Subcutaneous Nodules (SCN) May Predict Increased Risk for Cardiovascular Disease (CVD) in Patients from the CORRONA database with Rheumatoid Arthritis (RA): An Updated Analysis

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Abstract

Background: CVD is now known to be a major comorbidity of patients with RA. The possible association of extraarticular manifestations of RA with the development of CVD is largely unexplored although a previous report found that rheumatoid nodules predicted mortality from CVD in men (Arthritis Rheum 46:10-16, 2002).

Methods: We examined the association of the presence of SCN and incident cases of CVD in a cohort of 10,638 patients with RA from the CORRONA registry with at least one follow-up visit. A total of 22,367 patient years of follow-up were included with an average of 2.1 years follow-up per patient.

Results: The presence of SCN was associated with all of the outcomes of CV disease when considered together. The incident rate ratios (IRR) for CVD which achieved significance after adjustment for age and gender were CDAI (IRR 1.20 [conf 1.00 to 1.40] p=0.025), mHADQ (IRR 1.09 [conf 1.05 to 1.14] p=0.008), patient VAS (IRR 1.09 [conf 1.04 to 1.19] p=0.001), patient pain VAS (IRR 1.90 [conf 1.29 to 2.80] p=0.001). A multivariate regression model for all of the measures of disease activity.

Conclusion: We conclude that the presence of SCN on examination identifies a patient with RA who is at significantly greater risk for the development of CVD. It is possible that the association of SCN with CVD is due to a heretofore unrecognized biological relationship. With this report we confirm and expand our prior report of association of SCN with CVD in this very large cohort.

Background

Cardiovascular disease represents the leading cause of death in RA patients, accounting for approximately one-third to one-half of all RA related deaths (1,2). The increased prevalence of CVD in patients with RA cannot only be explained by the presence of traditional atherosclerotic risk factors (3). Chronic inflammatory status, accelerated atherosclerosis, systemic vascular inflammation, hyperhomo- cysteinemia, and the immunogenic effects of therapeutic interventions seem to increase CV risk in patients with RA (4). It is presently uncertain whether CVD in RA represents a comorbidity associated with inflammation or whether there is an inherent increased risk specific to the RA disease state (5,6).

Current evidence is inadequate to support screening for asymptomatic cardiac disease in patients with rheumatoid arthritis. It is thus critical to develop effective strategies to detect and optimally manage individuals with asymptomatic cardiac disease in patients with rheumatoid arthritis.

Methods

1. A cohort of 10,759 patients with RA from the CORRONA registry were included to determine the association of the presence of subcutaneous nodules (SCN) and CVD.

2. A total of 22,367 patient years of follow-up were included with an average of 2.1 years follow-up per patient.

3. The presence of SCN was recorded by the examining rheumatologist at the time of a clinical encounter.

4. Risk factors for CVD were simultaneously assessed and included age, gender, presence of hypertension, diabetes mellitus, disease severity (CDAI, DAS28, mHADQ), patient assessment of pain and global arthritis activity on a 10 cm visual analogue scale (VAS), ESR, CRP and history of prior myocardial infarction (MI) or cerebrovascular accident (CVA). We used generalized estimating equation (GEE) poisson regression models to determine if the presence of SCN on examination was associated with CVD events defined as MI or CVA after adjusting for the variables annoted above.

Results: The presence of SCN was associated with all of the outcomes of CV disease when considered together. The incident rate ratios (IRR) for CVD which achieved significance after adjustment for age and gender were CDAI (IRR 1.20 [conf 1.00 to 1.40] p=0.025), mHADQ (IRR 1.09 [conf 1.05 to 1.14] p=0.008), patient VAS (IRR 1.09 [conf 1.04 to 1.19] p=0.001), patient pain VAS (IRR 1.90 [conf 1.29 to 2.80] p=0.001). A multivariate regression model for all of the variables described a significant association with the presence of SCN (IRR p<0.05) while other disease outcome measures lost significance except patient VAS and patient pain VAS.

Conclusion: We conclude that the presence of SCN on examination identifies a patient with RA who is at significantly greater risk for the development of CVD. It is possible that the association of SCN with CVD is due to a heretofore unrecognized biological relationship. With this report we confirm and expand our prior report of association of SCN with CVD in this very large cohort.

Table 1. Baseline characteristics of patients with and without Cardiovascular disease events.

Table 2. Incident Rate Ratios for CVD (MI, stroke or CVD related death) after the adjustment for age and gender

Table 3. Multivariate model using Patient VAS for pain as the disease severity measures.

Table 4. Association of SCN with CVD in multivariate models that used different measures of disease activity.

Discussion

Cardiovascular disease is a major comorbidity in patients with RA. Subcutaneous nodules (SCN) are associated with CVD (1,2). The possible association of extraarticular manifestations of RA with the development of CVD is largely unexplored although a previous report found that rheumatoid nodules predicted mortality from CVD in men (Arthritis Rheum 46:10-16, 2002).

Discussions

Cardiovascular disease in a major comorbidity in patients with RA. Subcutaneous nodules (SCN) are associated with CVD (1,2). The possible association of extraarticular manifestations of RA with the development of CVD is largely unexplored although a previous report found that rheumatoid nodules predicted mortality from CVD in men (Arthritis Rheum 46:10-16, 2002).

Preliminary observations suggest that the presence of SCN may actually mediate the association between RA and CVD. Further research is needed to better understand the mechanisms by which RA may increase the risk of CVD.