strongly supports our intuitive understanding of obesity as a highly important risk factor for early death in RA. Because of the dynamic effects of weight over time and their relationship to disease activity and comorbid conditions, it is important to note that epidemiologic studies to date that have assessed associations between body mass and mortality are likely to have systematically underestimated the causal risks of obesity in RA.

Gremese et al appropriately distinguish between intentional and unintentional weight loss. We fully agree that while unintentional weight loss is hypothesized to be predictive of death, intentional weight loss would, in contrast, be hypothesized to be protective. Unfortunately in a large database study it is rarely possible to make this distinction. Fortunately, however, there are data from other populations within this age group suggesting that >60% of weight loss is unintentional (1–3), and in these previous studies, unintentional weight loss was associated with greater mortality but intentional weight loss was not. Therefore, it is likely that the associations between weight loss and death observed in our study are most representative of the risk posed by unintentional weight loss. We hope to further emphasize that overall, these observations should further support aims to promote intentional weight loss among patients with RA: there is no evidence to suggest that intentional weight loss would have anything but positive effects on health.

We also agree with Gremese and colleagues that weight loss is likely linked to disease activity over time. In fact, in studies published by us (using data from the same cohort) (4) and by others (1), it has been demonstrated that higher CRP levels and less improvement in these levels are associated with greater weight loss. While some analyses in our study were performed after adjustment for time-varying measures of CRP and other factors (4), we would not suggest that weight loss is itself causally associated with mortality risk. However, there is strong evidence that weight loss is an important time-dependent confounder between weight and mortality.

In basic terms, the recent observations suggest that both obesity and unintentional weight loss are indeed associated with poor long-term survival in RA. Although obese patients with RA seem to live longer, obesity is not likely to be biologically protective, but simply is a sign that the individual has not recently lost a substantial amount of weight.

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Cardiovascular events in rheumatoid arthritis—time to see beyond articular involvement in “real world” clinical practice: comment on the article by Mackey et al

To the Editor:

The recent study by Mackey and colleagues (1) underlines the role of rheumatoid arthritis (RA) as a predictor of cardiovascular events. In particular, the authors observed that RA was independently associated with an increased risk of incident coronary heart disease (CHD) and fatal cardiovascular disease (CVD), as determined using different Cox proportional hazards models. The hazard ratio for CHD and CVD in patients with RA was greater than that for hypertension and comparable only to that for diabetes. These findings are very impressive and strengthen our previously published data (2,3).

We previously observed at least 3 alterations that appeared to be typical of RA patients in the absence of any symptom of heart disease and defined this clinical picture as “silent rheumatoid heart disease” (2). Valvular thickening/calcifications and minimal pericardial effusion were the main findings. In a subsequent study, we observed left ventricular diastolic dysfunction in RA patients without clinically evident cardiovascular disease (3). In both studies, RA patients were compared with healthy subjects, and none of the patients or control subjects had any associated comorbidities to verify the effect of the disease on the heart.
Three successive systematic reviews with meta-analyses corroborated the above-described findings (4–6). The first meta-analysis used pooled data from 10 controlled studies and confirmed valvular and pericardial involvement in RA (4), the second confirmed the increased prevalence of left ventricular diastolic dysfunction in patients with RA (5), and the third highlighted the detrimental effect of RA on left ventricular mass (6). All 3 cardiac abnormalities are predictors of cardiovascular morbidity and mortality. However, diastolic dysfunction and left ventricular hypertrophy are well-defined cardiovascular risk factors in patients with hypertension and those with diabetes.

Unlike diabetes and hypertension, RA has paid the price for this strict vision, until now. We believe it is time to look beyond articular involvement in RA and to consider that it is associated with a high risk for cardiovascular disease. For all these reasons, echocardiography should be included in the panel of examinations for monitoring cardiovascular risk, detecting subsets of patients at high risk, and evaluating the cardiovascular effects of drug therapy. Obviously, the standard of care for RA patients should include more stringent assessment of comorbidities and classic modifiable cardiovascular risk factors in order to make drug therapy adjustments, reduce the number of cardiovascular events, and improve quality of life.

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Reply

To the Editor:

We appreciate the comments by Dr. Corrao and colleagues regarding our recent study that showed a ~1,5-fold increased risk of CHD and ~2,5-fold increased risk of fatal CVD in postmenopausal women with RA compared with those without RA, after adjustment for other risk factors. Our data are indeed consistent with those from the prior studies cited by Corrao et al, showing increased left ventricular mass and diastolic dysfunction in patients with RA compared with control subjects. Recent studies have shown that RA is also associated with higher levels of coronary plaque (1), an increased mortality risk (2), and higher levels of myocardial fibrosis (3), as measured by cardiac magnetic resonance, which are associated with an increased incidence of heart failure and increased mortality (4,5). Our current study showed that the incidence of CVD was 1,5-fold higher in women with RA, even those without any classic CVD risk factors, but also showed that anti-cyclic citrullinated peptide and rheumatoid factor positivity may not be reliable indicators of increased CVD risk in postmenopausal women with RA. In contrast, self-reported joint pain was significantly associated with an increased risk of CVD and, as previously reported, total mortality (2). Additional studies in patients with RA are needed to determine appropriate risk stratification and to evaluate the effects of therapeutic interventions in reducing the risks of CHD, CVD, and premature mortality.

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