Echocardiographic parameters associated with pulmonary congestion in Chagas cardiomyopathy

Parâmetros ecocardiográficos associados com a congestão pulmonar na miocardiopatia chagásica

Marsella Marques Barral¹, Maria Carmo Pereira Nunes¹,², Marcia Melo Barbosa², Cid Sérgio Ferreira³, Wilson Campos Tavares Júnior³ and Manoel Otávio da Costa Rocha¹,³

ABSTRACT

Introduction: Discrepancy between the intensity of pulmonary congestion and the grade of cardiomegaly seems to be a common finding of Chagas cardiomyopathy, in spite of significant systolic dysfunction of the left ventricle. Its mechanism has not been established. The aim of this study was to investigate pulmonary congestion and to analyze if it correlated with Doppler echocardiographic parameters in patients with Chagas dilated cardiomyopathy. Methods: Fifty-five patients with positive serology tests for Trypanosoma cruzi and Chagas dilated cardiomyopathy were studied. Chest x-rays, Doppler echocardiogram and plasmatic brain natriuretic peptide levels were obtained in all patients. The degree of pulmonary venous vessels changes on chest x-ray was graded using a pulmonary congestion score, and then compared to Doppler echocardiographic parameters. Results: Mean age was 48.5 ± 11.2 years and 29% were women. The majority (95%) of patients were in NYHA functional class I and II. Mild pulmonary congestion by chest x-ray was found in 80% of the patients. In a multivariate analysis, left ventricular ejection fraction, right ventricular TTE index and the color M-mode velocity correlated with the degree of pulmonary congestion. Conclusions: Pulmonary venous changes on chest x-rays are frequent, but usually mild in patients with Chagas dilated cardiomyopathy. The degree of pulmonary congestion correlates with Doppler echocardiographic left and right ventricular dysfunction and with color M-mode velocity.

Key-words: Chagas disease. Echocardiography. Pulmonary congestion.

RESUMO

Introdução: Na miocardiopatia chagásica, é considerado haver uma menor intensidade de congestão pulmonar, mesmo na vigência de disfunção ventricular esquerda importante, não havendo ainda explicação definitiva para este fenômeno. O objetivo deste estudo foi de investigar a presença de congestão pulmonar na miocardiopatia chagásica e analisar se a intensidade da congestão esteve associada com parâmetros morfofuncionais ecocardiográficos de disfunção cardíaca. Métodos: Cincuenta e cinco pacientes com sorologia positiva para Trypanosoma cruzi e portadores de miocardiopatia chagásica foram estudados. Todos os pacientes foram submetidos ao estudo radiológico do tórax, ecocardiograma e dosagem plasmática do peptídeo natriurético. Resultados: A idade média foi de 48.5 ± 1.2 anos e 29% eram mulheres. A maioria (95%) dos pacientes encontrava-se na classe funcional I e II. Mild pulmonary congestion by chest x-ray was found in 80% of the patients. In a multivariate analysis, left ventricular ejection fraction, right ventricular TTE index and the color M-mode velocity correlated with the degree of pulmonary congestion. Conclusões: Pulmonary venous changes on chest x-rays are frequent, but usually mild in patients with Chagas dilated cardiomyopathy. The degree of pulmonary congestion correlates with Doppler echocardiographic left and right ventricular dysfunction and with color M-mode velocity.


INTRODUCTION

Chagas disease is an important cause of death in several countries in Latin America, with great socioeconomic impact. The heart is the most frequently and severely involved organ in Chagas disease, and its impairment may result in death due to arrhythmia, heart failure or thromboembolic phenomena.

Chest x-ray is an important and inexpensive tool in the evaluation of patients with Chagas cardiomyopathy. An enlarged heart by this method indicates a poor prognosis. However, pulmonary venous circulation by chest x-ray usually shows mild signs of pulmonary congestion, in spite of significant systolic dysfunction. In patients with Chagas cardiomyopathy, it is common to find a discrepancy between the intensity of pulmonary congestion and the grade of cardiomegaly, in spite of significant left ventricular systolic dysfunction. The mechanism underlying the pulmonary congestion has not been established.

Doppler echocardiography provides a variety of anatomic and functional information in Chagas dilated cardiomyopathy and represents one of the most important methods in the evaluation of these patients. Dilatation of the heart, with systolic and diastolic dysfunction by Doppler echocardiography are major findings in Chagas cardiomyopathy.

Therefore, the aim of this study was to investigate the degree of pulmonary congestion by chest x-ray and to evaluate its correlation with left ventricular function by Doppler echocardiography in patients with Chagas dilated cardiomyopathy.

METHODS

Fifty-five consecutive patients with Chagas dilated cardiomyopathy were enrolled. All patients came from a tertiary referring center for Chagas disease at the Federal University of Minas Gerais, in Belo Horizonte, Brazil.
Following a pilot study with 10 patients, 52 patients were established as an adequate sample to conduct the present study.

Patients were included in the study if they had at least two positive serological tests for Chagas disease (indirect immunofluorescence, indirect hemagglutination and/or ELISA) and cardiomyopathy. Chagas dilated cardiomyopathy is characterized by the echocardiographic finding of a dilated left ventricle with impaired ventricular systolic function. Patients were selected if they had a left ventricular diastolic diameter/body surface area (BSA) ≥31mm and left ventricular (LV) ejection fraction <55%[12]. Patients were receiving optimized treatment for heart failure and inclusion was independent of drug regimen. Patients who had associated heart diseases or systemic arterial hypertension were excluded.

All patients underwent clinical examination and NYHA functional class was established. Medical therapy was individually adjusted according to a standardized treatment regimen. Chest x-rays, B-type natriuretic peptide (BNP) plasmatic levels, and Doppler echocardiograms were obtained on the same occasion in all patients. Chest x-ray was obtained in the postero-anterior and lateral positions. All films were acquired using the conventional technique of the Radiology Department of the University Teaching Hospital[13]. All radiological parameters were graded and the intensity of pulmonary venous vessels changes on chest x-ray was established (Table 1) using a previously described pulmonary congestion score (PCS)[14,15]. Two independent observers simultaneously evaluated the chest X-rays and any discordance were solved by consensus. The inter observer reproducibility was analyzed.

### Echocardiography

Images were acquired using a Sonos 5,500 (Hewlett-Packard Corporation, Palo Alto, CA) with 2.5-MHz to 3.5-MHz transducers. All recordings were performed by one investigator, who was blinded to the clinical evaluation of the patients. The echocardiographic techniques and calculations of different cardiac dimension and volumes were performed according to the recommendations of the American Society of Echocardiography. LV ejection fraction was calculated according to the modified Simpson’s rule[12].

Quantitative evaluation of global right ventricular (RV) function was performed by the Doppler-derived index of myocardial performance (Tei index), as previously described[16]. RV morphology and function were evaluated qualitatively on multiple echocardiographic views[17].

The presence and degree of mitral and tricuspid regurgitation were evaluated by pulsed and continuous wave Doppler guided by color flow mapping[18]. Maximal velocity of the tricuspid regurgitation flow was obtained and systolic pulmonary pressure calculated[19].

Diastolic function was assessed by pulsed-wave Doppler examination of mitral, pulmonary venous inflow and Doppler tissue imaging (systolic, E’ and A’ waves)[20,21]. The ratio between peak early diastolic transmitral flow velocity (E) and E’ was calculated. Color Doppler M-mode was also used to assess ventricular diastolic function[22]. According to these Doppler parameters, four patterns of diastolic function were established: normal, and grades I (abnormal relaxation pattern), II (pseudonormal pattern) and III (restriction to filling) of diastolic dysfunction.

### TABLE 1 - Pulmonary venous vessels of patients with Chagas dilated cardiomyopathy, seen using chest x-ray.

<table>
<thead>
<tr>
<th>Pulmonary venous vessels distribution</th>
<th>Physiopathology</th>
<th>Estimated pulmonary venous pressure</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>None</td>
<td>8-12mmHg</td>
<td>1</td>
</tr>
<tr>
<td>Equalization</td>
<td>Pulmonary venous hypertension</td>
<td>13-15mmHg</td>
<td>Mild</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inversion</td>
<td>Pulmonary venous hypertension</td>
<td>16-18mmHg</td>
<td>Mild</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perihilar haze</td>
<td>Interstitial edema</td>
<td>&gt;18mmHg</td>
<td>Mild</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subpleural thickening</td>
<td>Interstitial edema</td>
<td>&gt;18mmHg</td>
<td>Mild</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peribronchial cuffing</td>
<td>Interstitial edema</td>
<td>&gt;18mmHg</td>
<td>Mild</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>Interstitial edema</td>
<td>&gt;18mmHg</td>
<td>Mild</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kerley lines</td>
<td>Interstitial edema</td>
<td>&gt;18mmHg</td>
<td>Mild</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consolidation</td>
<td>Alveolar edema</td>
<td>&gt;25mmHg</td>
<td>11</td>
</tr>
</tbody>
</table>

*Value added to pulmonary venous vessels distribution grading on the corresponding chest x-ray film.
BNP levels

Venous blood samples were obtained by direct venous puncture on the same day of the echocardiogram. Serum NT-proBNP was determined with a sandwich immunoassay on an Elecsys 2010 (Roche diagnostics). The NT-proBNP method is considered precise, has a wide dynamic measuring range, is free from common interferences, and does not cross-react with BNP.[21]

Statistical analysis

Data were expressed as the mean value ± standard deviation for continuous variables and absolute or relative frequencies for categorical variables. Inter-observer reproducibility was evaluated by the Kappa coefficient, considering satisfactory if near to 1.

Correlations between PCS and echocardiographic variables were assessed using linear regression analysis.

Multiple linear regression analysis was constructed to obtain the best regression model, with the PCS as the dependent variable and the echocardiographic parameters as the independent variables. The permanence of all variables in the final model was established when the significance level was < 0.05. SPSS version 13 (SPSS Inc., Chicago, Illinois) was used for all analyses.

Ethical

The research protocol was approved by the Research Ethics Committee of the institution and a written informed consent was obtained from all patients.

RESULTS

A total of 55 patients were enrolled. The mean age was 48.5 ± 11.2 years and 29% were women. Twenty-five (46%) patients were in NYHA class I, 27 (49%) in class II, and only three (5%) in class III/IV. There was significant association between functional class and the degree of pulmonary congestion (p=0.005; r = 0.375). The heart failure treatment was analyzed and didn’t modified the grade of pulmonary congestion.

Chest x-ray was normal in 11 patients and showed some degree of pulmonary venous abnormalities in the remaining 44 (80%) patients. The radiological findings of pulmonary congestion are shown on Table 2. Mean value of lung congestion score was 4.22 ± 2.29. The kappa coefficient was 0.58 to perihilar haze; 0.86 to presence of subpleural thickening; 0.78 to peribronchial cufing; 1.0 to equalization, inversion ,consolidation and pleural effusion.

Doppler echocardiographic parameters associated with the PCS are shown on Table 3. The mean LV ejection fraction was 36.7 ± 10.5% (median: 40%). LV ejection fraction correlated with the degree of pulmonary congestion (r = -0.58; p=0.001), as shown on Figure 1. The PCS was also associated with systolic pulmonary artery pressure (r = 0.56; p=0.002), as shown on Figure 2.

Various parameters used to evaluate diastolic function were associated with pulmonary congestion (Table 3). According to the established classification of diastolic dysfunction, six (10.9%) patients had normal diastolic function, 36 (65.5%) showed grade I of diastolic dysfunction, five (9.1%) grade II and eight (14.5%) grade III. The degree of diastolic dysfunction was also associated with the PCS (p<0.001). The mean E/E’ ratio was 6.3 ± 2.8 and it did not correlate with pulmonary congestion.

Mitral regurgitation was mild in ten (18%) patients and moderate in five (9%). The degree of mitral regurgitation was also associated with PCS (p=0.003). BNP levels correlated with pulmonary congestion.

<table>
<thead>
<tr>
<th>TABLE 2 - Pulmonary congestion score.</th>
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<tbody>
<tr>
<td>Venous flow characteristics</td>
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<tr>
<td>--------------------------------------</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Mild equalization</td>
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<tr>
<td>Moderate equalization</td>
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<tr>
<td>Mild inversion</td>
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<tr>
<td>Moderate inversion</td>
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<tr>
<td>Severe inversion</td>
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<tr>
<td>Kerley lines</td>
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<tr>
<td>Mild subpleural thickening</td>
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<tr>
<td>Moderate subpleural thickening</td>
</tr>
<tr>
<td>Pleural effusion</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE 3 - Doppler echocardiographic parameters associated with the pulmonary congestion score.</th>
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</thead>
<tbody>
<tr>
<td>Variables</td>
</tr>
<tr>
<td>--------------------------------------------</td>
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<tr>
<td>LVd (mm)</td>
</tr>
<tr>
<td>LVs (mm)</td>
</tr>
<tr>
<td>LAd (mm)</td>
</tr>
<tr>
<td>FS (%)</td>
</tr>
<tr>
<td>EF (%)</td>
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<tr>
<td>E wave (cm/s)</td>
</tr>
<tr>
<td>A wave (cm/s)</td>
</tr>
<tr>
<td>E/A</td>
</tr>
<tr>
<td>DT (ms)</td>
</tr>
<tr>
<td>IVRT (ms)</td>
</tr>
<tr>
<td>dPVF (cm/s)</td>
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<tr>
<td>E wave (cm/s)</td>
</tr>
<tr>
<td>E/A</td>
</tr>
<tr>
<td>Color M-mode (cm/s)</td>
</tr>
<tr>
<td>SPAP (mmHg)</td>
</tr>
<tr>
<td>RV Tii index</td>
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<tr>
<td>BNP (pg/ml)</td>
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</tbody>
</table>

LVd: left ventricular diastolic diameter; LVs: left ventricular systolic diameter; LAd: diastolic diameter of the left atrium; EF: ejection fraction; FS: fractional shortening; E: early diastolic transmitral flow velocity; A: late transmitral flow velocity; E/A: ratio of early to late transmitral flow velocity; DT: deceleration time of the E wave; IVRT: isovolumic relaxation time; dPVF: diastolic component of pulmonary venous flow; E: early diastolic mitral annular velocity; A: late diastolic mitral annular velocity; E'/A': ratio of the early diastolic transmital flow velocity to early diastolic mitral annular velocity; color M-mode: velocity slope of the color M-mode; SPAP: systolic pulmonary artery pressure; RV: right ventricle; BNP: brain natriuretic peptide.
congestion. However, when we included variables of LV systolic and
diastolic function in the multivariate model, BNP levels were not
predictive of pulmonary congestion.

In multivariate analysis, the echocardiographic variables that
remained correlated with the PCS were LV ejection fraction, RV
Tei index and color M-mode velocity. The final regression equation
\( r = 0.56; p = 0.001 \) was: 

\[
\text{PCS} = 3.463 + 4.064 \times (\text{RV Tei index}) + 0.051 \times (\text{color M-mode}) - 0.069 \times (\text{LV ejection fraction})
\]

**DISCUSSION**

Chest x-ray is an important exam in dilated cardiomyopathy,
providing noninvasive information about heart dimension and
pulmonary vessels at low costs. To the best of our knowledge,
the present study is the first to correlate parameters of pulmonary
congestion by chest X-ray with ventricular dysfunction by Doppler
echocardiogram in patients with Chagas cardiomyopathy. Similar to
other studies, PCS correlated with several prognostic parameters
of heart failure, such as NYHA functional class, LV ejection fraction
and RV dysfunction. Abnormalities of venous pulmonary pressure
by chest x-ray have been compared to Doppler echocardiograms
in elderly patients with systolic dysfunction. Radiological changes
have been shown to present a sensitivity of 76% in detecting
echocardiographic parameters of LV dysfunction.

It has been previously reported that in Chagas dilated
cardiomyopathy, lungs usually do not show findings of severe
pulmonary congestion. This is a peculiar aspect of this cardiomyopathy,
which shows more congestion in the systemic circulation than in the
pulmonary territory. In the present study, some degree of pulmonary
congestion was present in 80% of the chest x-rays and it was usually
mild. The essential feature of LV dysfunction is an increase in left
atrial pressure and pulmonary venous congestion leading to fluid
flow across the pulmonary microvasculature. In fact, in our study,
ejection fraction remained an important factor associated with
pulmonary congestion.

Although left ventricular dysfunction was present, 20% of the
chest x-rays did not show any signs of pulmonary congestion. This
could be explained by the fact that, in the scenario of cardiac failure,
venocapilar marks on chest x-ray do not necessarily correlate with
capillary pulmonary pressure. The absence of interstitial or alveolar
edema doesn’t necessarily mean that capillary pressure is normal.

Our patients were in NYHA functional class I or II, so these
results can not be extrapolated to the whole population of patients
with Chagas cardiomyopathy.

Chagas cardiomyopathy is a chronic myocarditis of an
inflammatory nature with a progressive fibrotic process affecting
the myocardial of both ventricles. RV involvement may occur more
often in Chagas cardiomyopathy than in other forms of dilated
cardiomyopathy. Moreover, chagasic patients with RV dysfunction
present with more extensive left ventricular involvement due to the
pathologic process, and have a poorer prognosis. In the present
study, higher PCS was also observed when severe LV dysfunction
was associated with RV dysfunction.

The Tei index is easily obtained and has been reported to be clinically
useful in assessing global RV function. Because the index has a wide
numeric range, it may better assist in reflecting the various degrees of
RV dysfunction. In the present study, we showed a correlation between
a prolonged RV Tei index and pulmonary congestion, supporting the
hypothesis that the clinical severity of RV dysfunction was associated
with the impairment of LV function. Tei et al. have shown that the
index correlate with symptoms and survival in patients with primary
pulmonary hypertension. A previous study from our group has shown
the correlation of pulmonary artery pressure and RV dysfunction in
Chagas cardiomyopathy. Lewis et al. found the same correlation in
patients with idiopathic cardiomyopathy.

Although the E/E’ ratio has been shown to be associated with a
pulmonary capillary wedge pressure in patients with depressed
ejection fractions, in the present study, the E/E’ ratio did not remain
in the final regression model. This may be explained by the fact that
most of our patients were clinically stable, and probably had lower
LV filling pressures, as demonstrated by the lower values of E/E’ ratio
found in these patients.

The propagation velocity of the E wave, as assessed by color
Doppler M-mode, has been demonstrated to be a measure of
ventricular relaxation, which is essentially independent of preload.
In the present study, color-mode velocity emerged as an independent
predictor of pulmonary congestion, after adjusting for LV ejection
fraction and RV function. Similarly, Schwammenthal et al. found
that an index derived of color M-mode velocity, E/Vp, was the best
predictor of pulmonary congestion in a subgroup of patients who
underwent cardiac catheterization.

In conclusion, pulmonary venous changes are frequent but
usually mild in patients with Chagas cardiomyopathy. The degree of
pulmonary congestion correlates with LV ejection fraction, RV Tei
index and with color M-mode velocity. However, since most patients
were in NYHA classes I or II, our results can not be extrapolated to
the whole population of patients with Chagas dilated cardiomyopathy.

**CONFLICT OF INTEREST**

The authors declare that there is no conflict of interest.

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