Symptomatic Aortic Stenosis
Does Systemic Hypertension Play an Additional Role?

Francesco Antonini-Canterin, Guoqian Huang, Eugenio Cervesato, Pompilio Faggiano, Daniela Pavan, Rita Piazza, Gian Luigi Nicolosi

**Abstract**—Hypertension and aortic stenosis represent 2 different models of left ventricular systolic overload. Previous studies have observed different remodeling patterns in these conditions. There is, however, little information about patients with coexisting aortic stenosis and hypertension. Echocardiography was performed in 193 consecutive patients with symptomatic aortic stenosis (113 males, 80 females; mean age, 68±9 years). The prevalence of systemic hypertension was assessed. Left ventricular mass index and relative wall thickness were measured from M-mode echocardiography. Four different left ventricular remodeling patterns were identified: normal remodeling, concentric remodeling, concentric hypertrophy, and eccentric hypertrophy. A history of hypertension was present in 62 patients (32%), whereas 131 patients were normotensive. No significant differences were found between hypertensive and normotensive patients with respect to age, male/female ratio, mean New York Heart Association class, distribution of symptoms, left ventricular systolic and diastolic function, and remodeling patterns. In hypertensive patients, however, symptoms were present with larger aortic valve areas and lower stroke work loss. Systemic hypertension is not rare in patients with symptomatic aortic stenosis (32% in our series). Left ventricular remodeling patterns are quite similar in hypertensive and normotensive aortic stenosis. Our results suggest that symptoms of aortic stenosis develop with larger valve area and lower stroke work loss in hypertensive patients, probably because of the additional overload due to hypertension itself. It could suggest that in patients with coexisting hypertension and aortic stenosis, hypertension should be treated more aggressively to delay the occurrence of symptoms, and these patients should be followed-up more closely. (*Hypertension*. 2003;41:1268-1272.)

**Key Words:** aorta ▪ echocardiography ▪ hypertension, arterial ▪ hypertrophy ▪ remodeling

Left ventricular (LV) remodeling and LV hypertrophy are adaptive responses to chronic LV systolic pressure overload and are commonly encountered in patients with systemic hypertension and valvular aortic stenosis (AS). The adverse effect of LV hypertrophy on prognosis has already been well recognized in both pathological conditions.1 Echocardiography provides a very accurate and sensitive tool to detect LV hypertrophy. Taking into account the values of LV relative wall thickness (RWT) and LV mass index (LVMI), 4 different patterns of LV remodeling have been identified and proven to be associated with different hemodynamic profiles2 and prognosis.3

Although previous studies have observed different remodeling patterns in AS and hypertension,4 there is, however, little information about patients with coexisting AS and hypertension. Although there are some reports of the coexistence of these 2 diseases,5–9 the true prevalence of the association is unknown. In addition, whether systemic hypertension plays an additional role in LV remodeling and symptom development in patients with AS has not been extensively evaluated. The purposes of this study were to (1) determine the prevalence of coexisting AS and hypertension in a large series of patients with symptomatic aortic stenosis, (2) assess LV remodeling pattern distributions in AS patients with and without hypertension before aortic valve replacement, and (3) evaluate the additional effect of systemic hypertension on the clinical status and symptoms in patients with AS.

**Study Population**
The present study included 193 consecutive patients with symptomatic AS and an adequate ultrasound window (113 males, 80 females; mean age, 68±9 years) who were referred to our Echocardiographic Laboratory before aortic valve replacement. All patients underwent a complete examination, including 2D, M-mode, color-flow Doppler, and pulse/continuous-wave Doppler echocardiography. At the same time, an experienced cardiologist, unaware of the echocardiographic results, evaluated the patient’s clinical status and the main symptoms, including angina, heart failure, and syncope. The prevalence of history of systemic hypertension was assessed in the entire population. Systemic hypertension was defined as a history of arterial blood pressure >140/90 mm Hg and/or the administration of drugs for
anthy hypertensive treatment. The clinical status was defined according to the criteria of the New York Heart Association (NYHA)
classification.19

Two-Dimensional Echocardiography
Complete echocardiographic examination was performed with commercially available ultrasound instruments, an Aloka SSD770 or
2200 ultrasound imaging unit or a Hewlett-Packard 2500 or 5500 imaging system with 2.5- to 3.5-MHz phased-array transducers.
Standard views and techniques were used according to guidelines of the American Society of Echocardiography.11 LV volumes and LV
ejection fraction were determined from an apical maximized 5-chamber view by measuring the end-systolic and end-diastolic
volumes with the modified, single-plane Simpson method or the area-length method. All echocardiographic data were stored on
high-quality S-VHS videotape for offline analysis.

M-Mode Echocardiography
M-mode echocardiograms were derived from 2D images and recorded at 50 mm/s. Cardiac dimensions were measured according to
the recommendations of the American Society of Echocardiography.12 An optimized, parasternal short-axis view at the mid-LV
level, just below the mitral valve leaflets, was used to measure the following parameters: LV end-systolic and end-diastolic dimensions
and ventricular septum and LV posterior wall thicknesses. LV mass and LVMI (LV mass standardized by body surface area) were
measured by M-mode echocardiography with the use of the DeVereux formula.13,14 RWT was calculated as RWT=2×posterior
wall thickness/LV diastolic diameter.2

Doppler Echocardiography
The peak and mean aortic valve flow velocities were determined by continuous-wave Doppler echocardiography by systematically
sampling the flow from different windows and averaging the values for 3 to 5 beats. The maximal instantaneous gradient across the aortic
valve and the mean gradient were derived from aortic Doppler velocities by the modified Bernoulli equation. The aortic valve area
was calculated from the continuity equation as previously described.15 The percentage of stroke work loss, an alternative
pressure-corrected index reflecting the severity of AS, was calculated as the mean systolic pressure gradient divided by mean
ventricular systolic pressure×100%.16-18 LV systolic and diastolic function was evaluated by respectively considering the ejection
fraction, E and A wave velocities, E/A ratio, and the deceleration time of the E wave. Total ejection isovolume (TEI) index, a global
function was evaluated by respectively considering the ejection fraction, peak and mean aortic valve flow velocities by the modified Bernoulli
equation. The aortic valve area was calculated as RWT=2×posterior wall thickness/LV diastolic diameter.2

Definition and Classification of LV
Remodeling Patterns
By taking into account both values of LVMI and RWT, patients were classified into 4 different LV patterns, as previously reported2: (1)
normal remodeling, with RWT ≤0.44, LVMI ≤125 g/m²; (2) concentric remodeling, with RWT >0.44, LVMI ≤125 g/m²; (3)
concentric hypertrophy, with RWT >0.44, LVMI >125 g/m²; and (4) eccentric hypertrophy, with RWT <0.44, LVMI >125 g/m². A
further analysis was performed by taking into account previously reported sex-related cutoff values of hypertrophy (LVMI >135 g/m²
for males and >110 g/m² for females).21

Statistical Methods
Continuous data were expressed as mean±SD, and categorical data as percentage. For analysis comparing the 2 groups, the χ² test was
used for dichotomous variables and the Student t test for continuous variables. Probability values <0.05 were considered to be
significant.

Results
Prevalence of Systemic Hypertension in Patients
With Symptomatic AS
A history of systemic hypertension was present in 62 patients (32%), whereas the other 131 patients (68%) were normoten-
sive. As shown in Table 1, the systolic blood pressure in patients with coexisting AS and hypertension was 142±26 mm Hg, and in normotensive AS patients it was 134±23 mm Hg (P=0.032). The difference was significant despite therapy in most hypertensive patients. The diastolic
blood pressure was not significantly different in the 2 groups (70±13 mm Hg in hypertensive AS patients and 67±13 mm Hg in normotensive AS patients; P=NS).

Clinical Characteristics of Study Population
The main demographic and clinical characteristics of patients are summarized in Table 1. There were no significant differences between hypertensive and normotensive AS pa-
patients in demographic presentation. Age and sex did not affect the prevalence of hypertension. The mean NYHA class and the distribution of symptoms (including angina, heart failure, and
syncope) between the 2 groups were also not different.

Severity of Aortic Valvular Stenosis of
Hypertensive and Normotensive Patients
Compared with normotensive AS patients, hypertensive AS patients presented with larger aortic valve areas (0.82±0.2
cm² vs 0.74±0.2 cm², P=0.021) and lower stroke work loss (25.5±7% vs 28.0±7%, P=0.022) with a similar degree of
symptoms.

LV Remodeling Patterns of Hypertensive and
Normotensive Patients
The LV remodeling pattern distributions in hypertensive and normotensive patients with AS are shown in Table 2. In patients with coexisting AS and hypertension, concentric
hypertrophy was present in 50%, eccentric hypertrophy in 29%, concentric remodeling in 14.5%, and a normal remodeling
pattern in 6.5%. A similar distribution of LV remodeling patterns was also detected in patients without hypertension.
In this group, 49.6% had concentric hypertrophy, 31.3%
had eccentric hypertrophy, and 15.3% had concentric remodeling, whereas only 3.8% patients had normal remodeling.

After also taking into account sex-related cutoff values of hypertrophy (LVMI $>$135 g/m² for males and $>$110 g/m² for females), we did not find any difference in the prevalence of remodeling patterns between hypertensive AS patients and normotensive AS patients (Tables 3 and 4). Independently of hypertension, females showed a higher prevalence of concentric hypertrophy (71% vs 38%, $P$<0.001).

**Comparison of LV Functional Parameters Between Hypertensive and Normotensive AS Patients**

Table 5 shows the systolic, diastolic, and global LV functional parameters in the 2 groups. The values of LV systolic function parameter (ejection fraction), the diastolic functional parameters (velocity of E and A waves, deceleration time of the E wave, and the E/A ratio), and the global performance parameter (TEI index) were not significantly different between hypertensive and normotensive patients.

**Discussion**

LV geometric remodeling with or without LV hypertrophy is 1 of the mechanisms of chronic adaptation to pressure overload, which is common in both systemic hypertension and AS. LV remodeling and hypertrophy initially attenuate the untoward effect of pressure overload on the ventricular wall and preserve pump function. The presence of significant signs of LV hypertrophy on the surface electrocardiogram (ECG), however, has proven to be associated with a substantial increase in cardiovascular risk. In addition, it has been widely reported that LV hypertrophy is very commonly associated with cardiac failure, particularly due to diastolic dysfunction. There is also a 6-fold increase in the likelihood of sudden death from cardiac causes in patients with evidence of LV hypertrophy, which is likely related to myocardial ischemia, myocardial necrosis or fibrosis, and the increased prevalence of complex ventricular arrhythmias.

Echocardiography provides a more accurate and sensitive method of detecting LV hypertrophy than does ECG. As a result of using the echocardiography-derived indexes LVRWT and LVMI, 4 different geometric patterns of LV remodeling have been proposed, which were reported to be associated with different hemodynamic profiles and prognosis.

Systemic hypertension and AS represent 2 different pathological models of LV systolic overload. Previous studies have observed different remodeling patterns in these 2 conditions; concentric hypertrophy indeed has a higher prevalence in isolated AS. There is little information, however, about patients with coexisting AS and hypertension. Furthermore, in patients with coexisting AS and hypertension, it is also unknown whether hypertension plays an additional role in LV remodeling, LV function, and symptoms. To our knowledge, the present study is the first 1 to address to this issue in symptomatic AS.

Theoretically, severe AS might cause a small stroke volume (low-flow state), leading to either normal or low blood pressure in many cases. Frequently, the presence of hypertension would induce a clinician to consider an aortic systolic murmur to be functional. In 1931, Christian first reported 2 cases of hypertension from a group of 57 patients with AS. Since then, others have also reported the coexistence of systemic hypertension and AS, even though the exact prevalence is not completely known. Contralto and Levine reported a 9% incidence of hypertension in a series of 180 cases. McGinn and White reported that 27% of their patients with AS had systolic pressures $>$150 mm Hg. Ikram and colleagues found that in 50 patients with isolated AS confirmed by catheterization, 14% had moderate or severe

**TABLE 2. LV Remodeling Patterns in Hypertensive AS Patients and Normotensive AS Patients**

<table>
<thead>
<tr>
<th>LV Remodeling Patterns</th>
<th>Hypertensives</th>
<th>Normotensives</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal LV remodeling</td>
<td>6.5</td>
<td>3.8</td>
<td>NS</td>
</tr>
<tr>
<td>Concentric LV remodeling</td>
<td>14.5</td>
<td>15.3</td>
<td>NS</td>
</tr>
<tr>
<td>Concentric LV hypertrophy</td>
<td>50.0</td>
<td>49.6</td>
<td>NS</td>
</tr>
<tr>
<td>Eccentric LV hypertrophy</td>
<td>29.0</td>
<td>31.3</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Cut-off value for hypertrophy: left ventricular mass index $>$125 g/m².

**TABLE 3. LV Remodeling Patterns in Hypertensive AS Patients and Normotensive AS Male Patients**

<table>
<thead>
<tr>
<th>LV Remodeling Patterns</th>
<th>Hypertensives</th>
<th>Normotensives</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal LV remodeling</td>
<td>11.1</td>
<td>11.7</td>
<td>NS</td>
</tr>
<tr>
<td>Concentric LV remodeling</td>
<td>19.4</td>
<td>19.5</td>
<td>NS</td>
</tr>
<tr>
<td>Concentric LV hypertrophy</td>
<td>38.9</td>
<td>37.7</td>
<td>NS</td>
</tr>
<tr>
<td>Eccentric LV hypertrophy</td>
<td>30.6</td>
<td>31.1</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Cut-off value for hypertrophy: left ventricular mass index $>$135 g/m².

**TABLE 4. LV Remodeling Patterns in Hypertensive AS Patients and Normotensive AS Female Patients**

<table>
<thead>
<tr>
<th>LV Remodeling Patterns</th>
<th>Hypertensives</th>
<th>Normotensives</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal LV remodeling</td>
<td>3.8</td>
<td>1.9</td>
<td>NS</td>
</tr>
<tr>
<td>Concentric LV remodeling</td>
<td>3.8</td>
<td>3.7</td>
<td>NS</td>
</tr>
<tr>
<td>Concentric LV hypertrophy</td>
<td>69.2</td>
<td>72.2</td>
<td>NS</td>
</tr>
<tr>
<td>Eccentric LV hypertrophy</td>
<td>23.1</td>
<td>22.2</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Cut-off value for hypertrophy: left ventricular mass index $>$110 g/m².

**TABLE 5. Comparison of LV Functional Parameters Between Hypertensive AS Patients and Normotensive AS Patients**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Hypertensives</th>
<th>Normotensives</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF, %</td>
<td>59±8</td>
<td>58±10</td>
<td>NS</td>
</tr>
<tr>
<td>Vel E, m/s</td>
<td>0.87±0.41</td>
<td>0.86±0.45</td>
<td>NS</td>
</tr>
<tr>
<td>Vel A, m/s</td>
<td>0.99±0.25</td>
<td>0.93±0.36</td>
<td>NS</td>
</tr>
<tr>
<td>Ratio E/A</td>
<td>0.82±0.34</td>
<td>0.99±0.79</td>
<td>NS</td>
</tr>
<tr>
<td>DT, s</td>
<td>0.166±0.08</td>
<td>0.166±0.07</td>
<td>NS</td>
</tr>
<tr>
<td>TEI index</td>
<td>0.51±0.24</td>
<td>0.50±0.20</td>
<td>NS</td>
</tr>
</tbody>
</table>

LVEF indicates left ventricular ejection fraction; Vel E, velocity of E wave; Vel A, velocity of A wave; DT, deceleration time; and TEI index, total ejection isovolume index.
hypertension, and only 46% of patients had blood pressures <140/90 mm Hg. Our results, obtained in a large consecutive series of patients with symptomatic AS, are consistent with those previous reports. In our study population, 62 of 193 (32%) patients had a history of hypertension. Age and sex did not affect the prevalence of hypertension. This suggests that hypertension could be considered not absolutely rare in patients with symptomatic AS. On the other hand, in recent epidemiological investigations, hypertension has already been proven to be an independent risk factor of aortic sclerosis and calcification.27,28 The possible explanation of this association could be that hypertension might lead to abnormally high tensile stress on aortic leaflets, followed by endothelial injury or disruption.

In the present study, patients with symptomatic AS had a distribution of LV remodeling patterns similar to that in a previously published study.4 The distribution of LV remodeling patterns was, however, not significantly different between hypertensive and normotensive AS patients in the present study. Also, after taking into account sex-related cut-off values for hypertrophy, we did not find significant differences in the prevalence of remodeling patterns between hypertensive and normotensive AS patients. Independently of hypertension, as previously reported,29 we observed a higher prevalence of concentric hypertrophy in females.

The similarity of remodeling pattern distributions in hypertensive and normotensive patients suggests that in symptomatic AS, the presence of a “fixed” mechanical obstruction of the aortic valve might represent a relatively constant level of afterload and play a more significant role in LV remodeling and hypertrophy than does systemic hypertension itself. Coexisting systemic hypertension seems in fact not to have a significant influence on LV remodeling. As a result, it could also have no additional significant effect on LV function. In the present study, in fact, we did not find significant differences between normotensive and hypertensive AS patients so far as LV systolic function (ejection fraction), LV diastolic function (ie, the parameters derived from mitral inflow Doppler, including velocity of the E and A waves, E/A ratio, and wave deceleration time), and the parameter of global LV performance (TEI index) were concerned.

Hypertension, however, could play a role on the time of onset of symptoms in patients with AS, even though this information could not be directly derived from our retrospective study. Although the distribution of clinical symptoms and NYHA class were similar between hypertensive patients and normotensive patients in our series, symptoms seem to develop at a relatively earlier stage of the disease in patients with AS and hypertensive. Indeed, they had a larger aortic valve area and lower stroke work loss compared with patients without hypertension. It probably reflects that in patients with coexisting AS and hypertension, the LV is facing a higher-pressure afterload (double overload), resulting in significantly more severe myocardial damage and/or subendocardial ischemia; thus, the symptoms might appear at a relatively earlier phase.

It could be difficult to understand how hypertension per se causes symptoms to develop earlier in the course of AS without affecting LV patterns of remodeling, but it must be taken into consideration that symptoms in AS are not a “continuous variable” directly related to LV hypertrophy. Frequently, patients are referred to surgery after a single episode of acute heart failure, angina, or syncope that could be induced by the association of a paroxysmal hypertensive response and a sudden afterload increase. This could explain, at least in part, the earlier occurrence of symptoms in hypertensive AS patients that also occur in the absence of significant differences in the prevalence of LV remodeling patterns.

In patients with AS, the presence of clinical symptoms is a strong predictor of adverse prognosis.30–32 Early identification of symptoms is of major clinical importance to optimize the patients’ treatment. Whether systemic hypertension brings an additional influence to the prognosis of symptomatic AS has not been determined. However, the onset of symptoms at an earlier stage of the disease in patients with coexisting hypertension and AS should be relevant from a clinical point of view (ie, for these patients, hypertension should be treated and controlled more aggressively to delay the onset of symptoms, and this group of patients should be followed-up more closely for optimal clinical management).

It must be recognized, however, that AS affects the LV myocardium through almost entirely load-dependent mechanisms, whereas systemic hypertension extensively invokes neurohumoral mechanisms. On the other hand, interaction between the 2 mechanisms has not been completely clarified to date in the literature and is beyond the purposes of the present study.

Perspectives
Hypertension is not rare in patients with symptomatic AS (about one third of them are hypertensive). Age and sex do not significantly affect the prevalence of hypertension. LV remodeling patterns are quite similar in hypertensives and normotensives. Concentric hypertrophy is the most prevalent pattern in both groups, as was reported for isolated AS. We demonstrated for the first time, to our knowledge, that in hypertensive symptomatic AS patients, symptoms develop at a relative earlier stage of the disease, with larger valve areas and lower stroke loss, probably because of the additional overload due to the hypertension itself. These findings could suggest that in these patients, hypertension should be treated more aggressively, and this group of patients should also be followed-up more closely.

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