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 hypertension 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...
TABLE 1. Clinical Data in All Groups of Subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group 1 (n=29)</th>
<th>Group 2 (n=18)</th>
<th>Group 3 (n=47)</th>
<th>Group 4 (n=11)</th>
<th>Group 5 (n=4)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>47±12</td>
<td>51±10</td>
<td>58±10</td>
<td>52±8</td>
<td>62±8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Gender, male/female</td>
<td>8, 21</td>
<td>5, 13</td>
<td>23, 24</td>
<td>5, 6</td>
<td>3, 1</td>
<td>NS</td>
</tr>
<tr>
<td>BMI, Kg/m²</td>
<td>31±5</td>
<td>29±4</td>
<td>32±5</td>
<td>30±3</td>
<td>32±4</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of hypertension, wk</td>
<td>0</td>
<td>10±2</td>
<td>16±4</td>
<td>8±3</td>
<td>11±6</td>
<td>NS</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>118±12</td>
<td>146±16</td>
<td>157±25</td>
<td>145±16</td>
<td>150±35</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>75±8</td>
<td>93±11</td>
<td>92±12</td>
<td>91±9</td>
<td>90±26</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>MAP, mm Hg</td>
<td>43±11</td>
<td>54±12</td>
<td>64±22</td>
<td>54±8</td>
<td>60±10</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Antihypertensive treatment, No.</td>
<td>0</td>
<td>2</td>
<td>7</td>
<td>2</td>
<td>1</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are mean±SEM.
BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure.

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).

Left Ventricular 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 VE/V_A ratio was significantly diminished 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<.05 was considered statistically significant.
Backscatter Signal

When we analyzed the CV, subject heterogeneity was the only covariate that had a significant impact (P<0.05) and remained in the analysis. Because MWFS was shown to be different among the tested groups, it was also kept as a potential confounding variable. CV varied (P<0.001) throughout the myocardial regions, the maximal value being obtained in the septum and posterior wall and the minimum in the apex and anterior wall in the 5 groups.

As shown in Figure 1, CV was similar in both normotensives and hypertensives with preserved diastolic function, and it gradually diminished throughout the remaining groups of hypertensives, being significantly (P<0.01) lower in groups 4 (2.9±0.3 dB; range 2.4 to 3.5 dB) and 5 (2.1±0.4 dB; range 1.3 to 2.9 dB) compared with groups 1 (5.7±0.2 dB; range 5.3 to 6.1 dB), 2 (5.7±0.2 dB; range 5.3 to 6.2 dB), and 3 (5.3±0.1 dB; range 5.0 to 5.6 dB). These differences remained significant for all the regions studied (Figure 2).

K_{LV} was inversely correlated with CV measured in the septum (r=-0.26, P<0.05), inferior wall (r=-0.25, P<0.05), and apex (r=-0.31, P<0.05) in all hypertensives. In addition, MWFS was directly correlated with CV measured in the septum (r=0.36, P<0.02) and apex (r=0.29, P<0.05) in all hypertensives.

Regarding MI, the only covariates with a significant impact were 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-

<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>RWT, %</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>LVH, %</td>
<td>95±19</td>
<td>92±22</td>
<td>91±21</td>
<td>95±11</td>
<td>77±26</td>
<td>NS</td>
</tr>
<tr>
<td>V_{p}, mm Hg/mL</td>
<td>1.3±0.3</td>
<td>1.4±0.7</td>
<td>0.8±0.1</td>
<td>1.3±0.2</td>
<td>2.2±0.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DT, ms</td>
<td>204±42</td>
<td>205±35</td>
<td>200±65</td>
<td>201±41</td>
<td>115±13</td>
<td>NS</td>
</tr>
<tr>
<td>FS, %</td>
<td>32±4</td>
<td>33±6</td>
<td>34±6</td>
<td>39±7</td>
<td>30±10</td>
<td>NS</td>
</tr>
<tr>
<td>EF, %</td>
<td>60±5</td>
<td>62±8</td>
<td>59±7</td>
<td>62±9</td>
<td>50±18</td>
<td>NS</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>
<tr>
<td>K_{LV}, mm Hg/mL</td>
<td>0.11±0.07</td>
<td>0.11±0.08</td>
<td>0.13±0.08</td>
<td>0.18±0.08</td>
<td>0.35±0.07</td>
<td>&lt;0.001</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; RWT, isovolumic relaxation time; V_{p}, peak velocity of protodiastolic mitral inflow; V_{p}, peak velocity of end-diastolic mitral inflow; DT, deceleration time; FS, endocardial fractional shortening; MWFS, midwall fractional shortening; EF, ejection fraction; K_{LV}, left ventricular chamber stiffness.
ponents of the tissue smaller than its wavelength; the reflected signal is scattered, and a part of it (ie, backscatter) is directed toward the probe. Time-domain analysis of this radiofrequency signal provides its MI and the systolic-to-diastolic CV of the intensity. This CV is ≈5 dB in normal conditions and diminishes in a substantial way in the presence of contractile dysfunction, variation of the elastic properties, or alterations of the geometry of the scatter, etc. In systemic hypertension, an increase of collagen content takes place in the myocardium, so that changes are generated in the backscatter signal.

Whereas no significant changes were found in this study in MI, CV was seen to decrease in hypertensive patients in parallel with the compromise of diastolic function. In fact, values of CV measured in hypertensives with pseudonormal or restrictive filling patterns were below the interval of normal values measured in this study and reported in the literature.28,29 Several other investigators, using alternative methods, have confirmed the presence of diminished cardiac cycle-dependent variation of backscatter in the hypertrophied myocardium of hypertensive patients.30–32 In addition, Giorgi et al33 reported recently a direct correlation between CV and myocardium of hypertensive patients.30

Perspectives

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...
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


Ultrasonic Backscatter and Diastolic Function in Hypertensive Patients
Alicia M. Maceira, Joaquín Barba, Oscar Beloqui and Javier Díez

Hypertension. 2002;40:239-243; originally published online August 5, 2002;
doi: 10.1161/01.HYP.0000030154.90042.4C

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2002 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://hyper.ahajournals.org/content/40/3/239

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published
in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial
Office. Once the online version of the published article for which permission is being requested is located,
click Request Permissions in the middle column of the Web page under Services. Further information about
this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/