Heart Disease in RA Has Complex Etiology

BY DENISE NAPOLI

FROM THE ANNALS OF RHEUMATIC DISEASES

When it comes to heart disease in rheumatoid arthritis, the classic risk factors like body mass index and abnormal lipid profiles play a role, but a very different one than among the general population, according to Dr. George D. Kitas and Dr. Sherine E. Gabriel.

Moreover, systemic inflammation is likely just as important for the development of cardiovascular disease in this cohort. Therefore, "effective, even optimal control of traditional risk factors is imperative, but may be insufficient to reduce CV risk for people with RA," the investigators wrote (Ann. Rheum. Dis. 2010 Nov. 24 [doi:10.1136/ard.2010.142133]). Rather, "tight control of systemic inflammation is likely to be required for optimal results."

According to Dr. Kitas of the Arthritis Research U.K. Epidemiology Unit at Manchester (England) University, and Dr. Gabriel of the division of rheumatology at the Mayo Clinic, Rochester, Minn., one of the commonest and simplest risk factors for heart disease among the general population – increased body mass index – may, paradoxically, be associated with increased survival among RA patients.

They point to one study showing that even after the presence of diabetes mellitus, cardiac history, smoking, and hypertension were controlled for, lower BMI carried a threefold risk of death, compared with patients without RA (Arthritis Rheum. 2004;50:3450-7).

"RA appears to be associated with profound alterations in body composition, which are not reflected in the BMI thresholds used in the general population," the authors wrote.

These alterations include what the authors call "rheumatoid cachexia," characterized by low muscle mass combined with a high fat mass, which may represent "from the CV perspective, the 'worst of both worlds.' "

A similar paradoxical relationship appears to exist concerning lipids in RA. "Serum levels of total cholesterol and LDL cholesterol decline precipitously during the 3- to 5-year period before RA incidence," they wrote, citing a study by other investigators (Ann. Rheum. Dis. 2009;68[suppl. 3]:78).

On the other hand, dyslipidemia has been documented to affect "up to half" of hospitalized RA patients (Ann. Rheum. Dis. 2010;69:683-8).

Meanwhile, the landmark JUPITER study (Justification for the Use of Statins in Primary Prevention: An Intervention Trial Evaluating Rosuvastatin) excluded RA patients, because of C-reactive protein levels in excess of the "arbitrarily chosen threshold of 2 mg/L used in that trial, as well as a significant classical CV risk factor load, unlike the participants in JUPITER, who had no other risk factors." They reported that a trial of statins specifically in RA, enrolling 4,000 patients, is underway in the United Kingdom, but will not report results until 2016 (www.dgoh.nhs.uk/tracera).

Another area where research is lacking is concerning the effects of inflammation on CV risk. The authors pointed, for example, to the theory of "accelerated atherosclerosis," first postulated in the 1990s.

"The cell types, cytokine signaling, adhesion interactions, and tissue-damaging processes involved in the generation, progression, instability, and rupture of atheromatous plaques are reminiscent of those seen in chronic rheumatoid synovitis," they wrote.

Moreover, "effective RA treatment appears to be associated with some, often transient, improvements in vascular function," they added, although "there are no clear, consistent relationships between this and contemporary disease activity."

Another theory, that "high-grade systemic inflammation in RA does not necessarily imply accelerated atherosclerosis but rather an increased propensity to plaque instability and rupture," was confirmed in an autopsy analysis in one study (J. Rheumatol. 2007;34:937-42).

The work was funded by Arthritis Research U.K., the British Heart Foundation, the Medical Research Council, and the U.S. National Institute of Arthritis and Musculoskeletal Diseases. Dr. Kitas and Dr. Gabriel said they had no relevant financial disclosures. ■

TNF Inhibitor Users Report Less Sick Leave

BY HEIDI SPLETE

FROM THE ANNALS OF RHEUMATIC DISEASES

A significant 30% reduction in the number of sick leave days per month was seen in adults with rheumatoid arthritis after using TNF antagonists for 6 months.

The finding was observed in a population-based study of 365 RA patients aged 18-85 years.

VITALS

Major Finding: TNF-inhibitor users reduced the average sick leave time from 9.8 days per month at the start of treatment to 6.5 days after 6 months of treatment.

Data Source: A study of 365 Swedish adults aged 18-58 years with rheumatoid arthritis

Disclosures: The researchers said that they had no relevant financial disclosures.

The study is among the first to address the quantitative impact of TNF inhibitors on sick leave and disability pension, said Dr. Tor Olofsson of Lund (Sweden) University, and colleagues, whose study was published in the December issue of Annals of the Rheumatic Diseases.

They reviewed insurance database information on RA patients enrolled in the South Swedish Arthritis Treatment Group registry.

Each patient was matched with four controls from the general population.

The study population averaged 9 sick days per month in the first month of anti-TNF treatment. The monthly rate dropped to an average of 6.5 days after 6 months and remained steady at an average of 6.6 days per month for months 6-12 (Ann. Rheum. Dis. 2010;69:2131-6).

Compared with the controls in the general population, the relative risk of being on sick leave in the RA group was 6.6 at the start of treatment, but dropped to 5.1 after 6 months, and remained at an average of 5.2 for the rest of the year. The relative risk of being on disability pension was 3.4 at the start of treatment and 3.2 after one year of treatment.

Approximately 98% of the patients had tried at least one disease-modifying antirheumatic drug (DMARD) before starting anti-TNF therapy.

The average age of the patients was 46 years, and 82% were women. A total of 92 patients (25%) discontinued treatment, including 34 for adverse events, 32 for treatment failure, and 26 for other reasons. ■

Methotrexate Use in RA Shown to Be Protective Against Mortality

BY SHARON WORCESTER

FROM THE ANNUAL MEETING OF THE AMERICAN COLLEGE OF RHEUMATOLOGY

ATLANTA – Methotrexate use is strongly associated with longer survival in rheumatoid arthritis patients.

After taking into consideration the propensity for prescribing methotrexate, prednisone, and anti–tumor necrosis factor (TNF) agents over time, and after adjusting for potential confounding factors such as disease severity, a strong protective effect on mortality was shown for methotrexate (adjusted hazard ratio 0.23) but not for prednisone (adjusted hazard ratio 1.80), said Dr. Mary Chester Wasko.

Combined treatment with methotrexate and prednisone also had a significant protective effect (hazard ratio 0.34).

"Since methotrexate appeared to be strongly protective with respect to survival in these analyses, and because methotrexate and prednisone are often prescribed together in practice, we questioned whether there might be an interaction between the two drugs with respect to survival," said Dr. Wasko of the University of Pittsburgh.

Indeed, the strength of the association between methotrexate and improved mortality was only modestly reduced when methotrexate was used in combination with prednisone, she added.

Anti-TNF agents were associated with a slightly decreased risk of mortality. Although the result was not statistically significant (adjusted hazard ratio 0.15), follow-up was limited, as the analyses were based on only 10 deaths out of 598 treated patients with only 5 years of follow-up after these drugs were approved. Additional follow-up is needed to strengthen the results.

Dr. Wasko and her colleagues used the Arthritis, Rheumatism, and Aging Medical Information Systems (ARAMIS) database of patients from 10 U.S. rheumatology practices for their study. The median age of the 5,629 participants was 58 years, 75% were female, 90% were white, and follow-up was a median of 4 years and 3 months. A total of 1,027 patients died during 36,612 patient years of observation.

Patients were evaluated biannually from 1981 to 2003 using the Health Assessment Questionnaire (HAQ).

They reported on demographics, health status (including comorbidities), and medication use.

The outcome of interest was all-cause mortality as confirmed by next of kin. ■

VITALS

Major Finding: After taking into consideration the propensity for prescribing methotrexate, prednisone, and anti–tumor necrosis factor agents over time, and after adjusting for potential confounding factors such as disease severity, a strong protective effect on mortality in RA patients was shown for methotrexate (adjusted hazard ratio 0.23) but not for prednisone (adjusted hazard ratio 1.80).

Data Source: An analysis of data – using a novel propensity scoring method – from a longitudinal multicenter observational database of 5,629 RA patients.

Disclosures: Dr. Wasko disclosed that she has received research grants from Amgen, has served as the principle investigator for clinical trials for Centocor, and has served as a consultant for Centocor and UCB.