Ultrasonic Myocardial Texture Versus Doppler Analysis in Hypertensive Heart
A Preliminary Study

Vitantonio Di Bello, Roberto Pedrinelli, Davide Giorgi, Alessio Bertini, Massimiliano Bianchi, Marco Paterni, Maria Francesca Romano, Giulia Dell’Omo, Costantino Giusti

Abstract—Doppler-derived parameters of transmitral flow are useful indices of diastolic dysfunction in the hypertensive heart. Different degrees of myocardial involvement in hypertensive heart can be detected by videodensitometric myocardial textural analysis. The aim of this study was to compare Doppler-derived and ultrasonic videodensitometric parameters in the differentiation of healthy hearts from hypertensive hearts. We compared a group of age-matched (59±9 years) male essential hypertensive patients (n=53) with normotensive healthy subjects as controls (n=32). All subjects provided ambulatory blood pressure measurements for the evaluation of 24-hour mean systolic and diastolic blood pressure. A transmitral flow Doppler analysis was performed on all subjects. A quantitative analysis of the echocardiographic digitized imaging was performed with the help of a calibrated digitization system to calculate the septum and the posterior wall textural parameters. The myocardial mean gray level (MGL) was calculated to derive the cyclic variation index (CVI): \( \frac{(\text{MGL}_{\text{end-diastolic}} - \text{MGL}_{\text{end-systolic}})}{\text{MGL}_{\text{end-diastolic}}} \times 100 \). When compared with controls, the hypertensive patients showed a significantly lower CVI for both septum (–11.1±26.8% versus 34.7±16.3%; \( P < 0.001 \)) and posterior wall (–11.2±27.6% versus 38.2±15.4%; \( P < 0.001 \)). Individual analyses for the ratio of peak transmitral flow velocity in early diastole to the peak transmitral flow velocity in late diastole showed that only 24% of the patients (13/53) were discriminated from normal subjects by this parameter. Individual analyses for CVI, however, at both septum and posterior wall levels, showed that 74% of the patients (39/53) were discriminated from normal subjects by this second parameter. In comparison with Doppler-derived indices of diastolic filling, the videodensitometric parameters showed a significantly higher ability to discriminate between hypertensive subjects and normal controls. (Hypertension. 1999;33:66-73.)

Key Words: hypertension, arterial hypertrophy, left ventricular ventricular function, left echocardiography ultrasonography

Abnormalities of left ventricular diastolic function have been found in patients affected by arterial hypertension and left ventricular hypertrophy (LVH).\(^1\)\textendasymtext En Some experimental and autopsy data support the hypothesis that arterial hypertension per se could contribute to both an increase in intramyocardial fibrosis and an alteration in the microcirculatory system. A quantitative analysis of the 2-dimensional spatial pattern or the “texture” of the echocardiographic images represents a useful approach that allows ultrasound myocardial tissue characterization (quantitative texture analysis). This technique was effective in the identification of acutely ischemic and contused myocardium in animal models.\(^{1,2}\)\textendasciitext It was also applied to humans for the identification of amyloid and hypertrophic cardiomyopathies,\(^3\) myocarditis,\(^4\) myocardial ischemia,\(^5\) viable myocardium,\(^6\) and severe LVH in hypertension.\(^7\) The aims of our study were (1) the evaluation of myocardial texture through analysis of the first-order gray level in a group of age-matched hypertensive patients compared with normotensive subjects and (2) the evaluation of the power to discriminate between hypertensive and normal hearts of both pulsed Doppler analysis of transmitral flow (as an expression of diastolic left ventricular filling) and videodensitometric parameters (as an expression of intrinsic modifications of myocardial texture).

Methods

Study Population
Exclusion criteria were as follows: the presence of malignant hypertension, heart failure, cardiomyopathy, or valvulopathy; the coexistence of diabetes (fasting blood glucose >6.6 mmol/L [120 mg/dL]) or obesity (body mass index >30 kg/m\(^2\)); the presence of

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coronary artery disease (angina pectoris and/or previous myocardial infarction, evaluated on the basis of exercise ECG); a history of renal and connective tissue disease; or serum creatinine <106 μmol/L (1.2 mg/dL). Furthermore, after repeated casual blood pressure measurements and ambulatory 24-hour blood pressure monitoring, which allowed correct definition of hypertensive status, the patients were selected on the basis of left ventricular mass (LVM) index (LVM/body surface) (LVMbs), obtained by echocardiography. Patients with a full spectrum of LVMbs from a normal value to a value corresponding to severe LVH, were chosen. The patients were further distributed into 3 balanced subgroups: (1) patients with LVM values within the normal ranges of our laboratories, (2) patients with LVMbs values between 125 and 174 g/m², and (3) patients with LVM values >175 g/m². The conventional echocardiographic and tissue characterization determinations were obtained at the same time. In accordance with these criteria, 53 hypertensive subjects, all men with absent or a mild/moderate to severe degree of LVMbs, were recruited (hypertensive group). The subjects selected had to complete a full clinical, biochemical, and instrumental workup for secondary hypertension, including an angiographic procedure if needed. No patients were undergoing any antihypertensive therapy at the time of the study; an adequate pharmacological washout period was observed by all patients. This group of patients was compared with a group of 32 carefully age- and sex-matched normotensive subjects (normotensive group) on the basis of 24-hour ambulatory blood pressure monitoring. According to the institutional guidelines, all subjects were aware of the experimental nature of the study and had provided informed consent. The study was approved by the local ethical committee.

Conventional 2-Dimensional Doppler Echocardiography

M-mode and 2-dimensional echocardiograms by Doppler analysis were performed in all subjects by means of a commercially available machine (Hewlett-Packard Sonos 1000, with 2.5- or 3.5-MHz transducer). The following parameters were obtained from the M-mode echocardiographic tracings with 2-dimensional imaging: end-diastolic diameter (in millimeters); percent fractional shortening of the left ventricle; septal and posterior wall thickness at end diastole (in millimeters); LVMbs (in grams per square meter) according to the Penn convention and also normalized for height to the 2.7th power.23,24 The relative wall thickness was also measured at end diastole, as the ratio of $2(LVMI/end ventricular posterior wall thickness/left ventricular internal dimension).23 According to the model of Shimizu et al.,26,27 we calculated the midwall fractional shortening of the left ventricle to obtain a more appropriate evaluation of left ventricular systolic function. A pulsed Doppler transmural flow velocity profile was obtained from the apical 4-chamber view, and the sample volume was positioned just below the mitral valve leaflets. The following parameters were evaluated: peak E (peak transmural flow velocity in early diastole); peak A (peak transmitral flow velocity in late diastole); E/A ratio; mitral acceleration time (from baseline to peak E wave) corrected for heart rate; mitral deceleration time (from peak E wave to baseline) corrected for heart rate; isovolumic relaxation time corrected for heart rate (as the interval from the end of the left ventricular outflow velocity to the onset of mitral inflow by placing the sample volume at an intermediate point between the mitral and the aortic valves, ). Heart rate correction was performed with the application of Bazet’s formula (diastolic time/square root of R-R interval). We also measured the following: E wave velocity-time integrals (in centimeters); A wave velocity-time integrals (in centimeters); E/A velocity-time integrals; and atrial filling fraction (the percentage of atrial contribution to total diastolic filling). All measurements were derived from the average of ≥5 consecutive cardiac cycles. To assess the reproducibility of these measures, all recordings were analyzed on 2 separate occasions for intraobserver variability, as well as by a blinded investigator for interobserver variability. Intraobserver and interobserver global coefficients of variation averaged 7.5% and 10.2%, respectively; in these studies as well as in our laboratory, the reproducibility of measurements of the posterior wall was less than that of measurements of the septum (coefficients of variation averaged 8.2% and 11.3%, respectively).

Image Digitization

The gain settings and compensation profiles were adjusted for all study subjects to obtain apparently uniform myocardial brightness throughout the echocardiogram to achieve a precise and reproducible sampling of textural parameters. The gray scale transfer function was adjusted to be linear for the entire video signal range (no reject, enhancement, or dynamic range was used) with 25- to 30-dB amplification at a depth of 18 cm. The optimal echocardiographic images were transferred directly from the echocardiograph to a calibrated video digitization system (Tomtec Imaging Systems, Inc) to convert them into 256×256 pixels of 256 gray levels each (0=black, 255=white) with 8 bits of intensity range. Particular care was taken to ensure that the angle of incidence of the sonic beam was at ~90° to the area of interventricular septum or to the left ventricular posterior wall when the parasternal left ventricular long axis was scanned. The regions of interest (chosen by consensus of 2 observers, who were strictly blinded regarding the results of conventional echocardiography), which were always the same size (32×42 pixels), were placed in the same location in the septum (midseptum) and in the posterior wall (mid–posterior wall) at both end-systolic and end-diastolic frames; we took into account that there is a displacement of the heart during the cardiac cycle, which is evident in the sequence of frames that appeared on the computer screen. Only the myocardium was included; the endocardial and epicardial specular echoes were excluded to avoid areas of echo dropout and obvious artifacts. The mean gray level of each cavity region (background signal) was subtracted from the absolute mean gray level obtained for each region of interest (mean gray level, background corrected [MGL]). A histogram of the echocardiographic gray level distribution was generated for each region of interest by placing the gray level distribution on the abscissa and the frequency of the occurrence on the ordinate. A quantitative analysis of the shape of each distribution was also performed with the use of skewness and kurtosis. The cyclic variation index (CVI) of the gray level amplitude was calculated according to the following formula: (MGL of end-diastolic−MGL of end-systolic)/MGL of end-diastolic×100) (Figure 1).28 To assess the variability of these measures, all recordings were analyzed...
on 2 separate occasions for intraobserver variability, as well as by a
blinded investigator for interobserver variability. Intraobserver and
interobserver coefficients of variation averaged 8.5% and 10.4%,
respectively. Measurements were derived from the average of ≥5
consecutive cardiac cycles.

**Ambulatory Blood Pressure Measurements**
Clinical blood pressure was measured in each subject at the time of
the echocardiographic examination, 3 times at 5-minute intervals,
with the use of Korotkoff sounds phase I and V to identify systolic
and diastolic values, respectively. Ambulatory blood pressure was
recorded from the nondominant arm with an oscillometric device
(SpaceLabs 90202; SpaceLab Inc).29 The device was set to provide
automatic measurements every 15 minutes from 6 AM to midnight
and every 30 minutes from midnight to 6 AM. Twenty-four-hour
blood pressure values were then downloaded and processed on a PC
with specialized software to obtain the average daytime systolic and
diastolic blood pressure values; the daytime interval was arbitrarily
defined as that between 8 AM and 10 PM. The upper limits for normal
noninvasive ambulatory measurements of average daytime blood
pressure were 136 mm Hg for systolic and 87 mm Hg for diastolic
blood pressure, with the careful exclusion of patients with white-coat
hypertension.31

**Statistical Analysis**
The structure of the present study is reflected in the selection of the
population according to the criteria of a case-control study. Contin-
uous variables were expressed as mean±SD. Intergroup differ-
ences were tested for significance by unpaired Student’s t test, and
the subgroup analysis was tested by 1-way ANOVA followed by
Scheffé’s test. Quantitative histogram analyses were tested by the
Friedman rank test. Upper and lower 95% confidence limits for each
variable were calculated from the 2 tails of the Student’s t test
distribution by the following formulas: mean±(2.042×SD) and
mean±(2.042×SD), respectively. McNemar’s test was also applied
to determine the statistical significance of the comparison of the 2
methods (pulsed Doppler and videodensitometry). Correlation coef-
ficients were calculated according to standard methods. A P value
<0.05 was considered statistically significant.

**Results**
Age (59.9±9.5 versus 61.9±9.1 years) and body mass index
(24.5±2.8 versus 22.8±3.5 kg/m²) overlapped closely be-
tween hypertensives and normotensives. The mean daytime
ambulatory blood pressure was 147±7/93±4 versus 125±6/
78±5 mm Hg (P<0.0001); casual blood pressure averaged
156±18/94±8 versus 136±14/80±7 mm Hg (P<0.0001)
(Table 1). The septum and the posterior wall thickness were
greater in hypertensives, while the end-diastolic diameters
were comparable. LVMs was significantly higher in the
hypertensive group (Table 2). The left ventricular end-diast-
olic diameter and the relative fractional shortening overlapped
in the 2 groups (Table 2); in particular, fractional
shortening distribution was within the normal range of our
control group. Midwall fractional shortening was similar in
both groups. E/A ratio was significantly higher in normoten-
sive subjects (Table 2). In addition, the A velocity-time
integral was significantly higher in hypertensives than in
controls; of consequence, E/A velocity-time integral ratio
was significantly lower in hypertensives than in controls.
The other diastolic functional parameters, such as mitral acceler-
atation time (corrected for heart rate), mitral deceleration rate
(corrected for heart rate), and isovolumic relaxation time
(corrected for heart rate), and the atrial filling ratio also
overlapped.

### Table 1. Demographic and Clinical Parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Hypertensive</th>
<th>Normotensive</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>59.9±9.5</td>
<td>61.9±9.1</td>
<td>NS</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.72±0.07</td>
<td>1.72±0.06</td>
<td>NS</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>74.2±4.2</td>
<td>70.1±5.5</td>
<td>&lt;0.04</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.5±2.8</td>
<td>22.8±3.5</td>
<td>NS</td>
</tr>
<tr>
<td>Body surface, m²</td>
<td>1.93±0.15</td>
<td>1.88±0.18</td>
<td>NS</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>156.2±18.3</td>
<td>136.3±14.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>94.8±7.7</td>
<td>80.0±6.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MASBP, mm Hg</td>
<td>115.2±10.6</td>
<td>98.6±7.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MADBP, mm Hg</td>
<td>93.3±3.6</td>
<td>78.4±4.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>76.4±13.1</td>
<td>79.7±17.7</td>
<td>NS</td>
</tr>
</tbody>
</table>

**BMI** indicates body mass index; **SBP**, systolic blood pressure; **DBP**, diastolic blood pressure; **MASBP**, mean blood pressure; **MADBP**, mean daytime ambulatory systolic blood pressure; and **MADBP**, mean daytime ambulatory diastolic blood pressure.

**Subgroup Analysis**
Preliminarily, even with a relatively low number of cases,
hypertensive patients were studied in 2 different ways: (1) in
relationship to their LVMs values and (2) according to the
method of Ganau et al.,25 by taking into account the relative
wall thickness. To perform the first analysis (Table 3), the
hypertensive patients were divided into 3 subgroups follow-
ing prognostic criteria according to Devereux et al,:22 18
patients without LVH (LVMs within normal range: <124
g/m²); 23 with mild to moderate LVH (LVMs from 125 to
174 g/m²); and 12 patients with severe LVH (LVMs >175
g/m²) (Table 3). It is important to note that in the subgroup
without LVH, the CVI of both the septum and the posterior
wall was significantly lower in comparison with controls. In
contrast, the E/A ratio did not differentiate hypertensives
from controls. In the presence of a moderate degree of LVH,
the CVI for both the septum and the posterior wall was
significantly lower than that for hypertensives without LVH
and controls. A further increase in LVMs resulted in a small
and nonsignificant decrease in CVI values in the group of
hypertensives with severe LVH (Table 3). In the subgroup
with severe LVH, the E/A ratio showed moderate discrimi-
inating power in relation to normal patients.

On the basis of relative wall thickness and LVM, hyper-
tensive patients were divided into 4 groups (Table 4): hyper-
tensive patients with normal relative wall thickness and
LVM (n=9; 17%); patients with concentric remodeling
(n=9; 17%); patients with concentric hypertrophy (n=15;
28%); and patients with eccentric hypertrophy (n=20; 38%).
Midwall fractional shortening overlapped in all subgroups.
The ANOVA regarding CVI showed significantly lower CVI
of the posterior wall in the concentric hypertrophy group in
comparison with others (−13.4±12%; P<0.01); in addition,
the E/A ratio was lower in the concentric hypertrophy group
(0.72±0.2; P<0.07), but its significance was lower than that of
CVI (Table 4).

When we consider the sensitivity of the 2 tests in discrimi-
inating hypertensive patients from normal subjects, individual
analyses for E/A ratio showed that only 24% of patients (13/53) were discriminated from normal subjects, while individual analyses for CVI at both septum and posterior wall levels showed that 74% of patients (39/53; P < 0.01) were discriminated from normal subjects (Figure 2).

Ultrasonic Textural Data
The echo density of the septum and the posterior wall did not differ between the 2 groups at end diastole, but at end systole it was greater in the hypertensive than in the normotensive group (Table 5). The CVI, a parameter reflecting the variation in echo density from diastole to systole, was smaller in the hypertensive group than in the control group at both septum (P < 0.001) and posterior wall levels (P < 0.001) (Figure 1). Kurtosis and skewness results overlapped in the 2 groups for both septum and posterior wall.

Relationship Between Quantitative Texture Analysis Data, Echocardiographic Parameters, and Blood Pressure
CVI was unrelated to left ventricular fractional shortening and the diastolic functional parameters diastolic septum (r = −0.19, P = NS) and posterior wall thickness (r = −0.15, P = NS). A significant relationship was found between the E/A ratio and LVMbs (r = −0.52, P < 0.002). The mean daytime systolic ambulatory blood pressure values were closely linked to both CVI (midseptum: r = −0.54, P < 0.003; mid–posterior wall: r = −0.53, P < 0.005) and LVMbs (r = 0.52; P < 0.002). CVI at both septum and posterior wall showed an inverse low but significant correlation with LVMbs (r = −0.36, P < 0.05; r = −0.38, P < 0.04, respectively).

TABLE 2. Conventional Echo-Doppler Parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Hypertensive</th>
<th>Normotensive</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>End-diastolic diameter, mm</td>
<td>49.3</td>
<td>4.1</td>
<td>48.7</td>
</tr>
<tr>
<td>Fractional shortening, %</td>
<td>36.1</td>
<td>5.9</td>
<td>32.2</td>
</tr>
<tr>
<td>Diastolic interventricular septum thickness, mm</td>
<td>1.25</td>
<td>0.2</td>
<td>1.0</td>
</tr>
<tr>
<td>Diastolic posterior wall thickness, mm</td>
<td>1.15</td>
<td>0.2</td>
<td>1.0</td>
</tr>
<tr>
<td>Relative wall thickness</td>
<td>0.41</td>
<td>0.04</td>
<td>0.47</td>
</tr>
<tr>
<td>Midwall fractional shortening</td>
<td>16.6</td>
<td>5.2</td>
<td>18.7</td>
</tr>
<tr>
<td>LVMbs, g/m²</td>
<td>23.1</td>
<td>0.3</td>
<td>9.75</td>
</tr>
<tr>
<td>Peak E, m/s</td>
<td>0.65</td>
<td>0.15</td>
<td>0.75</td>
</tr>
<tr>
<td>Peak A, m/s</td>
<td>0.83</td>
<td>0.19</td>
<td>0.63</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>0.78</td>
<td>0.2</td>
<td>1.26</td>
</tr>
<tr>
<td>Mitral acceleration time</td>
<td>3.1</td>
<td>0.6</td>
<td>2.8</td>
</tr>
<tr>
<td>Mitral deceleration time</td>
<td>6.8</td>
<td>1.5</td>
<td>6.7</td>
</tr>
<tr>
<td>Isovolumic relaxation time</td>
<td>3.1</td>
<td>0.7</td>
<td>3.2</td>
</tr>
<tr>
<td>E Velocity-time integral</td>
<td>10.5</td>
<td>2.3</td>
<td>10.6</td>
</tr>
<tr>
<td>A Velocity-time integral</td>
<td>8.1</td>
<td>1.5</td>
<td>6.9</td>
</tr>
<tr>
<td>E/A Velocity-time integral</td>
<td>1.31</td>
<td>0.3</td>
<td>1.61</td>
</tr>
<tr>
<td>Atrial filling ratio</td>
<td>42.2</td>
<td>8.1</td>
<td>38.3</td>
</tr>
</tbody>
</table>

LVMbs indicates left ventricular mass index normalized for height.

TABLE 3. Subgroup Analysis of Hypertensive Patients

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Hypertensive Without LVH (Group 1)</th>
<th>Hypertensive With Mild/Moderate LVH (Group 2)</th>
<th>Hypertensive With LVM &gt;175 (Group 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>MASBP, mm Hg</td>
<td>125.0</td>
<td>5.6</td>
<td>141</td>
<td>4</td>
</tr>
<tr>
<td>MADBP, mm Hg</td>
<td>78.4</td>
<td>4.8</td>
<td>91</td>
<td>2</td>
</tr>
<tr>
<td>LVMbs, g/m²</td>
<td>97.5</td>
<td>25.6</td>
<td>102</td>
<td>14</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>0.26</td>
<td>0.4</td>
<td>0.89</td>
<td>0.22</td>
</tr>
<tr>
<td>CVIseptum, %</td>
<td>34.7</td>
<td>16.3</td>
<td>−0.18</td>
<td>16</td>
</tr>
<tr>
<td>CVIpw, %</td>
<td>38.2</td>
<td>15.4</td>
<td>−0.75</td>
<td>16</td>
</tr>
</tbody>
</table>

MASBP, mean daytime ambulatory systolic blood pressure; MADBP, mean daytime ambulatory diastolic blood pressure; and pw, posterior wall.

*Significant comparison between groups 1 and 2.
†Significant comparison between groups 1 and 3.
‡Significant comparison between groups 2 and 3.
Discussion
The main findings of this study were as follows: (1) an abnormality of CVI at both septum and posterior wall levels was present in hypertensive patients even when LVH was absent and also in hypertensives with mild/moderate to severe LVH (the highest alteration of this parameter was present in the concentric hypertrophy model); these patients did not present abnormalities of left ventricular systolic function; (2) CVI was more accurate than E/A ratio in the discrimination of hypertensive heart from normal heart.

Biological and Structural Determinants of Myocardial Acoustic Properties
Different structural components of myocardium can influence its acoustic properties under physiological and pathological conditions (Rayleigh scattering). Collagen is a primary determinant of both scattering and attenuation of myocardial tissue; a linear relationship was found between integrated backscatter and hydroxyproline content in autopsied human hearts with fibrotic changes associated with remote myocardial infarction; furthermore, a significant direct correlation was found between collagen content analyzed histopathologically and regional echo amplitude. Scatterer geometry is another determinant of myocardial reflectivity; in fact, myocardial scattering intensity depends directly on myocyte cellular size. The microstructural arrangement of myocardial cells embedded in a collagen matrix may provide a sufficient local acoustic impedance mismatch to account for the scattering from normal myocardium. Ventricular muscle fiber orientation might influence myocardial acoustic properties. In fact, the insonation angle might greatly influence the magnitude of both attenuation and backscatter; the backscatter would be maximal in a direction perpendicular to the fiber orientation. On the other hand, the middle portion of the left ventricular wall comprises mainly circumferentially oriented fiber bands. Tissue water content and blood flow both influence myocardial attenuation and scattering; the increase in water content (tissue edema) and to a lesser degree the reduction in coronary blood flow (myocardial ischemia) might influence the acoustic properties of myocardium.

### Table 4. Subgroup Analysis According to the Method of Ganau et al. of Hypertensive Patients

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Hypertensive With Normal LVM (n=9) (Group 1)</th>
<th>Concentric Remodeling (n=9) (Group 2)</th>
<th>Concentric Hypertrophy (n=15) (Group 3)</th>
<th>Eccentric Hypertrophy (n=20) (Group 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean SD</td>
<td>Mean SD</td>
<td>Mean SD</td>
<td>Mean SD</td>
</tr>
<tr>
<td>MASBP, mm Hg</td>
<td>138 3</td>
<td>144* 5</td>
<td>150† 6</td>
<td>148¶ 7</td>
</tr>
<tr>
<td>MADBP, mm Hg</td>
<td>92 2</td>
<td>91 3</td>
<td>94 6</td>
<td>93 3</td>
</tr>
<tr>
<td>Midwall fractional shortening</td>
<td>17 5</td>
<td>16 4</td>
<td>15 5</td>
<td>16 4</td>
</tr>
<tr>
<td>LVM, g/m²</td>
<td>100 16</td>
<td>104 13</td>
<td>167§ 23</td>
<td>154¶§ 27</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>0.97 0.2</td>
<td>0.80* 0.2</td>
<td>0.72† 0.2</td>
<td>0.80¶ 0.2</td>
</tr>
<tr>
<td>CVI, %</td>
<td>3.2 14</td>
<td>2.6 14</td>
<td>−13.4†</td>
<td>−3.1¶ 16</td>
</tr>
<tr>
<td>CVI, %</td>
<td>9.9 18</td>
<td>8.1 10</td>
<td>−12.5†</td>
<td>6.7 15</td>
</tr>
</tbody>
</table>

MASBP indicates mean daytime ambulatory systolic blood pressure; MADBP, mean daytime ambulatory diastolic blood pressure; and pw, posterior wall.

*Significant comparison between groups 1 and 2.
†Significant comparison between groups 1 and 3.
‡Significant comparison between groups 1 and 4.
§Significant comparison between groups 2 and 3.
¶Significant comparison between groups 2 and 4.

Figure 2. Left, Individual distribution of E/A ratio for the 2 examined groups. Right, Individual distribution of CVI at septum level for the 2 examined groups. See text for statistical comparison between groups.
DYNAMIC ASPECT OF SCATTERING MUST BE CONSIDERED; ACCORDING TO WICKLINE ET AL., PEAK VALUES OCCURRED AT END DIASTOLE AND MINIMAL VALUES AT END SYSTOLE, BUT THESE CYCLIC CHANGES IN THE ECHO AMPLITUDE ARE RELATED, ALTHOUGH NOT LINEARLY, TO INTRINSIC MYOCARDIAL CONTRACTILE PERFORMANCE.

LACK OF HISTOPATHOLOGICAL DATA AND HYPOTHESES ON MYOCARDIAL TEXTURAL MODEL IN HYPERTENSION

Although the lack of histopathological data is not ethically acceptable in this type of subject, some hypotheses might explain the alterations in the acoustic properties of myocardium, and in particular the dynamic aspects of scattering, on the basis of various experimental and human autopsy studies on the myocardium in hypertension: (1) the increase of the intermyocytic collagenic network that occurs in hypertension4,8,12 could determine, in systole, an increase in scattering causing a reduction of its normal cyclic variation, despite the reduction of length of myocardial fibers during contraction, which represents one of the elements that might explain the loss of acoustic myocardial reflectivity in normal subjects; (2) the pressure-volume overload of hypertension, causing a stimulus on myocardium mediated by complex mechanical and humoral factors, could determine the change in orientation, structure, or geometry of both the muscle fibers and the collagen network, thereby influencing the acoustic properties of the myocardium9,11; and (3) variations in the myocardial blood flow, possibly related to the development of alterations of the microcirculatory system, such as a reduction in capillary density in hypertrophied hypertensive myocardium,37 could help to explain, at least in part, the scattering alterations in hypertension.

The decrease in the cyclic variation of the echo amplitude in hypertensives in the presence of normal systolic indices (left ventricular fractional shortening and midwall fractional shortening), in a concentric LVH model, may suggest that the variation in echo amplitude could be considered a distinct, “early” index of altered myocardial function and a useful parameter indicating a potential evolution toward hypertensive heart failure.

Masuyama et al.38 found reduced cyclic variations of the integrated backscatter indices in the septum of a mixed population of patients with hypertensive and valvular hypertrophy and hypertrophic cardiomyopathy compared with normal subjects. CVI is thus probably a highly sensitive parameter in the identification of abnormal echo density in hypertension and other diseases.15–19 When the hypertensive subgroups are considered, the CVI was significantly lower in patients with LVM >175 g/m² and in patients with concentric hypertrophy, indicating the patients with the worst prognosis in terms of morbidity or mortality for cardiovascular events.24,39

The analysis of transmural flow velocity has provided a means of simple evaluation of global diastolic function.40 The diastolic abnormalities precede systolic impairment and the evolution toward congestive cardiopathy. In the pressure-volume hypertensive overload in particular, an alteration of the passive end-diastolic phase (increased stiffness) was observed. The E/A ratio in this study appeared to be inversely correlated to LVMₜₙ and mean systolic ambulatory blood pressure, in accordance with previous results; the fact that the E/A ratio is significantly lower in patients with the highest LVM and in the concentric hypertrophy group, thereby selecting the patients with the worst cardiovascular prognosis, was confirmed. According to these results, it appears evident that the ability of CVI to discriminate between normal heart and hypertensive heart is higher than that of the E/A ratio. The pressure-volume overload factor per se, or with the interaction of complex humoral factors, is able to induce the parallel replication of the myocytic component and the fibroblastic excessive production of collagen, which could alter the correct ratio of myocyte to collagen. The videodensitometric signal may be affected by a change in the orientation of the collagen fibers relative to muscle fiber orientation, modifications of structure, or geometry of individual

<table>
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<th>Normotensive</th>
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<td>CVIpw, %</td>
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<td>27.6</td>
<td>38.2</td>
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</table>

pw indicates posterior wall.

**TABLE 5. Ultrasonic Textural Data (Midseptum and Mid–Posterior Wall)**
muscle and collagen fibers, such as a shift from type III to type I collagen molecules and fibroblast replacement due to myocyte apoptosis. A second possibility relates the changes in acoustic properties of the myocardium to the development of the structural remodeling of the coronary arterioles, leading to a reduced myocardial blood flow reserve.

**Strength and Limitations of the Study**

Further studies are needed to establish the origin of the abnormal echo density in human hypertension and its real clinical and prognostic value. The strength of this study was in the recruitment of subjects with closely comparable cardiac mass and age and subjects of the same sex, as well as a selection procedure that excluded important confounding factors. However, the study has limitations as well: the relatively low number of study population and the aforementioned lack of histopathological data. Moreover, Feigenbaum has recently expressed a favorable opinion about the possibility, with the increasing use of digital recordings, to “anticipate advances in the making of tissue diagnoses using echocardiography.”

**Conclusion**

Changes in echo density from diastole to systole are blunted in hypertensive patients with absent to severe LVH. In our selected group of patients, the videodensitometric analysis showed a higher discriminating power between hypertensive and normal heart compared with traditional pulsed Doppler diastolic functional parameters. Furthermore, the maximal alterations of videodensitometric findings are present both in the subgroup with higher LVMt and in the concentric hypertrophy group, which had the worst prognostic impact in terms of mortality. Thus, videodensitometric analysis could provide information in addition to that offered by conventional Doppler echocardiography, possibly contributing to the identification of patients at risk of developing the clinical complications of hypertensive cardiopathy. Further work is needed to establish the clinical, therapeutic, and prognostic implications of these findings.

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**References**


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