

## Subtle Heart Failure Signs Increase RA Mortality Risk

BY DIANA MAHONEY  
New England Bureau

BOSTON — Heart failure appears to be treated less aggressively in people with concomitant rheumatoid arthritis, based on the results of a community-based cohort study.

The findings, which were reported at the annual meeting of the American College of Rheumatology, showed that treatment disparities may account for some of the excess cardiovascular mortality in RA patients.

Optimizing the treatment of heart failure in RA could lead to improved survival and should be a priority, according to one of the study's investigators, Dr. John M Davis III of the Mayo Clinic in Rochester, Minn.

"The clinical implication is that we need to maintain a high index of suspicion for signs and symptoms of heart failure, order appropriate work-up, and consider cardiovascular referral and/or therapies," he said in an interview.

Dr. Davis and his colleagues studied 309 patients, 103 with and 206 without RA. Their mean age was 78 years, and all had heart failure as defined by Framingham criteria. Medical charts were reviewed for data on the use of echocardiograms and the prescription of cardiovascular drugs, including ACE inhibitors,  $\beta$ -blockers, and diuretics, both before and after heart failure diagnosis. The researchers used chi-square tests and logistic regression models to examine

the differences between the two groups.

The prevalence of ischemic heart disease was 24% in those with RA and 40% in those without. Hypertension was less prevalent in the RA patients (60% vs. 70%), but smoking was more prevalent (55% vs. 44%).

Fewer than half (47%) of the RA patients and 61% of those without RA received an echocardiogram within 90 days of their heart failure diagnosis, a significant difference. The difference persisted after adjusting for ischemic heart disease, hypertension, and smoking, Dr. Davis stated, noting that the odds ratio for receiving an echocardiogram among RA patients, compared with those without RA, was 0.53. In addition, 40% of the heart failure patients with RA and 84% of those without RA received cardiovascular medications within 60 days following diagnosis.

"The signs and symptoms of heart failure appear to be more subtle in the RA population, so there may be some difficulty in terms of recognition," he said in an interview. Other disease factors might mask heart failure symptoms. "[Arthritis] patients' sedentary status limits the ability to develop exertional symptoms; interstitial lung changes can confound the pulmonary exam for edema; and swelling in the ankles could be interpreted as arthritis and not edema," he said. In addition, long medication lists might discourage adding cardiovascular treatments and introduce compliance issues in patients. ■

## Research Focus on Bone Could Yield Targeted Therapies for Osteoarthritis

BY BETSY BATES  
Los Angeles Bureau

BEVERLY HILLS, CALIF. — New ways of thinking about the underlying causes of osteoarthritis may lead to targeted therapeutic advances similar to those currently available for rheumatoid arthritis, Dr. Steven R. Ytterberg said at the annual meeting of the American Association for Hand Surgery.

The first conceptual shift is the notion that osteoarthritis probably is not a disease, but a clinical and pathologic outcome arising from a range of disorders, explained Dr. Ytterberg, a clinical rheumatologist and researcher at the Mayo Clinic, Rochester, Minn.

He noted wide disparities in the characteristics of primary vs. secondary osteoarthritis; localized, single-joint disease vs. generalized osteoarthritis; and osteoarthritis associated with osteophyte necrosis, inflammation, or crystal deposition.

Dr. Ytterberg compared, for instance, inflammatory, erosive osteoarthritis of the hands with diffuse idiopathic skeletal hyperostosis (DISH). "Is this all the same disease? I don't know that it makes sense that it is."

Another major shift is in the way researchers are studying development of osteoarthritis. "With osteoarthritis, the focus

has always been on cartilage. To begin to see frayed cartilage through the arthroscopy has always been presumed to be where the action is," he said.

Microscopic disruption of the extracellular matrix, and later, macroscopic clefts in the cartilage were seen as progressive evidence of encroaching disease.

Now, the focus has shifted, and the target of research is bone.

"A large amount of information is now calling attention to what's going on in the chondrocytes: potential changes in cell-signaling pathways."

Many researchers are now beginning to believe that "subchondral bone is where the problem is," with cartilage abnormalities perhaps the downstream effect of abnormal wear in response to bone changes, said Dr. Ytterberg.

Other researchers are pursuing the hypothesis that osteoarthritis is an enthesopathy.

These theoretical research constructs are currently in their infancy but could help to better characterize what is now a diffusely defined set of symptoms that may or may not have common mechanistic origins, he said.

"This may open avenues of thinking [regarding] therapy for osteoarthritis, much like [the targeted therapies] we now have for rheumatoid arthritis," he noted. ■

## Disability Seems Worse in RA Patients With Low Vitamin D

BY DIANA MAHONEY  
New England Bureau

BOSTON — Vitamin D deficiency is prevalent in rheumatoid arthritis patients and may influence patient disability, which makes a periodic assessment of vitamin D status a crucial part of their management, according to Dr. Uzma J. Haque of Johns Hopkins University in Baltimore.

Of 62 rheumatoid arthritis patients followed at the Johns Hopkins Arthritis Center, Baltimore, from December 2003 through November 2006, those patients with vitamin D deficiency (defined as a serum 25-hydroxyvitamin D [25(OH)D] level below 30 ng/mL) were significantly more likely to report major difficulties in performing activities of daily living than were patients with normal levels of vitamin D, Dr. Haque reported in a poster presentation at the annual meeting of the American College of Rheumatology. Vitamin D deficiency was not, however, significantly associated with markers of rheumatoid arthritis, she said.

The mean age of the predominantly

white, female (82%) study population was 57.6 years, and the mean disease duration was 11.6 years.

In addition to the serum concentration of 25(OH)D, the analysis included joint count, disease activity score, health assessment questionnaire (HAQ), and pain scores, Dr. Haque noted.

The investigators identified vitamin D deficiency in 37 of the 62 patients and observed that 25(OH)D levels fluctuated, ebbing lowest between April and June and highest between July and September, according to Dr. Haque.

Vitamin D deficiency was not significantly associated with any demographic or rheumatoid arthritis characteristics, nor were there any significant associations between vitamin D levels and disease activity score, joint counts, morning stiffness, or rheumatologist global assessments, she said.

"In contrast, [vitamin D] levels were significantly and inversely associated with HAQ, even after controlling for disease duration," Dr. Haque reported.

Dr. Haque reported no conflicts of interest relative to her presentation. ■

## Genetic Factors May Dictate Course of Knee Osteoarthritis

BY DAMIAN McNAMARA  
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FORT LAUDERDALE, FLA. — Symmetrical bilateral progression of knee osteoarthritis was a surprising result of a genetic study of people with hand osteoarthritis and their relatives.

"[This finding] indicates to me that there is probably a strong genetic factor for progression," Dr. Virginia Byers Kraus said in an interview during a poster session at the World Congress on Osteoarthritis.

Dr. Byers Kraus and her associates studied 1,333 patients with hand osteoarthritis for a median of 3.8 years. Participants whose osteoarthritis progressed in either the medial or lateral compartment of one knee were significantly more likely to show progression in the same compartments of the other knee.

There are clinical implications to the findings. For example, "if you see these individuals [with hand osteoarthritis], if they have an affected knee, the other is likely to be affected with osteoarthritis and they are likely to progress in parallel," said Dr. Byers Kraus, an internist in the division of rheumatology, Duke University Medical Center, Durham, N.C. "It's a probable prognostic factor for patients."

What makes the conclusions "particularly intriguing" is that the knee progression symmetry was observed in this study of people with hand osteoarthritis, Dr. Byers Kraus said at the meeting, which

was sponsored by the Osteoarthritis Research Society International.

The cohort came from the Genetics of Generalized Osteoarthritis (GOGO) study. In all, 79% were women and the mean age was 69 years. Researchers scored baseline and follow-up radiographs for changes in Kellgren-Lawrence grade, minimal joint space, presence of osteophytes, and joint space narrowing of the medial and lateral knee compartments. They also assessed at least two affected siblings with three-joint bilateral bony enlargements in their hands to assess any genetic correlations.

"In a cohort with hand osteoarthritis, they were more likely to have osteoarthritis [in other joints] if family members have hand osteoarthritis," Dr. Byers Kraus said. And "when you have a patient with hand osteoarthritis and relatives with hand osteoarthritis, there is an increased likelihood of bilateral knee osteoarthritis."

These findings support a strong genetic or constitutional risk for progression in knee osteoarthritis, Dr. Byers Kraus said.

The results also could have research implications, especially in studying people with osteoarthritis but in whom there is no progression, Dr. Byers Kraus said. This makes it difficult to assess the efficacy of a particular treatment compared with a control group. "This was responsible for the failure of a major trial on Acetone. Age, female gender, obesity—outside of these, we are not good at identifying definite progressors." ■