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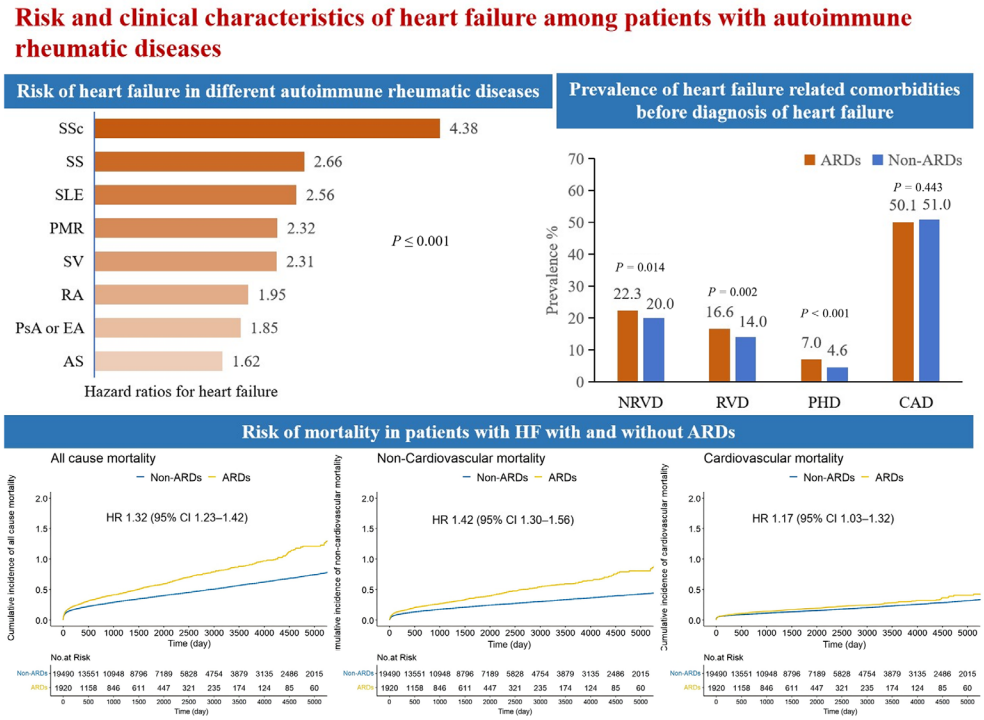
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Long-term risk of heart failure in patients with autoimmune rheumatic diseases

A population-based cohort study

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Graphical abstract



Abstract

Background: Rising evidence indicates that several autoimmune rheumatic diseases (ARDs) are associated with a higher risk of heart failure (HF); however, large-scale comparative studies across multiple ARDs are scarce.

Methods: In this cohort study, participants without prevalent HF from the UK Biobank were included. The relation between ARDs and the incidence of HF and mortality was analyzed using Cox proportional hazards models.

Results: Of 499,525 participants included in this study (n = 10,198 with ARDs, n = 489,327 without ARDs), 18,686 HF cases occurred over a median follow-up of 13.8 years. Significantly elevated risks for HF were observed among all patients with ARDs ($P < 0.05$), with the highest relative risk of HF in patients with systemic sclerosis (hazard ratio [HR]: 4.38; 95% confidence interval [CI]: 2.98–6.43; $P < 0.001$). Of patients who developed HF, those with ARDs exhibited a higher prevalence of rheumatic valvular disease (16.6% vs. 14.0%), non-rheumatic aortic valve disease (12.6% vs. 9.6%), and pulmonary heart disease (7.0% vs. 4.6%) before the diagnosis of HF ($P < 0.05$), while the prevalence of coronary artery disease, atrial fibrillation/atrial flutter, and hypertensive heart disease was similar. A history of ARDs was associated with increased all-cause mortality after diagnosis of HF (HR: 1.32; 95% CI: 1.23–1.42; $P < 0.001$), especially for non-cardiovascular mortality (HR: 1.42; 95% CI: 1.30–1.56; $P < 0.001$).

Conclusion: Various ARDs were associated with a higher risk of HF. Patients with HF and ARDs had a higher prevalence of valvular disease and pulmonary heart disease before HF diagnosis compared with other patients with HF. A history of ARDs was associated with higher mortality after diagnosis of HF.

Key words: autoimmune disease, heart failure, UK Biobank, rehospitalization, mortality

Nonstandard Abbreviations and Acronyms

AF/AFL	Atrial fibrillation/flutter
ARDs	Autoimmune rheumatic diseases
AS	Ankylosing spondylitis
APS	Antiphospholipid syndrome
BMI	Body mass index
CAD	Coronary artery disease
CI	Interval of confidence
CRP	C-reactive protein
DBP	Diastolic blood pressure
DM	Diabetes mellitus
DM/PM	Dermatomyositis/Polymyositis
HbA1c	Glycosylated Hemoglobin
HF	Heart failure
HFpEF	Heart Failure with preserved Ejection Fraction
HFrEF	Heart Failure with reduced Ejection Fraction
HR	Hazard ratio
ICD	International Classification of diseases
IPTW	Inverse-probability of treatment weighting
IQR	Interquartile range
IRB	Institutional Review Board
LDL-C	Low-density lipoprotein cholesterol
PMR	Polymyalgia rheumatica
PsA or EA	Psoriatic arthritis or enteropathic arthropathies
RA	Rheumatoid arthritis
SBP	Systolic blood pressure
SLE	Systemic lupus erythematosus
SS	Sjogren's syndrome
SSc	Systemic sclerosis
SV	Systemic vasculitis
UKB	UK biobank

Highlights

- Several ARDs have elevated risks of HF, with the highest risks observed for SSc.
- HF patients with ARDs had more valvular/pulmonary disease pre-HF than those without.
- CAD, hypertensive heart disease, and AF/AFL prevalence were similar to other HF patients.
- ARD patients have higher all-cause mortality post-HF, especially non-cardiovascular.

1. Introduction

Autoimmune rheumatic diseases (ARDs) are diverse inflammatory conditions affecting multiple organ systems, notably the cardiovascular system. Heart failure (HF) is a common cardiovascular manifestation in ARD patients and significantly contributes to their increased mortality risk.[1–3] Recent insights highlight an increased risk of HF in several ARDs such as rheumatoid arthritis (RA),[4–6] systemic lupus erythematosus (SLE),[7,8] and systemic sclerosis (SSc).[9,10] However, large-scale research on the relationship between HF and other ARDs like Sjogren syndrome (SS), polymyalgia rheumatica (PMR), and systemic vasculitis (SV) is lacking and contentious.[11–14] Besides, in previous studies, ARDs have been individually reported to have associations with HF, using different definitions of ARDs and HF. There is a lack of comprehensive studies simultaneously comparing the risk of HF between different ARDs.[15,16]

The mechanisms linking ARDs to HF are multifaceted, involving chronic inflammation, immune system activation, and endothelial dysfunction. Cardiac involvement varies among ARDs, with RA and SLE frequently causing myocardial inflammation, fibrosis, and pericardial involvement, while pulmonary hypertension is notably prevalent in SSc. Valvular damage, including conditions such as Libman-Sacks endocarditis in SLE, is also well-documented.[17,18] Despite the known associations between some ARDs and HF, there is a lack of systematic studies describing the HF-related comorbidities in patients with ARDs, highlighting the need for further research to better understand the etiology of HF in this population.

Given the distinct pathophysiological mechanisms in ARD-related HF, it is essential to investigate whether these factors contribute to different clinical outcomes compared with HF patients without ARDs. However, specific data on prognosis in HF patients with ARDs remain limited. Comprehensive studies focusing on these aspects could provide valuable insights into improving prognostic models and therapeutic strategies for this unique patient population.

The objectives of this study are to simultaneously evaluate the risk of HF across eight different ARDs, explore the differences in HF-related comorbidities in HF patients with and without ARDs, and compare the prognosis after diagnosis of HF in patients with and without ARDs. It is

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hypothesized that the relative risk of developing HF varies across different ARDs. Furthermore, the potential etiology and prognosis of HF in ARDs patients differ from other patients with HF.

2. Methods

2.1. Data sources

A detailed description of the aims of the UK Biobank has been published before.[19] In short, the UK Biobank is a population-based cohort study following over 500,000 participants 40 to 69 years of age from 22 assessment centers throughout the United Kingdom between 2006 and 2010. Through questionnaires, interviews, recurrent visits to assessment centers, and linkage to health records, a wide range of psychosocial, sociodemographic, physical, and genetic data were collected. The UK Biobank received ethical approval from the UK National Health Service, National Research Ethics Service Northwest, the National Information Governance Board for Health and Social Care in England and Wales, and the Community Health Index Advisory Group in Scotland. All participants provided written informed consent. This cohort study was approved by the UKB (application number 77740). The study was conducted complying with the Declaration of Helsinki.

2.2. Study population

We excluded participants diagnosed with HF before the initial assessment or those lacking informed consent for follow-up data collection. There is no universally accepted definition for ARDs. Commonly recognized ARDs include RA, psoriatic arthritis or enteropathic arthropathies (PsA or EA), ankylosing spondylitis (AS), SLE, SSc, PMR, SS, SV, mixed connective tissue disease, and idiopathic inflammatory myopathies.[20–22] To avoid low statistical power and random error from small sample sizes, and consistent with prior studies,[23,24] we only included ARDs with at least 100 prevalent cases at baseline and a minimum of 10 HF events during follow-up. Of the 10 ARDs assessed, mixed connective tissue disease and idiopathic inflammatory myopathies were excluded (1.7% of the ARDs population) due to an insufficient number of cases. Finally, eight common ARDs met these criteria and were included in the analysis: RA, PsA or EA, AS, SLE, SSc, PMR, SS, and SV (Supplementary Table 1, Supplemental Digital Content, https://links.lww.com/CARES/A19). ARDs were defined by ICD-10 codes extracted from records, including primary care, hospital inpatient, death registers, and self-reported medical conditions. Some ARDs (PMR, SS, and Behçet disease) were identified through hospital inpatient records due to the absence of ICD coding in other sources. Supplementary Table 2, Supplemental Digital Content, https://links.lww.com/CARES/A19, lists the ICD-10 codes for ARDs.

2.3. Comorbidity

Data on demographic factors (age, sex, ethnicity, education, and Townsend deprivation index), lifestyle (smoking, drinking, and physical activity), and medication history (cholesterol-lowering, blood pressure, and glucocorticoids) were collected via questionnaires and interviews at the assessment center. Additionally, during the initial assessment center visit, measurements were taken for body mass index (BMI), systolic and diastolic blood pressure (SBP and DBP), total cholesterol, LDL cholesterol (LDL-C), hemoglobin A1c (HbA1c), and C-reactive protein (CRP). The presence of comorbidities, including hypertension, diabetes mellitus (DM), coronary artery disease (CAD), atrial fibrillation/flutter (AF/AFL), and chronic kidney disease, was determined through interviews, questionnaires, and ICD codes recorded before the first assessment. Definitions and assessments of covariates are detailed in Supplementary Table 3, Supplemental Digital Content, https://links.lww.com/CARES/A19.

2.4. Analysis

In the initial analysis, we assessed the risk of HF across various ARDs. Patients with prevalent ARDs at baseline were classified as the exposure group. Participants were continuously monitored for HF occurrences through linked health-related records, which included primary care, hospital inpatient records, death registers, and self-reported medical conditions. Incident cases of HF were identified based on the ICD-10 code I50 (category ID in UK Biobank 131354). Participants who reported the date of their first HF occurrence after the initial assessment were classified as having HF.

For the secondary analysis, we included all patients diagnosed with HF in the database and identified those with pre-existing ARDs and HF-related comorbidities before the HF diagnosis. We compared the prevalence of HF-related comorbidities between HF patients with ARDs and those without. The selection of HF-related comorbidities was based on the European Society of Cardiology guidelines for HF[25] and expert opinion. These comorbidities included hypertensive heart disease, CAD, rheumatic valve disorders, non-rheumatic valve disorders, cardiomyopathy, pulmonary heart diseases, and AF/AFL. Data on these comorbidities were collected from hospital admissions, primary care records, death registers, and self-reported sources, using ICD-10 codes. Detailed definitions of these comorbidities are provided in Supplementary Table 4, Supplemental Digital Content, https://links.lww.com/CARES/A19.

In the third analysis, we compared the prognosis of patients with incident HF based on their history of ARDs. The prognosis measures of interest included all-cause mortality, cardiovascular mortality, non-cardiovascular mortality, and hospitalizations for HF. Information on the date and primary cause of death was sourced from death registries. Cardiovascular death was defined using ICD-10 codes for the underlying cause of death, including

diseases of the heart (I00–I09, I11, I13, and I20–I51), essential hypertension or hypertensive renal disease (I10, I12, and I15), cerebrovascular diseases (I60–I69), and peripheral vascular disease (I73). Hospitalization for HF was defined as the first hospital admission with a primary diagnosis of HF occurring after the initial HF diagnosis. The primary diagnosis of HF was identified from "Hospital inpatient—main Diagnoses" records using the ICD-10 code I50 (category ID in UK Biobank 41202).

2.5. Statistics

Baseline characteristics and characteristics in patients with HF were presented as median (interquartile range [IQR]) for continuous variables and percentages for categorical variables. Differences in characteristics between groups were assessed using the Wilcoxon test for continuous variables and the chi-square test for categorical variables. Missing data were handled using multiple imputation under the missing at random (MAR) assumption, generating five imputed datasets.

To compare the incidence of HF in patients with and without a history of ARDs, Cox regression models were used to estimate the hazard ratio (HR) and 95% confidence intervals (CIs). We assessed the proportional hazards assumption using Schoenfeld residuals, and the proportional hazards assumption was met. Multicollinearity was assessed using the variance inflation factor (VIF), and only predictors with a variance inflation factor below five were retained for analysis to reduce redundancy in the model. To identify confounding factors, the minimal adjustment set of adjustment variables was constructed from the potential covariates by using a directed acyclic graph (DAG) based on DAGitty (Supplementary Fig. 1, Supplemental Digital Content, https://links.lww.com/CARES/A19). The Cox regression models were adjusted for age at baseline, gender, smoking status, BMI, ethnicity, and the Townsend deprivation index. Patients were followed from the initial assessment center visit until the occurrence of HF, death, emigration, or the end of the study (December 19, 2023), whichever came first. When comparing the risk of HF between patients with certain ARDs and those without ARDs, patients with other autoimmune diseases were excluded. To test the robustness of our findings, we further conducted several sensitivity analyses. First, we additionally adjusted for the history of hypertension, DM, CAD, physical activity level, and the use of glucocorticoids and disease-modifying antirheumatic drugs (DMARDs) in the Cox model to estimate the direct effect of ARDs on HF. Second, we conducted a sensitivity analysis that excluded participants with missing data. Third, inverse-probability of treatment weighting (IPTW) with stabilized weights based on propensity scores was applied to address baseline differences between individuals with and without ARDs. The following variables were included for IPTW: age, gender, year of admission, history of hypertension, and history of chronic renal failure. The weights were then employed in weighted Cox proportional hazards regression models to analyze the associations between various ARDs and the outcomes. Fourth, considering mortality as a significant competing risk for the incidence of HF, we performed a sensitivity analysis using the Fine–Gray model. To compare the prognosis between patients with incident HF with and without a history of ARDs, Cox proportional hazards models were used. The Cox regression models were adjusted for age at baseline, gender, smoking status, BMI, ethnicity, and the Townsend deprivation index. Patients were followed from the date of their first HF diagnosis until the occurrence of hospitalization for HF, death, date of emigration, or the end of the study period (December 19, 2023), whichever came first. The reported HRs were adjusted for age at HF diagnosis and gender.

All analyses were performed using IBM SPSS Statistics version 25 (IBM Corporation, Armonk, New York) and R project, version 4.2.2 (R Project for Statistical Computing, Vienna, Austria). A P value of < 0.05 was considered to be statistically significant. To account for multiple comparisons on the association of the eight ARDs with HF risk, Bonferroni correction was used, and $P < 0.00625$ (0.05/8) was considered as statistically significant.

3. Results

3.1. Population characteristics

By 2024, the UK Biobank database included 502,269 participants. After excluding 2,742 participants diagnosed with HF before the first assessment and 2 participants who did not provide informed consent, 499,525 participants were included in this study. At baseline, 10,198 participants were diagnosed with ARDs, including 6,712 with RA, 395 with PsA or EA, 750 with SLE, 215 with SSc, 266 with PMR, 243 with SS, 636 with SV, and 1,554 with AS (Fig. 1).

Table 1 presents the baseline characteristics of patients with ARDs compared with the general population. Patients with ARDs were, on average, 2 years older and more likely to be female than those without ARDs. They also had higher levels of BMI, SBP, HbA1c, and CRP. Additionally, they had a higher prevalence of current smoking, hypertension, diabetes, CAD, AF/AFL, and chronic kidney disease.

3.2. Incidence of HF

After a median follow-up of 13.8 years (IQR 12.9–14.5), a total of 1,086 participants (0.2%) were lost during follow-up. A total of 844 participants with ARDs (8.3%) and 17,842 participants without ARDs (3.6%) developed HF. After adjusting for potential confounders, all ARDs were associated with a significantly increased risk of incident HF, compared with a reference rate of 2.7/1,000 patient-years in those without ARDs. The highest relative risk was observed in patients with SSc (9.8/1,000 patient-years; HR: 4.38; 95% CI: 2.98–6.43), followed by SS (6.9/1,000; HR: 2.66; 95% CI: 1.73–4.08), SLE (5.4/1,000; HR: 2.56; 95% CI:

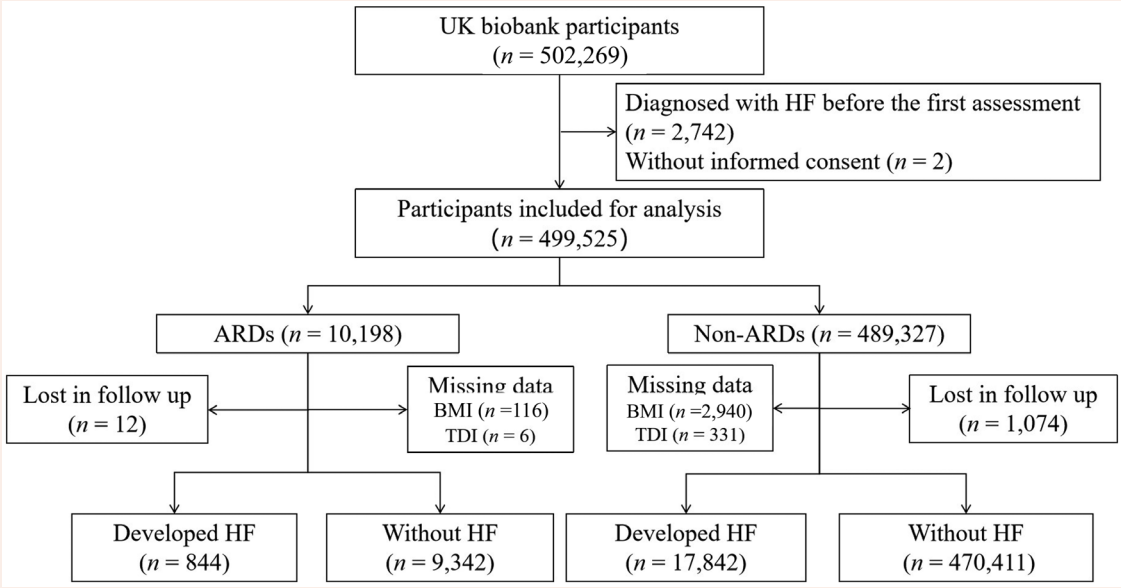


Figure 1. Flow chart for study participants. ARDs = autoimmune rheumatic diseases, AS = ankylosing spondylitis, PMR = polymyalgia rheumatica, PsA or EA = psoriatic or enteropathic arthropathies, RA = rheumatoid arthritis, SLE = systemic lupus erythematosus, SS = Sjogren syndrome, SSc = systemic sclerosis, SV = systemic vasculitis.

1.95–3.37), PMR (10.2/1,000; HR: 2.32; 95% CI: 1.65–3.27), SV (8.1/1,000; HR: 2.31; 95% CI: 1.81–2.60), RA (6.4/1,000; HR: 1.95; 95% CI: 1.82–2.08), PsA or EA (6.1/1,000; HR: 1.85; 95% CI: 1.30–2.63), and AS (5.4/1,000; HR: 1.62; 95% CI: 1.34–1.96) (Table 2). In the sensitivity analysis, we found results similar to the main analysis after additionally adjusting for the history of hypertension, DM, CAD, physical activity level, and use of glucocorticoids in the Cox model (Supplementary Table 5, Supplemental Digital Content, https://links.lww.com/CARES/A19), excluding participants with missing data (Supplementary Table 6,

Table 1

Baseline characteristics of participants with and without ARDs.

	Participants with ARDs (*n* = 10,198)	Participants without ARDs (*n* = 489,327)	*P*
Age, median (IQR), year	60 (11)	58 (13)	< 0.001
Women, no. (%)	6,648 (65.2)	265,854 (54.3)	< 0.001
White, no. (%)	9,774 (95.8)	467,410 (95.5)	0.620
College or university degree, no. (%)	2,396 (23.5)	158,136 (32.3)	< 0.001
Townsend deprivation index	–1.7 (4.8)	–2.2 (4.2)	< 0.001
BMI, median (IQR), kg/m^2	27.4 (6.6)	26.7 (5.7)	< 0.001
SBP, median (IQR), mmHg	138.0 (25.5)	136.5 (25.0)	< 0.001
DBP, median (IQR), mmHg	81.5 (13.5)	82.0 (13.5)	0.009
Total cholesterol, median (IQR), mmol/L	5.5 (2)	5.7 (2)	< 0.001
LDL-C, median (IQR), mmol/L	3.4 (1)	3.5 (1)	< 0.001
HbA1c, median (IQR), mmol/mol	35.5 (6)	35.2 (5)	< 0.001
CRP, median (IQR), mg/L	2.5 (5)	1.3 (2)	< 0.001
Current smoking, no. (%)	1,229 (12.1)	51,469 (10.5)	< 0.001
Current alcohol drinking, no. (%)	8,737 (85.7)	449,131 (91.8)	< 0.001
Moderate-vigorous activity, no. (%)	7,488 (73.4)	403,561 (82.5)	< 0.001
Hypertension, no. (%)	6,595 (64.7)	274,477 (56.1)	< 0.001
Diabetes, no. (%)	833 (8.2)	25,035 (5.1)	< 0.001
Coronary artery disease, no. (%)	701 (6.9)	17,493 (3.6)	< 0.001
AF or AFL, no. (%)	232 (2.3)	7,222 (1.5)	< 0.001
Chronic kidney failure, no. (%)	339 (3.3)	5,432 (1.1)	< 0.001
Blood pressure lowering medication, no. (%)	1,288 (12.6)	53,278 (10.9)	< 0.001
Cholesterol-lowering medication, no. (%)	1,089 (10.7)	49,638 (10.1)	0.080
Glucocorticoid and DMARDs, no. (%)	3,710 (36.4)	5,038 (1.0)	< 0.001

ARDs = autoimmune rheumatic diseases, AF and AFL = atrial fibrillation/atrial flutter, BMI = body mass index, CRP = C-reactive protein, DBP = diastolic blood pressure, DMARDs = disease-Modifying Antirheumatic Drugs, LDL-C = low-density lipoprotein cholesterol, SBP = systolic blood pressure.

Table 2

Incidence of HF in participants with and without ARDs.

	HF event				
	With ARDs		Without ARDs		
ARDs	*n*/*N*** (%)	Event rate per 1,000 person-years (95% CI)	*n*/*N*** (%)	Event rate per 1,000 person-years (95% CI)	HR* (95% CI)
RA	572/6,712 (8.5%)	6.4 (6.0–6.9)	17,842/489,327 (3.6%)	2.73 (2.70–2.78)	1.95 (1.82–2.08)
PsA or EA	31/395 (7.8%)	6.1 (4.2–8.7)	17,842/489,327 (3.6%)	2.73 (2.70–2.78)	1.85 (1.30–2.63)
SLE	52/750 (6.9%)	5.4 (4.0–7.1)	17,842/489,327 (3.6%)	2.73 (2.70–2.78)	2.56 (1.95–3.37)
SSc	26/215 (12.1%)	9.8 (6.6–14.6)	17,842/489,327 (3.6%)	2.73 (2.70–2.78)	4.38 (2.98–6.43)
AS	110/1,554 (7.1%)	5.4 (4.5–6.6)	17,842/489,327 (3.6%)	2.73 (2.70–2.78)	1.62 (1.34–1.96)
PMR	33/266 (12.4%)	10.2 (7.2–14.5)	17,842/489,327 (3.6%)	2.73 (2.70–2.78)	2.32 (1.65–3.27)
SV	64/636 (10.1%)	8.1 (6.3–10.4)	17,842/489,327 (3.6%)	2.73 (2.70–2.78)	2.31 (1.81–2.60)
SS	21/243 (8.6%)	6.9 (4.4–10.7)	17,842/489,327 (3.6%)	2.73 (2.70–2.78)	2.66 (1.73–4.08)

ARDs = autoimmune rheumatic diseases, AS = ankylosing spondylitis, HF = heart failure, PMR = polymyalgia rheumatica, PsA or EA = psoriatic or enteropathic arthropathies, RA = rheumatoid arthritis, SLE = systemic lupus erythematosus, SS = Sjogren syndrome, SSc = systemic sclerosis, SV = systemic vasculitis.
*Hazard ratios and 95% CIs were calculated using Cox proportional hazards models. Models were adjusted for age at baseline, gender, smoking status, BMI, Ethnic, and Townsend deprivation index. **n/N: number of patients who develop heart failure (n) out of the total number of patients (N) in each group.

Supplemental Digital Content, https://links.lww.com/CARES/A19), and considering the competing risk of death (Supplementary Table 7, Supplemental Digital Content, https://links.lww.com/CARES/A19). IPTW analysis yielded results similar to the main analysis (Supplementary Table 8, Supplemental Digital Content, https://links.lww.com/CARES/A19) with one exception: unlike in the main analysis, SS was not significantly associated with an increased risk of incident HF compared with control subjects (HR: 1.81; 95% CI: 0.74–4.42).

3.3. Characteristics of patients with ARDs and HF

Among the 21,410 patients diagnosed with HF, 1,920 had a history of ARDs either before or at the time of their HF diagnosis. Table 3 summarizes the characteristics of patients with HF with and without ARDs. Patients with HF and ARDs had a higher prevalence of rheumatic valvular disease, non-rheumatic aortic valve disease, and pulmonary heart disease before their HF diagnosis ($P < 0.05$). In contrast, the prevalence of CAD, AF/AFL, and hypertensive heart disease was similar between the two groups.

Figure 2 illustrates the prevalence of HF-related comorbidities among patients with different ARDs. CAD and AF/AFL were the most common comorbidities among patients with different ARDs, affecting approximately half and 40% of patients, respectively. Valvular disease (both rheumatic and non-rheumatic) followed, with a prevalence of about 20%, after CAD and AF/AFL. Hypertensive heart disease, cardiomyopathy, and pulmonary heart disease were less common. Notably, in patients with SSc and HF, pulmonary heart disease was the most prevalent comorbidity, affecting 40.7% of this group. Supplementary Table 9, Supplemental Digital Content, https://links.lww.com/CARES/A19 compared the comorbidities in patients with HF and ARDs versus those without ARDs.

3.4. Mortality and rehospitalization for HF in patients with ARDs and HF

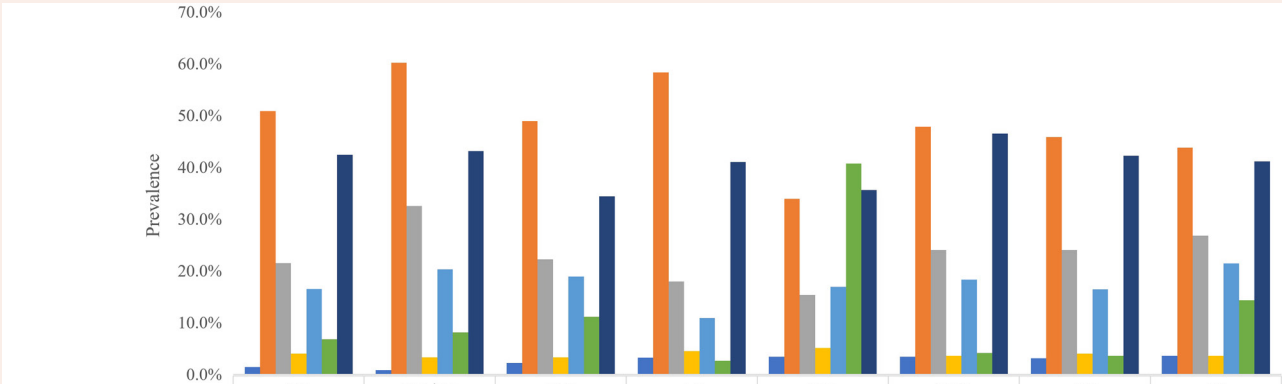
During a median follow-up of 3.3 years (IQR 0.9–7.7) after HF diagnosis, 853 patients with ARDs (44.4%) and 7,491 patients without ARDs (38.4%) died. After adjusting for potential confounding factors, a history of ARDs

Table 3

Characteristics of heart failure patients with and without ARDs.

	With ARDs *n* = 1,920	Without ARDs *n* = 19,490	*P*
Age at HF diagnosis, median (IQR), year	72.8 (9.6)	70.3 (11.7)	< 0.001
Female, no. (%)	1,035 (53.9)	6,725 (34.5)	< 0.001
Hypertensive heart disease, no. (%)	40 (2.1)	442 (2.3)	0.602
Coronary artery disease, no. (%)	962 (50.1)	9,944 (51.0)	0.443
Rheumatic valve disorders, no. (%)	319 (16.6)	2,736 (14.0)	0.002
Non-rheumatic valve disorders, no. (%)	429 (22.3)	3,897 (20.0)	0.014
Non-rheumatic mitral valve disorders, no. (%)	185 (9.6)	1,964 (10.1)	0.540
Non-rheumatic aortic valve disorders, no. (%)	241 (12.6)	1,870 (9.6)	< 0.001
Cardiomyopathy, no. (%)	79 (4.1)	1,185 (6.1)	< 0.001
Pulmonary heart diseases, no. (%)	134 (7.0)	905 (4.6)	< 0.001
Atrial fibrillation/flutter, no. (%)	817 (42.6)	8,249 (42.3)	0.851

ARDs = autoimmune rheumatic diseases, HF = heart failure.



	RA	PsA/EA	SLE	AS	SSc	PMR	SV	SS
Hypertensive heart disease	1.4%	0.8%	2.2%	3.2%	3.4%	3.4%	3.1%	3.6%
Coronary artery disease	50.8%	60.2%	48.9%	58.3%	33.9%	47.8%	45.8%	43.8%
Nonrheumatic valve disorders	21.5%	32.5%	22.2%	17.9%	15.3%	24.0%	24.0%	26.8%
Cardiomyopathy	4.0%	3.3%	3.3%	4.5%	5.1%	3.6%	4.0%	3.6%
Rheumatic valve disorders	16.5%	20.3%	18.9%	10.9%	16.9%	18.3%	16.4%	21.4%
Pulmonary heart diseases	6.8%	8.1%	11.1%	2.6%	40.7%	4.1%	3.6%	14.3%
Atrial Fibrillation/Flutter	42.4%	43.1%	34.4%	41.0%	35.6%	46.5%	42.2%	41.1%

Figure 2. Prevalence of HF-related comorbidities in patients with HF and different ARDs. ARDs = autoimmune rheumatic diseases, AS = ankylosing spondylitis, HF = heart failure, PMR = polymyalgia rheumatica, PsA or EA = psoriatic or enteropathic arthropathies, RA = rheumatoid arthritis, SLE = systemic lupus erythematosus, SS = Sjogren syndrome, SSc = systemic sclerosis, SV = systemic vasculitis.

was associated with an increased risk of all-cause mortality after HF diagnosis (125.6/1,000 patient-years vs. 71.0/1,000 patient-years, HR: 1.32; 95% CI: 1.23–1.42). Regarding the cause of death, ARDs were linked to both a higher risk of non-cardiovascular death (HR: 1.42; 95% CI: 1.30–1.56; $P < 0.001$) and cardiovascular death (HR: 1.17; 95% CI: 1.03–1.32; $P = 0.02$) (Fig. 3).

Among ARDs with over 100 cases and more than 10 reported deaths, RA (HR: 1.36; 95% CI: 1.24–1.49; $P < 0.001$), SV (HR: 1.39; 95% CI: 1.15–1.70; $P = 0.001$), and SS (HR: 1.48; 95% CI: 1.10–1.99; $P = 0.010$) were associated with a higher risk of all-cause death, whereas AS, PMR, and PsA or EA were not associated with an increased risk of all-cause death (Supplementary Table 10, Supplemental Digital Content, https://links.lww.com/CARES/A19).

After a median follow-up of 2.8 years (IQR: 0.8–5.5), 233 patients with ARDs (12.4%) and 2,381 patients without ARDs (12.5%) were re-hospitalized for HF. A history of ARDs was not associated with an increased risk of HF rehospitalization (HR: 1.02; 95% CI: 0.87–1.15; $P = 0.88$) after diagnosis of HF.

4. Discussion

In this long-term cohort study with approximately 13 years of follow-up, we identified three major findings. First, several ARDs were associated with an elevated risk of HF. SSc was associated with the highest risk of HF, followed by SS. Second, unlike other HF patients, those with ARDs and HF had a higher prevalence of valvular disease and pulmonary heart disease before HF diagnosis. In

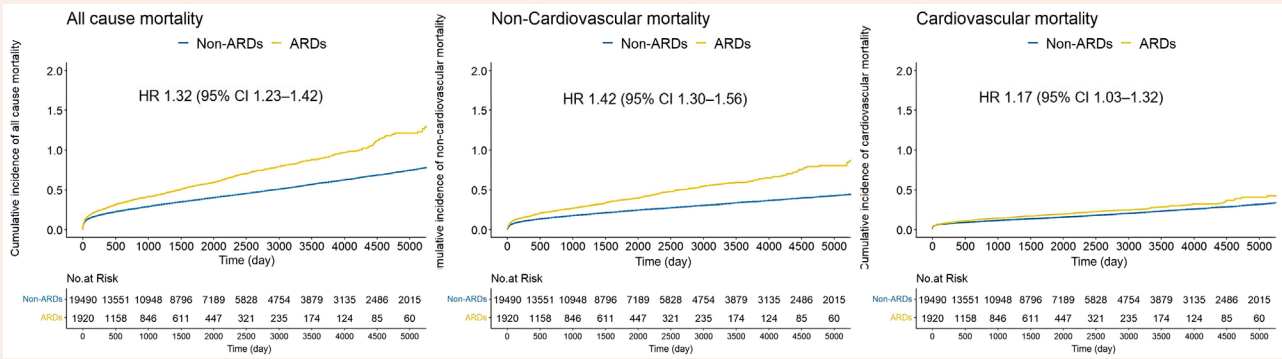


Figure 3. Risk of mortality in HF patients with and without ARDs. Hazard ratios and 95% CIs were calculated using Cox proportional hazards models. Models were adjusted for age at HF diagnosis, gender. ARDs = autoimmune rheumatic diseases, HF = heart failure.

contrast, the prevalence of CAD, hypertensive heart disease, and AF/AFL remained comparable to that of other HF patients. Third, HF patients with a history of ARDs had a higher risk of all-cause mortality compared with those without ARDs. This increased risk was predominantly attributable to non-cardiovascular mortality.

Previous studies have primarily examined the correlation between specific ARDs and HF in isolation, with limited research exploring the relationship between multiple ARDs and HF. The largest study to date, which included 446,449 patients with ARDs, found a general association between ARDs and an increased risk of HF (HR: 1.72; 95% CI: 1.65–1.80).[15] However, this study did not assess the risk of HF associated with specific ARDs, leaving unclear whether HF risk varies among different autoimmune conditions. In this study, we found that patients with SSc exhibited the highest relative risk of developing HF, with a 4.38-fold increased risk compared with individuals without ARDs. Consistent with our study, a single-center study involving 18,278 patients with chronic inflammatory diseases also reported that patients with SSc (HR: 7.26; 95% CI: 5.72–9.21; $P < 0.01$) had the highest risk of developing HF compared with matched patients without chronic inflammatory diseases.[16] SSc is an autoimmune-mediated connective tissue disease resulting from excessive accumulation of collagens and small artery vasculitis. The prevalence of cardiac involvement in SSc is estimated to be approximately 15% and is associated with poor survival.[26] Besides, a considerable risk of HF was observed for Sjögren syndrome, second only to SSc. It was traditionally thought that while systemic manifestations occur in about 30% of patients with SS, cardiovascular involvement is rare.[27] However, a growing body of research suggests potential cardiac involvement in association with SS. Limited studies have specifically evaluated the correlation between SS and HF with conflicting results. One study of 5,092 patients with primary SS found that those with primary SS had a higher risk of developing HF (HR: 1.42; 95% CI: 1.20–1.68).[11] Conversely, another cohort study of 16,466 patients found no significant difference in HF-related hospitalization rates compared with individuals without SS (HR: 0.98; 95% CI: 0.84–1.14).[14] These inconsistencies may be attributed to variations in the definitions of outcome events. Given the elevated risk of developing HF, our findings support early HF screening in patients with ARDs, particularly for those diagnosed with SSc or SS.

The development of HF in patients with ARDs may involve several distinct mechanisms. Chronic inflammation, along with glucocorticoids, can accelerate coronary atherosclerosis, contributing to ischemic heart disease. Furthermore, extra-cardiac involvement of ARDs—such as the kidneys and lungs—may indirectly promote HF. Additionally, ARDs may directly affect cardiac structures, including the myocardium, valves, and conduction system, thereby driving HF progression.[21,28] In this study, there are several notable observations about the potential mechanisms underlying the development of HF. First, the prevalence of CAD and hypertensive heart disease was similar among patients with HF, regardless of ARDs status. This aligns with previous research indicating that patients with HF associated with DM/PM,[21] SSc,[10] SS,[11] and SLE[7] have a comparable or even lower prevalence of ischemic heart disease than other HF patients. Traditionally, the elevated incidence of cardiovascular events in patients with ARDs has been largely attributed to accelerated atherosclerosis. Our findings, however, suggest that the development of HF in this population is only partially explained by traditional risk factors, which indicates that other pathophysiological mechanisms may be involved. Notably, our study identified a higher prevalence of valvular disease and pulmonary vascular disease in HF patients with ARDs compared with those without. This suggests that valvular and pulmonary vascular involvement may play a significant role in HF development among ARDs patients. Valvular manifestations are common among patients with ARDs, particularly in patients with RA, SLE, APS, or AS.[29] Various ARDs can directly or indirectly affect the valves, especially the aortic valve.[30] Besides, it is noteworthy that pulmonary vascular diseases were the most common comorbidities in patients with both HF and SSc, affecting approximately 40% of this population. Pulmonary hypertension is a frequent systemic manifestation in SSc patients and is associated with poor outcomes. Prior research has highlighted a notably higher incidence of right HF (31%) among patients with HF and SSc compared with those with HF and other chronic inflammatory diseases.[16] Though speculative, findings from our study, along with prior research, point to pulmonary hypertension as a principal driver in the pathogenesis of HF in patients with SSc. Greater attention should be given to the prevention and management of pulmonary hypertension in SSc patients.

Few cohort studies have investigated the mortality risk among patients with ARDs and HF. A history of SSc (HR: 2.16; 95% CI: 1.54–3.03)[10] and RA (HR: 1.89; 95% CI: 1.26–2.84)[31] was associated with elevated all-cause mortality in HF patients. Conversely, patients with SS exhibited comparable all-cause mortality rates after HF diagnosis to those without SS (HR: 0.94; 95% CI: 0.74–1.19).[11] Consistent with previous studies, our findings indicate that patients with ARDs and HF experience a higher risk of all-cause death. Moreover, our study revealed that patients with ARDs and HF face a higher risk of non-cardiovascular mortality rather than cardiovascular mortality. The increased non-cardiovascular mortality observed in ARD patients with HF may be linked to the following aspects. First, as systemic disorders, ARDs often lead to multiorgan damage (e.g., renal or pulmonary impairment), which can contribute directly to fatal non-cardiac outcomes. Second, immunosuppressive therapies such as glucocorticoids and disease-modifying agents may increase susceptibility to severe infections and malignancies, further elevating non-cardiovascular mortality. This finding highlights the necessity for multiorgan protection and optimization of medication use in managing ARDs. Our study also found that a history of ARDs was not

associated with an increased risk of HF rehospitalization, which is consistent with findings from another study involving HF patients with autoimmune diseases.[32] The lack of a significant increase in HF rehospitalization risk may be attributable to two potential explanations. First, once HF develops, the severity of HF in patients with concurrent ARDs may be similar to that in other HF patients. Second, some studies have indicated that patients with RA face a higher all-cause rehospitalization risk after HF diagnosis, primarily driven by elevated non-cardiovascular hospitalization rates.[33] The competing high risk of non-cardiovascular hospitalizations in ARDs patients may lead to an underestimation of HF rehospitalization risk, thus complicating the interpretation of the results. Additionally, recent research has observed an association between autoimmune disorders and a higher HF rehospitalization risk in HFpEF patients.[34] Whether the relationship between ARDs and HF rehospitalization differs across HF subtypes (HFrEF vs. HFpEF) requires further investigation.

Several limitations of this study warrant acknowledgment. First, due to its observational nature, the study cannot establish causal relationships between ARDs and HF. Second, the absence of detailed clinical data, such as medical history, echocardiography results, natriuretic peptide levels, and cardiac magnetic resonance imaging, precludes a thorough investigation of the specific causes of HF in patients with and without ARDs. Additionally, we were unable to evaluate differences in ejection fraction between HF patients with ARDs and those without. Third, although we adjusted for potential confounders in the Cox models and conducted sensitivity analyses to confirm the robustness of the findings, residual confounding due to unmeasured factors remains possible. Furthermore, due to the incomplete data on drug usage, we cannot adjust all drugs that might potentially affect the occurrence of HF. Fourth, because the number of patients with some types of ARDs is relatively small, there may be bias when assessing the prognosis of HF patients with specific types of ARDs. Therefore, the results should be interpreted with caution as they are considered exploratory.

5. Conclusions

In this cohort study, we found that several ARDs were associated with elevated risks of HF, with the highest relative risks observed for SSc and SS. Unlike other HF patients, those with HF and ARDs had a higher prevalence of valvular disease and pulmonary vascular disease before HF diagnosis, while the prevalence of CAD, hypertensive heart disease, and AF/AFL was similar. Among patients with incident HF, a history of ARDs was linked to increased all-cause mortality, particularly non-cardiovascular mortality. Further research is needed to elucidate the underlying pathophysiological mechanisms of HF in this population to enhance prevention strategies.

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Ethical statements

The UK Biobank study was approved by the North West Multicentre Research Ethics Committee (reference 11/NW/0382) and conducted in accordance with the principles of the Declaration of Helsinki. All participants provided written informed consent to participate in the UK Biobank study. This study was approved by the Institutional Review Board (IRB) of Beijing Anzhen Hospital (Approval No. 2025227X). This study was conducted in accordance with the Declaration of Helsinki.

Conflict of interest

The authors have no conflicts of interest to disclose.

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Data availability statement

The datasets generated during and analyzed during the current study are available in the UKbiobank .

Author contributions

Had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis: Xin Du.

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Drafting of the manuscript: Chang Hua and Xin Du.

Critical revision of the manuscript for important intellectual content: Zhiyan Wang and Xin Du.

Statistical analysis: Chang Hua.

Obtained funding: Xin Du.

Supervision: Qiang Lv, Xin Du, Jianzeng Dong, Changsheng Ma.

AI statement

No generative AI or AI-assisted technologies or systems were used in the preparation of this manuscript. All authors confirm that they take full responsibility for the accuracy, integrity, and originality of the content.

References

[1] Wang B, Liu J, Zhao L. Association of congestive heart failure with mortality in individuals with rheumatoid arthritis: a cohort study. *Clin Rheumatol*. 2024;43:1287–97.

[2] Nicola PJ, Crowson CS, Maradit-Kremers H, et al. Contribution of congestive heart failure and ischemic heart

disease to excess mortality in rheumatoid arthritis. *Arthritis Rheum*. 2006;54:60–7.
[3] Pinheiro FA, Souza DC, Sato EI. A study of multiple causes of death in rheumatoid arthritis. *J Rheumatol*. 2015;42:2221–8.
[4] Mantel A, Holmqvist M, Andersson DC, Lund LH, Askling J. Association between rheumatoid arthritis and risk of ischemic and nonischemic heart failure. *J Am Coll Cardiol*. 2017;69:1275–85.
[5] Logstrup BB, Ellingsen T, Pedersen AB, et al. Development of heart failure in patients with rheumatoid arthritis: a Danish population-based study. *Eur J Clin Invest*. 2018;48:e12915.
[6] Ahlers MJ, Lowery BD, Farber-Eger E, et al. Heart failure risk associated with rheumatoid arthritis-related chronic inflammation. *J Am Heart Assoc*. 2020;9:e014661.
[7] Yafasova A, Fosbol EL, Schou M, et al. Long-term cardiovascular outcomes in systemic lupus erythematosus. *J Am Coll Cardiol*. 2021;77:1717–27.
[8] Kim CH, Al-Kindi SG, Jandali B, Askari AD, Zacharias M, Oliveira GH. Incidence and risk of heart failure in systemic lupus erythematosus. *Heart*. 2017;103:227–33.
[9] Lin CY, Chen HA, Chang TW, Hsu TC, Su YJ. Association of systemic sclerosis with incident clinically evident heart failure. *Arthritis Care Res (Hoboken)*. 2023;75:1452–61.
[10] Sun G, Yafasova A, Andersson C, et al. Gender- and age-specific rates of heart failure and other adverse cardiovascular outcomes in systemic sclerosis. *Rheumatology (Oxford)*. 2022;61:4374–83.
[11] Sun G, Fosbol EL, Yafasova A, et al. Long-term risk of heart failure and other adverse cardiovascular outcomes in primary Sjogren's syndrome. *J Intern Med*. 2023;293:457–69.
[12] Sun G, Yafasova A, Baslund B, et al. Long-term risk of heart failure and other adverse cardiovascular outcomes in granulomatosis with polyangiitis: a nationwide cohort study. *J Rheumatol*. 2022;49:291–8.
[13] Nygaard L, Polcwiartek C, Nelveg-Kristensen KE, et al. Long-term cardiovascular outcomes and temporal trends in patients diagnosed with ANCA-associated vasculitis: a Danish nationwide registry study. *Rheumatology (Oxford)*. 2023;62:735–46.
[14] Lin CY, Chen HA, Chang TW, Hsu TC, Hsu CY, Su YJ. Association of primary Sjogren's syndrome with incident heart failure: a secondary analysis of health claims data in Taiwan. *Ther Adv Chronic Dis*. 2022;13:20406223221078083.
[15] Conrad N, Verbeke G, Molenberghs G, et al. Autoimmune diseases and cardiovascular risk: a population-based study on 19 autoimmune diseases and 12 cardiovascular diseases in 22 million individuals in the UK. *Lancet*. 2022;400:733–43.
[16] Prasada S, Rivera A, Nishtala A, et al. Differential associations of chronic inflammatory diseases with incident heart failure. *JACC Heart Fail*. 2020;8:489–98.
[17] Zagouras AA, Tang WHW. Myocardial involvement in systemic autoimmune rheumatic diseases. *Rheum Dis Clin North Am*. 2023;49:45–66.
[18] Moysidou G-S, Dara A, Arvanitaki A, et al. Understanding and managing cardiac involvement in systemic sclerosis. *Expert Rev Clin Immunol*. 2023;19:293–304.
[19] Sudlow C, Gallacher J, Allen N, et al. UK Biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med*. 2015;12:e1001779.
[20] Moutsopoulos HM. Autoimmune rheumatic diseases: one or many diseases? *J Transl Autoimmun*. 2021;4:100129.
[21] Goldblatt F, O'Neill SG. Clinical aspects of autoimmune rheumatic diseases. *Lancet*. 2013;382:797–808.
[22] Mavrogeni SI, Sfikakis PP, Koutsogeorgopoulou L, et al. Cardiac tissue characterization and imaging in autoimmune rheumatic diseases. *JACC Cardiovasc Imaging*. 2017;10:1387–96.
[23] He MM, Lo CH, Wang K, et al. Immune-mediated diseases associated with cancer risks. *JAMA Oncol*. 2022;8:209–19.
[24] Yu Y, Sun Y, Wang Y, et al. Immune-mediated diseases and risk of incident cardiovascular diseases: a prospective cohort study. *Rheumatology (Oxford)*. 2024;63:706–14.
[25] McDonagh TA, Metra M, Adamo M, et al.; ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2021;42:3599–726.
[26] Muangchan C, Baron M, Pope J; Canadian Scleroderma Research Group. The 15% rule in scleroderma: the frequency of severe organ complications in systemic sclerosis. a systematic review. *J Rheumatol*. 2013;40:1545–56.
[27] Maleki-Fischbach M, Kastsianok L, Koslow M, Chan ED. Manifestations and management of Sjogren's disease. *Arthritis Res Ther*. 2024;26:43.
[28] Wright K, Crowson CS, Gabriel SE. Cardiovascular comorbidity in rheumatic diseases: a focus on heart failure. *Heart Fail Clin*. 2014;10:339–52.
[29] Lee KS, Kronbichler A, Eisenhut M, Lee KH, Shin JI. Cardiovascular involvement in systemic rheumatic diseases: an integrated view for the treating physicians. *Autoimmun Rev*. 2018;17:201–14.
[30] Grygiel-Gorniak B, Oduah MT, Olagunju A, Klokner M. Disorders of the aorta and aortic valve in connective tissue diseases. *Curr Cardiol Rep*. 2020;22:70.
[31] Davis JM, Roger VL, Crowson CS, et al. The presentation and outcome of heart failure in patients with rheumatoid arthritis differs from that in the general population. *Arthritis Rheum*. 2008;58:2603–11.
[32] Sun G, Faurschou M, Vinding NE, et al. Mortality in heart failure with and without autoimmune disease. *Eur J Prev Cardiol*. 2023;30:1308–14.
[33] Myasoedova E, Davis JM, Matteson EL, et al. Increased hospitalization rates following heart failure diagnosis in rheumatoid arthritis as compared to the general population. *Semin Arthritis Rheum*. 2020;50:25–9.
[34] Tada A, Doi S, Harada T, et al. Autoimmune disorders in heart failure with preserved ejection fraction. *JACC Heart Fail*. 2024;12:1257–69.