not related to aortic regurgitation independent of age, aortic stenosis, or mitral stenosis and higher log urinary albumin/creatinine.32 In the Framingham Heart Study,28 the OR for aortic regurgitation associated with male gender was 0.6, adjusted for age, body mass index, and hypertension. Further investigation is required on the relation of gender to valve disease.

Conclusions

Uncontrolled hypertension was associated with slightly larger sinuses of Valsalva diameter, which, however, did not result in a greater prevalence of sinuses of Valsalva dilatation or aortic regurgitation compared with groups with controlled BP or normotensives. Subjects with aortic root dilatation had higher LV mass, independent of aortic regurgitation, and lower LV chamber systolic function, independent of overt ischemic heart disease, which may contribute to increase the cardiovascular risk associated with hypertension. Sinuses of Valsalva dilatation was a strong independent correlate of aortic regurgitation. Further investigation is needed on the relation of aortic dilatation to ischemic heart disease, as well as the potential benefit of antihypertensive therapy on the prevention or reversal of aortic dilatation.
References

Aortic Root Dilatation at Sinuses of Valsalva and Aortic Regurgitation in Hypertensive and Normotensive Subjects: The Hypertension Genetic Epidemiology Network Study
Vittorio Palmieri, Jonathan N. Bella, Donna K. Arnett, Mary J. Roman, Albert Oberman, Dalane W. Kitzman, Paul N. Hopkins, Mary Paranicas, D. C. Rao and Richard B. Devereux

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