Evaluation of Segmentary Contractility in Chagas’ Disease by Using the Integral of the Myocardial Velocity Gradient (Myocardial Strain) Obtained Through Tissue Doppler Echocardiography

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Objective

To quantify the percentage of contractility of different myocardial segments in patients with Chagas’ disease by measuring myocardial strain and to assess the differences in the radial and longitudinal ventricular contractile function in the undetermined and dilated forms of chronic chagasic cardiomyopathy as compared with those in a group of healthy individuals.

Methods

The study comprised 39 individuals [20 (51.3%) of the male sex] divided into the following 4 groups: 1) Ni: 17 (43.6%) healthy individuals; 2) Und: 7 (17.9%) patients with the undetermined form of Chagas’ disease; 3) C1: 7 (17.9%) patients with the chronic form of Chagas’ disease with ejection fraction < 50%; and 4) C2: 8 (20.5%) patients with the chronic form of Chagas’ disease with ejection fraction > 50%. After performing baseline echocardiography, Doppler tissue images were recorded to measure myocardial strain in different segments on longitudinal and transversal parasternal, and apical 2- and 4-chamber views.

Results and Conclusion

The percentage of contractility in the different myocardial segments, both the radial and longitudinal components, is greater in healthy individuals than in patients with the chronic form of Chagas’ disease, and in those with the undetermined form of the disease as compared with that of chronic chagasic patients with EF < 50%. Left ventricular radial contractility is greater than left ventricular longitudinal contractility in all groups (Ni, Und, and Chronic). The data presented allow us to propose a progressive character of myocardial impairment in patients with Chagas’ disease.

Key words

Chagas’ disease, echocardiography, tissue Doppler, myocardial strain

Chagas’ disease became known worldwide with the pioneering study of Carlos Chagas, who, in 1909, described, not only the clinical manifestations, but also the etiologic agent, the transmitting agent, and the reservoirs of that disease 1. It is considered a great public health problem, mainly in developing countries. According to the World Health Organization, 20 million infected individuals live on the American continents, of whom, more than 6 million are in Brazil 2.

The disease may be clinically divided into 2 phases: acute and chronic. After regression of the acute phase, individuals experience a variable period characterized by positive serology and the absence of clinical, electrocardiographic, and radiological manifestations, which is called the undetermined form 3.

The chronic phase occurs in 25 to 30% of infected individuals, affecting mainly male adult individuals in the third or fourth decade of life. Clinically, it may be classified as dilated, arrhythmogenic, thromboembolic, mixed, and silent, and approximately 10% of the patients evolve to severe forms of the disease 3.

Echocardiography represents, currently, one of the most important complementary methods for assessing chronic Chagas’ heart disease, because it allows functional and anatomic evaluation, as well as the evolutionary follow-up of the disease. The echocardiographic findings vary from normal examinations to severe systolic and diastolic functional impairment. Approximately 75% of the patients have segmentary contractile alterations, which predominate in the left ventricular postero-inferior wall and apical region.

Recently, the incorporation of the tissue Doppler technique to conventional echocardiography allowed the more detailed evaluation of the systolic and diastolic myocardial functions in an overall and regional form 4-11.

The major limitations of Doppler tissue imaging are its dependency on the angle of incidence of the ultrasound beam in regard to the mobility of the segment to be studied and the fact that it does not differentiate between the presence of an active contraction of a healthy segment and the passive contraction of an akinetic segment, whose mobility depends on the healthy adjacent myocardium.

The search for a method that could overcome those limitations led to the development of a new technology derived from Doppler
tissue imaging; the measurement of the intramyocardial gradient of velocity or strain rate \(12^{15}\).

In general terms, strain represents the deformation of a tissue undergoing the application of a certain force. The concept of strain was described in 1973 by Minsky and Parmley \(^6\), and it expresses the local dynamics of myocardial performance. Differently from Doppler tissue imaging, strain rate provides information about the local instantaneous measurement of the myocardial compression or expansion rate, independently of the cardiac translation movement \(^7\).

A tendency exists towards considering myocardial thickening, or its radial contractile function, the major component of ventricular systolic function. However, the excursion of the ventricular base towards the apex is known to be approximately 1.5 to 2 cm during systole, while the wall thickening does not exceed 0.5 cm\(^8\)\(^-\)\(^20\). Nevertheless, the visual analysis is still inadequate to detect those subtleties, and more accurate data about radial and longitudinal ventricular contractile function are still required.

Muscle may be considered an incompressible tissue, which means that its longitudinal deformation is inversely proportional to the alterations observed in its thickness, i.e., the more the muscle stretches, the thinner it gets; and the more it contracts, the thicker it gets. Thus, by quantifying the stretching/shortening of the myocardial fiber, its degree of relaxation/contractility can be inferred \(^21\).

The strain rate is the measurement of the myocardial deformation velocity, defined by the formula \(\frac{V2-V1}{d}\), where \(V1\) and \(V2\) are the velocities of myocardial shortening (cm/s) in 2 points separated by a distance (cm) \(^{16}\) (fig. 1). That \(d\) distance may be adjusted by the operator and should usually be approximately 9 mm. Smaller distances increase the degree of noise, while greater distances decrease the resolution of the method.

That measurement provides the intramyocardial gradient of velocities per unit of time and represents the degree of deformity of the fiber. Because the intramyocardial gradient of velocity represents the difference of velocities (cm/s) between 2 points divided by the distance (cm) between those same 2 points, its unit is s\(^-\)1 [(cm/s)/cm].

Doppler tissue imaging, used in the parasternal views, assesses the radial component of myocardial contractility; when used in the apical views, it assesses the longitudinal contractility of the muscle. Based on those observations, a new technique assessing the gradient of velocity between 2 points close to the myocardium was developed. In other words, it quantifies the stretching/shortening of the fiber, and, indirectly, its thickening, which appears to be a much more effective method for assessing myocardial contractility.

Another form of assessing the deformity of the myocardial segments is through the integral of the strain rate. That measurement, simply called myocardial strain, provides information about the deformation of the fiber in terms of percentage.

This study aimed at measuring the percentage of contractility of the several myocardial segments in patients with Chagas’ disease by measuring the myocardial strain obtained on tissue Doppler echocardiography, and also at defining whether differences exist in the radial and longitudinal myocardial contractile function in the undetermined and chronic forms of the disease when compared with those of a group of healthy individuals.

**Methods**

This prospective study comprised healthy adult individuals and patients with Chagas’ disease of both sexes, with a satisfactory echocardiographic window, who agreed to sign a written informed consent. Thirty-nine individuals were studied, 20 (51.3%) being of the male sex. They were divided as follows: 1) group NI, comprising 17 (43.6%) asymptomatic individuals with normal electrocardiograms and echocardiograms, constituting the healthy control group; 2) group Und, comprising 7 (17.9%) asymptomatic individuals with positive serology for Chagas’ disease, with normal electrocardiograms, chest X-rays, contrast studies of the esophagus, and contrast enemas, characterizing the undetermined form of Chagas’ disease; 3) group C1, comprising 7 (17.9%) patients with Chagas’ disease in its chronic form, who, in addition to electrocardiographic or radiographic alterations, or both, also had left ventricular ejection fraction < 50% on echocardiograms; and 4) group C2, comprising 8 (20.5%) patients with the chronic form of Chagas’ disease, who had, in addition to electrocardiographic or radiographic alterations, or both, left ventricular ejection fractions > 50%. For comparing the radial and longitudinal contractility, the groups of chronic chagasic patients were considered as a single group (C1 + C2). The groups did not differ in regard to age (47.2 ± 9.4 years) or body mass index (25.4 ± 3.5).

The following individuals were excluded from the study: patients with significant valvular or pulmonary diseases, coronary heart disease, individuals with a recent history of drug use or alcoholism, and pregnant women.

After performing the clinical examination and characterizing each group, the patients underwent the echocardiographic study in a device with second harmonic and Doppler color-flow tissue imaging (System V and Vivid Five, GE-Vingmed Ultrasound, Horten, Norway). The images were obtained with the patient in the left lateral decubitus position. The echocardiogram was recorded in the digital format with the file of static and dynamic images of several
echocardiographic sections. The following measurements were taken: dimensions of the aorta (Ao); left atrium (LA); left ventricular diastolic and systolic diameters (LVDD and LVSD); diastolic thickness of the ventricular septum and of the left ventricular posterior wall (DTVS and DTLVPW); and left ventricular ejection fraction (EF) according to the Pombo method. After performing a complete baseline echocardiography, Doppler tissue images were recorded for measuring the velocities and myocardial strain. A complete cardiac cycle was recorded and digitally stored in the following 4 different echocardiographic views: longitudinal and transversal parasternal, and apical 2- and 4-chamber. In the first 2, the radial component of myocardial contractility (fig. 2) was assessed in the basal and middle segments of the septal and posterior walls (in the longitudinal parasternal view) and in the middle segments of the septal and posterior wall (in the transversal parasternal view). In the apical views, the longitudinal component of myocardial contractility was assessed in the basal, middle, and apical segments of the septal, lateral, anterior, and inferior walls (fig. 3).

The moving digital images were transferred to a Macintosh computer (Apple Computer Inc., Cupertino, California, USA) coupled to the echocardiograph. The measurements of myocardial strain were obtained later by using a specific computer program (EchoPAC GE-Vingmed Ultrasound, Horten, Norway). The distance between the points where the myocardial velocities were collected for calculating strain was fixed as 9.2 mm.

The data were typed in Microsoft Excel 2000 worksheets, and the statistical calculations and analyses were performed with the SigmaStat program for Windows, version 2.0 (Jandel Corporation, 1992-1995). For comparing the values obtained in the different segments assessed in the 4 groups studied, the Kruskal-Wallis test (analog of analysis of variance) was used. When P values < 0.05 were obtained, the Dunn test was used for multiple comparisons between the 4 groups, 2-by-2. For comparing, in each group, the mean values of radial contractility and longitudinal contractility, the Mann-Whitney test was used. For all tests used, the alpha error value was fixed as 0.05 or 5%. The values presented represent the median followed by the 25th and 75th percentiles (between parentheses).

The studies were carried out at InCor of the Medical School of the USP and at the laboratory of the OMNI-CCNI Medicina Diagnóstica de São Paulo. The study was approved by the committees on ethics of the 2 institutions.

**Results**

In regard to the usual echocardiographic measurements, the 4 groups had no statistical differences in the aortic and left atrial diameters, and in the diastolic thickness of the ventricular septum and left ventricular posterior wall. In the groups with the dilated form of chronic chagasic heart disease (C1 and C2), the left ventricular (diastolic and systolic) diameters were greater and the ejection fraction was lower compared with those in the group of healthy individuals and the group of patients with the undetermined form of Chagas’ disease (NI and Und) (tab. I).

In regard to the myocardial strain measurements, when each segment was individually assessed between the groups, contractility was observed to be significantly smaller in all segments of the septal, posterior, and inferior walls, and in the middle segment of the anterior wall in the C1 group as compared with those in the NI group. The C1 group had a decreased strain in the basal, middle, and apical segments of the septal wall, in the basal and middle segments of the posterior wall, in the middle and apical segments of the inferior wall, and in the middle segment of the anterior wall as compared with those in healthy individuals. Finally, the Und group had a reduced myocardial strain only in the middle segment of the posterior wall. The other segments of the Und, C1, and C2 groups showed no statistical difference in strain measurements despite the mild tendency of the median towards being increased in the basal, middle, and apical segments of the septal and lateral walls, and in the basal segments of the inferior and anterior walls in the Und group as compared with those in the healthy individuals group.

When the radial and longitudinal ventricular contractile function was assessed, both the radial and longitudinal contractilities were observed to be greater in the NI group than in the C1 and C2 groups, and in the Und group as compared with the C1 group (tab. IIa). Individually inside each group, radial contractility was greater than longitudinal contractility in healthy individuals and chronic chagasic patients (C1+C2), with a tendency towards being greater also in the undetermined form (P=0.053) (tab. IIb).
The median of the radial strain values (measurements performed in the longitudinal and transversal parasternal views) was 33.7% (30.4%; 38.2%) in healthy individuals; 32.3% (28.7%; 33.6%) in the Und group; 21.7% (18.5%; 25.3%) in the C1 group; and 24.7% (15.2%; 27.8%) in the C2 group (tab. III).

In the assessment of the longitudinal contractile function (measurements performed in the apical 2- and 4-chamber views), the mean percentages of contractility of the segments were as follows: 25.9% (24.5%; 30.7%) in the Nl group; 28% (24.7%; 29.7%) in the Und group; 16.8% (13.2%; 19.2%) in the C1 group; and 19.1% (15.8%; 22.3%) in the C2 group (tab. IV).

**Discussion**

The left ventricular contractile function in patients with heart disease is routinely assessed by using echocardiography. However, the visual assessment of segmentary contractility is a relative limitation of the method. Although objective indices of ventricular function quantification, such as ejection fraction, end-diastolic volume, systolic volume, and shortening fraction, are routinely used, those parameters are still greatly influenced by the variations in pre- and afterload.

The color kinesis technique may also be used to quantify the contractile function on echocardiography; however, as it depends on the appropriate identification of the excursion of myocardial segments, its performance in individuals with a little satisfactory echocardiographic window may be difficult 23,24.

Recently, Yamada et al 25 showed that the peak systolic velocity measured with Doppler tissue imaging correlated with dP/ dt\textsubscript{max} in individuals undergoing cardiac catheterization. Myocardial strain has also been proposed as an index of contractility of the muscle fiber 16.

The Doppler effect was described in 1842 by the Austrian physicist Christian Johann Doppler; its use in medicine, mainly in echocardiography, began approximately 100 years later 26.

When the ultrasound beam reaches a moving structure, such as blood cells, the reflected wave suffers an alteration in its frequency, returning to the transducer with a frequency different from that of the wave originally emitted. Thus, when that beam reaches the blood cells that are moving towards the transducer, the frequency of the reflected wave increases, and, therefore, it will be greater than that of the wave emitted. On the contrary, if the blood ce cells are moving away from the transducer, the frequency of the reflected wave will be smaller than that of the wave emitted. Therefore, a variation in frequency occurs, and it may be measured by the equipment, being proportional to blood velocity.

Similarly to the use of Doppler for measuring blood flow velocity inside the heart and vessels, the method allows the identification and measurement of the velocity of the movement of other tissues, such as myocardium. Such a technique is called Doppler tissue imaging (DTI).

Several studies have reported the normal patterns of the systolic and diastolic velocities for each myocardial segment 27-29. The use of DTI allows the assessment of the overall and regional systolic and diastolic functions 24. However, it has the limitation of depending on the angle of incidence of the ultrasound beam and of not allowing the assessment of the movement of a segment separated from that of its adjacent segment.
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The strain technique can solve that problem partially. Although it is even more dependent on the angle of incidence of the beam, the fact of assessing the difference of velocities between 2 close myocardial segments reduces the influence of the cardiac rotation and translation movements and of the movement of adjacent segments (tethering) 30,31.

The measurement of the intramyocardial gradient of velocity, a technique used to calculate the myocardial strain on Doppler echocardiography, has already been approached by several authors 32,33.

In our study, we used that technique to quantify the segmentary contractility in healthy individuals and patients with Chagas' disease, in addition to comparing the radial and longitudinal components of the ventricular contractile function.

The baseline echocardiographic measurements, as expected, showed increased left ventricular diameters in the C1 and C2 groups (dilated form of chronic chagasic cardiomyopathy), and a decreased ejection fraction in the same groups when compared with those in the NI and Und groups.

On quantifying segmentary contractility by use of the strain technique, some very interesting data were observed. In the group of the dilated form of chronic chagasic cardiomyopathy with ejection fraction < 50% (C1), a decreased percentage of contractility was observed in all segments of the septal, posterior, and inferior walls, in addition to the middle segment of the anterior wall, confirming the segmentary nature of chagasic cardiomyopathy and its predilection for the left ventricular apical and posteroinferior regions. In the C2 group, in which the systolic impairment was milder (ejection fraction > 50%), decreased myocardial strain was observed in a smaller number of segments (middle of the septal wall, basal and middle of the posterior wall, middle and apical of the inferior wall, and middle of the anterior wall).

In the undetermined form, however, an interesting behavior could be the vicarious nature of healthy segments after myocardial aggression in that disease. Unfortunately, the number of patients in that group was small, and this may have been the cause of the lack of a significant statistical difference.

<p>| Table III - Myocardial strain measurements in each segment according to the groups involved for assessing radial contractility |</p>
<table>
<thead>
<tr>
<th>NI</th>
<th>Und</th>
<th>C1</th>
<th>C2</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SepBas PL</td>
<td>32,0 (28,5;33,3)</td>
<td>35,0 (30,0;41,5)</td>
<td>26,0 (20,3;26,0)</td>
<td>31,0 (19,5;39,0)</td>
</tr>
<tr>
<td>SepMed PL</td>
<td>32,0 (28,8;34,7)</td>
<td>32,0 (27,8;38,7)</td>
<td>19,0 (13,0;24,5)</td>
<td>23,0 (17,5;28,5)</td>
</tr>
<tr>
<td>PostBas PL</td>
<td>42,0 (28,8;45,3)</td>
<td>38,0 (29,0;41,5)</td>
<td>19,0 (14,5;30,5)</td>
<td>18,0 (13,0;21,0)</td>
</tr>
<tr>
<td>PostMed PL</td>
<td>32,0 (25,8;38,2)</td>
<td>15,0 (12,8;21,2)</td>
<td>15,0 (9,5;22,0)</td>
<td>14,5 (11,0;21,0)</td>
</tr>
<tr>
<td>AntMed PT</td>
<td>33,0 (28,8;37,0)</td>
<td>30,0 (24,3;37,0)</td>
<td>32,0 (24,0;37,3)</td>
<td>26,0 (17,5;33,2)</td>
</tr>
<tr>
<td>PostMed PT</td>
<td>35,0 (33,3;43,0)</td>
<td>38,0 (33,5;49,5)</td>
<td>17,0 (11,3;29,8)</td>
<td>23,0 (14,3;31,0)</td>
</tr>
<tr>
<td>Median</td>
<td>33,7 (30,4;38,2)</td>
<td>32,3 (28,7;33,6)</td>
<td>21,7 (19,1;23,6)</td>
<td>24,7 (15,2;27,8)</td>
</tr>
</tbody>
</table>

<p>| Table IV - Myocardial strain measurements in each segment according to the groups involved for assessing longitudinal contractility |</p>
<table>
<thead>
<tr>
<th>NI</th>
<th>Und</th>
<th>C1</th>
<th>C2</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SepBasPost A4</td>
<td>26,0 (23,8;30,8)</td>
<td>32,0 (30,3;38,3)</td>
<td>19,0 (16,8;28,0)</td>
<td>15,5 (10,5;25,5)</td>
</tr>
<tr>
<td>LatBas A4</td>
<td>25,0 (23,5;29,3)</td>
<td>31,0 (26,5;33,5)</td>
<td>27,0 (22,5;29,8)</td>
<td>27,0 (19,5;31,0)</td>
</tr>
<tr>
<td>SepMedPostA4</td>
<td>26,0 (24,8;36,3)</td>
<td>33,0 (30,3;43,0)</td>
<td>13,0 (9,3;18,0)</td>
<td>25,5 (18,5;29,5)</td>
</tr>
<tr>
<td>LatMed A4</td>
<td>27,0 (23,0;30,3)</td>
<td>29,0 (24,3;29,8)</td>
<td>22,0 (16,0;28,8)</td>
<td>21,0 (16,0;28,8)</td>
</tr>
<tr>
<td>SepApic A4</td>
<td>25,0 (22,0;29,5)</td>
<td>17,0 (12,7;32,5)</td>
<td>16,0 (11,0;19,0)</td>
<td>12,0 (11,0;21,0)</td>
</tr>
<tr>
<td>LatApic A4</td>
<td>22,0 (19,0;25,3)</td>
<td>25,0 (6,3;32,0)</td>
<td>17,0 (10,8;24,0)</td>
<td>15,5 (13,0;18,0)</td>
</tr>
<tr>
<td>AntBas A4</td>
<td>31,0 (27,3;34,3)</td>
<td>34,0 (28,8;35,0)</td>
<td>23,5 (19,0;39,0)</td>
<td>29,5 (21,3;35,0)</td>
</tr>
<tr>
<td>InfrBas A2</td>
<td>25,0 (20,8;32,8)</td>
<td>28,0 (22,3;34,0)</td>
<td>13,5 (12,0;16,0)</td>
<td>16,0 (12,5;24,5)</td>
</tr>
<tr>
<td>AntMed A2</td>
<td>30,0 (25,3;33,8)</td>
<td>25,0 (21,0;27,3)</td>
<td>13,0 (11,0;27,0)</td>
<td>16,5 (15,5;25,5)</td>
</tr>
<tr>
<td>InfrMed A2</td>
<td>26,0 (22,3;35,3)</td>
<td>29,0 (24,0;35,8)</td>
<td>10,0 (8,0;11,0)</td>
<td>15,5 (12,0;20,5)</td>
</tr>
<tr>
<td>AntApic A2</td>
<td>20,0 (17,0;23,0)</td>
<td>14,0 (5,0;34,0)</td>
<td>14,0 (7,0;14,0)</td>
<td>11,0 (8,5;24,0)</td>
</tr>
<tr>
<td>InfrApic A2</td>
<td>30,0 (23,8;33,0)</td>
<td>25,0 (13,8;29,5)</td>
<td>11,5 (9,0;17,0)</td>
<td>14,0 (5,5;22,0)</td>
</tr>
<tr>
<td>Median</td>
<td>25,9 (24,5;30,7)</td>
<td>28,0 (24,7;29,7)</td>
<td>16,8 (13,3;19,2)</td>
<td>19,1 (15,8;22,3)</td>
</tr>
</tbody>
</table>

SepBas - basal segment of the septal wall; SepMed - middle segment of the septal wall; PostBas - basal segment of the posterior wall; PostMed - middle segment of the posterior wall; AntMed - middle segment of the anterior wall; PL - longitudinal parasternal; PT - transversal parasternal; *C1 < Und; C1 < Nl; C2 < Nl; **Nl > C1; Nl > C2; ***Nl > Und; Nl > C1; Nl > C2; ****Nl > C1; C1 < Und. The values represent the medians of myocardial strain; the figures between parentheses are the 25th and 75th percentiles, respectively.
function, although the left ventricular longitudinal shortening was up to 2 cm and its thickening did not exceed 0.5 cm, both the radial and longitudinal strains were greater in the NI group as compared with those in the C1 and C2 groups, and in the Und group as compared with those in the C1 group. This, once again, showed the intermediate characteristic of the undetermined form. When each group was individually analyzed, the radial strain was greater than the longitudinal strain in healthy individuals, in patients with the undetermined form, and in the chronic chagasic patients (C1 + C2 groups).

Our study shows the importance of that new technique for quantifying the myocardial contractile function, which can safely identify subtleties not evidenced on visual analysis.

Recently, a study of Doppler tissue imaging revealed something similar. That study assessed 339 patients, 92 of whom had systolic heart failure, 73 had diastolic heart failure, 68 had isolated diastolic dysfunction on echocardiography, and 106 healthy individuals for control. The authors reported that the systolic and diastolic velocities of the myocardial segments measured with Doppler tissue imaging were significantly decreased in the 3 groups when compared with those in the control group. Moreover, a 4.4-cm/s velocity predicted systolic dysfunction in 92% of the patients with systolic heart failure, in 52% of those with diastolic heart failure, and in 14% of those with diastolic dysfunction. In other words, tissue Doppler enabled the detection of alterations in the systolic function of patients previously labeled as having diastolic heart failure (therefore with normal ejection fraction), and even in those with isolated diastolic dysfunction on echocardiography. The new question would be: does pure diastolic heart failure really exist? Or, are the diagnostic methods used so far not sufficiently sensitive to detect more delicate alterations in myocardial function? Returning to our study, quantification of the radial and longitudinal contractile function by use of the strain technique enabled the detection of subclinical alterations in myocardial contractility, which were not perceptible on visual analysis (fig. 4). This may have a great prognostic significance.

References

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