MI Risk Starts Rising 1 Year After Arthritis Dx

BY MITCHEL L. ZOLER

COPENHAGEN — The increased risk for myocardial infarction in patients with rheumatoid arthritis starts to become apparent a year after rheumatoid arthritis is first diagnosed, based on a case-control study with more than 45,000 people.

"The increased risk of myocardial infarction is evident earlier in the course of rheumatoid arthritis than previously thought," Marie Gunnarsson said at the annual European Congress of Rheumatology. "The finding underscores the need for early heart-disease prevention measures in this population," added Ms. Gunnarsson, an epidemiology researcher in the Institute of Environmental Medicine at the Karolinska Institute in Stockholm.

The spike in MI risk occurs precipitously with RA diagnosis. In a prior report, Ms. Gunnarsson and her associates showed no excess risk for MI exists when RA is first diagnosed.

The study included 7,653 patients diagnosed with RA during 1996-January 2007 and entered into the Swedish RA register. Each of these patients was newly diagnosed, within 18 months from when RA symptoms first appeared. Each patient was matched by gender, age, and residential area with five people from the general Swedish population. The average age of the RA patients and matched comparators was 57 years, and 71% were women.

Patients with RA faced a 70% increased risk for being hospitalized for an acute MI.

MS. GUNNARSSON

During an average follow-up of almost 5 years in both groups, patients with RA faced a 70% increased risk for being hospitalized for an acute MI during the second through fourth year following their RA diagnosis, compared with controls, a statistically significant difference, Ms. Gunnarsson reported.

Hospitalizations for MI also were 70% higher among patients with RA during years 5-10 following their diagnosis. (See box.) In contrast, during the first year following RA diagnosis the patients also had an increased rate of MI hospitalizations, compared with controls, but the difference was not statistically significant.

The analysis showed no significant differences in the rates of MI death between the RA patients and controls during any follow-up period. The rate of death from any cause was also not significantly different between the two groups during most follow-up periods. The exception was during the period 5-10 years following RA diagnosis, when the RA patients had a 10% increased rate compared with the controls, a difference on the cusp of statistical significance.

Another analysis looked at the interaction of rheumatoid factor and MI hospitalizations. RA patients positive for rheumatoid factor had a slightly higher hospitalization rate than all RA patients, peaking with a rate twice the control rate at 5-10 years following RA diagnosis.

The study was funded in part by Astra Zeneca. Ms. Gunnarsson and her colleagues had no other disclosures to report. ■

Relative Risk for Myocardial Infarction in RA Patients

	Overall relative risk	Risk 0-11 months after RA diagnosis	Risk 1-4 years after RA diagnosis	Risk 5-10 years after RA diagnosis
Hospitalization for acute myocardial infarction	1.6*	1.4	1.7*	1.7*
Death from myocardial infarction	1.1	1.3	1.0	1.1
Death from any cause	1.0	0.7	1.0	1.1*

*Statistically significant difference in RA patients, compared with controls
Note: Findings from a study of 7,653 patients diagnosed with rheumatoid arthritis and 37,837 matched controls without rheumatoid arthritis.

ELSEVIER GLOBAL MEDICAL NEWS

Hyperuricemia Linked to Atherosclerosis in Young Adults

BY MITCHEL L. ZOLER

COPENHAGEN — Young, asymptomatic adults with elevated serum uric acid levels had a significantly increased risk for coronary atherosclerosis in a study of nearly 3,000 people.

"Hyperuricemia seems to be an independent risk factor for atherosclerosis in young adults with no other risks for atherosclerosis," Dr. Eswar Krishnan said at the annual European Congress of Rheumatology.

Each 1 mg/dL increase in the level of serum uric acid was linked with a statistically significant 15% increased risk of coronary atherosclerosis that was independent of other risk factors, judging from findings from a logistic regression analysis. The same relationship held in a subgroup that did not have metabolic syndrome, said Dr. Krishnan, a rheumatologist at Stanford (Calif.) University.

Results from prior studies had established a link between hyperuricemia and cardiovascular disease, but it wasn't clear what mechanism explains this link. The new finding implicates high serum uric acid as an apparent cause of atherosclerosis, both in coronary arteries and potentially in other vessels too, which in turn would produce cardiovascular disease events. The results "established that a higher rate of atherosclerosis is the pathway," Dr. Krishnan said in an interview.

Whether treatment that reduces hyperuricemia would blunt the atherosclerotic effect and improve outcomes is a hypothesis that needs testing, he cautioned. Allopurinol, the standard treatment for elevated serum uric acid levels, "is not a benign drug. It does other things" than just lower serum uric acid, Dr. Krishnan said.

Another option now available for reducing serum uric acid is febuxostat (Uloric), a selective xanthine oxidase inhibitor approved by the Food and Drug Administration for treating gout last February and on the U.S. market since March.

Dr. Krishnan said he received research support from and has been a consultant to Takeda, the company that markets Uloric, and two of his collaborators on the study are employees of Takeda. Dr. Krishnan said that he also owns stock in Savient Pharmaceuticals, the company developing pegloticase (Krystexxa), another drug for lowering serum uric acid and treating gout.

The new study used data collected from 5,115 asymptomatic people, aged 18-30 years, in the longitudinal Coronary Artery Risk Development in Young Adults (CARDIA) study. Participants were enrolled in four U.S. cities: Birmingham, Ala.; Chicago; Minneapolis; and Oakland, Calif. Half of the participants were African American, half were white, half were younger than 25, and none had long-standing risk factors for coronary disease. Fifteen years after enrollment, 2,997 participants had an electron beam coronary CT scan. For this analysis, any coronary calcification seen on the CT scan indicated coronary atherosclerosis.

The prevalence of coronary atherosclerosis was nearly doubled in the highest uric acid quartile.

DR. KRISHNAN

Dr. Krishnan and his associates divided the subjects into quartiles based on their serum uric acid levels. The highest quartile level was 6.7-11.6 mg/dL among men and 4.9-10.7 mg/dL among women. Fewer than 10 had gout, although with serum uric acid levels this high many more would likely develop gout as they aged, Dr. Krishnan said.

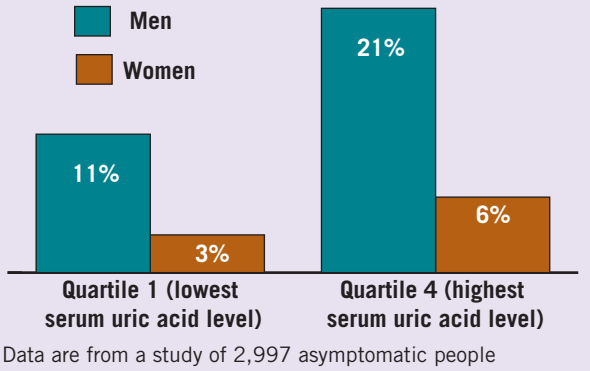
The prevalence of coronary atherosclerosis was nearly doubled in the highest uric acid quartile as compared with the lowest quartile for both men and women. (See box.) For example, men in the lowest quartile for serum uric acid had an 11% prevalence of coronary calcification; those in the highest quartile had a 21% prevalence.

In the logistic regression analysis, men and women in the highest quartile had a statistically significant, 73% increased risk of coronary atherosclerosis after adjustment for age, sex, body mass index, lipid levels, hypertension, type 2 diabetes, alcohol use, and renal disease. In this case, too, the relationship was similar when the analysis included only those without metabolic syndrome.

A second analysis looked at the link between serum uric acid levels and their Agatston score, which is the average amount of calcium in their coronary arteries on CT scan. Men in the highest quartile had an average score that was fourfold higher than that of men in the lowest quartile. In women, the score averaged threefold higher in the highest quartile compared with the lowest.

Several mechanisms might explain the uric acid–atherosclerosis link. Hyperuricemia might be a marker for oxidative stress or for inflammation, or uric acid itself could be atherogenic, Dr. Krishnan said. ■

Coronary Atherosclerosis Prevalence Increases With Rise in Serum Uric Acid Levels



Note: Data are from a study of 2,997 asymptomatic people aged 18-39 years.
Source: Dr. Krishnan

ELSEVIER GLOBAL MEDICAL NEWS