

Light Exercise Best to Prevent Knee Osteoarthritis

BY SUSAN BIRK

FROM THE ANNUAL MEETING OF
THE RADIOLOGICAL SOCIETY OF
NORTH AMERICA

CHICAGO – The wisdom about practicing everything in moderation also may hold true for knees, especially in middle-aged adults with risk factors for osteoarthritis.

Light exercise, such as walking, appears to protect against OA, but the extremes – a sedentary lifestyle or more aggressive workouts – may accelerate OA onset in at-risk individuals, according to baseline data from the Osteoarthritis Initiative, a longitudinal, multicenter, observational study funded by the National Institutes of Health.

Osteoarthritis risk can be reduced by avoiding aggressive exercise and exercising safely, said the study's lead author, Dr. Thomas M. Link, professor of radiology and chief of musculoskeletal imaging at the University of California, San Francisco.

Among at-risk patients, light exercisers had significantly less degeneration of the cartilage surrounding the knees on

Moderate-strenuous exercise may accelerate cartilage degeneration and increase osteoarthritis risk in women who engage in more intense workouts.

magnetic resonance imaging (MRI) than did those whose exercise routines were characterized as either minimal or moderate to strenuous.

Middle-age adults, particularly those with OA risk factors, need to be "extremely careful" with their cartilage, Dr. Link said in a press briefing Nov. 29 during the annual meeting of the Radiological Society of North America. "Once cartilage is gone, it's gone forever."

This doesn't mean that patients should stop running, but it does mean they must make sure they are exercising safely to avoid sustaining an injury that could "initiate an osteoarthritis cascade, which will be very difficult to stop," he said.

Research associate Keegan K. Hovis, R.N., said the key for patients who exercise strenuously is to focus on modifiable risk factors, such as maintaining a healthy weight and strengthening the knee stabilizing muscles, including the quadriceps.

Subjects included 132 at-risk patients and 33 controls matched for age and body mass index (99 women and 66 men between the ages of 45 and 55 years, BMI range of 18-27 kg/m²). Risk factors for OA included a previous knee injury or knee surgery, a family history of total knee replacement surgery, bone spurs on the fingers, and occasional knee symptoms.

Based on responses to the leisure activity component of the Physical Activity Scale for the Elderly, study participants

were stratified according to intensity of exercise habits into sedentary, light, or moderate-strenuous exercisers. Patients also were grouped by whether they engaged in frequent knee-bending activities. These activities included climbing at least 10 flights of stairs daily, lifting objects weighing more than 25 pounds, or squatting, kneeling, or deep-knee-bending for at least 30 minutes per day.

Sedentary exercisers walked less than

or equal to 2 days a week for less than 2 hours per day. Light exercisers walked or participated in other forms of light exercise such as table tennis or Frisbee at least 3 days a week for less than 2 hours a day. Moderate-strenuous exercisers engaged in sports such as running, tennis, or soccer at least 3 days a week for greater than or equal to 1 hour per day.

To assess cartilage health, researchers used T2 mapping, a quantitative and

qualitative MRI technique that, unlike anatomic imaging, reveals the chemical composition and structure of the cartilage (including collagen and water content) and can provide an image marker of cartilage degeneration in its earliest stages.

"T2 values can detect changes in cartilage at the molecular level, prior to irreversible changes in the structure; therefore, it has the potential to identify, with

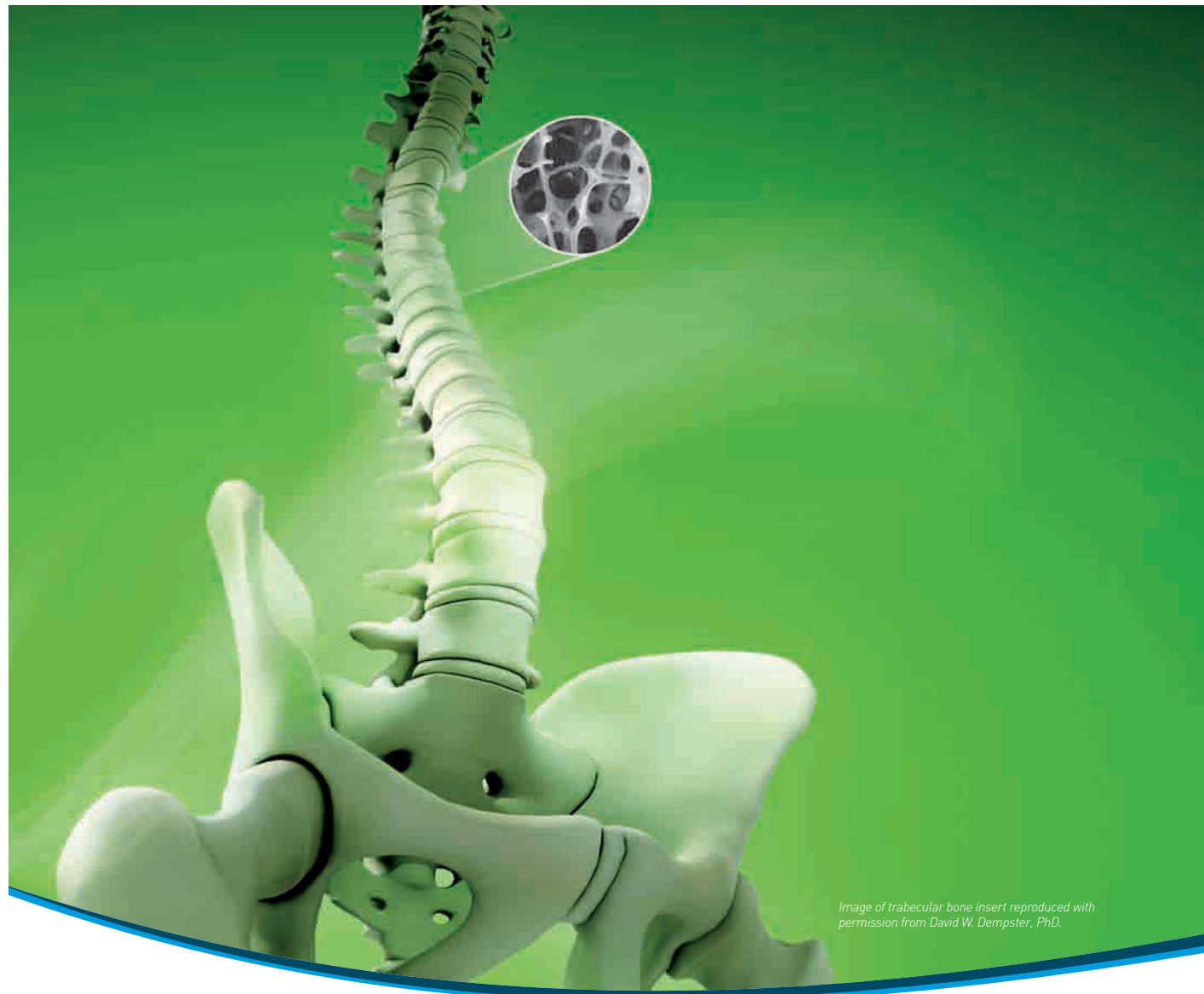


Image of trabecular bone insert reproduced with permission from David W. Dempster, PhD.

INDICATION

Prolia™ is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, Prolia™ reduces the incidence of vertebral, nonvertebral, and hip fractures.

IMPORTANT SAFETY INFORMATION

Hypocalcemia: Prolia™ is contraindicated in patients with hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating Prolia™. Hypocalcemia may worsen, especially in patients with severe renal impairment. In patients predisposed to hypocalcemia and disturbances of mineral metabolism, clinical monitoring of calcium and mineral levels is highly recommended. Adequately supplement all patients with calcium and vitamin D.

Serious Infections: In a clinical trial (N = 7808), serious infections leading to hospitalization were reported more frequently in the Prolia™ group than in the placebo group. Serious skin infections, as well as infections of

the abdomen, urinary tract and ear, were more frequent in patients treated with Prolia™. Endocarditis was also reported more frequently in Prolia™-treated subjects. The incidence of opportunistic infections was balanced and the overall incidence of infections was similar between the treatment groups. Advise patients to seek prompt medical attention if they develop signs or symptoms of severe infection, including cellulitis.

Patients on concomitant immunosuppressant agents or with impaired immune systems may be at increased risk for serious infections. In patients who develop serious infections while on Prolia™, prescribers should assess the need for continued Prolia™ therapy.

Dermatologic Adverse Reactions: Epidermal and dermal adverse events such as dermatitis, eczema and rashes occurred at a significantly higher rate in the Prolia™ group compared to the placebo group. Most of these events were not specific to the injection site. Consider discontinuing Prolia™ if severe symptoms develop.

Osteonecrosis of the Jaw (ONJ): ONJ, which can occur spontaneously, is generally associated with tooth extraction and/or local infection with delayed healing, and has been reported in patients receiving Prolia™. An oral exam should

the earliest signs of degeneration, who may benefit from early treatment or behavioral intervention," said Dr. Link.

Two radiologists analyzed T2 values in five cartilage areas – patella, medial femur, medial tibia, lateral femur, and lateral tibia – and graded overall visible signs of cartilage and meniscus damage using a modified whole-organ MRI scoring method (WORMS).

Among the 132 at-risk patients, T2 values were significantly lower, indicating less cartilage degeneration, in light exercisers than sedentary and moderate-strenuous exercisers in the overall av-

erage of all compartments (43.5 vs. 44.5 and 45.0, respectively) and in the lateral tibia (38.0 vs. 39.7 and 40.2). "Light exercise was associated with more intact collagen structure and lower cartilage water content, which are indicative of healthier cartilage," said Ms. Hovis.

Moderate-strenuous exercise in women was significantly correlated with higher T2 values in the medial femur, indicating that moderate-strenuous exercise may accelerate cartilage degeneration and increase osteoarthritis risk in women who engage in more intense workouts, she reported.

Differences in cartilage health were not found in any of the three exercise groups in the control cohort. However, knee-bending activities were associated with higher T2 values in both the at-risk and control cohorts. In the at-risk cohort, those who engaged in frequent knee-bending activities had significantly higher T2 values in all compartments than those who did not (44.7 vs. 43.2) and a significantly higher WORMS score, indicating visible signs of cartilage degeneration. In the normal cohort, knee-bending activities were associated with higher T2 values in the medial femur and

the medial tibia (49.9 vs. 47.0 and 35.4 vs. 32.5, respectively) with a trend toward significance in the overall average in all compartments.

"Knee-bending activity may accelerate cartilage degeneration in all individuals, but potentially to a greater degree in subjects already at risk for knee osteoarthritis," Ms. Hovis said.

The researchers plan to collect longitudinal data at 2 and 4 years and are finishing an analysis of data on strength training.

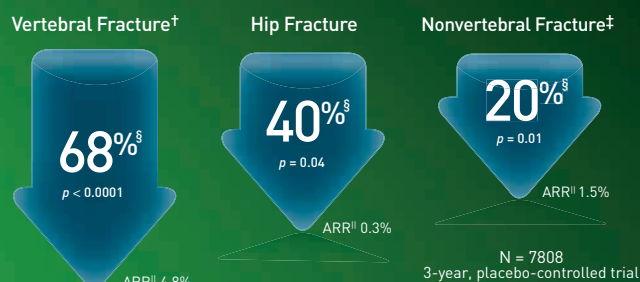
Dr. Link disclosed that he has received research support from Merck. ■

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be performed by the prescriber prior to initiation of Prolia™. A dental examination with appropriate preventive dentistry should be considered prior to treatment in patients with risk factors for ONJ. Good oral hygiene practices should be maintained during treatment with Prolia™.

For patients requiring invasive dental procedures, clinical judgment should guide the management plan of each patient. Patients who are suspected of having or who develop ONJ should receive care by a dentist or an oral surgeon. Extensive dental surgery to treat ONJ may exacerbate the condition. Discontinuation of Prolia™ should be considered based on individual benefit-risk assessment.

Suppression of Bone Turnover: Prolia™ resulted in significant suppression of bone remodeling as evidenced by markers of bone turnover and bone histomorphometry. The significance of these findings and the effect of long-term treatment are unknown. Monitor patients for consequences, including ONJ, atypical fractures, and delayed fracture healing.

Adverse Reactions: The most common adverse reactions (> 5% and more common than placebo) are back pain, pain in extremity, musculoskeletal pain, hypercholesterolemia, and cystitis. Pancreatitis has been reported with Prolia™.

The overall incidence of new malignancies was 4.3% in the placebo and 4.8% in the Prolia™ groups. A causal relationship to drug exposure has not been established. Denosumab is a human monoclonal antibody. As with all therapeutic proteins, there is potential for immunogenicity.

Prolia™ Postmarketing Active Safety Surveillance Program: The Prolia™ Postmarketing Active Safety Surveillance Program is available to collect information from prescribers on specific adverse events. Please go to www.proliasafety.com or call 1-800-772-6436 for more information about this program.

* Key sites: vertebral, hip, and nonvertebral.^{1,2}
† Includes 7393 patients with a baseline and at least one post-baseline radiograph.^{1,2}
‡ Composite measurement excluding pathological fractures and those associated with severe trauma, fractures of the vertebrae, skull, face, mandible, metacarpals, fingers, and toes.^{1,2}
§ RRR = relative risk reduction.
|| ARR = absolute risk reduction.

References: 1. Prolia™ (denosumab) prescribing information, Amgen. 2. Cummings SR, San Martin J, McClung MR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. *N Engl J Med*. 2009;361:756-765.

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