Normal Ultrasonic Myocardial Reflectivity in Hypertensive Patients
A Tissue Characterization Study

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Ultrasonic backscatter of myocardial walls is directly related to the morphometrically evaluated collagen content in humans. The integrated backscatter is also increased in hypertrophic cardiomyopathy, whereas it gives normal values in the physiological hypertrophy of elite athletes. We assessed the quantitatively evaluated myocardial reflectivity, in mild to moderate, clinically uncomplicated essential hypertensive patients, with echocardiographically assessed normal regional and global left ventricular function, and 22 age- and sex-matched normotensive control subjects. With an echo prototype implemented in our institute, we performed an on-line radiofrequency analysis to obtain quantitative operator-independent measurements of the integrated backscatter signal of the ventricular septum and posterior wall. The integrated values of the radiofrequency signal of myocardial walls were normalized for those of the pericardial interface and expressed as a percent (integrated backscatter index). Hypertensive patients and control subjects differed in mean blood pressure (119±11 versus 95±5 mm Hg, p<0.001) and left ventricular mass index (134±31 versus 105±21 g/m², p<0.001). However, integrated backscatter index overlapped for both the septum (28±17% versus 25±6%, p=NS) and the posterior wall (13±7% versus 13±4%, p=NS). In the hypertensive group, there was no detectable correlation between septal integrated backscatter index and either septal thickness (r=−0.26, p=NS) or mean arterial pressure (r=−0.14, p=NS). Hypertensive patients showed a normal pattern of quantitatively assessed ultrasonic backscatter, even in the presence of left ventricular hypertrophy. This suggests that, in the absence of overt cardiac dysfunction, disproportionate connective tissue growth does not necessarily accompany the compensatory hypertrophic response to arterial hypertension in humans. (Hypertension 1993;21:329–334)

KEY WORDS • hypertrophy • ultrasonics • myocardium • hypertension, essential


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Ultrasonic tissue characterization consists of the identification and characterization of the abnormalities in the physical or physiological state of biological structures based on analyzing interactions between ultrasound and tissue. This approach has proved accurate with a variety of methods in identifying several cardiovascular disease conditions, including acute myocardial ischemia, infarction, cardiomyopathies, and atherosclerotic plaque. Of all proposed methods, measurement of radiofrequency ultrasound signals (integrated backscatter) may permit an objective and reliable assessment of the acoustic properties of myocardium in humans. In myocardial hypertrophy, integrated backscatter has been useful in differentiating between primitive hypertrophic cardiomyopathy, characterized by an abnormally increased wall reflectivity, and hypertrophy of athletes, in which backscatter values fall within the normal range. This different acoustic behavior is thought to reflect different structural and architectural properties of myocardial tissue. In particular, the increased wall reflectivity of hypertrophic cardiomyopathy is probably due to the presence of abnormal myocardial fiber architecture ("disarray"), increased collagen, or both, whereas in athletes the normal reflectivity should mirror the physiological nature of the hypertrophic process, with a proportionate increase in muscle and connective tissue per unit volume of tissue. In fact, in humans a direct correlation exists between the amount of fibrotic tissue and the quantitatively assessed myocardial reflectivity, in full agreement with theoretical and experimental data suggesting that collagen concentration is a primary determinant of myocardial reflectivity. In this conceptual framework, another target of ultrasonic tissue characterization of great potential interest is hypertensive heart disease. Previous observations concerning the deposition of collagen in pressure-overload hypertrophy have varied. Some authors have found an increase in regional fibrosis, assessed either histologically or biochemically, whereas others have found an increase in total collagen but not in the concentration of collagen in hypertensive left ventricular hypertrophy. The measurement of ultrasound backscatter, which is a robust although technically demanding method for the identification of abnormalities in myocardial composition, therefore appears ideally...
suited for noninvasive assessment of myocardial fibrosis in hypertensive heart.

The purpose of this study was to evaluate the acoustic properties of myocardial tissue, assessed by means of ultrasonic integrated backscatter, in a group of mild to moderate, clinically uncomplicated essential hypertensive patients with variable degrees of left ventricular hypertrophy, as assessed by conventional two-dimensional echocardiography.

Methods

The study population comprised 46 mild to moderate, clinically uncomplicated essential hypertensive patients with echocardiographically assessed normal regional and global left ventricular function. Twenty-two patients were not taking any antihypertensive therapy at the time of the study; 26 were under treatment with antihypertensive agents: angiotensin converting enzyme inhibitors in 14, β-blockers in seven, diuretics in 13, and calcium antagonists in eight. The control group was composed of 22 age- and sex-matched normotensive subjects. Table 1 shows the demographic features of both groups.

Echocardiography

Conventional echocardiographic studies were performed with a 77020A phased array scanner (Hewlett-Packard Co., Andover, Mass.) with a 2.5- or 3.5-MHz transducer. Two-dimensional images were obtained in the parasternal long-axis and short-axis views and apical two- and four-chamber views. Left ventricular diameters and wall thicknesses were measured from the two-dimensional targeted M-mode echocardiographic tracings, according to the criteria of the American Society of Echocardiography. The quantitative analysis system was developed in our electronics laboratory and is suited for noninvasive assessment of myocardial fibrosis in hypertensive heart.

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Ultrasonic Tissue Characterization

The quantitative analysis system was developed in our institution and already had been in use in a different study population.

An SIM 3000 two-dimensional mechanical sector scanner echocardiograph (ESAOTE Biomedica, Genoa, Italy) was used for spatial orientation of the ultrasound beam; quantitative analysis of ultrasonic reflectivity was performed in the regions of interest, i.e., the ventricular septum and the posterior wall of the left ventricle. These regions were visualized in the parasternal long-axis view. The acquisition of the backscattered signal was performed at end diastole, because a systematic variation in backscatter amplitude occurs during the cardiac cycle. A 3.5-MHz frequency transducer (focal distance, 7 cm; 3- to 6-mm focal region, 6 cm) was used.

The “native” radiofrequency signal was sampled before the processing chain of the two-dimensional instrument. The radiofrequency signal underwent preamplification, bypassing the receiving circuits of the ultrasonic equipment. The analog signal was fed to an amplifier, and the gain sweep of the amplifier (2–60 dB) was accomplished in 30 steps. This allows the full use of the input dynamic range of the analog-to-digital convertor. Sampling was performed by a flash convertor with 8 bits of amplitude resolution at a rate of 40 MHz. The digitized signal, from the analog-to-digital convertor, was analyzed in real time by a hardware prototype developed in our electronics laboratory. The two-dimensional acquisition gate was visualized on the two-dimensional image so as to ensure its proper positioning.

For analysis of the myocardium, the gate width was kept at 3 μsec, which corresponds to 2.35 mm (for 64 points), given the velocity of ultrasound in biological tissues of 1.57 mm/μsec. This allowed sampling the radiofrequency signal in the subendocardial–middle layers of the myocardium, thus excluding epicardial and endocardial specular reflections. The acquisition gate was placed immediately behind the specular echo of the endocardium (left endocardium for the septum) to minimize the transmural variations in backscatter that are due to the position from which the signal is acquired within the wall. For evaluation of the pericardial echo, a 1.5-μsec gate length was used (which corresponds to 1.2 mm, for 32 points). The acquisition gate was centered on the strongest pericardial reflections, immediately behind the mitral leaflets. The representative value of reflectivity for both myocardial walls and pericardium was calculated as the mean of three measurements.

The hardware analysis involved the measurement of the integrated amplitude of the rectified radiofrequency signal corresponding to the two-dimensional area selected from the echocardiographic image. More analytically, the two-dimensional integrated backscatter index (2D-IB) was calculated over a tissue area, i.e., corresponding to an (n–m) segment in depth and an (r–l) segment in lateral displacement, as follows:

\[ 2D-IB = \frac{1}{x_r - x_l} \sum_{j=1}^{t} IB(X_j) \]

where

\[ IB(X_j) = \frac{1}{y_n - y_m} \sum_{i=1}^{m} |S(x_i,y_j)| \]

represents the processing over the depth of the interrogated tissue; \( S(x_i,y_j) \) is the sequence of the digitized backscattered echoes over the selected two-dimensional area expressed in millivolts.

The system provides a simultaneous display of conventional information together with tissue characteriza-
Echocardiographic Findings

Conventional echocardiographic findings of the two groups are displayed in Table 2. In comparison with normotensive subjects, hypertensive patients showed higher values of left ventricular septal thickness (1.33±0.31 versus 0.95±0.16 cm, \(p<0.001\)), posterior wall thickness (1.19±0.23 versus 0.97±0.13 cm, \(p<0.001\)), and left ventricular mass index (134±31 versus 105±21 g/m², \(p<0.001\)). Hypertensive patients showed a lower value of left ventricular end-diastolic diameter (4.90±0.29 versus 4.90±0.29 cm, \(p<0.05\)).

### Table 2. Conventional Echocardiographic Data of Control Subjects and Hypertensive Patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls</th>
<th>Hypertensives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septal end-diastolic thickness (cm)</td>
<td>0.95±0.16</td>
<td>1.33±0.31*</td>
</tr>
<tr>
<td>Posterior wall thickness (cm)</td>
<td>0.97±0.13</td>
<td>1.19±0.23*</td>
</tr>
<tr>
<td>LV end-diastolic diameter (cm)</td>
<td>4.90±0.29</td>
<td>4.59±0.68†</td>
</tr>
<tr>
<td>LV mass index (g/m²)</td>
<td>105±21</td>
<td>134±31*</td>
</tr>
<tr>
<td>Fractional shortening (%)</td>
<td>36±5</td>
<td>34±4</td>
</tr>
<tr>
<td>LV, left ventricular.</td>
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Ultrasonic Quantitative Data Analysis

Primary 2D-IB values are highly influenced by inter-patient differences in chest morphology, heart structure depth, and ultrasonic impedance. Therefore, to quantitatively assess the reflectivity of the interventricular septum and posterior free wall, we used the percent 2D-IB (as related to the pericardial interface).5,7,9,20,23,24

In particular, 2D-IB results for each heart structure, initially displayed in millivolts, were expressed as percent values, assuming the pericardial interface (from which the peak echo intensity was consistently recorded in each patient) to be 100%. In this manner, the individual pericardial signal strength was used to normalize myocardial signals in each patient, following this procedure: the radiofrequency primary measurement (in millivolts) of myocardial wall (septum or posterior wall) reflectivity divided by the radiofrequency primary measurement (in millivolts) of pericardial reflectivity, the result multiplied by 100, to obtain the percent integrated backscatter index.

Together with the percent 2D-IB, we also displayed the normalized 2D-IB values, expressed in decibels (that is, a relative unit measurement of sound energy, conventionally used), of primary measurements, referred in each subject to the pericardial reflection and calculated as follows: 20 log V/Vr. V and Vr are both primary 2D-IB values and expressed in millivolts. In particular, V is the amplitude value corresponding to the myocardial wall (septum or posterior wall), and Vr is the amplitude value corresponding to the reference pericardial reflection of that subject.

Statistical Analysis

Data are reported as mean±SD. Intergroup differences were tested for significance using the unpaired Student’s t test. Relations between radiofrequency and two-dimensional echocardiographic measurements were expressed in terms of linear regression analysis. A value of \(p<0.05\) was considered to be statistically significant.

Results

Demographic characteristics of hypertensive patients and control subjects are shown in Table 1. Arterial blood pressure markedly differed between the two groups. In each subject, the conventional echocardiographic and radiofrequency quantitative ultrasound measurements were obtained.

Hypertensive hypertensive patients (n=24) were indistinguishable from nonhypertrophic hypertensive patients (n=22) as to value of percent integrated backscatter of both the septum and the posterior wall (Table 4).

### Table 3. Quantitative Acoustic Data of Control Subjects and Hypertensive Patients

<table>
<thead>
<tr>
<th>Index</th>
<th>Controls</th>
<th>Hypertensives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septal 2D-IB (%)</td>
<td>25.1±6.4</td>
<td>28.3±16.6</td>
</tr>
<tr>
<td>Posterior wall 2D-IB (%)</td>
<td>13.0±4.3</td>
<td>12.9±7.2</td>
</tr>
<tr>
<td>Septal normalized 2D-IB (dB)</td>
<td>-12.5±2.2</td>
<td>-12.0±4.9</td>
</tr>
<tr>
<td>Posterior wall normalized 2D-IB (dB)</td>
<td>-18.6±2.7</td>
<td>-18.8±4.2</td>
</tr>
</tbody>
</table>

2D-IB, two-dimensional integrated backscatter.

Discussion

The population of hypertensive patients in this study showed a definite increase in cardiac mass index compared with age-matched control subjects. These findings are in agreement with those reported in current literature.19 Several studies have demonstrated that hypertrophy as an adaptive response to excessive loading conditions is an important compensatory mechanism that tends to minimize abnormalities in myocardial stress related to the inciting load.25 However, hypertrophied muscle may differ from normal muscle in many respects, including the structural composition, with an increase in collagen content that adversely affects mechanical and electrophysiological properties of the myocardium. In the present study, we used an on-line radiofrequency analysis system to obtain quantitative, operator-independent measurements of the acoustic properties of the myocardium.
myocardium in a population of mild to moderate, clinically uncomplicated hypertensive patients, with and without left ventricular hypertrophy. This technique has been shown to provide reliable quantitative measurements of myocardial acoustic properties in humans. In the present study, we found that hypertensive patients showed a normal pattern of quantitatively assessed ultrasonic backscatter, even in the presence of left ventricular hypertrophy. This suggests that, in the absence of overt cardiac dysfunction, disproportionate connective tissue growth does not necessarily accompany the compensatory hypertrophic response to arterial hypertension in humans.

The studied population consisted of clinically uncomplicated, mild to moderate essential hypertensive patients. We excluded patients with decompensated hypertensive heart disease, because it has already been shown that at the stage of overt cardiomyopathy there is a marked increase in connective tissue content per unit volume of myocardium, inducing a proportional increase in backscatter.9

Another peculiarity of this study is that most patients were under antihypertensive treatment. Myocardial structure can be affected differently by various antihypertensive treatments, which show different capabilities to induce the regression of myocardial hypertrophy; furthermore, the latter may asymmetrically affect the fibrous and muscular components of myocardial hypertrophy.26 This patient selection makes our population even more representative of that encountered in the present clinical practice.

Biological Basis of Myocardial Acoustic Reflectivity

The two main potential determinants of alterations in backscatter amplitude are myocardial fiber architecture and abnormal fibrotic tissue accumulation. The well-known diffuse myocardial fiber disarray of hypertrophic cardiomyopathy may play a role in the increased backscatter noted in this condition,4,2 as backscatter techniques are sensitive to the anisotropic properties of tissue.27,28 The normal backscatter of hypertensive hearts is therefore well in agreement with morphometric studies showing that fiber architecture is generally well maintained despite hypertrophy in the compensated and decompensated pressure-overloaded heart.29 Regarding fibrosis, ample experimental evidence exists in left ventricular pressure overload indicating that myocardial collagen growth is increased with the hypertrophic process.12-15 However, the evidence obtained in humans is substantially less convincing and is related to advanced stages of hypertrophy. In a morphometric autopsy study by Pearlman et al,29 five hearts with "compensated" arterial hypertension actually had longstanding hypertension, marked left ventricular hypertrophy (with an average mass of approximately 400 g), and, in three cases, even an enlarged heart by chest x-ray. Furthermore, experimental observations regarding collagen deposition in pressure-overload hypertrophy have varied. Some authors have found an increase in regional fibrosis, assessed either histologically or biochemically,12-16 whereas others found an increase in total myocardial collagen but not in the concentration of

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Hypertensives with LVH (n=24)</th>
<th>Hypertensives without LVH (n=22)</th>
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<tbody>
<tr>
<td>LVMI (g/m²)</td>
<td>156±29</td>
<td>112±14*</td>
</tr>
<tr>
<td>Septal 2D-IB (%)</td>
<td>27.3±13.2</td>
<td>29.4±19.9</td>
</tr>
<tr>
<td>Posterior wall 2D-IB (%)</td>
<td>12.8±7.3</td>
<td>13.1±7.2</td>
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</tbody>
</table>

LVH, left ventricular hypertrophy; LVMI, left ventricular mass index; 2D-IB, two-dimensional integrated backscatter.

*p<0.001.
collagen in hypertensive left ventricular hypertrophy.16
in particular when arterial hypertension was created by
banding the infrarenal abdominal aorta.17

Comparison With Previous Studies

Ultrasonic tissue characterization of hypertensive left
ventricular hypertrophy has been attempted with several
methods, including texture analysis, cyclic backscatter
evaluation, and radiofrequency analysis. Chandrasekaran
et al85 differentiated amyloid and hypertrophic cardiomy-
opathy with the use of computerized quantitative texture
analysis of conventional echocardiographic data. How-
ever, consistent with our results, they were unable to
distinguish patients with left ventricular hypertrophy due
to hypertension from normal control subjects. The
vodendensitometric approach has the advantage of analyzing
standard, clinical echocardiograms recorded on videod-
tape. Unfortunately, it also has significant drawbacks,
particularly the need for complex, off-line assessment of
echocardiographic amplitude data with an additional,
time-consuming computing system. Furthermore, the
many image-processing manipulations performed when
an echocardiogram is recorded (altering gain, time gain
compensation, and gray scale mapping functions) may
have dramatic and confounding effects on image appear-
ance. Therefore, ultrasound imaging systems were devel-
oped based on direct sampling of the total amount of
ultrasonic energy returning to the transducer from the
target wall. The measurement of the “integrated back-
scatter” can be expressed either as a cyclic (systolic-to-
diastolic) variation or as an amplitude value, either
absolute or, as done in this study and by other investiga-
tors,22 23 in comparison with pericardial reflection.

Masuyama et al31 showed that the cyclic backscatter
variation was reduced in the septum of patients with
pressure-overload hypertrophy, as well as in hyper-
trophic cardiomyopathies, when compared with normal
subjects. However, the cyclic backscatter variation
seems to provide different information from that of
absolute amplitude backscatter measurements. Al-
though the physiological basis of normal cardiac cycle-
dependent backscatter variation has not been com-
pletely elucidated, it may be related to cardiac
contractile performance, the elasticity of myocardial
tissue, or contraction-dependent variations in myocar-
dial scatterer geometry.32 33 A different kind of informa-
tion is provided by ultrasonic backscatter amplitude
measurement. This index, which we used in the present
study, is mostly related to the structural components of
the tissue, first of all to the collagen content. Our results
are also consistent with the preliminary data of Anger-
mann et al14 who found normal or even subnormal
values of absolute measurements of myocardial back-
scatter intensity in hypertensive patients with moderate
to severe myocardial hypertrophy. Therefore, our re-
sults are congruent with those of Masuyama et al,85 and
Chandrasekaran et al86 and consistent with the prelimi-
nary data of Angermann et al84; they outline a pattern of
backscatter response closer to the physiological hy-
pertrophy of athletes6 than to the abnormally in-
creased echodensity found in hypertrophic8 and in
dilated9 35 cardiomyopathy.

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References

1. Miller JS, Perez JE, Sobel BE: Ultrasonic characterization of
myocardium. Prog Cardiovasc Dis 1985;28:85–110
JE: Ultrasonic characterization of cardiovascular tissue, in Marcus
ML, Schelbert HR, Skorton DJ, Wolf GL (eds): Cardiac Imaging.
3. Skorton DJ: Noninvasive assessment of myocardial composition and
function in the hypertrophied heart. Circulation 1989;80:
1095–1097
(editorial) J Am Coll Cardiol 1991;17:1091–1093
A, Vecchio C: Quantitative assessment of ultrasonic myocardial
reflectivity in hypertrophic cardiomyopathy. J Am Coll Cardiol
1991;17:1085–1090
6. Lattanzi F, Di Bello V, Pizzico E, Caputo MT, Talarico L, Di Muro
C, Landini L, Santoro G, Giusti C, Distante A: Normal ultrasonic
myocardial reflectivity in athletes with increased left ventricular
mass: A tissue characterization study. Circulation 1992;85:
1828–1834
P, Santoro G, Distante A, Giusti C. Left ventricular performance and
ultrasonic myocardial quantitative reflectivity in endurance
senior athletes: An echocardiographic study. Eur Heart J (in press)
8. Hoyt RH, Collins SM, Skorton DJ, Ericksen EF, Conyers D:
Assessment of fibrosis in infarcted human hearts by analysis of
L'Abbate A: In vivo quantitative ultrasonic evaluation of myocar-
10. Mimb TW, O'Donnell M, Bawens D, Miller JR, Sobel BE: The
dependence of ultrasonic attenuation and backscatter on collagen
collagen and ultrasonic backscatter in myocardial tissue. J Acoust
Soc Am 1991;89:1580–1588
12. Weber KT, Brill CJ: Pathological hypertrophy and cardiac inter-
itis: Fibrosis and renin-angiotensin-aldosterone system. Circu-
lation 1991;83:1849–1865
13. Tamaki M, Fujihara H, Onodera T, WU DJ, Hamashima Y, Kawai
C: Quantitative analysis of myocardial fibrosis in normal, hyper-
tensive hearts, and hypertrophic cardiomyopathy. Br Heart J 1986;
55:575–581
fibrosis and pathologic hypertrophy in the rat with renovascular
hypertension. Am J Cardiol 1990;65:7G–7G
15. Capasso JM, Palackal T, Olivetti G, Anversa P: Left ventricular
failure induced by long-term hypertension in rats. Circ Res 1990;
66:1400–1412
the rat right and left ventricle in experimental hypertension. Circ
Res 1990;67:1355–1364
17. Coppaci PG, Newcomb M, Gibson K, Harris R: Collagen in the
11:554–558
regarding quantitation of myocardial fibrosis in normals, hyper-
tensive hearts, and hypertrophic cardiomyopathy. Br Heart J
1986;55:575–581
fibrosis and pathologic hypertrophy in the rat with renovascular
hypertension. Am J Cardiol 1990;65:1G–7G
20. Devereux S: Detection of left ventricular hypertrophy by
M-mode echocardiography: Anatomic validation, standardization,
and comparison to other methods. Hypertension 1987;9(suppl II):
II–19–II–26
Distante A, L'Abbate A: In vivo radio-frequency ultrasound anal-
371–375
myocardial backscatter throughout the cardiac cycle. Ultrasound
Imaging 1989;5:229–233
23. Landini L, Salvadori M, Mazzarisi A, Benassi A: On-line evalua-
tion of ultrasonic integrated backscatter. J Biomed Eng 1985;7:
301–305


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