Biomarkers Indicate HT Use Reduces Cartilage Turnover

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CHICAGO — Current hormone therapy use in postmenopausal women reduces cartilage turnover, Joanne M. Jordan, M.D., said at the 2004 World Congress on Osteoarthritis.

The study included 168 postmenopausal women, of whom 49% were African American, 23% were current hormone therapy (HT) users, and 63% had knee osteoarthritis (OA).

Rates of type II collagen cleavage measured by levels of the cartilage degradation assay and collagen II synthesis measured by type II procollagen (CPII) synthesis were lower in current HT users than in nonusers.

Taken together, these results demonstrate reduced collagen II turnover in HT users with and without osteoarthritis, Dr. Jordan reported in a poster at the meeting, sponsored by the Osteoarthritis Research Society International.

Dr. Jordan and colleagues at the Thurston Arthritis Research Center at the University of North Carolina at Chapel Hill previously reported that current HT use is associated with lower levels of serum cartilage oligomeric matrix protein, another marker of cartilage degradation.

In the current study, led by doctoral student Anca D. Dragomir, separate analyses of covariance models were used to evaluate the relationship between current HRT use and biomarker levels.

After controlling for ethnicity, age, body mass index, and knee OA status, only the reduction in mean CPII associated with current HT use was significantly associated with collagen II synthesis.

There was evidence of an association between current HT use and knee OA status for another biomarker, chondroitin sulphate epitope 846 (CSE 846), thought to be a marker of newly synthesized cartilage proteoglycan. HT users without OA had higher levels of CSE 846, compared with HT users with OA. This suggests that HT use could increase proteoglycan aggrecan production in postmenopausal women with no radiographic evidence of knee or hip OA. ■

Composite MRI Evaluation More Telling of OA Pathology

CHICAGO — The association between knee pain and the presence of pathologic features varies by the different compartments of the knee, Kathryn Wildy, M.D., reported at the 2004 World Congress on Osteoarthritis.

Using the Whole-Organ Magnetic Resonance Imaging Score (WORMS) system, a semiquantitative method that systematically scores 11 structural features, including articular cartilage, subarticular marrow edema, cysts, and bone attrition in eight different locations in the knee, Dr. Wildy and colleagues demonstrated how MRI studies that show the worst pathologically affected compartment, or even the total knee, often fail to correspond to the pain.

"When you look at the total knee, you probably are losing the story. We're looking at each compartment, rather than just the worst compartment, and you need to look at the different regions within each compartment," Dr. Wildy said at the meeting sponsored by the Osteoarthritis Research Society International.

In their multicenter study involving 263 elderly men and women with discordant knee pain, axial, coronal, and sagittal plane studies were obtained on fast spin echo MRI and the WORMS system was used to score pathologic features of the knee. The patient's nonpainful knee served as a control.

Knee pain was defined as pain on most days of the month in the past year or moderate pain on the Western Ontario and McMaster University Osteoarthritis (WOMAC) index in the past 30 days; the mean WOMAC score was 6.2 for the painful knee and 0.4 for the nonpainful knee.

In this community-based population, the severity of cartilage damage, osteophytes, and synovitis were each independently associated with knee pain, reported Dr. Wildy, who led the study while at the University of Pittsburgh.

In the medial tibiofemoral compartment, bone attrition and bone marrow edema scores greater than 0 were significantly associated with knee pain; in the lateral tibiofemoral compartment the presence of all measured features was significantly associated with pain.

In the patellofemoral compartment, no feature was associated with pain. For the total knee, cartilage damage, bone attrition, and bone marrow edema scores greater than 0 were associated with knee pain, said Dr. Wildy, who now practices in Omaha, Neb.

Interaction between features revealed that bone marrow edema,which was common in the painful knees, was significantly associated with pain when accompanied by high cartilage damage in either the total knee (OR 3.27) or the medial tibiofemoral compartment (OR 2.0). ■

MMP-3 Levels May Predict Joint Space Narrowing in OA Patients

CHICAGO — Baseline plasma matrix metalloproteinase 3 levels predicted joint space narrowing over 16 months in patients with knee osteoarthritis, according to findings from a pilot study.

However, the predictive accuracy of MMP-3 declines somewhat between 16 months and 30 months, Steve A. Mazzuca, Ph.D., reported at the 2004 World Congress on Osteoarthritis.

MMP-3, which is produced by chondrocytes and synoviocytes, has been implicated in the degradation of articular cartilage in osteoarthritis (OA). Compared with healthy subjects, patients with knee OA have higher concentrations of MMP-3 in their synovial fluid and blood.

"We are unable to answer the question right now if MMP-3 is an adequate surrogate for joint space narrowing, but it does correlate in real time," said Dr. Mazzuca, professor and senior scientist at Indiana University, Indianapolis.

The 30-month study, led by Stefan Lohmander, M.D., of Lund (Sweden) University, involved 120 obese women 45-64 years old with unilateral knee OA.

Study participants were selected from a larger randomized trial of doxycycline, a disease-modifying OA drug. An equal number of patients had progressive radiographic knee OA and stable disease.

During the follow-up period, mean joint space narrowing in the index knee was 0.97 mm among those with progressive disease. There was the slightest increase, 0.03 mm, in joint space width in those with stable disease.

After adjustment for age, baseline joint space width, and treatment, a regression analysis showed that patients with the highest MMP-3 concentrations at baseline (more than 11.85 ng/mL) were more than three times as likely to progress to joint space narrowing in both knees at 16 months than patients with the lowest MMP-3 concentrations (1.5 ng/mL to 6.42 ng/mL) at baseline (odds ratio 3.48).

The association was less striking at 30 months, although the risk of progression remained significantly higher among patients with the highest MMP-3 levels (OR 2.09), Dr. Mazzuca reported at the congress, sponsored by the Osteoarthritis Research Society International.

The study also evaluated whether plasma MMP-3 values could have served as a surrogate marker in the original doxycycline trial. Serial MMP-3 levels examined at two time intervals (0-16 months and 16-30 months) found that both mean and maximal MMP-3 levels were significantly related to joint space narrowing in patients treated with placebo. For the doxycycline group, there was not a significant association at the first time interval, and a reverse association at the second interval. Dr. Mazzuca concluded that serum MMP-3 correlates with concurrent joint space narrowing in knees not treated with doxycycline. ■