Ultrasonic Backscatter and Diastolic Function in Hypertensive Patients

Alicia M. Maceira, Joaquín Barba, Oscar Beloqui, Javier Díez

Abstract—This study was designed to assess whether ultrasonic reflectivity, evaluated by a real-time integrated backscatter analysis, was related to the severity of diastolic dysfunction, as studied by Doppler echocardiography in patients with essential hypertension. One hundred nine subjects were included in the study. Diastolic function was assessed by mitral-inflow Doppler ultrasound recordings. Backscatter cyclic variation and maximal intensity were measured in 6 regions throughout the left ventricle. The subjects were classified in 5 groups according to blood pressure and diastolic function: 29 normotensives with normal diastolic function (group 1), 18 hypertensives with normal diastolic function (group 2), 47 hypertensives with a delayed relaxation pattern (group 3), 11 hypertensives with a pseudonormal filling pattern (group 4), and 4 hypertensives with a restrictive filling pattern (group 5). The highest cyclic variation was found in groups 1 and 2, the lowest in groups 4 and 5 (5.7 ± 0.2 dB in group 1 and 5.7 ± 0.2 dB in group 2 versus 2.9 ± 0.3 dB in group 4 and 2.1 ± 0.4 dB in group 5; P < 0.001), with intermediate values in group 3 (5.2 ± 0.2 dB). Cyclic variation was inversely correlated with left ventricular chamber stiffness (P < 0.05) and directly correlated with midwall fractional shortening (P < 0.02) in all hypertensives. No differences in maximal intensity were found among the 5 groups of subjects. These results show an association between diminished cyclic variation of backscatter and deterioration of diastolic function in hypertensive patients. Thus, alterations in this parameter may be useful for the assessment of diastolic dysfunction in hypertension. (Hypertension. 2002;40:239-243.)

Key Words: diastole ■ hypertension, essential ■ ultrasonography

An exaggerated accumulation of fibrillar collagens type I and type III occurs throughout the free wall and interventricular septum of animals1,2 and humans3,4 with primary arterial hypertension and left ventricular hypertrophy (LVH). A number of experimental5–7 and clinical8–11 studies have shown that myocardial fibrosis is mainly caused by an excessive synthesis of fibrillar collagens. This rise in collagen content has been shown to raise myocardial stiffness and promote abnormalities of diastolic and systolic cardiac function, electrical activity, and intramyocardial perfusion.12 In this regard, we have reported recently13 that a correlation exists between myocardial collagen content and left ventricular chamber stiffness, as assessed from the deceleration time of the early mitral filling, as measured by Doppler echocardiography, in hypertensive patients.

Quantitative characterization of myocardial texture by means of analysis of ultrasonic reflectivity has been experimentally14–17 and clinically18–21 shown to correlate with the collagen content of the myocardial tissue. We, thus, have hypothesized that the severity of diastolic dysfunction in hypertensive subjects should be associated with alterations in myocardial ultrasonic reflectivity detected by backscatter analysis. To test our hypothesis, maximal intensity (MI) and cyclic variation (CV) of backscatter signal were analyzed in normotensive subjects and hypertensive patients classified according to their diastolic function.

Methods

Subjects

The study population consisted of 109 subjects (43 men and 66 women; mean age 53 years; range 22 to 80 years) who were referred to our unit for routine cardiac evaluation. Eighty subjects presented elevated systolic blood pressure > 139 mm Hg and diastolic blood pressure > 89 mm Hg. The study was approved by the review committee of the University Clinic of Navarra, and all the subjects gave informed consent.

All patients had appropriate clinical, laboratory, and radiological evaluations to exclude secondary hypertension, diabetes mellitus, and cardiac disease that was not hypertensive heart disease. None of the subjects exhibited clinical manifestations suggestive of heart failure.

Assessment of Left Ventricular Anatomy and Function

2D targeted M-mode and Doppler ultrasound recordings were obtained in each patient as described previously.10,11 Left ventricular mass and interventricular septal thickness were measured, and left ventricular mass index was calculated by dividing left ventricular mass by body surface area. The following pulsed Doppler measurements were obtained: maximal early transmitral velocity in diastole...
ventricular endocardial fractional shortening and ejection fraction deceleration time (DT), and isovolumic relaxation time (IVRT). Left ventricular dysfunction was defined as alterations in VE/VA ratio, and/or IVRT, and/or DT, and was classified in the following patterns according to the method of Garcíeta al.: delayed relaxation (VE/VA > 1; IVRT > 60 ms; DT > 150 ms), restrictive filling (VE/VA < 1; IVRT > 60 ms; DT < 150 ms), and pseudonormal filling (IVRT = 60 to 100 ms; DT = 150 to 200 ms), and normal filling pattern (IVRT < 60 ms; DT < 150 ms).

Analysis of Backscatter Signal

To perform the backscatter tissue characterization, a SONOS 5500 ultrasound system (Philips) with backscatter software was used. Six regions of interest were chosen throughout the left ventricular anatomy and function. The prevalence of LVH was significantly higher in the 4 groups of hypertensives compared with the remaining groups. In addition, parameters assessing left ventricular mass and dimensions were significantly higher in hypertensives from group 5 than in normotensives from group 1. Although subjects from group 1 were younger than subjects from the other groups, no significant differences in age were observed among the 4 groups of hypertensives.

Statistical Analysis

For the statistical analysis, the 10.0 version of SPSS software (SPSS Inc) was used. All the quantitative variables were tested for Gaussian distribution with the Kolmogorov-Smirnov test; all of them followed this distribution and are presented as mean±SD.

A repeated-measures mixed-factorial design, with myocardial region as intrasubject factor and group of inclusion as intersubject factor, was used. The statistical analysis used was a 3-way ANOVA (criteria were subjects, group of inclusion, and myocardial segments). Age, sex, blood pressure, intersubject heterogeneity of the signal, fractional shortening, ejection fraction, MWFS, left ventricular mass index, and echocardiographic time gain compensation and depth were included as covariates in the analysis. The Bonferroni post-hoc test was used whenever a difference was statistically significant. The correlation between continuously distributed variables was tested by univariate regression analysis. In all cases, \( P < 0.05 \) was considered statistically significant.

Results

Clinical Data

Subjects included in the study were classified in 5 groups according to values of blood pressure and diastolic function as follows: 29 normotensive subjects with normal diastolic function (group 1), 18 hypertensive patients with preserved diastolic function (group 2), 47 hypertensives with a delayed relaxation pattern (group 3), 11 hypertensives with a pseudonormal filling pattern (group 4), and 4 hypertensives with a restrictive filling pattern (group 5).

Clinical parameters evaluated in the 5 groups are presented in Table 1. As expected, values of blood pressure were significantly higher in hypertensives from groups 2 through 5 than in normotensives from group 1. Although subjects from group 1 were younger than subjects from the other groups, no significant differences in age were observed among the 4 groups of hypertensives.

Anatomy and Function

Table 2 shows the echocardiographic parameters assessing left ventricular anatomy and function. The prevalence of LVH was significantly higher in the 4 groups of hypertensives than in the group of normotensives. In addition, parameters assessing left ventricular mass and dimensions were significantly higher in hypertensives from group 5 than in hypertensives from the other groups. Whereas no significant differences were found either in IVRT or DT among the different groups, the \( \text{VE/VA} \) ratio was significantly diminished in group 5 hypertensives compared with the remaining groups. No differences were found in either ejection fraction or fractional shortening among the different groups. MWFS was significantly decreased in group 5 hypertensives compared with the remaining groups. In addition, \( K_{LV} \) was significantly higher in hypertensives from group 5 than in the other groups.
The main findings of this study are as follows: (1) an association exists between echocardiographically assessed altered myocardial ultrasonic reflectivity and progressive deterioration of diastolic filling in patients with arterial hypertension; and (2) alteration of CV of backscatter signal is related to alterations of both left ventricular chamber stiffness and systolic performance.

Several echocardiographic approaches have been used to quantitatively define changes in myocardial ultrasonic reflectivity, among them analysis of the backscatter signal. This signal is produced when the ultrasound interacts with com-

### TABLE 2. Echocardiographic Data in All Groups of Subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
<th>Group 5</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVM, g/m²</td>
<td>95±25</td>
<td>110±31</td>
<td>133±56</td>
<td>128±54</td>
<td>173±35</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>IVST, mm</td>
<td>9.2±1.5</td>
<td>10.1±2.1</td>
<td>11.9±3.1</td>
<td>11.2±2</td>
<td>13.3±2.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IVF, %</td>
<td>38±6</td>
<td>47±12</td>
<td>53±17</td>
<td>48±17</td>
<td>48±13</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LHV, %</td>
<td>13</td>
<td>55</td>
<td>76</td>
<td>90</td>
<td>100</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MWFS, %</td>
<td>17±2</td>
<td>15±2.2</td>
<td>14±3</td>
<td>14±2</td>
<td>13±2</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Values are mean±SEM.

LVM indicates left ventricular mass index; IVST, interventricular septal thickness; RWT, relative wall thickness; LHV, left ventricular hypertrophy; IVF, isovolumic relaxation time; Vₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑطور | 1.3±0.3 | 1.4±0.7 | 0.8±0.1 | 1.3±0.2 | 2.2±0.2 | <0.001|
| DT, ms    | 204±42  | 205±35  | 200±65  | 201±41  | 115±13  | NS  |
| FS, %     | 32±4    | 33±6    | 34±6    | 39±7    | 30±10   | NS  |
| EF, %     | 60±5    | 62±8    | 59±7    | 62±9    | 50±18   | NS  |
| MWFS, %   | 17±2    | 15±2.2  | 14±3    | 14±2    | 13±2    | <0.01|
| Kₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑطور | 0.11±0.07 | 0.11±0.08 | 0.13±0.08 | 0.18±0.08 | 0.35±0.07 | <0.001 |

Regarding MI, the only covariate with a significant impact was intersubject heterogeneity and time-gain compensation (P<0.01), and both remained in the analysis. MI also varied (P<0.001) among all the myocardial regions in all groups because it was higher in apex and lower in the lateral wall. We did not find significant differences in MI among groups for either global (Figure 1) or regional values (data not shown).

### Discussion

The main findings of this study are as follows: (1) an association exists between echocardiographically assessed altered myocardial ultrasonic reflectivity and progressive deterioration of diastolic filling in patients with arterial hypertension; and (2) alteration of CV of backscatter signal is related to alterations of both left ventricular chamber stiffness and systolic performance.

Several echocardiographic approaches have been used to quantitatively define changes in myocardial ultrasonic reflectivity, among them analysis of the backscatter signal. This signal is produced when the ultrasound interacts with com-
The mechanism for the reduction in CV of backscatter in hearts of patients with severe diastolic dysfunction is not clear. Several structural components of the myocardium affect its acoustic properties under physiological and pathological conditions, among them collagen with its complex structure, quantity, geometry, and orientation of the fibers. In hypertension, collagen accumulation in the myocardium occurs, and this fibrotic process causes diastolic dysfunction. In this regard, Ciulla et al. have reported that in hypertensive patients with LVH and histologically assessed myocardial fibrosis, echo amplitude during cardiac cycle is abnormally diminished. Furthermore, we have shown recently that the presence of biochemically assessed severe myocardial fibrosis is associated with decreased CV in patients with essential hypertension. Thus, our finding of decreased CV in hypertensives with pseudonormal and restrictive patterns of diastolic filling would suggest that this ultrasonic abnormality is associated with severe myocardial fibrosis in these patients.

As proposed by Weber et al., an increase in collagen content adversely influences diastolic stiffness of the myocardium and facilitates diastolic dysfunction. In fact, we have shown recently that in humans with hypertensive heart disease, exaggerated myocardial collagen content is associated with excessive KLV, as assessed noninvasively. Thus, the finding here that CV is inversely correlated with KLV further suggests that fibrosis is involved in diminished CV in hypertensives with severe patterns of diastolic dysfunction.

The present study demonstrates that cardiac cycle-dependent variation of backscatter signal is abnormally diminished in hypertensive patients with pseudonormal and restrictive patterns of diastolic filling as assessed by Doppler echocardiography. Furthermore, the associations here reported of CV with both KLV and MWFS suggest that both changes in the composition of myocardial tissue (ie, fibrosis) and abnormalities of left ventricular midwall contractile performance may contribute to altered CV in hypertensive patients with severe hypertension.
diastolic dysfunction. On the other hand, depressed MWFS has been shown to be an independent predictor of cardiac death and also contributes independently to the prediction of cardiovascular morbid events in patients with arterial hypertension.23 Thus, the association of low MDFS with severe LVH and enhanced LV chamber stiffness in hypertensives with a restrictive filling pattern of diastolic dysfunction would suggest a poor cardiac prognosis for these subset of patients. Further studies are required to test this possibility and how antihypertensive treatment would influence these alterations and cardiac outcome in hypertensives.

References


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