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

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Conclusion

Our findings demonstrate a longer survival for females compared to males in a cohort of patients with RA and concomitant HF. The difference 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.

Results

Out of 15,917 cohort participants (11,835 females, 74%), 718 patients were identified as prevalent HF cases (473 females, 66%).

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

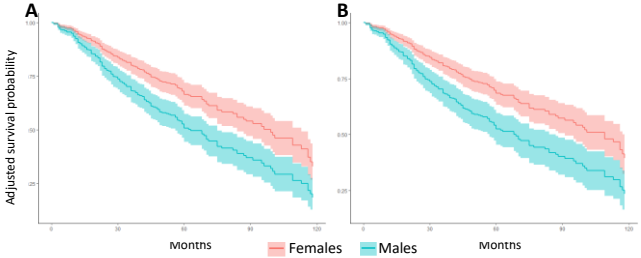
	Female	Male
N	473	245
Age [years]	70.4 ± 9.5	68.7 ± 10.4
RA disease duration [years]	15.2 ± 11.6	10.5 ± 9.0
Rheumatoid factor positive	314 (66.4)	160 (65.3)
DAS28-ESR	4.5 ± 1.4	4.3 ± 1.6
CRP [mg/l]	14.5 ± 23.2	15.7 ± 19.1
% of full physical function [0-100]	49.1 ± 23.8	59.5 ± 25.6
Treatment		
Glucocorticoid dose ≥10 mg/d	66 (14.0)	29 (11.8)
B cell targeted therapy	69 (14.6)	27 (11.0)
Interleukin-6 inhibitor	44 (9.3)	26 (10.6)
T cell co-stimulation modulator	40 (8.5)	32 (13.1)
Tumour necrosis factor inhibitor	146 (30.9)	82 (33.5)
Janus kinase inhibitor	31 (6.6)	13 (5.3)
csDMARDs	105 (22.2)	48 (19.6)
History of comorbidities		
No. of comorbidities	5.8 ± 3.0	6.2 ± 3.3
Chronic liver disease	29 (6.1)	28 (11.4)
Chronic lung disease	95 (20.1)	65 (26.5)
Chronic renal disease	150 (31.7)	92 (37.6)
Diabetes	134 (28.3)	79 (32.2)
Ischemic heart disease	164 (34.7)	127 (51.8)
Malignancy	42 (8.9)	35 (14.3)
Osteoporosis	216 (45.7)	61 (24.9)

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

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).

Mortality risk:
25% (n=117) of the females and 34% (n=84) of the males died after a mean follow-up time of 39 and 36 months, respectively. Females had a significant lower risk of death compared to males regardless of adjustment (model A: HR=0.57 [0.43-0.76]; model B: HR=0.52 [0.38-0.73], Figure).

Figure: Sex differences in adjusted survival curves.
A: adjusted for age; B: adjusted for age, RA disease duration, rheumatoid factor, CRP, % of full physical function and high glucocorticoid dose at baseline, year of HF >2012, DMARD treatment as cumulative exposure in months divided by the total observation months, chronic liver disease, chronic lung disease, chronic renal disease, depression/mental illness, diabetes, history of ischemic heart disease, malignancy, osteoporosis.



References

(1) PMID: 32378457; (2) PMID: 31544235; (3)PMID: 36386322;

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