# DMARDs Offer Cardiac Protection to RA Patients

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SAN FRANCISCO — The increased risk for cardiovascular disease associated with the diagnosis of rheumatoid arthritis was offset by the protective effects of disease-modifying antirheumatic drugs but heightened by prednisolone therapy in a large community-based study.

The study used data on individuals registered in the United Kingdom General Practice Research Database who were treated for rheumatoid arthritis between 1987 and 2002. This period predates the widespread use of anti–tumor necrosis factor (TNF) agents, so the findings offer no information on whether these agents are protective against cardiovascular disease, Dr. Christopher J. Edwards said at the annual meeting of the American College of Rheumatology.

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The research involved about 35,000 individuals diagnosed with RA and compared their rates of myocardial infarction (as a surrogate marker for cardiovascular disease) with those of 100,000 matched healthy controls.

The incidence of MI in patients with RA was 6.49/1,000 person-years vs. 2.96/1,000 person-years for controls.

The incident rate ratio was increased for MI by an RA diagnosis (2.23), according to a Poisson regression analysis.

The increased risk persisted even after a multifactor regression analysis controlled for traditional cardiovascular disease risk factors, including age, BMI, sex, smoking, serum lipid levels, hypercholesterolemia, and hypertension.

Of the 966 patients with RA who had an MI during the study period, 705 (73%) received treatment with either a disease-modifying antirheumatic drug (DMARD) or prednisolone during that time.

Of these 705, a total of 538 took either DMARDs or prednisolone within the 2 months that immediately preceded their MI.

The incident rate ratio for MI among patients on either a DMARD or prednisolone, compared with those not on these agents, was 0.94. Further analysis of DMARDs showed that the individual incident rate ratio for hydroxycholoroquine, methotrexate, and sulfasalazine vs. no drug were 0.42, 0.67, and 0.69, respectively. In contrast, use of prednisolone vs. no drug was associated with an incident rate ratio of 1.49. The effect sizes remained similar after controlling for traditional cardiovascular disease risks but were no longer significant.

The strong anti-inflammatory effects of DMARDs are the likely explanation of their protective effect against MI, Dr. Edwards said in an interview. Data from a number of trials have shown that these agents lower C-reactive protein (CRP) levels. It is reasonable but still pure conjecture to conclude that lowering CRP levels in RA patients lowers the risk of cardiovascular disease, said Dr. Edwards, consultant rheumatologist and senior lecturer at Southampton University Hospital (England).

While prednisolone has similarly strong anti-inflammatory effects in RA, these effects do not translate into protection against cardiovascular disease. Prednisolone use is associated with increased blood pressure and serum lipids levels and weight gain, which offset any anti-inflammatory benefits for the cardiovascular system, he continued in the interview.

In contrast to data presented by Dr. Edwards, findings from the recent QUEST-RA (Quantitative Patient Questionnaires in Standard Monitoring of Patients with Rheumatoid Arthritis) study show that prednisolone was protective against cardiovascular disease in RA (Ann. Rheum. Dis. 2007;66:1491-6). As an explanation for the conflicting findings, Dr. Edwards suggested that the difference may be that the patients in the British cohort had earlier RA and were more susceptible to the adverse effects of prednisolone than were the cohort patients in QUEST-RA, all of whom were referred to the study from tertiary care centers with advanced RA.

Dr. Edwards reported he has no conflict of interest concerning this research. ■