Obesity Does Not Hamper New Knees

BY JONATHAN GARDNER
London Bureau

Obese patients with osteoarthritis experience greater gains in physical function 7 years after undergoing total knee arthroplasty than do obese controls who did not have the surgery, according to an English study.

Based on data from 688 patients, there is no justification to withhold knee replacements from obese patients on the grounds that obesity is a risk factor for OA. At least one National Health Service trust has been reported to apply such a policy, the investigators wrote (Ann. Rheum. Dis. 2008 July 24 [doi:10.1136/ard.2008.093229]).

In a subgroup of 108 obese patients (body mass index greater than or equal to 30 kg/m^2) who underwent total knee arthroplasty (TKA), the median physical function score on the Short Form-36 Health Survey improved from 17 points at baseline to 20 points at a median 7-year follow-up; 36 obese controls who did not have TKA saw their scores decline from a median of 61 to 25 points.

"Improvements in physical function following [TKA] for osteoarthritis are sustained," wrote Janet Cushnaghan of the University of Southampton, England, and her associates. "These benefits extend to [obese patients] and, provided appropriate selection criteria are applied with regard to fitness for surgery, there seems no justification for withholding TKA."

The researchers studied patients and controls aged 45 and older who had taken part in an earlier case-control study of knee OA. That study compared patients placed on a waiting list for TKA between 1995 and 1997 with controls in the community. Functional status and BMI were measured as part of data collection.

During 2001-2004, the authors wrote to the original study group with a questionnaire about their surgery and included the functional status sections of the SF-36 form. A total of 325 patients and 363 controls were included in this analysis.

Overall, at a mean follow-up of 7 years, median physical function scores in patients who underwent TKA improved from 20 to 26; scores in controls fell from 89 to 75.

Mental health scores on the SF-36 form improved equally in both groups. Vitality scores declined in both groups, but the decline was greater in patients than in controls (a loss of 10 points vs. a loss of 5 points).

Of 82 patients older than age 75, the median physical function score stayed steady at 17 points; scores declined from 83 to 43 points in 87 controls in that age group.

The researchers said their findings might have been biased by migration, although subjects were as likely to have moved, demonstrating greater function, as to have entered nursing care, demonstrating poorer function.

They also said OA might have been undetected in the controls at baseline, which would have biased their findings in favor of the intervention group. ■

Combo Useful in Methotrexate Failure

BY NANCY WALSH
New York Bureau

PARIS — The combination of leflunomide and rituximab may offer an effective therapeutic option for patients with rheumatoid arthritis who can't tolerate methotrexate, a small study suggests.

The most effective therapy thus far for RA is a combination of a traditional disease–modifying antirheumatic drug (DMARD) and a biologic. While methotrexate is the most widely used DMARD, a significant number of patients are unable to tolerate this drug, said Dr. Edward M. Vital of the academic unit of musculoskeletal disease, University of Leeds (England).

Combination therapy substituting leflunomide for methotrexate has therefore been tried, first with infliximab as the biologic component. Initial experience, however, demonstrated that this combination was problematic, with a high incidence of vasculitis and 100% of patients who were on the regimen for an extended period developing antinuclear antibodies (ANA). Many also became positive for anti–double stranded (ds) DNA antibodies, Dr. Vital said at the annual European Congress of Rheumatology.

The probable reason for this induction of autoimmunity is that the removal of tumor necrosis factor (TNF) results in a shift in T cells from a predominant Th1 RA-type response to a Th2 lupus-type re-

sponse, with the production of autoantibodies. "Therefore, using a strategy of B-cell depletion with rituximab seems logical and potentially synergistic in combination therapy," he said.

Leflunomide in doses of 10-20 mg/day was administered to 15 patients with active RA in combination with rituximab, given as two infusions of 1,000 mg on days 1 and 15 following pretreatment with 100 mg methylprednisone. The primary end point was a EULAR moderate/good response at 6 months.

The mean age of the patients was 55 years and the mean disease duration was 10 years. The patients had received a mean of four previous DMARDs, and five had previously been treated with anti-TNF drugs.

All were inadequate responders to leflunomide alone.

Mean tender joint count was 18 and mean swollen joint count was 12. The mean disease activity score (DAS) was 6.8 and mean health assessment questionnaire disability index (HAQ-DI) was 2.3.

Thirteen of the patients were rheumatoid factor positive and the remaining two were positive for anticyclic citrullinated peptide (anti-CCP) antibody.

A total of 80% of patients achieved a EULAR moderate/good response with significant reductions in DAS28, said Dr. Vital, who had no financial disclosures.

ACR20, 50, and 70 responses were seen in 68%, 33%, and 20%, respectively, with significant improvements being seen in each component of the ACR core set.

Reductions were also seen in rheumatoid factor, IgM, and IgA.

At the time of Dr. Vital's presentation, eight patients had relapsed, at a mean time of 46 weeks post treatment. Four had not relapsed, with follow-up time of 62-85 weeks. Three partial responders were retreated with good results.

"Relapse-free survival has been somewhat better than expected, with one-third of responders still responding 20 months after treatment," he said.

In contrast, mean time to retreatment among patients treated with rituximab and methotrexate is 45.5 weeks after an inadequate response to methotrexate (Arthritis Rheum. 2007;56:3896-908).

One serious adverse event, a case of gastroenteritis that required 24 hours of hospitalization, was seen. There were no infusion reactions and none of the patients developed ANA or anti-dsDNA antibodies.

"This is a potential treatment option—and a much needed one—for patients who are intolerant of methotrexate," Dr. Vital said. ■

Factors Predict Remission With DMARD Use

PARIS — Factors that predict which rheumatoid arthritis patients will achieve and maintain remission after disease-modifying drugs include low body mass index, low erythrocyte sedimentation rate levels, and absence of anti–cyclic citrullinated peptide antibody at baseline.

"Remission is increasingly becoming an attainable goal in rheumatoid arthritis treatment, and it would be useful to be able to predict which patients are likely to achieve remission in the long run, and so to be able to avoid overly aggressive treatment," Dr. Diane van der Woude said at the annual European Congress of Rheumatology.

Although factors have been identified that predict the achievement of very low disease activity with biologics, little is known about the predictive factors of patients treated with DMARDs, said Dr. van der Woude of the department of rheumatology at Leiden (the Netherlands) University Medical Center.

She analyzed clinical, laboratory, and genetic data from patients enrolled in an inception cohort at the Leiden Early Arthritis Clinic between 1993 and 2003.

Among more than 1,900 patients referred to the clinic, 454 were diagnosed with RA and treated with chloroquine, sulfasalazine, or methotrexate, she said.

Sustained remission, or the absence of synovitis for longer than 1 year without DMARDs, was achieved by 69 patients (15%) with an average follow-up of 8 years. Six patients discharged because of remission had a recurrence of synovitis and were excluded from the remission group.

Univariate analysis revealed the following were significantly associated with less likelihood of achieving DMARD-free remission: positive family history (hazard ratio 0.56); high body mass index (HR 0.90); long duration of symptoms at presentation (HR 0.93); smoking (HR 0.55); and the presence of IgM rheumatoid factor (HR 0.17), anti–cyclic citrullinated peptide (CCP) antibodies (HR 0.09), and shared epitope alleles (HR 0.47).

Multivariate analysis identified older age, low BMI, low ESR, short duration of symptoms, nonsmoking status, and the absence of anti-CCP antibodies as independent predictors for DMARD-free remission.

—Nancy Walsh