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Priority Paper Evaluation
Future Rheumatology

Heart failure in patients with rheumatoid arthritis is clinically different and has a worse prognosis

Mario H Cardiel†
†Author for correspondence: Research Unit. Hospital General "Dr. Miguel Silva". Isidro Huarte y Samuel Ramos S/N. Col. Centro. CP 58000. Morelia, Mich, Mexico ■ Tel.: +52 443 313 9552 ■ Fax: +52 443 299 3231 ■ mhcardiel@hotmail.com

Evaluation of: Davis JM III, Roger VL, Crowson CS, Maradit Kremers H, Therneau TM, Gabriel SE: The presentation and outcome of heart failure in patients with rheumatoid arthritis differs from that in the general population. *Arthritis Rheum.* 58, 2603–2611 (2008). A community-based cohort study was undertaken in Olmsted County, Minnesota, USA, from 1979 to 2000 to compare the clinical presentation, management and outcome of incident heart failure in patients with rheumatoid arthritis (RA) compared with non-RA patients. This paper by Davis et al. studied 103 patients with RA and 852 non-RA patients who were compared with age- and sex-adjusted rates and multivariable logistic regresion models to evaluate clinical features and mortality. Patients with RA were more often female and had less frequency of obesity, hypertension and ischemic heart disease. Patients with RA had fewer typical symptoms of heart failure and were less likely to have undergone echocardiography. Patients with RA were more likely to have preserved ejection fraction. Mortality at 1 year was higher in RA patients (35 vs 19%; multivariable hazard ratio: 1.89; 95% confidence interval: 1.26–2.84). These findings support a more subtle clinical presentation, but increased mortality from heart failure in RA patients.

Methods

This community-based study was conducted in adult residents of Olmsted County, Minnesota, USA [1]. Only incident cases with clearly defined Framingham criteria for heart failure were included during the period from January 1, 1979 to January 1, 2000. Rheumatoid arthritis (RA) patients were obtained from an established population-based incidence cohort of 603 patients with RA, while non-RA patients were identified from the same community using the resources of an ongoing investigation project on heart failure. Medical records were abstracted by trained and blinded assessors. Data on diabetes, hypertension, dyslipidemia and ischemic heart diseases were gathered in all cases. Clinical data on presentation looked at Framingham criteria on heart failure. Data on echocardiography within 90 days of the onset of heart failure were reviewed. Current recommendations of the American Society of Echocardiography were used to define variables. A preserved ejection fraction was considered if the value was 50% or greater. Data on treatment were obtained from medical records from diagnosis to 60 days following the diagnosis of heart failure. Mortality data were derived from medical records, death certificates and state and national death indexes. Comparison of both cohorts was carried out using parametric and non-parametric tests. Logistic regression models were used to determine the likelihood of having a preserved ejection fraction in patients with RA in models adjusted for age, sex, calendar year and the likelihood of having undergone echocardiography.

Results

In total, 103 RA patients with heart failure were compared with 852 non-RA patients. As expected, the RA patient group had a higher proportion of female subjects (70 vs 54%; $p < 0.001$). Patients with RA were less likely to have a history of ischemic heart disease (24 vs 35%; $p = 0.02$, adjusted for age and sex), hypertension (60 vs 71%; $p = 0.03$) and obesity (10 vs 23%; $p = 0.002$). Clinical presentation differed in both groups. RA patients with heart failure were less likely to present with paroxysmal nocturnal dyspnea (odds ratio [OR]: 0.62; 95% confidence interval [CI]: 0.35–1.10); hepatojugular reflux (OR: 0.50; 95% CI: 0.26–0.96); dyspnea on exertion (OR: 0.64; 95% CI: 0.41–1.01) and orthopnea (OR: 0.53; 95% CI: 0.32–0.87). RA patients with heart failure were more likely to have rales (OR: 2.24; 95% CI: 1.04–4.81) and less likely to present with

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elevated systolic blood pressure (OR: 0.58; 95% CI: 0.38–0.89) or elevated diastolic blood pressure (OR: 0.34; 95% CI: 0.19–0.60).

In total, 47% of RA patients and 58% of non-RA patients underwent an echocardiography. A total of 79% were performed at the time of heart failure diagnosis. Patients with RA were 33% less likely to undergo this test. The mean ejection fraction was significantly higher in RA patients (50 vs 43%, p = 0.007). The proportion of patients with preserved ejection fraction (>50%) was higher in RA patients (58 vs 41%, p = 0.02). After adjustment for several variables, RA patients were almost twice as likely to have preserved ejection fraction (OR: 1.90; 95% CI: 0.98–3.67). Patients with RA and heart failure were less likely to receive ACE inhibitors (15 vs 30%) and β-blockers (10 vs 23%).

Mortality 30 days after heart failure onset was higher in RA patients (15.5 vs 6.6%, p = 0.001). This was similar at 1 year (35 vs 19.3%, p = 0.01). After adjustment for age, sex and calendar year, the risk of death in RA patients remained higher at 30 days (hazard ratio [HR]: 2.39; 95% CI: 1.36–4.18) and 1 year (adjusted HR: 2.02; 95% CI: 1.40–2.90). This excess in 1-year mortality was similar after adjusting for cardiovascular medications and ischemic heart disease (HR: 1.89; 95% CI: 1.26–2.84).

Discussion

This important paper clearly defines that patients with RA with heart failure had a different clinical presentation with less symptoms and signs than non-RA subjects [1]. They were also less likely to have undergone an echocardiography evaluation. These RA subjects were treated differently to the non-RA subjects – they received ACE inhibitors and β-blocker agents less frequently. Echocardiographic findings were different in RA patients. They were more likely to have preserved ejection fraction. Mortality was increased in RA patients at 30 days and 1 year, even after adjusting for important variables.

Authors support the idea that this preserved ejection fraction can be taken as a surrogate of diastolic dysfunction in RA. They postulate that this echocardiographic finding is consistent with multiple echocardiographic studies carried out in a small number of RA patients that provided similar results [2–4]. They speculate that heart failure in RA might have a mechanism in which diastolic dysfunction can be a possible explanation [5]. They describe immunologic pathways that could lead to myocardial fibrosis and diastolic dysfunction, such as that described in animal models [6].

Future perspective

This paper is relevant, since it provides evidence of a different clinical presentation, echocardiographic findings, treatment and outcome of heart failure in RA patients. Diastolic dysfunction is presented as the most likely explanation for these results. Important physiopathogenic mechanisms should be elucidated to try to improve this important cause of mortality in RA patients. Prospective clinical and ecocardiographic evaluations in RA cohorts are urgently needed to dissect the importance of the disease itself, the treatments currently in use (particularly important NSAIDs, steroids and anti-TNF-α blockers) [7,8], disease duration, disease activity, comorbid conditions such as hypertension, obesity, diabetes, hyperlipidemia on heart failure, and the poor outcome it carries in RA patients [9].

Rheumatologists should be fully aware that heart failure is an important comorbid situation in RA patients. The near future will be awaiting some clarifications on the mechanistic pathways that lead to a better understanding of diastolic dysfunction in RA. This information is needed by clinicians, who should try to implement preventive and therapeutic strategies while treating these patients.

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Executive summary

- Davis *et al.* present a unique community-based cohort study on incident cases of heart failure in rheumatoid arthritis (RA) patients and compare clinical features, diagnosis, treatment and outcome with non-RA patients.
- Patients with RA and heart failure have a more subtle clinical presentation, were less likely to have an echocardiography study, were more likely to have preserved ejection fraction, were treated differently and had greater mortality, at 30 days and 1 year.
- Diastolic dysfunction in RA is presented as the most likely explanation of these findings, and the possible mechanisms of disease are speculated.

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Papers of special note have been highlighted as:
- ▪ of interest
- ▪▪ of considerable interest

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▪▪ **Outstanding paper reporting on a community-based study that clearly describes differences in clinical presentation, echocardiographic findings, treatment and outcome of heart failure in rheumatoid arthritis (RA) patients compared with non-RA patients.**

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Affiliation

- Mario H Cardiel, MD, MSc
Research Unit. Hospital General 'Dr Miguel Silva'. Isidro Huarte y Samuel Ramos S/N, Col. Centro, CP 58000, Morelia, Mich, Mexico
Tel.: +52 443 313 9552
Fax: +52 443 299 3231
mhcardiel@hotmail.com