Elastic properties of the ascending aorta in patients with rheumatoid arthritis

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Rheumatoid arthritis
Aortic stiffness and distensibility
Left ventricular mass mass
Left ventricular diastolic function

Systemic inflammatory rheumatic diseases, such as rheumatoid arthritis (RA), are associated with increased cardiovascular mortality, on account of the high prevalence of ischemic heart disease and accelerated atherosclerosis, compared with age- and sex-matched controls [1]. The higher risk of cardiovascular disease (CVD) in RA patients seems to be independent of traditional cardiovascular risk factors. Different pathogenic mechanisms including pro-inflammatory cytokines, hyperglycemia, insulin resistance, prothrombotic state and hyperhomocysteinemia have been described [2]. However, immune activation is a key mechanism that promotes structural and functional abnormalities of the vascular bed. Arterial stiffness, usually measured by pulse-wave velocity analysis, is considered a marker of subclinical vascular disease and increased CVD risk, and it is markedly abnormal in patients with RA [3,4]. Large left ventricular (LV) mass has also been associated with RA, suggesting a link between chronic inflammation and LV hypertrophy [5]. We investigated the elastic properties of the aorta and systo-diastolic function in RA patients without CV disease, compared with healthy controls.

In our study, RA was diagnosed according to American College of Rheumatology criteria [6]. Disease activity was assessed at time of cardiovascular evaluation using a composite index, called DAS44, including swollen and tender joint count (on 44 joints), global health assessment, physician and patient's global assessment, and ESR value. The patients had a cardiological examination, 12-lead electrocardiography (ECG) and two-dimensional and Doppler trans- thoracic echocardiography. The exclusion criteria of the study were: (a) arterial hypertension (blood pressure ≥140/90 mmHg in more than three consecutive readings or use of any hypotensive drugs); (b) diabetes; (c) smoke; (d) symptomatic dyspnea or chest pain; (e) use of any cardiovascular drugs (including statins); (g) any previous myocardial infarction, surgical or percutaneous revascularization, a positive ECG result, perfusion or echocardiographic exercise or pharmacological stress test; (h) more than mild aortic or mitral regurgitation and/or stenosis; (i) any previous surgical or interventional cardiac or vascular procedure; (l) familial hypercholesterolemia; (m) any genetic risk, and it is markedly abnormal in patients with RA[3,4]. Large left ventricular mass (155±47 vs. 140±31 g; p=0.01), LV mass index (mean 140±13 vs. 92±25 g/m² p<0.001) and indexing to height in meters to the power 2.7 (43.4±12 vs. 31.10 g/m²; p=0.0043) than controls.

We also found lower mean aortic strain (7.7±3% vs. 13±5%; p=0.001) and distensibility (2.8±12 vs. 5.4±2.6 cm²dyn⁻¹ × 10⁻⁶; p=0.001) with a higher mean stiffness index (9.2±6.05 vs. 5.06±2.9; p=0.001) in RA cases, compared with controls. There was also a significant difference between RA patients and controls in terms of E/A (1.1±0.7 vs. 1.7±0.6, p=0.001), deceleration time (225±56 vs. 190±50 ms, p=0.004) and E/E' (10.3±5.5 vs. 7.3±3.5, p=0.01). A comparison of aortic distensibility and other morphological and functional cardiac parameters showed no significant association between LV mass with aortic distensibility, aortic strain and stiffness. In addition, RA duration, disease activity index (DAS 44) and CRP did not correlate with either LV mass or aortic elastic properties.

Increased aortic stiffness and decreased aortic distensibility were closely associated with diastolic filling indexes measured by conventional and tissue Doppler echocardiography. In particular, we found a significant association between aortic distensibility, E/A (p<0.0001) and E'/E' (p=0.013), aortic stiffness and deceleration time (p=0.01) and between aortic strain, E/A (p<0.0001) and E'/E' (p=0.02). After adjustment for age and systolic blood pressure, at multivariable stepwise regression analysis, RA (p<0.0001) and systolic blood pressure (p=0.022) were independently related with distensibility, only RA was independently related with stiffness (p=0.0003) and with strain (p<0.0001). Age (p=0.0004) and RA (p=0.0014) were independently related with E/A, while only RA (p=0.0069) was independently related with E/E'. RA (p=0.00154) and age (p=0.0076) were independently related with DT.

At a multivariable stepwise regression analysis, rheumatoid factor, DAS, anti-CCP status were not related with aortic stiffness, distensibility, LV mass. Stratifying cases on the basis of RA duration (more or less than ten years), we also found no differences for LV mass and other elastic properties of the aortic wall. When considering RA treatment, prednisone, methotrexate or anti-TNF agents were not related with stiffness, distensibility, LV mass. The results of this study are that, first, patients with RA without CV disease or any CV risk factors had an increase in LV mass and abnormal elastic properties of the aorta (increased arterial stiffness, lower
Antigen carbohydrate 125 in heart failure: A promising clinical tool

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ARTICLE INFO

Article history:
Received 29 April 2011
Accepted 14 May 2011
Available online 2 June 2011

Keywords:
Antigen carbohydrate 125
Serosal effusion
Heart failure
Prognosis

Dear editor,

We want to acknowledge Topatan and Başaran for their contribution toward a better understanding of the pathophysiology of antigen carbohydrate 125 (CA125) in heart failure (HF) [1].

First, we want to clarify to the authors that longitudinal results presented in our letter entitled “Antigen carbohydrate 125 in heart failure: Not just a surrogate for serosal effusions?” were misinterpreted and no methodological issues are present in our calculation [2]. These results (which are also presented in figure 1 – see explanation at the bottom of the figure), were expressed as median (interquartile range), and not as median (min-max range).

Second, our disagreement with the above authors can be summarized into two aspects: 1) the role of CA125 within the very complex and poorly understood pathophysiological cascade that ultimately leads to an elevation of pro-inflammatory markers in acute heart failure syndromes (AHF), and; 2) clinical usefulness of CA125 serum levels in HF.

There is plenty of evidence showing a significant elevation in CA125, proinflammatory markers as well as systemic volume expansion in AHF [3–6]. How these factors are inter-related is still a matter of controversy. Is the mesothelial cells activation by volume expansion/serosal effusions the main mechanism for triggering the production of CA125, or is it the already heightened background inflammation in AHF that triggers the activation of the mesothelial cells, leading ultimately to CA125 elevation? We believe that the amount of evidence available is insufficient to dissect the exact role of CA125 within the (most likely) multifactorial cascade that ultimately leads to an elevation of pro-inflammatory markers in AHF.

Therefore, it seems unfair to conclude that CA125 is no more than a simple surrogate for the presence of serosal effusions and mesothelial stimulation. We cautiously have suggested that CA125 may increase in HF patients, not only as a consequence of serosal effusion but, perhaps

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Table 2

Left ventricular (LV) structure and function parameters in RA patients and controls.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>RA patients (n. 44)</th>
<th>Controls (n. 35)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior wall thickness mm</td>
<td>8.9±1.2</td>
<td>8.2±1.2</td>
<td>0.01</td>
</tr>
<tr>
<td>LV end-diastolic dimension mm</td>
<td>47±7</td>
<td>47±4</td>
<td>0.93</td>
</tr>
<tr>
<td>LV end-systolic dimension mm</td>
<td>25±3.4</td>
<td>27±7</td>
<td>0.25</td>
</tr>
<tr>
<td>Ejection fraction %</td>
<td>63±7</td>
<td>64±4.4</td>
<td>0.26</td>
</tr>
<tr>
<td>LV mass, g</td>
<td>135±47</td>
<td>140±31</td>
<td>0.012</td>
</tr>
<tr>
<td>LV mass index, g/m²</td>
<td>140±31</td>
<td>92±25</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LV mass index, g/m²</td>
<td>43±12</td>
<td>31±10</td>
<td>0.0043</td>
</tr>
<tr>
<td>E/A</td>
<td>1.1±0.7</td>
<td>1.7±0.6</td>
<td>0.0003</td>
</tr>
<tr>
<td>DT msec</td>
<td>234±55</td>
<td>190±50</td>
<td>0.005</td>
</tr>
<tr>
<td>E/E</td>
<td>11±5.8</td>
<td>73±3.6</td>
<td>0.0034</td>
</tr>
<tr>
<td>AoS mm</td>
<td>3.2±0.4</td>
<td>3.05±0.4</td>
<td>0.01</td>
</tr>
<tr>
<td>AoD mm</td>
<td>3±0.4</td>
<td>2.7±0.4</td>
<td>0.0054</td>
</tr>
<tr>
<td>Distensibility cm² dyne⁻¹ 10⁻⁶</td>
<td>3±1.2</td>
<td>5±2.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stiffness index</td>
<td>8.3±4.5</td>
<td>5±2.9</td>
<td>0.002</td>
</tr>
<tr>
<td>Strain %</td>
<td>8.1±3.1</td>
<td>13±7</td>
<td>0.0003</td>
</tr>
</tbody>
</table>

These two conditions probably influence the prognosis of RA patients and provide a plausible mechanism for their increased cardiovascular morbidity and mortality. Although our patients did not have active disease at the time of cardiologic assessment, the longstanding chronic systemic inflammatory state may accelerate the atherosclerotic process, increasing aortic stiffening and LV mass.

Further prospective studies are needed to establish whether abnormal elastic aortic properties really correspond to an increased risk of cardiovascular disease in RA.

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [7].

References