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The Presentation and Outcome of Heart Failure in Persons with Rheumatoid Arthritis Differs from that of the General Population

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Abstract

Objective—To compare the clinical presentation, management, and outcome of heart failure in subjects with rheumatoid arthritis (RA) compared to subjects without RA.

Methods—We conducted a community-based cohort study in the setting of Olmsted County, Minnesota, 1979 - 2000. 103 RA subjects and 852 non-RA subjects with incident heart failure (physician diagnosed and Framingham criteria validated) were compared. Age- and gender-adjusted rates/frequencies and multivariable logistic regression models were used to compare the heart failure clinical features and mortality following the onset of heart failure between the groups.

Results—The RA subjects were more often female and less frequently had obesity, hypertension, and ischemic heart disease. RA subjects with heart failure had fewer typical symptoms and signs and were less likely to undergo echocardiography compared to non-RA subjects. After adjusting for differences, the RA subjects with heart failure were more likely to have preserved ejection fraction ($\geq 50\%$). RA subjects experienced higher mortality at one year following heart failure (35% vs. 19%; multivariable HR: 1.89, 95% CI: 1.26, 2.84).

Conclusions—Both the clinical presentation and the outcome of heart failure differ significantly between RA and non-RA subjects from the same population. Among RA subjects, the presentation of heart failure is more subtle, myocardial function is more likely preserved, while mortality from heart failure is significantly higher. These findings emphasize the importance of more vigilant screening of RA patients for early signs of heart failure and may represent important insights into the biological mechanisms underlying heart failure in patients with RA.

Keywords

rheumatoid arthritis; heart disease; epidemiology

INTRODUCTION

In recent years, the medical community has become increasingly aware of the higher rate of heart failure suffered by patients with rheumatoid arthritis (RA), and of the profound impact of this comorbidity on mortality (1-3). Among individuals 65 years and older in the general population, heart failure occurs at a rate of nearly 10 per 1000 individuals and is responsible for approximately 20% of all hospitalizations (4). The burden of heart failure is even greater

among RA patients (2,5,6), with a 2-fold higher incidence of heart failure for patients with RA compared to members of the general population (2). Indeed, heart failure is a major contributor to mortality for patients with RA (3).

Higher mortality following a first myocardial infarction or stroke has been reported for RA patients compared to members of the general population (7). However, little is known regarding the comparative case fatality associated with heart failure for RA patients compared to other community-dwelling patients. Moreover, it remains unclear whether RA is an independent risk factor for mortality following onset of heart failure. These data are necessary to clarify our understanding of why RA subjects experience increased mortality, and to devise strategies for improving the survival of patients with this chronic disease.

Furthermore, knowledge of the pathophysiology of heart failure among RA patients, and how this differs compared to patients without this condition, is critical to develop new treatments. Structural and functional alterations of the myocardium have been reported in numerous controlled, cross-sectional studies of RA subjects without known cardiovascular disease, suggesting impairment of diastolic function (8-17). These findings indicate that, compared to non-RA subjects, heart failure in RA may be more often related to diastolic dysfunction in comparison to the general population. To date, no studies have assessed myocardial function at the onset of heart failure for RA patients. This is an important question because the management of heart failure may differ depending on the etiology of myocardial dysfunction.

Similarly, little is known regarding the clinical presentation of heart failure among RA patients compared to the general population. For example, RA patients may manifest less dyspnea on exertion due to the debility resulting from chronic arthritis. Information on presentation is paramount to better understand factors that affect patient diagnosis, management, and the long-term outcome of heart failure.

Therefore, we conducted a population-based study of RA and non-RA subjects from the same underlying population with a first diagnosis of heart failure, to test the hypotheses that: 1) the clinical presentation of heart failure in subjects with RA differs from that of non-RA subjects; 2) RA subjects have a higher frequency of heart failure with preserved ejection fraction as compared to non-RA subjects; and, 3) RA subjects experience a higher risk of death following onset of heart failure compared to non-RA subjects.

PATIENTS AND METHODS

Study design and populations

We conducted a community-based study of all adult (age ≥ 18 years) residents of Olmsted County, Minnesota with incident heart failure—including a cohort of RA subjects as well as a cohort of subjects from the same population with no history of RA (non-RA). We used the resources of the Rochester Epidemiology Project (18), a population-based medical records linkage system, to review the complete inpatient and outpatient medical records of all subjects from all community providers, including Mayo Medical Center, Olmsted Medical Center, local nursing homes, and the few remaining community providers. The institutional review boards of the Mayo Foundation and the Olmsted Medical Center approved this study.

The RA heart failure cohort included all subjects with a first episode of heart failure identified during the period January 1, 1979 to January 1, 2000, from among an established population-based incidence cohort of 603 RA subjects (2). RA was defined by the 1987 American College of Rheumatology criteria (19). The non-RA heart failure cohort included all subjects with a first episode of heart failure identified from among a population-based

cohort of subjects from the community with incident heart failure during the same time period (January 1, 1979 to January 1, 2000) using the resources of an ongoing epidemiologic investigation of heart failure in Olmsted County, Minnesota, after excluding all subjects with RA (20,21). In both cohorts, the first episode of heart failure, ascertained by review of the complete inpatient and outpatient medical records, was defined as the date each subject first fulfilled the Framingham criteria (2 major or 1 major and 2 minor criteria) (22). Twenty-eight patients with heart failure prior to the occurrence of RA were excluded. Trained abstractors reviewed the records, blinded to the present study hypotheses.

Data collection and definitions

Diabetes mellitus was defined according to the diagnostic criteria adopted by the World Health Organization consultation group in 1998 and included physicians' diagnoses (23). Hypertension was defined by a recorded physician diagnosis or use of antihypertensive agents. Dyslipidemia was defined by a recorded physician diagnosis or use of anti-lipid agents. Ischemic heart disease included previous myocardial infarction (hospitalized or silent) and coronary revascularization procedures (i.e. coronary artery bypass surgery and percutaneous coronary interventions).

Data regarding the clinical presentation of heart failure were collected for all subjects based on the Framingham criteria (22). The following features were considered present if documented in the medical record during the first episode of heart failure: paroxysmal nocturnal dyspnea, engorged jugular veins, rales, cardiomegaly, acute pulmonary edema, S3 gallop, hepatojugular reflux, swollen extremities, cough, dyspnea on exertion, hepatomegaly, pleural effusion on chest x-ray, tachycardia (heart rate ≥ 120 beats per minute), and orthopnea.

Echocardiography data obtained within 90 days of the onset of heart failure were collected retrospectively using the resources of a longitudinal registry of all echocardiograms performed at Mayo Clinic Rochester since 1979 (24). Echocardiography variables were defined in accordance with current recommendations of the American Society of Echocardiography (25). Ejection fraction was measured by M-mode, 2-dimensional, or semi-quantitative estimate, and the average of these values was used when more than one measure was available. Preserved ejection fraction was defined as $\geq 50\%$ (26).

Information on use of heart failure medications (angiotensin converting enzyme [ACE] inhibitors and beta blockers) was abstracted from the medical records beginning at the time of diagnosis until 60 days following the diagnosis of heart failure.

Mortality data were derived from the medical record, death certificates, and the state and national death indexes.

Statistical methods

The distributions of patient characteristics at the onset of heart failure were described. Differences between the two cohorts were tested using the chi square test for categorical variables and the t-test for continuous variables. Wilcoxon rank sum tests were used to compare the mean ejection fraction between the cohorts. The age and sex distributions of the non-RA cohort were adjusted to the age and sex distributions of the RA cohort to facilitate comparison.

Logistic regression models were used to determine the likelihood of having a preserved ejection fraction (defined as $\geq 50\%$) for the RA compared to non-RA cohorts. Models were adjusted for age, gender, calendar year, as well as the likelihood of having had an echocardiogram. To adjust for the latter, the probability of receiving an echocardiogram was

determined using a logistic regression model containing all available covariates. The analyses of the main effects were stratified by quintiles of the resulting probability variable.

Kaplan-Meier methods were used to examine the mortality rates following heart failure. Predictions from Cox models were used to obtain estimates of the expected mortality for the non-RA cohort, adjusted to the same age and sex distributions as the RA cohort. Cox regression models were used to model the risk of mortality at various time points following heart failure, adjusting for age, sex, and calendar year. We tested the null hypotheses that there were no differences in the risk of mortality following heart failure between RA and non-RA subjects.

RESULTS

Description of study cohorts

The RA cohort included 103 residents of Olmsted County, Minnesota with RA who experienced a first episode of heart failure between 1979 and 2000 as defined by the Framingham criteria. Of these, 102 had a physician diagnosis of heart failure, and one subject was suspected to have heart failure. The non-RA cohort included 852 residents of Olmsted County with no history of inflammatory arthritis who experienced a first episode of heart failure over the same time period.

Table 1 shows the characteristics of the RA and non-RA heart failure subjects at the onset of heart failure. As expected based on RA epidemiology, there were differences in these characteristics. For example, a higher proportion of the RA compared to non-RA subjects was female (70% vs. 54%, $p<0.001$; Table 1). These differences were accounted for in subsequent analyses. A history of ischemic heart disease prior to heart failure was significantly less common in the RA compared to non-RA cohort, at 24% versus 37%, respectively (age, sex and calendar year adjusted, $p=0.02$). Additionally, a history of either hypertension or obesity ($\text{BMI} \geq 30 \text{ kg/m}^2$) was less likely among the RA subjects compared to the non-RA subjects, at 60% vs. 71% ($p=0.03$) and 10% versus 23% ($p=0.002$), respectively. The other cardiovascular risk factors were similar for both cohorts.

Clinical presentation of heart failure

The clinical features of heart failure for the RA subjects differed from the non-RA subjects (Table 2). Compared to the non-RA subjects, RA subjects 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). The RA subjects were significantly more likely to have rales as compared to non-RA subjects (OR: 2.24; 95% CI: 1.04 - 4.81). Additionally, RA subjects were far less likely to present with elevated systolic blood pressure ($\geq 140 \text{ mmHg}$) (OR: 0.58; 95% CI: 0.38 - 0.89) or elevated diastolic blood pressure ($\geq 90 \text{ mmHg}$) (OR: 0.34; 95% CI: 0.19 - 0.60).

Echocardiography data

Among the RA subjects, 48 (47%) of 103 HF subjects received an echo within 90 days whereas among the non-RA subjects, 497 (58%) of 852 HF subjects received an echo in this time window. Compared to non-RA subjects with heart failure, RA subjects with heart failure were significantly less likely to have undergone echocardiography within 90 days of onset of heart failure (47% vs. 58%; $p=0.02$). The majority of these echocardiograms (79%) were performed at the time of heart failure diagnosis. Adjusting for age, sex, calendar year, comorbidities, and history of ischemic heart disease, RA subjects were 33% less likely to receive an echocardiogram compared to non-RA subjects (OR: 0.67; 95% CI: 0.42, 1.08).

Although use of echocardiography has increased over time in both groups, RA subjects were significantly less likely to receive an echocardiogram over the entire study period.

The mean ejection fraction was significantly higher for RA subjects compared to non-RA subjects with incident heart failure at 50% vs. 43%, respectively ($p = 0.007$) (Figure 1). The proportion of heart failure subjects with preserved ejection fraction ($\geq 50\%$) was significantly higher for RA compared to non-RA subjects at 58% vs. 41%, respectively ($p = 0.02$). Adjusting for age, sex, calendar year, history of ischemic heart disease and the probability of having received an echocardiogram, RA patients were approximately twice as likely to have preserved ejection fraction (OR: 1.90; 95% CI: 0.98, 3.67). A sensitivity analysis was also conducted allowing for different time windows between echocardiography and the diagnosis of heart failure; the results were unchanged.

Use of cardiovascular drugs

RA subjects with heart failure received treatment with ACE inhibitors (15% vs. 30%) and beta blockers (10% vs. 23%) less frequently compared to non-RA subjects.

Mortality rates following heart failure

The 30-day mortality rate following the onset of heart failure was higher for RA compared to non-RA subjects at 15.5% vs. 6.6%, respectively ($p=0.001$) (Table 3 and Figure 2). The 1-year mortality rate following heart failure remained higher for RA compared to non-RA subjects at 35% vs. 19.3%, respectively ($p=0.01$). After adjusting for age, sex, and calendar year, RA subjects experienced a 2.39-fold higher risk of death 30 days following onset of heart failure compared to non-RA subjects (HR: 2.39; 95% CI: 1.36, 4.18). At 1 year, this mortality difference was similar but less pronounced (adjusted HR: 2.02; 95% CI: 1.40, 2.90). After also adjusting for use of cardiovascular medications and ischemic heart disease, the excess 1-year mortality was similar (HR: 1.89; 95% CI: 1.26, 2.84) (Table 3). Among those who survived the first year after onset of heart failure, there was no difference in overall survival between RA and non-RA subjects with heart failure in the subsequent years (data not shown).

DISCUSSION

In this community-based cohort study comparing RA and non-RA subjects with heart failure, we have shown that both the clinical presentation and the outcome of heart failure appear to differ in important ways for RA as compared to non-RA subjects. The RA subjects with heart failure were less likely to have typical symptoms and signs than non-RA subjects. Some of these differences could be due, in part, to the debility of the RA cohort. For example, RA patients are more likely to be sedentary and therefore may be less likely to develop exertional symptoms. In addition, the higher frequency of rales observed for the RA subjects may be explained by the presence of rheumatoid lung disease.

Additionally, we have shown that at first diagnosis of heart failure, RA subjects have a higher frequency of preserved ejection fraction as compared to non-RA subjects. This is despite adjustment for age, gender, calendar year, and history of ischemic heart disease. Overall, these findings suggest the possibility that RA patients experience a higher rate of heart failure with preserved ejection fraction in comparison to patients from the general community. This suggests that diastolic dysfunction may play an important role in the pathophysiology of heart failure for RA patients. Diastolic dysfunction can be defined as impairment of diastolic distensibility, relaxation, or ventricular filling (27). Heart failure with normal or 'preserved' ejection fraction is often considered as a surrogate for diastolic heart failure (28,29), although important caveats must be considered (for example, valvular

heart disease can cause heart failure with a normal ejection fraction). However, diagnostic criteria for diastolic heart failure remain controversial (26), mainly due to lack of agreement regarding definitions and methodology for defining diastolic dysfunction (26,29,30). Several cross-sectional studies have assessed parameters of myocardial function in RA using 2-dimensional, M-mode, and Doppler echocardiography, as reviewed by Giles et al (1). These studies (typically conducted among small groups of RA subjects without known cardiovascular disease) have demonstrated a higher frequency of left ventricular diastolic impairment in comparison to healthy control subjects (8,9,13,14,31-34). Our findings are consistent with these early reports. Further research into the pathophysiological implications of diastolic dysfunction, including the potential link with systemic inflammatory diseases, is eagerly awaited.

Perhaps most importantly, we have shown that RA subjects experience significantly higher mortality following the onset of heart failure compared to non-RA subjects despite lower rates of hypertension, ischemic heart disease, and obesity. This is commensurate with our previous reports showing the lesser contribution of conventional cardiovascular risk factors to the development of heart failure in the RA population (35). Notably, the effect of BMI is paradoxical among RA subjects compared to unaffected persons; indeed, low BMI is more predictive of increased cardiovascular mortality than elevated BMI (36). This may be related to well-described cachexia consequent to the chronic inflammatory state. The excess mortality among RA subjects is particularly noteworthy in light of the higher rate of preserved ejection fraction in the RA cohort since the presence of a preserved ejection fraction is generally associated with a lower mortality rate in subjects with heart failure (37).

Considerable evidence now suggests that chronic immune activation and inflammatory mechanisms participate in the development and progression of heart failure, including the induction of myocardial hypertrophy, fibrosis, and contractile dysfunction (38). It may be anticipated that patients with chronic, systemic inflammatory diseases such as RA, who have markedly elevated levels of inflammatory mediators such as cytokines and C-reactive protein, would therefore be at particularly high risk of heart failure progression, and consequently, of higher mortality. However, further research is necessary to identify the mechanisms of heart failure progression and the factors responsible for increased mortality among RA patients.

We have also shown that the RA subjects with heart failure receive different evaluation and treatments compared to their non-RA counterparts. This may be due in part to the clinical differences between these populations. RA subjects with heart failure were less likely to undergo echocardiography than non-RA subjects. Additionally, in this study, RA subjects were less likely to have hypertension, ischemic heart disease, and obesity compared to non-RA subjects. Therefore, our finding of lower utilization of ACE inhibitors and beta blockers may be explained by less need for anti-hypertensive therapy. The *American College of Cardiology/American Heart Association 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult* currently recommends evaluation of left ventricular function as well as the prescription of beta blockers and ACE inhibitors for all patients with heart failure (in the absence of contraindications) given compelling evidence for reduction in heart failure signs and symptoms, reduced risk of hospitalizations, and for reduction in mortality with such treatment (39). However, ACE inhibitors were not a standard therapy for heart failure during the majority of the study period. It is perilous to compare heart failure treatments in the two groups because of the likelihood of confounding by indication and/or contraindication. Therefore, we can make no definitive conclusions about the treatment differences between the study cohorts.

However, our findings strongly suggest that the clinical presentation differs for RA patients with heart failure in comparison to heart failure subjects from the general population who do not have RA, and furthermore, that RA patients suffer significantly higher mortality following heart failure. It is conceivable that the subtle presentation of heart failure among RA subjects leads to difficulty in diagnosis and influences management. Our study points to the need for increased vigilance for the signs and symptoms of heart failure in RA patients. Although it is premature to advocate routine echocardiography for RA patients, these findings lead us to hypothesize that more aggressive screening for presymptomatic left ventricular dysfunction (including diastolic dysfunction) as well as early therapeutic strategies may be beneficial in RA. In the general population, various indices of diastolic dysfunction have been shown to predict future development of heart failure as well as increased mortality (40,41). Future studies should address the potential utility of screening RA patients with echocardiography to identify early asymptomatic ventricular dysfunction and to evaluate the role of potential interventions aimed at reducing the excess mortality associated with heart failure.

Several limitations of this study should be considered. The physicians caring for RA patients may not have assessed symptoms and signs of heart failure as aggressively as physicians caring for non-RA subjects, creating the possibility of systematic bias in the reporting of clinical findings in RA compared to non-RA subjects with heart failure. However, most of the patients would have seen multiple physicians including internists and likely cardiologists. Thus, this potential bias is unlikely to be the sole explanation for our findings. It was not possible from our dataset to compare the stage (such as New York Heart Association classification) or severity of heart failure at presentation between the two patient groups. The possibility that the RA patients were diagnosed at an earlier or later stage of heart failure cannot be excluded, which could potentially contribute to the observed differences in clinical presentation. However, the lack of this information does not change the clinical implications of our findings. Additionally, the echocardiography data were unavailable for a large proportion of the RA population, so we cannot exclude bias regarding the ejection fraction data. However, such a bias would imply that RA subjects with heart failure and an abnormal ejection fraction were less likely to undergo echocardiography than RA subjects with heart failure and preserved ejection fraction, which seems unlikely. Although we adjusted for factors associated with the clinical intervention of undergoing echocardiography, residual confounding of the association between RA and echocardiography is possible. To further validate diastolic heart failure in this study, it would have been advantageous to assess diastolic function more completely using Doppler echocardiography or cardiac catheterization, but this was not feasible in this study.

With regard to cardiovascular medication use, it was not possible to determine the indications for the various drug treatments that were considered. It was not possible to analyze the pattern of medication use with respect to ejection fraction, which is important because of differences in treatment of heart failure with reduced ejection fraction compared to preserved ejection fraction. This is a limitation because knowledge of why medications were or were not prescribed would provide an understanding of what factors affect treatment decisions in RA heart failure patients. Additionally, certain medications used to treat RA patients, including glucocorticoids (42,43) and nonsteroidal anti-inflammatory drugs (44,45), are associated with heart failure and could conceivably increase the risk of mortality for these patients. However, the relationship between such drugs and disease-related outcomes is potentially confounded by disease severity (46); it was beyond the scope of this paper to disentangle the effects of RA treatment from the underlying disease. Finally, the study population included the white, primarily rural and well-educated population of Rochester, Minnesota; thus, the generalizability of the findings to groups not represented in our study is limited.

Several strengths of the study should be underscored. The study sample included RA and non-RA subjects with incident heart failure identified from the same underlying population, minimizing selection bias. The availability of the complete medical records using the Rochester Epidemiology Project resources facilitated the identification of RA and non-RA subjects with follow-up through the medical records for the outcomes of incident heart failure. On average, each RA subject had 27 years and each non-RA subject 41 years of medical history prior to the occurrence of RA, lessening the likelihood of misclassifying the ‘first’ episode of heart failure. Additionally, these resources facilitated the collection of echocardiography data, cardiovascular risk factors, and drug treatment data. Validated cases of heart failure were evaluated, and a reasonable and practical surrogate for diastolic heart failure was used. The echocardiograms for this study were all performed at the same institutional laboratory, and the methodology for defining ejection fraction was constant over time. Although more detailed information on myocardial function would be of interest, diastology is a controversial field. Therefore, these data are best considered as preliminary and await subsequent studies using enhanced, consensus definitions for diastolic dysfunction.

In summary, RA patients with heart failure appear to have a more subtle presentation, with lower frequency of typical heart failure symptoms and signs, compared to heart failure patients without RA. RA patients with heart failure also experience a higher frequency of heart failure with preserved ejection fraction compared to those without RA, suggesting a greater importance of diastolic dysfunction in the pathophysiology of heart failure for persons with RA. Importantly, RA patients suffer higher mortality in the year following heart failure compared to their non-RA counterparts. Our data suggest that new approaches to screening for early left ventricular dysfunction in RA patients should be investigated. In addition, further research into the mechanisms of heart failure and the potential role of active systemic inflammation (as exemplified in RA) is needed. It is hoped that the new knowledge gleaned from such investigations could lead to the early identification of RA patients at risk of heart failure, so that these patients might be treated with state-of-the-art cardiovascular agents as well as anti-inflammatory agents in order to optimize survival.

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Figure 1.
Distribution of ejection fraction (EF) between RA and non-RA subjects.

Figure 2.
Mortality through 1 year following the onset of heart failure for the RA and non-RA cohorts.

Table 1

Characteristics of the RA and non-RA subjects at onset of heart failure

Characteristic	RA (N = 103)	Non-RA (N = 852)
Age, yrs. (mean $\pm$ SD)	78.0 $\pm$ 9.0	76.5 $\pm$ 12.2
Female	72 (70%)	457 (54%)
RA disease duration, yrs. (mean $\pm$ SD)	12.7 $\pm$ 9.0	--
Rheumatoid factor positive	68 (66%)	--
Ischemic heart disease	25 (24%)	318 (35%) [†]
Diabetes mellitus	28 (27%)	191 (23%) [†]
Dyslipidemia	22 (21%)	221 (24%) [†]
Hypertension	62 (60%)	576 (71%) [†]
Smoking (current or former)	57 (55%)	424 (54%) [†]
Obesity (BMI $\geq$ 30 kg/m ²)	9 (10%)	191 (23%) [†]

Values are number (%) except as indicated otherwise.

Abbreviations: RA, rheumatoid arthritis.

Bold values are statistically significant ($p < 0.05$).

[†] Percentages are age and sex adjusted to the distribution of the RA cohort.

Table 2

Clinical features of heart failure (based on the Framingham criteria) and treatment for the RA and non-RA cohorts*

<i>Clinical Features</i>	<i>RA (N = 103)</i>	<i>Non-RA†(N = 852)</i>	<i>OR (95% CI)</i>
Symptoms			
Paroxysmal nocturnal dyspnea	16 (16%)	180 (23%)	0.62 (0.35, 1.10)
Cough	39 (38%)	301 (37%)	1.05 (0.68, 1.61)
Dyspnea on exertion	69 (67%)	615 (76%)	0.64 (0.41, 1.01)
Orthopnea	22 (21%)	271 (34%)	0.53 (0.32, 0.87)
Swollen extremities	70 (68%)	494 (62%)	1.26 (0.81, 1.97)
One or more symptoms**	76 (74%)	681 (84%)	0.54 (0.33, 0.87)
Signs			
Engorged jugular veins	60 (58%)	481 (62%)	0.87 (0.57, 1.32)
Rales	95 (92%)	522 (84%)	2.24 (1.04, 4.81)
S3 gallop	28 (27%)	224 (28%)	0.94 (0.59, 1.50)
Hepatojugular reflux	11 (11%)	153 (20%)	0.50 (0.26, 0.96)
Hepatomegaly	9 (9%)	58 (6%)	1.43 (0.68, 3.04)
Tachycardia	14 (14%)	129 (18%)	0.77 (0.42, 1.42)
One or more signs	99 (96%)	747 (93%)	1.86 (0.65, 5.28)
Radiography			
Cardiomegaly	55 (55%)	466 (64%)	0.69 (0.45, 1.05)
Acute pulmonary edema	34 (34%)	275 (37%)	0.87 (0.56, 1.36)
Pleural effusion	44 (44%)	310 (42%)	1.10 (0.72, 1.69)
One or more radiographic findings	83 (83%)	633 (85%)	0.87 (0.49, 1.54)
Hypertension			
Systolic blood pressure ≥ 140 mm Hg	48 (47%)	468 (60%)	0.58 (0.38, 0.89)
Diastolic blood pressure ≥ 90 mm Hg	15 (15%)	271 (34%)	0.34 (0.19, 0.60)

Abbreviations: RA, rheumatoid arthritis; OR, odds ratio; CI, confidence interval.

Bold values are statistically significant.

* Values are number (%) unless specified otherwise. Percentages are age and sex adjusted to the distribution of the RA cohort.

** Excluding swollen extremities because this is unreliable as a sign of heart failure in RA patients.

Table 3

Mortality following heart failure for RA and non-RA subjects at 30 days, 6 months and 1 year*

<i>Time Point</i>	<i>Mortality</i>		<i>HR (95% CI)</i>	
	<i>RA N = 103</i>	<i>Non-RA N = 852</i>	<i>Model 1</i>	<i>Model 2</i>
30 days	15.5%	6.6%	2.39 (1.36, 4.18)	1.66 (0.85, 3.22)
6 months	25.2%	14.0%	1.93 (1.26, 2.95)	1.70 (1.05, 2.76)
1 year	35.0%	19.3%	2.02 (1.40, 2.90)	1.89 (1.26, 2.84)

* The column labeled Model 1 displays Cox regression models adjusted for age, sex, and calendar year. The column labeled Model 2 displays models also adjusted for use of cardiovascular medications and ischemic heart disease. RA = rheumatoid arthritis; OR = odds ratio; CI = confidence interval.