Normal Ultrasonic Myocardial Reflectivity in Athletes With Increased Left Ventricular Mass

A Tissue Characterization Study

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Background. Ultrasonic integrated backscatter of myocardial walls is directly related to the morphometrically evaluated collagen content. The integrated backscatter is also increased in hypertrophic cardiomyopathy, probably because of fiber disarray. The purpose of this study was to investigate myocardial tissue reflectivity in subjects with physiological hypertrophy caused by intense physical training and to assess the relation between the acoustic properties of myocardial tissue and left ventricular wall thickness assessed by conventional two-dimensional echocardiography.

Methods and Results. Twenty-four young male athletes (14 professional cyclists and 10 weight lifters, all in full agonistic activity) were studied together with 10 normal age-matched controls with sedentary life. By means of a commercially available two-dimensional echocardiograph, standard measurements were obtained according to the recommendations of the American Society of Echocardiography. With a prototype implemented in our Institute, an on-line radiofrequency analysis of ultrasound signals was also performed to obtain quantitative operator-independent measurements of the integrated backscatter of the myocardial walls. The integrated values of the radiofrequency signal were normalized for the pericardial interface and expressed in percent integrated backscatter (%IB). Compared with control subjects, athletes showed greater thickness values of septum (controls, 9±1; cyclists, 14±2; weight lifters, 15±1 mm, mean±SD; p<0.01) and posterior wall (9±1, 12±2, and 12±1 mm, respectively; p<0.01) but similar values of %IB for both septum (23±4%, 21±7%, and 23±8%, p=NS) and posterior wall (10±2%, 9±2%, and 11±2%, p=NS). In athletes, no correlation was found between septal and posterior wall thickness and the corresponding regional myocardial reflectivity (r=0.23, p=NS and r=0.01, p=NS, respectively).

Furthermore, we compared the quantitative ultrasonic data between two subsets of 10 athletes and 10 patients with hypertrophic cardiomyopathy and similar degrees of septal thickness (16±1 versus 17±1 mm, respectively, p=NS). Septal and posterior wall %IB results were significantly higher in patients with hypertrophic cardiomyopathy (53±13% and 36±9%, respectively) than in athletes (21±7% and 10±3%, respectively; p<0.01 for both).

Conclusions. We conclude that 1) endurance athletes show a normal pattern of quantitatively assessed ultrasonic backscatter despite of a marked left ventricular hypertrophy and 2) athletes and patients with hypertrophic cardiomyopathy and similar degrees of myocardial wall thickness can be differentiated on the basis of quantitative analysis of backscattered signal. (Circulation 1992;85:1828–1834)

Key Words • mass, left ventricular • ultrasound • radiofrequency
myocardial tissue and left ventricular wall thickness, assessed by conventional two-dimensional echocardiography, in subjects with physiological hypertrophy caused by intense physical training. To determine the true clinical potentialities of integrated backscatter to distinguish patients with hypertrophic cardiomyopathy, which we have previously evaluated and described, versus athletes with left ventricular hypertrophy, we also compared the backscatter data in two subsets of athletes and patients with hypertrophic cardiomyopathy matched for left ventricular wall thickness.

Methods

Study Population

The present study population comprises 24 young male athletes: 14 professional cyclists and 10 weight lifters, all in full agonistic activity. A control group of 10 male age-matched subjects was also considered. All study subjects were asymptomatic and had normal physical examination and no family history of cardiac disease. The demographic features of these three groups are reported in Table 1.

In the same period, we also studied 10 male patients with hypertrophic cardiomyopathy. These patients had echocardiographic documentation of a nonluted, hypertrophied left ventricle in the absence of cardiac or systemic diseases that could produce left ventricular hypertrophy. All of them had a sedentary life-style. Patients with hypertrophic cardiomyopathy were selected so as to have similar values of septal thickness with respect to the 10 athletes with the highest values of septal thickness.

Echocardiography

Conventional echocardiographic studies were performed with a Toshiba Sonolayer SSA270A or Hewlett-Packard 77020A phased-array sector scanner 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, using standard transducer positions. Thickness of the anterior ventricular septum and posterior free wall, end-diastolic dimension of the left ventricular cavity, and left atrial size were measured from the M-mode echocardiographic tracings according to the criteria of the American Society of Echocardiography. Ejection fraction was calculated by Teicholtz rule. In our laboratory, the upper limit of the normal range for adult males is 122 g/m² for left ventricular mass index and 12 mm for both septal and posterior wall thickness.

Ultrasonic Tissue Characterization

An OTE Biomedica SIM 3000 two-dimensional mechanical sector scanner echocardiograph was used for spatial orientation of the ultrasound beam; quantitative analysis of ultrasonic reflectivity was performed in the regions of interest, i.e., the pericardium, the ventricular septum, and the posterior left ventricular free wall. These regions were visualized and analyzed in the parasternal long-axis view. The backscattered signal was acquired 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-dB focal region, 6 cm) was used. The transducer bandwidth, measured at -3 dB with respect to the 3.5-MHz central frequency, is 700 kHz.

The “native” (raw) radiofrequency signal was sampled before undergoing the processing chain of the two-dimensional instrument. The radiofrequency signal undergoes preamplification, bypassing the receiving circuits of the ultrasonic equipment. The analog signal is fed to an amplifier, and the gain sweep of the amplifier (from 2 to 60 dB) is accomplished in 30 steps. This allows full utilization of the input dynamic range of the analog-to-digital converter. Sampling is performed by a flash converter with 8 bits of amplitude resolution at a rate of 40 MHz. The digitized signal from the analog-to-digital converter is analyzed in real time by a hardware prototype developed in our electronics laboratory. The acquisition of the two-dimensional gate is visualized on the two-dimensional image to ensure its proper positioning (Figure 1).

For analysis of the myocardium, the gate width was kept at 3 usec, 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 middle layers of the myocardium, excluding epicardial and endocardial specular reflections. The acquisition gate was kept just behind the specular echo of the endocardium (left endocardium for the septum) to minimize the transmural variations in backscatter related to the position from which the signal is acquired within the wall. The representative value for the ventricular septum and the posterior free wall was calculated as the average of three measurements. 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, just behind the mitral leaflets. The representative value for the pericardial echo was calculated as the average 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 at a tissue area corresponding to an n-m segment in depth and an r-l segment in lateral displacement, as follows:

<table>
<thead>
<tr>
<th>Table 1. Demographic Features of the Study Subjects</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td>Subjects (n)</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Weight (kg)</td>
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<tr>
<td>Body surface (m²)</td>
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<tr>
<td>Blood pressure (mm Hg)</td>
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<tr>
<td>Systolic</td>
</tr>
<tr>
<td>Diastolic</td>
</tr>
</tbody>
</table>

*p<0.01 vs. control group; t*<0.01 vs. cyclists.
Ultrasonic Quantitative Data Analysis

Primary, not normalized or compensated, 2D-IB values were not considered for analysis, being highly influenced by chest morphology, heart structure depth, and ultrasonic impedance. Therefore, two different methods were implemented to obtain a quantitative assessment of the reflectivity of the ventricular septum and posterior free wall: 1) percent two-dimensional integrated backscatter, expressed as a comparison with the pericardial interface, and 2) compensated two-dimensional integrated backscatter according to off-line compensation procedure.

Percent two-dimensional integrated backscatter. Two-dimensional integrated backscatter values for each heart structure, initially displayed in millivolts, were then converted into percent values, assuming 100% for the pericardial interface (from which the maximum echo intensity was consistently recorded in the individual patients). The individual pericardial signal strength was used to normalize myocardial signals in each patient.3,5,15

Compensated two-dimensional integrated backscatter. In this study, a compensation procedure was adopted to overcome problems caused by the variable attenuation effects of the interposed tissue. The rationale for this approach has been discussed extensively by Melton and Skorton.16 This procedure was performed off-line by determining the correction coefficient for each tissue layer that constitutes the interposed tissues (each layer was assumed to behave homogeneously as to frequency-dependent losses) and then multiplying this correction term by the amplitude signal originating from the tissue target (radiofrequency gated signal). The correction term was evaluated as follows: the thickness of each tissue layer was measured from two-dimensional targeted time–motion tracings; each thickness was doubled, then multiplied by the average amplitude attenuation coefficient measured with a 3.5-MHz transducer (0.13 cm⁻¹ for chest wall, 0.13 cm⁻¹ for myocardium, and 0.032 cm⁻¹ for blood) over the operating frequency range; and finally, the exponential amplification (i.e., opposite to the attenuation law) that represents the correction factor was measured.17 As primary 2D-IB values, the compensated data are measurements of electrical tension and are expressed in millivolts.

Statistical Analysis

Data were reported as mean±SD. Intergroup differences were tested for significance by ANOVA with subgroup analysis by Newman-Keuls test or Student’s t test. Relations between radiofrequency and two-dimensional echocardiographic measurements were expressed in terms of linear regression analysis. A value of p<0.01 was considered statistically significant.

Results

Clinical and Demographic Features

By inclusion criteria, there were no differences in sex and age among the three study groups. All controls showed myocardial wall thickness and left ventricular mass index values within normal range, considering the criteria adopted in our laboratory. In contrast, most athletes showed abnormally increased values of septal (n=22, 92%) and posterior wall (n=12, 50%) thickness and left ventricular mass index (n=24, 100%). Weight lifters presented with higher values of body weight and systolic blood pressure than either controls or cyclists (Table 1).

No patients with hypertrophic cardiomyopathy had clinical or echo Doppler signs of left ventricular outflow obstruction. They all had abnormal septal thickness,
TABLE 2. Conventional Two-dimensional Echocardiography Measurements in the Study Subjects

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Cyclists</th>
<th>Weight lifters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septal end-diastolic thickness (mm)</td>
<td>9.4±1.2</td>
<td>13.5±1.7*</td>
<td>14.5±0.7*</td>
</tr>
<tr>
<td>Posterior wall end-diastolic thickness (mm)</td>
<td>9.1±0.9</td>
<td>12.7±1.3*</td>
<td>11.7±0.9*</td>
</tr>
<tr>
<td>LV end-diastolic diameter (mm)</td>
<td>51.8±2.2</td>
<td>56.7±3.9*</td>
<td>53.0±4.3</td>
</tr>
<tr>
<td>LV mass index (g/m²)</td>
<td>109.6±15.2</td>
<td>209.2±30.7*</td>
<td>176.9±25.4*</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>73±7</td>
<td>66±7</td>
<td>70±10</td>
</tr>
<tr>
<td>Left atrium diameter (mm)</td>
<td>32.1±3.5</td>
<td>40.0±5.5*</td>
<td>34.7±5.5†</td>
</tr>
</tbody>
</table>

LV, left ventricular.  
*p<0.01 vs. control group.  
†p<0.01 vs. cyclists.

whereas posterior wall thickness was abnormally high only in one patient.

Technical Feasibility and Conventional Echocardiographic Findings

Technically satisfactory conventional echocardiographic images and radiofrequency ultrasonic signals were obtained in each subject. Conventional echocardiographic measurements are displayed in Table 2. Ventricular septal and posterior wall thicknesses, as well as left ventricular mass index, were significantly higher in athletes than in normal control subjects; all these parameters show similar values in the two subgroups of athletes. Left ventricular end-diastolic diameter and left atrial diameter were significantly higher in cyclists than in either controls or weight lifters. Ejection fraction values were similar in the three study groups.

Quantitative Analysis of Ultrasound Backscatter

Percent and compensated two-dimensional integrated backscatter mean values of the ventricular segments analyzed in athletes and in the normal control subjects are reported in Table 3. Percent and compensated values of both ventricular septum and posterior left ventricular free wall were similar in athletes and in control subjects. No detectable difference in myocardial reflectivity could be found between cyclists and weight lifters. Percent and compensated backscatter values are similar in each subject and between different groups, in agreement with data recorded for other populations.

Septal backscatter measurements show higher values than posterior wall in both controls and athletes. This finding has been previously and consistently reported in normal subjects and is probably a result of the ultrasonic beam attenuation and technical characteristics of the acquisition system used.

Conventional and quantitative echocardiographic data for each athlete are displayed in Table 4.

Relation Between Conventional Echocardiographic Measurements and Radiofrequency Analysis

In athletes, no significant correlation was found between regional myocardial reflectivity (considered as percent integrated backscatter) of septal and posterior wall and the corresponding wall thickness (r=0.23, p=NS, and r=0.01, p=NS, respectively; Figure 2). Similarly, no correlations were found between septal percent backscatter value and left ventricular end-diastolic diameter (r=0.20, p=NS) and left atrial diameter (r=0.15, p=NS).

Comparison Between Patients With Hypertrophic Cardiomyopathy and Athletes With Physiological Hypertrophy

A further comparative analysis was performed between 10 male patients with hypertrophic cardiomyopathy and 10 athletes of this study (four cyclists and six weight lifters). Patients’ as well as athletes’ individual data concerning conventional and quantitative echocardiographic findings are presented in Table 4. Patients and athletes were retrospectively selected on the basis of the comparable myocardial septal wall thickness (so as to include the patients with the thinnest and the athletes with the thickest septum). Conventional and quantitative mean ultrasound data of the two groups are presented in Table 5 and Figure 3. Although no significant differences were recorded between septal and posterior wall thickness (by selection criteria), the quantitative reflectivity values of these structures were found to be significantly higher in patients with hypertrophic cardiomyopathy than in athletes.

Discussion

The population of athletes of this study showed a definite increase in cardiac mass index compared with age-matched sedentary subjects. These findings agree with those found in current literature. Several studies have demonstrated that physical training is able to induce an increase in left ventricular mass, a functional response aimed at normalization of parietal stress increased by repeated exercise.

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 in a population of subjects with physiological hypertrophy. It has been shown previously that this technique can provide reliable quantitative measurements of myocardial acoustic properties in humans.
Biological Basis of Myocardial Acoustic Reflectivity

Two main structural and histological features can increase the reflectivity of the myocardial walls: an abnormal deposition of fibrous tissue and abnormal myocardial fiber architecture. In fact, in humans a direct correlation exists between the amount of fibrotic tissue and the quantitatively assessed myocardial reflectivity,522-24 in full agreement with theoretical and experimental data suggesting that collagen concentration is a primary determinant of myocardial reflectivity.532 On the other hand, we also found an increased myocardial reflectivity in hypertrophic as well as nonhypertrophic myocardial segments in hypertrophic cardiomyopathy.8 In this case, the abnormal acoustic properties of the myocardium are an expression of the intrinsic myopathic process, probably because of the characteristic histological abnormalities of hypertrophic cardiomyopathy (such as cardiac muscle disorganization and abnormalities in intramural coronary arteries) that are also present in segments of the wall that are of normal thickness.

In the physiological hypertrophy, myocardial reflectivity showed a complete overlap with control subjects. The normal reflectivity is consistent with the lack of fibrous tissue deposition and the absence of cardiac tissue disorganization that appear to characterize this kind of hypertrophy. This finding is consistent with experimental data showing that the development of exercise-induced cardiac hypertrophy in rats is accompanied by only minimal connective tissue hyperplasia, determining a rise in the total amount of myocardial hydroxyproline of only 10%27 — a value well below the critical threshold needed for evoking a detectable increase in myocardial reflectivity.25,26 The increased myocardial cell size per se seems to be unable to provoke abnormal myocardial reflectivity. No difference could be found between isotonic exercise such as cycling, which resembles volume overload and causes both an increase in left ventricular diastolic volume and an eccentric myocardial hypertrophy, and isometric exercise such as weight lifting, which resembles pressure overload and causes a prevalent increase in wall thickness.

Clinical Implications and Comparison With Hypertrophic Cardiomyopathy

The left ventricular hypertrophy detected by conventional echocardiography is a heterogeneous entity from...
myocardial tissue characteristics. Further studies on left ventricular hypertrophy caused by pathological rather than physiological pressure or volume overload will be

TABLE 5. Demographic and Ultrasound (Conventional and Quantitative) Data in the Subgroup of Patients With Hypertrophic Cardiomyopathy and Athletes With Similar Myocardial Wall Thickness

<table>
<thead>
<tr>
<th></th>
<th>HCM pts</th>
<th>Athletes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects (n)</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Age (years)</td>
<td>44±12</td>
<td>25±6*</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Male</td>
</tr>
<tr>
<td>Septal end-diastolic thickness (mm)</td>
<td>16.9±1.0</td>
<td>15.5±1.4</td>
</tr>
<tr>
<td>Posterior wall end-diastolic thickness (mm)</td>
<td>10.2±1.1</td>
<td>12.3±1.3</td>
</tr>
<tr>
<td>LV end-diastolic diameter (mm)</td>
<td>45.2±6.8</td>
<td>53.9±5.5</td>
</tr>
<tr>
<td>Septal compensated IB (mV)</td>
<td>147.9±48.1</td>
<td>74.6±17.1*</td>
</tr>
<tr>
<td>Posterior wall compensated IB (mV)</td>
<td>114.4±22.5</td>
<td>54.4±10.7*</td>
</tr>
<tr>
<td>Septal percent IB</td>
<td>53.0±13.3</td>
<td>20.5±7.0*</td>
</tr>
<tr>
<td>Posterior wall percent IB</td>
<td>36.2±9.2</td>
<td>10.4±2.7*</td>
</tr>
</tbody>
</table>

HCM, hypertrophic cardiomyopathy; LV, left ventricular; IB, integrated backscatter.

*p<0.01.

FIGURE 2. Scatterplots showing linear regression analysis between percent integrated backscatter of septum (upper panel) and posterior wall (lower panel) and the corresponding septal and posterior wall thickness in athletes (○, cyclists; ◆, weight lifters).

The results of this study suggest that quantitative assessment of myocardial reflectivity might be helpful in achieving the occasionally difficult task of differentiating physiological hypertrophy from milder forms of hypertrophic cardiomyopathy. It should be emphasized that the technology we used to obtain quantitative measurements of myocardial ultrasonic reflectivity is relatively simple and can be added to commercially available echocardiographic instruments. Therefore, once the relation between abnormal tissue reflectivity and cardiac disease has been definitively clarified, this technique may become an attractive additional tool in the routine ultrasound examination of the heart and may complement conventional echocardiographic measurements of cardiac dimensions and function with information on
needed, however, for a complete assessment of myocardial acoustic reflectivity in different forms of myocardial hypertrophy.

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A tissue characterization study.  
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