The Intensive Diet and Exercise for Arthritis Trial: 18-Month Clinical Outcomes

Written by Debra Gordon, MS

Excess weight is a well-established risk factor for osteoarthritis (OA). The Arthritis, Diet, and Activity Promotion Trial (ADAPT) demonstrated for the first time that exercise that is combined with calorie restriction, designed to reduce body mass index (BMI), could also improve physical function and reduce knee pain [Messier SP et al. *Arthritis Rheum* 2004]. The trial, however, did not demonstrate any effect of diet and exercise on OA progression.

The same authors embarked on a long-term study to test the hypothesis that intensive weight loss (at least 10% of total body weight), along with exercise, would significantly impact the mechanical and inflammatory pathways of OA. Stephen P. Messier, PhD, Wake Forest University, Winston-Salem, North Carolina, USA, and colleagues launched the Intensive Diet and Exercise for Arthritis [IDEA; NCT00979043] trial, an 18-month study that was designed to evaluate the impact of intensive weight loss, with or without exercise, on disease progression.

A primarily Caucasian, female patient population (n=454) with radiographic knee OA and a mean age of 65 years and body mass index (BMI) of 33.6 kg/m^2 were randomized to one of three arms: (1) intensive dietary restriction alone; (2) intensive dietary restriction plus exercise; or (3) exercise alone. An intention-to-treat analysis was used to compare changes in pain, function, and mobility between groups at 18 months of follow-up.

Eighty-eight percent of patients completed the study. Eighty-five percent of participants had bilateral knee OA. Mean weight loss was 9.5 kg (9.5%) in the dietary restriction-only group, 10.6 kg (11.4%) in the dietary restriction-plus-exercise group, and 2.0 kg (2.2%) in the exercise-only group. None of the participants regressed to her baseline weight during follow-up.

At 18 months, all subjects experienced a decrease in Western Ontario and McMaster University Osteoarthritis (WOMAC) pain scores from baseline. Pain was significantly lower in the dietary restriction-plus-exercise group (51% lower than baseline pain), compared with the 27% reduction in the dietary restriction-only group and 29% reduction in the exercise-only group ($p<0.0004$). The dietary restriction-plus-exercise group also significantly improved ($p=0.003$) on the WOMAC function scale (47% relative to the 30% improvement in the dietary restriction-only group and 24% in the exercise-only group).

All groups demonstrated improvements in walking speed, a measure of mobility. However, walking speed was significantly faster in the dietary restriction-plus-exercise group ($p<0.004$) than either the dietary restriction- or exercise-only group.

"Generally, there is a 1% to 2% decrease in walking speed per decade up to age 62," said Dr. Messier. "When a 12% to 16% decline occurs, it is unexpected." In contrast, the intensive dietary restriction-plus-exercise cohort increased their walking speed by 12%, for a walking speed that was faster than that of healthy women aged 40 to 62 years and equivalent to that of healthy middle-aged men. The study cohort reversed the trend of declining mobility that is seen in older adults. Pain can be significantly reduced and mobility and function improved with long-term, intensive dietary restriction and moderate exercise.

Genome-Wide Analysis of Imputed Genotypes Identifies CCR1/CCR3 As Novel Risk Locus in Behçet Disease

Written by Rita Buckley

Behçet disease (BD) is a genetically complex condition that is characterized by recurrent inflammatory attacks that affect the orogenital mucosa, eyes, and skin. Earlier genomewide association studies (GWAS) have linked the *IL10* and *IL23R-IL12RB2* loci to BD susceptibility [Remmers EF et al. *Nat Genet* 2010; Mizuki N et al. *Nat Genet* 2010]. Yohei Kirino, PhD, National Institutes of Health, Bethesda, Maryland, USA presented the findings of a GWAS analysis of imputed genotypes that are associated with BD.

According to Dr. Kirino, whole-genome imputation was used to identify additional BD susceptibility loci using 96 healthy Turkish controls who were genotyped on Illumina HumanOmni1M-Quad single-nucleotide polymorphism (SNP) chips as a reference. Imputation was conducted using MACH v1.0.15, providing 814,474 SNPs for analysis in 1215 BD cases and 1278 healthy controls. Sequenom iPLEX assays were used to validate the imputation results and to fine map the associated region. Two independent replication sets were genotyped for the most significant SNP.