Sex-related differences in characteristics and mortality of patients with rheumatoid arthritis and concomitant heart failure

Tatjana Rudi1, Vera Zietemann1, Yvette Meissner1, Matthias Schneider1, Thilo Klopfch1, Matthias Worsch4, Anja Strangfeld1–5
1German Rheumatism Research Centre Berlin (DRFZ), Epidemiology and Health Services Research, Berlin; 2University Hospital Düsseldorf, Rheumatology, Düsseldorf; 3Rheumatologist, Neubrandenburg; 4Rheumatologist, Private Practice, Mühlhausen, 5Department of Rheumatology and Clinical Immunology, Charité University Medicine Berlin, all Germany

German Rheumatism Research Centre Berlin, Epidemiology and Health Services Research

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Introduction
Sexual differences in the characteristics and outcomes of patients with rheumatoid arthritis (RA) have been observed in clinical trials and observational studies, yet the mechanisms underlying these sex differences remain incompletely understood. This study aimed to investigate sex differences in the characteristics and mortality of a cohort of RA patients with concomitant heart failure (HF).

Methods
Patients with RA and HF were identified from the German biologics register RABBIT between 01/2007 and 04/2022. The analysis included 15,917 cohort participants (11,835 females, 74%). For each patient, we extracted baseline characteristics, including demographics, disease activity, comorbidities, and treatment data. Kaplan-Meier survival analysis was used to compare survival curves between females and males.

Results
Out of 15,917 cohort participants (11,835 females, 74%), 718 patients were identified as prevalent HF cases (473 females, 66%). Cox proportional hazards regression models were used to analyze the impact of sex on survival, adjusted for age, disease duration, and comorbidities. Females with HF were on average 1.7 years older, had worse physical function, and longer RA disease duration compared to males. Females were more likely to have osteoporosis and less likely to have ischemic heart disease (Table).

Table: Baseline characteristics by sex at time of first report of HF

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Female</th>
<th>Male</th>
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<tbody>
<tr>
<td>N</td>
<td>473</td>
<td>245</td>
</tr>
<tr>
<td>Age [years]</td>
<td>70.4 ± 9.5</td>
<td>68.7 ± 10.4</td>
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<tr>
<td>RA disease duration [years]</td>
<td>15.2 ± 11.6</td>
<td>10.5 ± 9.0</td>
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<tr>
<td>Rheumatoid factor positive</td>
<td>314 (66.4)</td>
<td>160 (65.3)</td>
</tr>
<tr>
<td>CRP [mg/l]</td>
<td>4.5 ± 14</td>
<td>4.3 ± 15</td>
</tr>
<tr>
<td>% of full physical function [0-100]</td>
<td>49.1 ± 23.8</td>
<td>59.5 ± 25.6</td>
</tr>
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</table>

Treatment
- Glucocorticoid dose ≥10 mg/d: 66 (14.0) vs. 29 (11.8)
- B cell targeted therapy: 69 (14.6) vs. 27 (11.0)
- Interleukin-6 inhibitor: 44 (9.3) vs. 26 (10.6)
- T cell co-stimulation modulator: 40 (8.5) vs. 32 (13.1)
- Tumour necrosis factor inhibitor: 146 (30.9) vs. 82 (33.5)
- Janus kinase inhibitor: 31 (6.6) vs. 13 (5.3)

Comorbidity
- Ischemic heart disease: 42 (8.9) vs. 7 (3.0)
- Female
- Diabetes: 134 (28.3) vs. 76 (31.7)
- Chronic lung disease: 164 (34.7) vs. 127 (51.8)
- Malignancy: 42 (8.9) vs. 35 (14.3)
- Osteoporosis: 216 (45.7) vs. 61 (24.9)

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References
1 PMID: 32378457; 2 PMID: 31544235; 3 PMID: 36386322; 4 PMID: 37378143

Conclusion
Our findings demonstrate a longer survival for females compared to males in a cohort of patients with RA and concomitant HF. The differences could not be explained by age, comorbidities, and RA-related characteristics at baseline. The observed differences in the clinical profile and mortality highlight the need for research stratifying by sex when investigating cardiac events.

Background
Heart failure (HF) is a common co-morbidity of rheumatoid arthritis (RA) with high mortality risk [1]. In the general population, significant sex-related differences in HF including aetiology, pathophysiological mechanisms and age are observed, emphasizing the importance to stratify analyses by sex [2]. There is increasing evidence that mortality rates of females are lower, which cannot be explained by comorbidities, HF characteristics or HF medical treatment [3].

Objectives
To investigate sex-specific differences in patient characteristics and the association of sex with mortality in RA patients with concomitant HF.

Methods
RA-patients enrolled and observed in the German biologics register RABBIT between 01/2007 and 04/2022 were selected for the analysis if they presented HF either at enrolment or during follow-up. Observation started with the first report of HF (baseline) and ended at death, dropout or end of follow-up, whichever came first. Cox proportional hazard regression with sex as exposure of interest was applied, adjusted for age (model A) and further adjusted for comorbidities and RA specific characteristics (model B). Missing values were imputed once.

Values are numbers (percent) or means ± standard deviation.