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A meta-analysis of the effect size of rheumatoid arthritis on left ventricular mass: comment on the article by Rudominer et al

To the Editor:

We appreciate the work of Rudominer et al, who recently published a report describing the association of rheumatoid arthritis (RA) with increased left ventricular mass (1). The findings of Rudominer and colleagues are consistent with the findings of our own previous study of RA patients, which is cited by the authors (2). Patients with RA have both structural and functional left ventricular involvement. In these patients, we have previously demonstrated that diastolic dysfunction (detected as impaired relaxation abnormalities during left ventricular filling) is directly correlated with structural changes in the left ventricle, specifically, changes involving left ventricular mass, interventricular septal thickness, and left ventricular posterior wall thickness (2). In RA patients, these all seem to be features of the systemic disease process, and diastolic dysfunction seems to be a consequence of left ventricular structural changes. However, it is probable that these findings only partially explain the cardiovascular morbidity in RA.

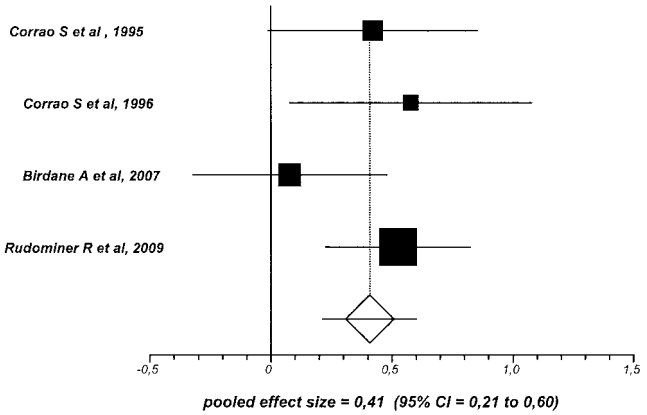

Figure 1. Forest plot of the effect size in the meta-analysis, using a fixed-effects model. Squares represent the effect sizes in the previous studies. The diamond and dotted line represent the pooled effect size in the meta-analysis. Horizontal lines represent the 95% confidence interval (95% CI). The Glass statistic (mean difference standardized by pooled standard deviation) and 95% CI are shown as the pooled mean effect size estimate. For the overall fixed-effects model, $P < 0.0001$.

Indeed, in a study of RA patients (with no exclusion criteria), we observed a peculiar cardiac picture among patients who had no symptoms of cardiac disease (3). The population of RA patients in that study seemed to share 3 characteristics: minimal posterior pericardial effusion, alteration of the aortic root (detected as an increased prevalence of Valsalva sinus aneurysms), and both valvular and valvular cord thickening. However, even though left ventricular mass was greater overall in the RA group, the difference was not statistically significant in patients versus controls. We believe that heart involvement in RA results from the disease's systemic inflammatory process, which explains the high rates of cardiac mortality in RA patients. Thus, we completely agree with the conclusions discussed by Rudominer et al and think that the collective scientific community has achieved an important goal in demonstrating that different populations with RA (both Mediterranean [2,3] and North American [1]) have the same clinical cardiac features (i.e., a higher left ventricular mass index and abnormalities consistent with impaired left ventricle relaxation).

We undertook a meta-analysis of previously published reports (1–4) to summarize the effect size of RA on left ventricular mass index in patients compared with healthy controls. We searched for data pertaining to left ventricular mass index, which had been determined using echocardiography. Unfortunately, in the studies by Arslan et al (5) and Gonzalez-Juanatey et al (6), left ventricular mass index was not calculated; therefore, we excluded these studies from our analysis. We computed the modified Glass statistic using pooled sample standard deviation and Cochran's Q statistic. The pooled mean effect size estimate was calculated according to methods described by Hedges and Olkin (7). Figure 1 shows the pooled estimation of effect size using a fixed-effects model

(7). This model was used since there was low interstudy variation. The data from our meta-analysis support the findings of Rudominer et al, and help to describe the effect of RA on the heart. In conclusion, we believe that left ventricular structural and functional changes are one of the established clinical features of RA, and the challenge will now be to find ways to utilize this information both to optimize clinical monitoring and to reduce cardiovascular mortality in RA patients.

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Aortic stiffness and left ventricular hypertrophy in rheumatoid arthritis: comment on the article by Rudominer et al

To the Editor:

In the recent article by Rudominer et al (1), the authors reported an association of rheumatoid arthritis (RA) with increased left ventricular (LV) mass but not with reduced ejection fraction. Rudominer and colleagues also suggested that a pathophysiologic link might exist between chronic inflammation and LV hypertrophy, even though LV systolic function was preserved in their study population.

LV hypertrophy might be useful in predicting cardiovascular events independent of traditional risk factors. In addition, arterial stiffness has been described as an independent predictor of cardiovascular mortality both in patients with cardiovascular disease and in the general population (2–4).

In a population of patients with RA, we investigated both ventricular mass and aortic elasticity, which is considered an important determinant of LV function and coronary blood flow. Aortic elasticity was assessed using a 2-dimensional guided M-mode evaluation of the systolic aortic diameter (D_s) and the diastolic aortic diameter (D_d) at a location 3 cm above the aortic valve; using simultaneous electrocardiography, D_d was measured at the peak of the R wave, and D_s was measured at the point of maximal anterior motion of the aortic wall. For both diameters, 5 measurements were taken and then averaged. Indices of aortic elasticity were calculated as follows: aortic strain = $100(D_s - D_d)/D_d$; aortic distensibility = $(2[D_s - D_d]/D_d[PP])$ (given as $cm^2/dyn \times 10^{-6}$) where PP is pulse pressure (calculated as $P_s - P_d$); and aortic stiffness = $\ln(P_s/P_d)/([D_s - D_d]/D_d)$ where P_s and P_d are systolic and diastolic blood pressures, respectively, measured in mm Hg, and where $\ln(P_s/P_d)$ refers to the natural logarithm of the relative pressure.

In a population of 93 randomly enrolled RA patients, we observed increased mean ± SD LV mass (101 ± 29 gm/m^2), decreased aortic strain and distensibility indices (8 ± 5% and 3.2 ± 2.5 $cm^2/dyn \times 10^{-6}$, respectively), and an increased stiffness index (10.5 ± 9.7). From this cohort, we then selected 35 patients who had no hypertension, valve disease, or history of cardiovascular disease (mean ± SD age 57.8 ± 7.7 years, mean ± SD RA disease duration 10 ± 8 years). In these patients, we observed increased mean ± SD LV mass (92 ± 53.1 gm/m^2), decreased aortic strain and distensibility indices (9 ± 3.8% and 3.6 ± 0.8 $cm^2/dyn \times 10^{-6}$, respectively), and an increased stiffness index (7.6 ± 2.6).

Patients were then divided into 2 subgroups based on their C-reactive protein levels (≤0.5 mg/dl versus >0.5 mg/dl); LV mass was not significantly different between the 2 groups. LV mass and other morphologic and functional cardiac parameters were compared. In a univariate analysis, indexed LV mass tended to correlate with aortic distensibility, but this was not significant ($P = 0.069$). In a multivariate analysis, LV mass significantly correlated with aortic distensibility ($P = 0.04$) but only tended to correlate with aortic strain ($P = 0.06$).

The stiffening of the aorta and other central arteries represents a potential risk factor for increased cardiovascular morbidity and mortality (2–4). Furthermore, an association between impaired aortic elasticity and LV hypertrophy has been demonstrated in previous studies (5,6). Our findings confirm those of Rudominer and colleagues (1) and demonstrate an association between some aspects of impaired aortic elasticity and increased LV mass in RA patients. These findings suggest that patients with RA could have preclinical atherosclerosis, even without having hypertension or other cardiovascular risk factors. A decrease in aortic elasticity could influence the natural history of RA and contribute to the development of cardiovascular disease and left ventricular dysfunction.

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