MMP3 Predicts Progression Of Ankylosing Spondylitis

BY JEFF EVANS
Senior Writer

WASHINGTON — Elevated expression of matrix metalloproteinase-3 in patients with ankylosing spondylitis may independently predict radiographic disease progression, Dr. Walter P. Maksymowych reported at the annual meeting of the American College of Rheumatology.

Joint and bone damage progression in ankylosing spondylitis becomes evident radiographically over a very long period and further damage can only be predicted from damage already visible on radiographs, making it difficult to diagnose and predict the disease course, said Dr. Maksymowych of the University of Alberta, Edmonton (Arthritis Rheum. 2004;50:2622-32).

This is "perhaps one of the greatest challenges in the field of spondylitis research," he said. The dependence on radiographic evidence of progression poses major difficulties in "the design of clinical trials of agents that evaluate disease modification."

Matrix metalloproteinase-3 (MMP3) was the only independent and significant biomarker to predict progression in a panel of nine serologic proteins involved in disease activity and structural damage progression in inflammatory forms of arthritis, as well as osteoclast regulation.

Dr. Maksymowych and his colleagues analyzed the proteins in 100 patients with ankylosing spondylitis in the OASIS (Outcome in Ankylosing Spondylitis International Study) longitudinal cohort that began in 1996 at four centers in the Netherlands, Belgium, and France. The patients had a mean age of 43 years and a mean disease duration of 10.6 years.

The level of MMP3 was the only biomarker that was significantly associated with the progression of structural damage at 2 years, after adjustment for age, sex, disease duration, C-reactive protein levels, and modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) at baseline. A cutoff level of 68 ng/mL MMP3 in serum and a cutoff score of 10 units on the mSASSS predicted progression at 2 years.

Radiographic progression was 78 times more likely to occur with an MMP3 level of at least 68 ng/mL and an mSASSS of at least 10 units or more than with a lower MMP3 level and a lower damage score. Overall, 15% of the patients fell into that high-risk category. Of those who developed radiographic progression by 2 years, 67% had a high MMP3 level and a high damage score.

"Neither MMP3 nor baseline mSASSS alone are of prognostic value in individual patients. However, the combination of a high MMP3 and a high baseline mSASSS score, as defined by those cutoffs, is of prognostic value in individual patients," Dr. Maksymowych said. The next step is to test these cutoffs in another cohort of ankylosing spondylitis patients. ■

Should a Swollen Joint Count Be Conducted at Every Office Visit?

BY DIANA MAHONEY
New England Bureau

BOSTON — Because patient self-reported rheumatoid arthritis outcomes are insufficient on their own for making therapeutic decisions, a swollen joint count should be conducted at every visit, according to Dr. Edward Keystone.

In a small clinical study, Dr. Keystone and his colleagues of the University of Toronto's Mount Sinai Hospital surveyed 66 rheumatoid arthritis patients about their disease status during routine visits.

"Patients were asked to rate how they were feeling—very well, well, fair, poor, or very poor—on the day of their visit with respect to their rheumatoid arthritis," Dr. Keystone said at a meeting on rheumatology sponsored by Harvard Medical School. The investigators then correlated the self-reported outcomes with a variety of disease measures including pain and fatigue visual analog scales, physician global assessment quality of life and disease activity scales, and formal joint counts.

"By and large, pain and fatigue dictated the self-assessments," said Dr. Keystone. Patients who had high scores on these measures were most likely to report "poor" or "very poor." Yet there was only a modest correlation between patient self-assessment and swollen joint count. In fact, he said, some of the patients with the most swollen joints reported "fair," "well," or "very well" with respect to their disease.

The fact that swollen joint count does not correlate with patients' perceptions of their conditions is especially troublesome in light of a recent study suggesting that many rheumatologists don't perform a formal quantitative joint count during routine visits with patients under their care, said Dr. Keystone.

For the study, investigators queried approximately 600 rheumatologists attending the annual European League Against Rheumatism (EULAR) meeting regarding their use of formal joint counts in routine care (Ann. Rheum. Dis. 2006;65:820-2). "More than half [of the respondents] reported performing a joint count at fewer than half of the routine visits, and 45% said they performed joint counts at less than 25% of the visits," said Dr. Keystone. Thirteen percent of the respondents said they never perform a formal joint count, he noted.

'Performing a swollen joint count is easy and extremely valuable in clinical practice.'

DR. KEYSTONE

As a result, many physicians are missing signs of disease progression as well as important windows of opportunity for effective intervention, said Dr. Keystone. "Patients with mild to moderate disease activity might report that they're doing 'well,' when in fact a joint count might suggest disease progression," he said. "And we know that tight, early control of moderate disease can substantially improve patient outcomes."

It's not enough to ask patients how they are doing and leave it at that, Dr. Keystone stressed. "While it's not feasible to get an MRI or radiographic assessment of disease status at every visit, performing a swollen joint count is easy and extremely valuable in clinical practice." ■

Quadriceps Strength, Mass May Predict Course of Knee OA

BY JEFF EVANS
Senior Writer

WASHINGTON — Strong quadriceps muscles appear to protect against cartilage loss in some parts of the knee in most people, but larger muscle mass in the knee may be associated with x-ray progression of knee osteoarthritis in women, according to findings from two studies presented at the annual meeting of the American College of Rheumatology.

Specifically, strong quadriceps muscles protected the patellofemoral joint from cartilage loss and did not worsen its loss in the tibiofemoral joint in both men and women. A large leg muscle mass overall did not appear to influence the x-ray progression of osteoarthritis (OA) in the patellofemoral joint, except for the medial aspect of the joint in women.

Speaking during a press conference, Dr. Shreyasee Amin of the Mayo Clinic, Rochester, Minn., noted that strong quadriceps have generally been viewed as protective against knee OA. But some previous studies have found evidence that greater quadriceps strength may actually do more harm than good in the tibiofemoral joint in knees with mechanical malalignment.

But these earlier studies used x-rays to measure progression, which is an indirect measure of cartilage loss, the hallmark of OA. Pathologic changes to the meniscus on x-ray also can appear to cause an increase in joint-space narrowing, yet not reflect any real change in cartilage, she said.

Dr. Amin and colleagues prospectively performed MRI scans at baseline, 15 months, and 30 months, and measured the quadriceps strength at baseline in a cohort of 265 men and women with symptomatic knee OA. The patients had a mean age of 67 years and a mean body mass index (BMI) of 31.5 kg/m^2. Upon dividing the patients into three levels of strength for each gender, the investigators found that men and women who had the greatest quadriceps strength were 60% less likely to lose cartilage in the lateral aspect of the patellofemoral joint after 30 months than were those who had the least strength.

"The quadriceps muscle could help stabilize the patella and prevent it from subluxing laterally, and so we feel that that might be a reason why greater quadriceps strength protects against cartilage loss at the lateral patellofemoral joint," she said.

MRI scans showed no evidence that greater quadriceps strength either protected or worsened cartilage loss at other areas of the knee. The analyses were adjusted for age, BMI, gender, and baseline cartilage scores.

In a subgroup analysis of patients who had their knees measured for malalignment, varus alignment (bow leg) of 5 degrees or more did not increase the risk for tibiofemoral joint cartilage loss. There were too few people who had a valgus alignment (knock knee) of 5 degrees or more for analysis.

During a separate presentation at the same meeting, Dr. David J. Hunter of Boston University reported that a large amount of lean muscle mass in the leg had no effect on the x-ray progression of patellofemoral OA, after correcting for race, height, and total percentage of fat. But women with the largest muscle mass were more likely to experience progression of medial patellofemoral OA than were women with the least amount of leg muscle mass, even after adjusting for those confounding variables.

"I really want to emphasize that a lot of the effects that we saw with muscle mass were largely mitigated when we adjusted for total percent fat and race. The differences in prevalence [of joint space narrowing progression] were quite profound in this study, such that it was much more common in blacks, particularly in black women," Dr. Hunter said.

Dr. Hunter and his associates measured OA progression with weight-bearing, skyline x-rays that were taken at baseline and after 36 months in a subset of 796 patients with and without knee pain on most days of the month. The patients were originally part of a cohort of 3,075 white and black men and women aged 70-79 years in the multicenter, community-based Dynamics of Health, Aging, and Body Composition (Health ABC) study on knee OA.

The results could possibly be explained by an increased pull of the vastus medialis oblique muscle in patients with large muscle mass, which would pull the patella medially and increase the potential for medial patellofemoral joint space narrowing progression. The force of knee flexion might also be increased in people with large leg muscle mass because of a large hamstring muscle, which could potentially increase the patellofemoral joint reaction force. Muscle mass itself also might be a proxy for physical activity, which itself may predispose a person toward progression, according to Dr. Hunter. ■