

Joint Distraction May Stall Knee Replacement in OA

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Joint distraction, a surgical technique that involves the placement of an external fixation frame around a degenerated joint, may help postpone the need for total knee replacement in young patients with severe osteoarthritis.

The cartilage in end-stage OA is severely damaged, with fissuring; altered chondrocyte distribution and death; and a significant loss of extracellular matrix constituents. These changes in cartilage are accompanied by characteristic changes in

periarticular bone and soft tissue. All these structural changes mean severe pain and functional limitations for patients, who typically rate their pain with a score of 80% out of a maximum of 100%, according to Dr. Floris P.J.G. Lafeber, of the University Medical Center Utrecht (the Netherlands).

The standard treatment for these patients is total knee replacement. However, "Total knee prostheses don't last forever," Dr. Lafeber said. "They last on average 15 years, so if you have one placed at age

60 you are likely to need a replacement at 75, which is complicated and expensive, and the results are often disappointing. And then if you need another at age 90 the difficulties are really serious," he said, adding that in the Netherlands, approximately 1,000 total knee prostheses are placed each year in patients younger than 60.

"This is a major socioeconomic problem and will only grow with the aging of the population," he said.

The rationale for joint distraction lies in

the hypothesis that osteoarthritic cartilage is capable of self-repair if the joint is unloaded and chondrocyte nutrition is maintained. Pins are drilled through the soft tissue and bone just above and below the joint, and when the frame is in place the distance between the cartilaginous surfaces of the joint is increased by 5 mm. This transfers the load and stresses on cartilage away from the joint, eliminating further wear and tear. Then, springs within the distraction frame cause changes to occur in flu-



PHOTOS COURTESY DR. FLORIS P.J.G. LAFEBER

This knee has OA at baseline on x-ray (top). Cartilage repaired itself after 2 years of treatment (bottom). Distraction may alleviate the need for total knee arthroplasty.

Iowa's Experience With Ankle OA

Ankle distraction also has been performed and is being evaluated in a randomized study led by Dr. Annunziato Amendola of the University of Iowa, Iowa City.

The study, funded by the National Institutes of Health, prospectively enrolled about 40 patients with post-traumatic OA of the ankle. They used the same ankle distraction technique as did Dr. Lafeber's group, but patients were randomized to distraction alone or with the addition of continuous passive joint motion.

Patients have been evaluated clinically and radiographically, and with a special three-dimensional CT scanning technique to look at cartilage regeneration.

All but three patients have now undergone 2- and 3-year evaluations, and the results thus far have been comparable to the results they have had in Utrecht in terms of relief of pain, according to Dr. Amendola. Additional improvements have been seen over time, and patients in the motion group did significantly better at every time point than did the non-motion group.

"I think this is quite an intriguing technique," Dr. Amendola said.



1. Wortmann RL, Kelley WN. Gout and hyperuricemia. In: Harris ED Jr, Budd RC, Genovese MC, et al, eds. *Kelley's Textbook of Rheumatology*. 7th ed. Philadelphia, Pa: Elsevier Saunders; 2005:1402-1429. 2. Emmerson BT. The management of gout. In: Hochberg MC, Silman AJ, Smolen JS, Weinblatt MR, Weisman MH, eds. *Rheumatology*. 3rd ed. Edinburgh: Mosby; 2003:1929-1936.

id pressure in the joint, with increases during loading and normalization with unloading. This continuous change in fluid pressure is important for the cartilage, because chondrocytes depend on synovial flow for nutrition, Dr. Lafeber explained.

The loading onto the frame also results in periarticular osteopenia, which in turn permits the sclerotic, osteoarthritic bone to become more flexible and the mineral content to normalize once the frame is removed. Furthermore, the periarticular bone turnover results in the release of multiple growth factors that can help repair the cartilage.

In collaboration with his center's or-

thopedic department, Dr. Lafeber and his colleagues in the department of rheumatology and clinical immunology began exploring this technique in a proof-of-concept study with ankle distraction. Although ankle OA is much less common than knee OA, in the case of failure an arthrodesis could be performed without much risk, he said.

A total of 73 patients underwent ankle distraction for 3 months, with the result that pain scores—rated at an average of 75% of 100%—fell to 20%, while scores for function and clinical condition rose from 25% at baseline to 80%. Some of these patients now have been followed for as long

as 10 years, with continuing benefits.

They next did a feasibility study that included three patients with knee OA, and found similar results on pain and function scores as well as on stiffness scores. They then undertook a larger prospective study in which 19 patients with severe knee OA (mean age, 48 years) have been treated with 2-month periods of distraction. Thus far, six have been followed for up to 2 years. Functional ability and clinical condition, poor at the onset with scores of 39% and 32%, respectively, increased to 82% and 81%.

Serum and urinary biomarkers of cartilage turnover were measured throughout a 12-month follow-up. During the distrac-

tion phase there was an enormous turnover, with elevations of markers of both synthesis and breakdown, but after the distraction phase there was a gradual decrease of breakdown markers and an increase in the markers of synthesis, indicating repair of the cartilage, Dr. Lafeber said.

Imaging studies also demonstrated improvements. In seven patients who have been followed for more than 12 months, joint space width shown on x-rays increased from slightly greater than 2.5 mm to more than 3.5 mm. "And on MRI studies done after 1 year and read in a blinded fashion in collaboration with Prof. Felix Eckstein, who is one of the leading re-

At what point should urate-lowering therapy be initiated in patients with gout?

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- Maintaining even lower uric acid levels may accelerate the dissolution of urate crystals⁴

To learn more about managing hyperuricemia and gout, visit

www.Gout.com

3. Shoji A, Tamai H, Kamatani NA. Retrospective study of the relationship between serum urate level and recurrent attacks of gouty arthritis: evidence for reduction of recurrent gouty arthritis with antihyperuricemic therapy. *Arthritis Rheum.* 2004;51:321-325. 4. Perez-Ruiz F, Calabozo M, Pijoan JJ, Herrero-Beites AM, Ruizbal A. Effect of urate-lowering therapy on the velocity of size reduction of tophi in chronic gout. *Arthritis Rheum.* 2002;47:356-360. ©2008 Takeda Pharmaceuticals America, Inc. TXF-00011 Printed in U.S.A. 09/08



Biomarkers of bone breakdown and synthesis increase during distraction.

COURTESY DR. FLORIS P.J.G. LAFEBER

searchers in this field, the amount of subchondral bone covered with cartilage was shown to have increased by 40%, cartilage volume increased by 50%, and cartilage thickness over the bone increased by 5%," Dr. Lafeber said.

The overall conclusion is that joint distraction is clinically very effective in young patients with end-stage knee arthritis, with cartilage repair presumably responsible for the clinical benefit, he said. However, more prolonged follow-up is needed.

Some of the ankle patients have had a second distraction, but whether this will be feasible and advisable in the knee patients remains to be seen, because the follow-up is too short.

"It may be possible, and of course we hope [that] it's not just a delay before joint replacement, but that we can really cure the joint. That's only wishful thinking so far, though," he said.

Dr. Lafeber acknowledged that his study was not placebo controlled.

"Of course it would be better to have a good control, which in this case would be placement of the complete frame but without the distraction," he said.

Currently, however, they are offering this treatment only to patients with end-stage OA who otherwise would be considered for joint replacement. "We cannot ethically allow these patients to go without any treatment for 2 years," he said.

Moreover, with benefits persisting for up to 10 years for the ankle patients, placebo effects are hardly likely to still be in play. "Maybe for the first year, because these patients are seeing their physicians more frequently than they would otherwise, but certainly after several years the placebo effect would have vanished," he said. ■