Myocardial Stiffness evaluation by shear wave elastography in transthyretin amyloidosis with and without cardiac involvement

A.C. Comte de Alencar Neto¹, C.R.F.C. Caio Reboucas Fonseca Cafezeiro¹, B.V.K.B. Bruno Vaz Kerges Bueno¹, J.H.R. Joao Henrique Rissato¹, V.T.H. Viviane Tiemi Hotta¹, A.C.A.F. Aristoteles Comte De Alencar Filho¹, F.L.P. Fernando Linhares Pereira², K.C. Katia Couceiro³, C.E.R. Carlos Eduardo Rochitte¹, J.M.B.B. Joao Marcos Bemifica Barbosa³, J.S.J.Jose Soares Junior¹, F.J.A.R. Felix Jose Alvarez Ramires¹, R.K.F. Roberto Kalil Filho¹, W.M.J. Wilson Mathias Junior¹, F.F. Fabio Fernandes¹

¹Heart Institute of the University of Sao Paulo (InCor), Sao Paulo, Brazil
²Clinical Hospital of the University of Sao Paulo, Sao Paulo, Brazil
³Amazonas State University, Manaus, Brazil

On behalf of INCOR HCFMUSP Amyloidosis Study Group

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Introduction: Cardiac involvement (CI) in hereditary transthyretin amyloidosis (ATTRh) occurs by deposition of amyloid fibrils in the heart, resulting in stiffening and diastolic dysfunction. Shear wave elastography, non-invasively and without the emission of ionizing radiation, quantitatively assesses tissue stiffness, a passive component of diastole, complementing the complex echocardiographic assessment.

Objective: To evaluate myocardial stiffness, through diastolic myocardial elasticity (DME), in ATTRh patients with and without CI and a healthy control group (CG).

Methodology: Prospective, cross-sectional study, 60 patients divided into 3 groups: ATTRh with CI (n:20), ATTRh without CI (n:20) and CG (n:20). DME was evaluated in the septal wall of the left ventricle (LV) (basal, middle, and apical segments) and in the free wall of the right ventricle (RV). They were also submitted to 2D-ECO, EKG, troponin, BNP, 6-minutes-walking test and pyrophosphate-labeled scintigraphy (Tc-99m-PYP). Data were analyzed using a one-way ANOVA, verifying myocardial stiffness, measured by DME, among the 3 groups. Then, pairwise comparisons were adjusted using Tukey’s technique.

Results: DME was a significant factor for distinguishing between groups when analyzed in the parasternal long axis (PLAX) basal septum (p=0.013), parasternal short axis (PSAX) basal septum (p=0.03) and in the PLAX RV free wall (p=0.004). Was observed in the apical septum segment similar stiffness between groups, suggesting a pattern of apical preservation. In the post hoc evaluation, DME in the basal septum region was significantly higher among the ATTRh with CI group than in the control group, but without significant difference between ATTRh with CI and ATTRh without CI, suggesting that the latter group has intermediate values between the sick patient and the healthy patient. Also, right ventricle DME in ATTRh with CI was greater than in the other two groups (Table 1 and Figure 1). In a regression model, the results indicate that 17.2% of the DME variance can be attributed to 3-hour scan uptake on the Tc-99m-PYP (R²=0.172, F (1-36) =7.2, p < 0.011), estimated by the equation: 3-hour scan uptake = 0.91 +0.078 x DME.

Conclusion: Myocardial stiffness is increased in ATTRh with CI, showing a decreasing pattern of stiffness in the apex direction, suggesting a pattern of apical preservation. Cardiac elastography has the potential to be an important tool in the assessment of cardiac involvement in systemic amyloidosis.
Table 1 Cardiac elastography

<table>
<thead>
<tr>
<th>Elastography</th>
<th>ATTRh with CI (n=20)</th>
<th>ATTRh without CI (n=19)</th>
<th>Control (n=20)</th>
<th>P-value</th>
<th>η²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal Septum (PLAX) (kPa)</td>
<td>6.6 ± 1.4</td>
<td>5.6 ± 1.4</td>
<td>5.4 ± 1.1</td>
<td>P=0.013*</td>
<td>0.14</td>
</tr>
<tr>
<td>Basal Septum (PSAX) (kPa)</td>
<td>6.7 ± 1.4</td>
<td>5.8 ± 1.4</td>
<td>5.6 ± 1.2</td>
<td>P=0.03*</td>
<td>0.11</td>
</tr>
<tr>
<td>Middle Septum (PSAX) (kPa)</td>
<td>5.1 ± 1.7</td>
<td>5.3 ± 1.4</td>
<td>5 ± 0.8</td>
<td>P=0.065</td>
<td>-</td>
</tr>
<tr>
<td>Apical Septum (PSAX) (kPa)</td>
<td>4.5 ± 0.9</td>
<td>4.3 ± 0.8</td>
<td>4.5 ± 0.8</td>
<td>P=0.6</td>
<td>-</td>
</tr>
<tr>
<td>RV (PLAX) (kPa)</td>
<td>5.4 (3.8 – 7)</td>
<td>3.7 ± (3.1-4.1)</td>
<td>4 ± (3.5 – 4.8)</td>
<td>P=0.004**</td>
<td>0.23</td>
</tr>
</tbody>
</table>

kPa = Kilopascal; RV = right ventricle
PLAX = Parasternal short-axis; PSAX = Parasternal long-axis
*In patients ≥50 years, of the ATTR group without CI, it was not possible to acquire apical hardness (PLAX) due to acoustic window limitation.
**In patients ≥50 years, of the ATTR group without CI, it was not possible to acquire hardness at all 3 points due to technical difficulty due to acoustic window limitation.

**In this comparison with three independent groups, there was a statistically significant difference only between the ATTR and control group (ATTR vs CONTROL).**

**In this comparison with three independent groups, there was a statistically significant difference between the ATTR and control group (ATTR vs CONTROL) and the ATTR and ATTR without AC (ATTR vs ATTR without AC).**

Figure 1 DME variation (mean) in basal-middle-apical segments in the ATTRh without CI, ATTRh with CI and control group.