Abnormal Concentric Ventricular Remodeling in Rheumatoid Arthritis

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Disclosure

We have no financial or other relationship to disclose.

Background

• Heart failure (HF) is an important complication of rheumatoid arthritis (RA)
  • Significantly increased incidence in RA
    • Unexplained by traditional risk factors
  • HF-related mortality is high in RA
  • Preserved systolic function
    • LV diastolic dysfunction

Rationale

• Distinct pathogenesis of HF complicating RA?
  • Inflammatory immune mechanisms
  • Structural changes in the myocardium
• Analysis of left ventricular geometry elucidates patterns of remodeling.
  • New mechanistic insights
  • Prognostic & therapeutic implications

Purpose

To compare left ventricular geometry between patients with RA and subjects without any history of arthritis from the same community.
**Methods**

- **Design:**
  - Cross-sectional study
  - Population-based cohorts
  - RA vs. non-RA

- **Study population:**
  - Olmsted County, MN residents
  - Age ≥ 50 years
  - No history of clinical heart failure

- **Data collection:**
  - BMI, CV risk factors, RA data
  - Lab: CRP, RF, ACPA
  - 2D/Doppler echocardiography

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**Methods**

**Key Parameters of LV Geometry**

- Posterior wall thickness
- Left ventricle internal diameter

**Relative wall thickness (RWT)**

- Normal
- Eccentric hypertrophy
- Concentric remodeling

**LV mass index (LVM)**

- Normalized to body surface area

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**Classification of LV Geometry**

<table>
<thead>
<tr>
<th>LV mass index</th>
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</tr>
</thead>
<tbody>
<tr>
<td>≤95 (female)</td>
<td>&gt;95 (female)</td>
</tr>
<tr>
<td>≤115 (male)</td>
<td>&gt;115 (male)</td>
</tr>
</tbody>
</table>

- RWT ≤0.42
- RWT >0.42

- Normal
- Eccentric hypertrophy
- Concentric remodeling

Methods

• Statistical analysis:
  • Contingency tables
  • Chi square tests
  • Logistic regression models
    • Model 1: fit all adjustors
    • Model 2: assess variable of interest holding the adjustors constant
    • Reduce overfitting bias

Results

Characteristics of the RA Cohort (N = 210)

<table>
<thead>
<tr>
<th>Disease duration, yrs</th>
<th>10.1 ± 7.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid factor or ACPA positive</td>
<td>69%</td>
</tr>
<tr>
<td>Pain, 100 mm VAS (0 – 100)</td>
<td>29.7 ± 24.1</td>
</tr>
<tr>
<td>HAQ disability index (0 – 3)</td>
<td>0.6 ± 0.6</td>
</tr>
<tr>
<td>C-reactive protein, mg/L (&lt;3.0 – 8.0)</td>
<td>4.4 ± 6.8</td>
</tr>
<tr>
<td>Methotrexate use</td>
<td>56%</td>
</tr>
<tr>
<td>Biologic use</td>
<td>14%</td>
</tr>
<tr>
<td>Prednisone use</td>
<td>29%</td>
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Results

Comparison of RA and non-RA subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>RA (N = 210)</th>
<th>Non-RA (N = 1446)</th>
<th>P-value</th>
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<tr>
<td>Age, yrs</td>
<td>65.1 ± 9.9</td>
<td>65.0 ± 9.4</td>
<td>0.84</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28.7 ± 5.9</td>
<td>28.2 ± 5.4</td>
<td>0.16</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>132 ± 18</td>
<td>125 ± 19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>71 ± 9</td>
<td>68 ± 10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV mass index, g/m²</td>
<td>85 ± 16</td>
<td>91 ± 22</td>
<td>&lt;0.001</td>
</tr>
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<td>RWT, cm</td>
<td>0.43 ± 0.07</td>
<td>0.39 ± 0.08</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>EF, %</td>
<td>62 ± 7</td>
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All values are sex-adjusted.

Results

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All values are sex-adjusted.
Results
Abnormal LV geometry in RA and non-RA

Adjusted OR = 1.3 (95% CI: 0.9, 1.8), p=0.13

Results
Concentric remodeling in RA and non-RA

*Adjusted OR = 3.8 (95% CI: 2.6 to 5.6) p<0.001

Results
Concentric remodeling in RA and non-RA
Patients with abnormal geometry

*Adjusted OR = 6.7 (95% CI: 3.8 to 11.9), p<0.001

Results
Predictors of Abnormal LV Geometry in RA

<table>
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<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
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<tr>
<td>RA duration</td>
<td>0.99</td>
<td>0.94, 1.04</td>
</tr>
<tr>
<td>RF+</td>
<td>1.37</td>
<td>0.72, 2.61</td>
</tr>
<tr>
<td>ACPA+</td>
<td>1.50</td>
<td>0.79, 2.85</td>
</tr>
<tr>
<td>CRP &gt;8 mg/L</td>
<td>2.30</td>
<td>0.88, 6.02*</td>
</tr>
<tr>
<td>Pain score</td>
<td>1.43</td>
<td>0.91, 2.26</td>
</tr>
<tr>
<td>HAQ disability index</td>
<td>1.76</td>
<td>0.98, 3.12†</td>
</tr>
<tr>
<td>MTX</td>
<td>2.22</td>
<td>1.14, 4.34‡</td>
</tr>
<tr>
<td>Anti-TNF</td>
<td>1.00</td>
<td>0.99, 1.00</td>
</tr>
<tr>
<td>Prednisone</td>
<td>0.94</td>
<td>0.47, 1.88</td>
</tr>
</tbody>
</table>

*P = 0.088. †P = 0.058. ‡P = 0.019.
Odds ratios are adjusted for all covariates.

Summary
- RA is associated with abnormal LV geometry
  - Concentric remodeling, in particular
- Significant after adjustment for CV risk factors
- Association with markers of RA severity

Possible Implications
- Pathogenesis
  - RA-associated remodeling suggests a distinct pathogenesis of heart failure
  - Concentric remodeling is related to aging, obesity, and metabolic syndrome1-3
    - New hypotheses?
- Clinical management
- Screening for ventricular remodeling?
- Different approach to prevention of HF?

Conclusions

• RA is associated with concentric remodeling

• Further research is necessary to understand:
  • Biological mechanisms involved
  • Impact on diagnosis and treatment
  • Impact on cardiovascular outcomes

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