

Collagen Biomarkers Predict OA Progression

Measuring the collagen degradation chemicals may help identify high-risk knee OA patients.

BY DIANA MAHONEY
New England Bureau

BOSTON — Disease progression in early osteoarthritis is associated with combined increases in biochemical markers for the synthesis and degradation of type II collagen, and these changes can be identified before radiologic evidence of the disease is apparent, a study has shown.

The findings suggest that measuring these biomarkers may help identify patients with early knee osteoarthritis who are at high risk for rapid progression, Dr. Patrick Garnero said at the 10th World Congress on Osteoarthritis.

“Currently, the only validated methodology for assessing progression in osteoarthritis is the measurement of joint space width by radiography, which has limited sensitivity,” said Dr. Garnero of the Institut National de la Santé et de la Recherche Médicale

in Lyon, France. “When there is radiologic evidence of osteoarthritis, significant joint damage has already occurred,” he said at the congress, which was sponsored by the Osteoarthritis Research Society International. Previous short-term studies in advanced osteoarthritis have shown that baseline levels of serum concentration of the N-propeptide of collagen type IIA (PII-ANP) and the urinary excretion of cross-linked C-telopeptide (CTX-II) are associated with disease progression.

Dr. Garnero and his associates at the University of Bristol in England followed 84 patients with early osteoarthritis in one or both knees for 5 years. All of the patients, mean age 62 years, had experienced persistent pain in one or both knees for more than 3 months, and 39% presented with a Kellgren-Lawrence score of less than 2. Using specific ELISA assays, the investigators measured each patient’s PII-ANP and CTX-II levels and obtained knee radiographs at baseline and at 2, 3, and 5 years. The radiographs were read by two independent readers. “Of interest,” Dr. Garnero said, independent readings showed that “about 60% of the patients had Kellgren-Lawrence scores lower than 2 and about 42% had scores below 0, suggesting a large proportion of this cohort had very early disease.”

“We defined disease progression as either a reduction in the tibiofemoral joint space by at least 2 mm or total replacement of either knee during the 5-year follow up,” Dr. Garnero said. Based on these criteria, 24 had progressive disease and 60 did not.

In the overall cohort there was a “slight but significant” mean PII-ANP increase of 1.6% per year and no increase in urinary CTX-II levels during the 5-year follow up. When patients with and without progressive disease were considered independently, however, there were substantial differences. “Both measures

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were significantly higher throughout the study in the 24 patients with progressive disease compared with the remaining 60 patients,” Dr. Garnero said. Even so, “we could not differentiate the two groups according to x-ray measurements,” suggesting that detectable biomarker changes precede radiologic progression.

When classified by quartile of mean 5-year levels for both PII-ANP and CTX-II measures, patients in the highest quartile of PII-ANP and in the two highest quartiles for CTX-II were associated with increased risk for progression. The odds ratio for increased progression risk for the highest quartile PII-ANP measures alone and the two highest quartiles for CTX-II measures alone were 3.2 and 3.4, respectively, compared with 11.8 for the combination of both markers.

The sensitivity and specificity of the PII-ANP top quartile alone were 42% and 82%, respectively, compared with 71% and 58% for the CTX-II top two quartiles. “Combined, the sensitivity and specificity for both markers was 92% and 52%, respectively,” Dr. Garnero said. Because progression of joint damage likely results primarily from an imbalance between degradation and reparative processes, “combining these two markers is more effective in predicting progression than the measurement of a single marker.”

Predicting progression in osteoarthritis is notoriously difficult “because the outcomes vary substantially from patient to patient even if other considerations are the same,” he said.

The findings need to be validated in a larger study, he noted. ■

Patellar Immobility Associated With Severe Chondral Damage

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — Restricted patellar mobility in patients with anterior knee pain is associated with chondral damage in the patellofemoral compartment, results from a large study demonstrated.

Knees with patellar tightness were three times more likely to have severe patellofemoral damage compared with those without tightness, Dr. J. Richard Steadman reported at a symposium sponsored by the International Cartilage Repair Society.

Many causes for patellar immobility exist, including compartmentalization by plica, suprapatellar scarring, and anterior interval contracture. “If you look at the patellar tendon and its relationship to the tibia going into flexion you’ll find that patellar tendon actually separates from the tibia,” explained Dr. Steadman, of the Steadman Hawkins Research Foundation, Vail, Colo. “So if you have a scarring ... between the patellar tendon and the tibia, you’ve eliminated the slack in the joint that allows you to have noncompressed cartilage as you go through a range of motion.”

Preoperatively, he and his associates subjectively measured and documented patellar tight-

ness in the superior, inferior, medial, or lateral directions in 410 knees between November 2004 and November 2005. At surgery, the researchers collected data on knee pathology and documented chondral defects in all compartments of the knee. Grade 3 or 4 defects on the Outerbridge classification system were considered severe chondral damage.

Slightly more than half of the study participants (52%) were female and their average age was 44 years.

Dr. Steadman reported that preoperatively, 41% of patients had patellar tightness in at least one direction, 24% had patellar tightness in all four directions, 9% had inferior and superior tightness only, and 3% had medial and lateral tightness only. At surgery, 40% of patients had severe chondral damage of the patellofemoral compartment.

In addition, 54% of knees with patellar tightness had severe patellofemoral chondral damage while only 29% without patellar tightness had severe patellofemoral chondral damage.

Knees with patellar tightness were three times more likely to have severe patellofemoral damage compared with those without tightness. The highest odds of severe patellofemoral defects were associated with superior tightness (3.0) and inferior tightness (2.4). ■

Functional Therapy Aids Knee OA Rehab

BY DIANA MAHONEY
New England Bureau

BOSTON — Exercises that simulate the mechanically challenging activities of daily living lessen energy expenditures and compensations associated with knee osteoarthritis, Dr. Anthony M. Reginato said at the 10th World Congress on Osteoarthritis.

As such, functional interventions should be an important component of rehabilitation therapy, he said at the congress, which was sponsored by the Osteoarthritis Research Society International.

In a double-blind, randomized trial, Dr. Reginato and his colleagues at Massachusetts General Hospital in Boston analyzed chair rise and box lifting in patients with knee osteoarthritis to determine if functional training or strengthening exercises led to improvements in mechanical energy expenditures (MEE), mechanical energy compensations (MEC), linear and angular momentum, and/or performance duration.

The study included 26 individuals, aged 43-86 years, who had Kellgren-Lawrence grade 2 or 3 knee osteoarthritis and at least two functional limitations on the SF36 physical functioning subscale. Participants were randomized to receive 8 weeks of physical therapy comprising either strength training or functional training.

“The goal of strength training is to address specific impairments, including range of motion and the ability to generate muscle force,” Dr. Reginato said.

In contrast, functional training simulates activities of daily living, such as gait, rising from a chair, and stair climbing, at different speeds and levels of difficulty, the goal of which is to improve neuromuscular control of the whole body, with specific focus on the individual’s abilities and safety limits, he explained.

At baseline and postintervention, each participant completed a chair rise test, which required arising from a backless chair, and a box lift test, which required hoisting a plastic case holding a 5-kg metal disk onto a table. During both tasks, investigators calculated ankle, knee, hip, and back MEE and MEC. They also assessed maximum whole body angular momentum, maximum whole body anterior posterior linear momentum, and maximum whole body vertical linear momentum, as well as the intervals between the start and end of each task.

Using univariate analysis of covariance and multivariate analysis of variance to compare between-group differences in score changes relative to baseline, the investigators determined that, in the chair rise, the functional training group had significantly more improvement in energy expenditures and compensations by increasing ankle energy expenditure and decreasing back compensation, compared with the strength training group. And while there were no significant differences in chair rise interval times between the groups, the functional training group had a greater change from baseline in this measure.

In the box lift test, both groups increased their MEE in the back during the “no transfer” phase of lifting, although the strength training group had significantly higher changes in this measure, Dr. Reginato reported. In the transfer phase, the strengthening group had a significantly greater change in MEE in the back, compared with the functional group, which showed a decrease in this measure, and greater change in maximum whole body angular momentum.

The findings suggest that both functional and impairment-level interventions have important roles in the treatment of knee osteoarthritis, he said. ■