No beneficial effects of joint distraction on early microscopical changes in osteoarthrotic knees

A study in rabbits

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Background **Although promising results have been reported, on the use of joint distraction in osteoarthrotic joints, the mechanism behind the effects has not yet been expland.**

Material and methods **24 rabbits were randomly divided into 4 groups and osteoarthrosis was induced by papain injection. The first group served as control and the others were treated by simple external fixation (group 2), articulated distraction (group 3) or nonarticulated distraction (group 4).**

Results **Histologically, there was no significant difference between the first, the second and the third groups. However, osteoarthrosis increased in group 4.**

Interpretation **We conclude that joint distraction has no beneficial effect on the osteoarthrotic cartilage in papain-induced osteoarthrosis, and nonarticulated distraction worsens the results.**

Joint distraction, using an external fixation frame bridging the joint, is an alternative approach in the treatment of osteoarthrosis (OA). Although clinical results in the ankle and hip joints are promising (Aldegheri et al. 1994, van Valburg et al. 1999, Marijnissen et al. 2002), the mechanism behind the effects has not yet been explained (van Valburg et al. 2000, Hunziker 2001). We evaluated quantitatively the effects of simple external fixation, and articulated and nonarticulated distraction on the knee joint in a rabbit model.

Animals and methods

24 mature New Zealand male rabbits ranging in weight from 1.6 to 2.3 kg were used in the study. The rabbits were divided into 4 groups with 6 animals in each. Experimental OA was induced in the right knees of the first group and both knees of the others by injecting 0.2 mL 4% papain solution with 0.1 mL 0.03 M cysteine as activator. The same amount of saline was injected into the left knees of the first group. Injection was repeated on the 4th and 7th days.

At 6 weeks, unipolar external fixators were applied across the right knees of the rabbits in groups 2, 3 and 4, under ketamin anesthesia (35 mg/kg) with 4 Schanz screws (Figure 1). The rabbits received seftriakson (50 mg/kg) during the first 2 days after surgery. Radiographs were taken on the first postoperative day to exclude a fracture.

No distraction was performed in the second group. The right knees of the rabbits in the third and fourth group were distracted at a rate of 0.5 mm × 2 per day for 2 days but the fixation of the fourth group was locked at 135 degrees in order to prevent motion. Then radiographs of the third and fourth groups were taken, both at the beginning and at the end of the study. Either external fixation or distraction was performed with the rabbit's knee in a neutral position, i.e. 135 degrees of flexion. Throughout the study the rabbits were loading their extremities.

The rabbits were killed by intravenous anesthesia at 12 weeks and both knees were removed,

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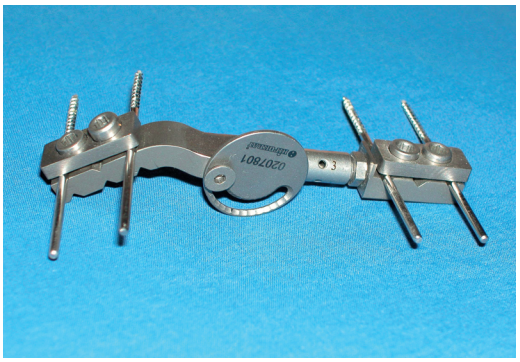
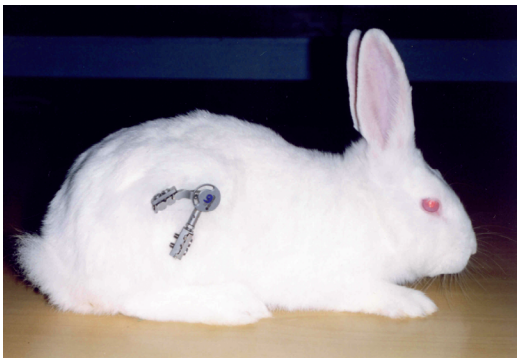


Figure 1. External fixator.



External fixator in situ.

washed in saline and fixed in 10% neutral buffered formalin. They were decalcified with 10% aqueous formic acid and embedded in paraffin to allow cutting of 4 µm sections. The sections were stained with hematoxylin and eosin and with toluidine blue for microscopic examination. The sections were examined using the modified Mankin score for the structure of the cartilage, cell appearance, staining of the cartilage matrix by toluidine blue, tidemark and pannus formation (Yoshimi et al. 1994). By this system, a maximum of 32 points can be reached in cases of severe OA.

The results were analyzed first by Kruskal-Wallis test. Then the groups were compared in pairs by Mann Whitney U test. The protocol of the study was approved by the local ethical committee for animal research.

Results (Table)

None of the rabbits lost weight and no pin-tract infection was observed. Radiographs taken throughout the study revealed no fractures, but distraction in the third and fourth group was confirmed (Figure 2). The difference between the papain and saline injected groups (p = 0.0002) provided proof that the model worked well to produce OA. Although there was no significant difference whether simple external fixator was applied or whether the joints were distracted permitting motion (articulated distraction), as compared with the papain injected knees, these procedures worsened the results. The median Mankin score of simple external fixation group was 23, but 12 and 14 for papain and articulated distraction groups, respectively. However, nonarticulated distraction increased OA (p = 0.001).

Median (range) modified Mankin score of the group

Groups	Scores	P-value
Saline	2.5 (0–7)	–
Papain	11.5 (3–26)	0.0002 [a]
External fixation	22.5 (8–28)	0.2 [b]
Articulated distraction	14 (13–25)	0.1 [b]
Nonarticulated distraction	23.5 (16–31)	0.001 [b]

[a] Difference from saline
[b] Difference from papain
Mann Whitney U-test

When the left knees of groups 2, 3 and 4 were compared with the right knees of the first group, the differences were not significant (p = 0.5, p = 0.7, and p = 0.3, respectively. Kruskal Wallis test).

Discussion

Joint distraction is based on the hypothesis that osteoarthrotic cartilage has some reparative activity when there is a release of mechanical stress on the cartilage, as intraarticular intermittent fluid pressure is maintained and subchondral sclerosis diminished (van Roermund et al. 2002). Although promising results have been reported for ankle and hip joints (Aldegheri et al. 1994, van Valburg et al. 1999, Marijnissen et al. 2002), there is no rational biological basis for this therapy, since it is known that joint immobilization leads ultimately to the degeneration of articular cartilage (Hunziker 2002). The result of the present study revealed no beneficial effects of joint distraction on articular

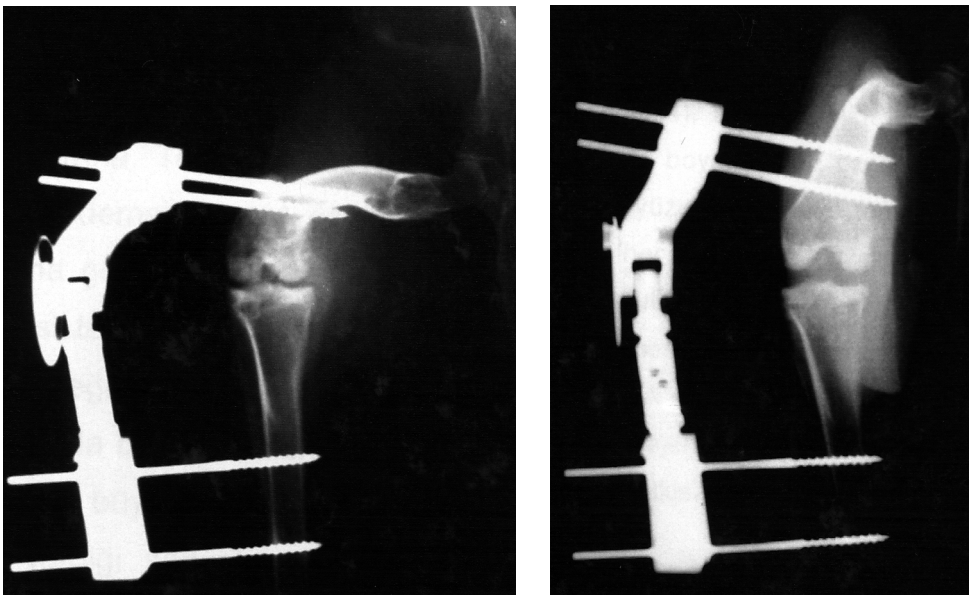


Figure 2. Knee joint before distraction (left) and during distraction (right).

cartilage. Nonarticulated distraction worsened the results very significantly, while simple external fixation or articulated distraction had no statistically significant effect on the osteoarthrotic cartilage (Table). Theoretically, these results are not surprising, as the continuous distraction in a moving joint causes morphological changes in chondrocytes prior to degeneration and the forces exerted on cells distort their shape and stimulate alteration in cellular biochemistry and matrix metabolism (Hung et al. 1997).

Contrary to our results, van Valburg et al. (2000) found no difference between the histology of the cartilage of distracted and non-distracted knees. This may be due to differences in the model of OA. The anterior cruciate ligament transection model used by van Valburg et al. (2000) acts by producing joint instability and the application of external fixator later prevents instability. In our opinion, however, papain-induced OA simulates cartilage pathology as in primary OA (Bentley 1971).

The use of the contralateral knee as a control has been reported to be legitimate (Manicourt and Pita 1988). However, it can be argued that the non-operated knees would be loaded more. In our study, there was no statistically significant difference between the non-operated knees of groups 2–4 and the OA-induced but non-operated rabbits (group 1). These results clearly indicate that contralateral knees can be used as controls, with the clinical relevance that the application of an external fixator to a knee may have little effect on the contralateral knee.

Application of an external fixator itself has been suspected to cause changes similar to OA (Hung et al. 1997). Our results reveal that there is no significant effect of simple external fixation of the joints, and it can be used safely for fractures around osteoarthrotic joints. Although our study indicates no beneficial effects of distraction on the osteoarthrotic joints, the study has some limitations. Firstly, experimental studies are not always applicable to clinical work, and secondly, studies with longer follow-up are necessary because distraction treatment requires up to a year before a substantial clinical benefit may be achieved.

The external fixator was produced by Hipokrat, Izmir, Turkey.

Aldegheri R, Trivella G, Saleh M. Articulated distraction of the hip. Conservative surgery for arthritis in young patients. Clin Orthop 1994; (301): 94-101.

Bentley G. Papain-induced degenerative arthritis of the hip in rabbits. J Bone Joint Surg (Br) 1971; 53: 324-37.

Hung S C, Nakamura K, Shiro R, Tanaka K, Kawahara H, Kurokawa T. Effects of continuous distraction on cartilage in a moving joint: an investigation on adult rabbits. J Orthop Res 1997; 15: 381-90.

Hunziker E B. Articular cartilage repair: basic science and clinical progress. A review of the current status and prospects. Osteoarthritis Cartilage 2002; 10: 432-63.

Manicourt D H, Pita J C. Progressive depletion of hyaluronic acid in early experimental osteoarthritis in dogs. Arthritis Rheum 1988; 31: 538-44.

Marijnissen A C, Van Roermund P M, Van Melkebeek J, Schenk W, Verbout A J, Bijlsma J W, Lafeber F P. Clinical benefit of joint distraction in the treatment of severe osteoarthritis of the ankle: proof of concept in an open prospective study and in a randomized controlled study. Arthritis Rheum 2002; 46: 2893-902.

van Roermund P M, Marijnissen A C, Lafeber F P. Joint distraction as an alternative for the treatment of osteoarthritis. Foot Ankle Clin 2002; 7: 515-27.

van Valburg A A, van Roermund P M, Marijnissen A C, van Melkebeek J, Lammens J, Verbout A J, Lafeber F P, Bijlsma J W. Joint distraction in treatment of osteoarthritis: a two-year ollow-up of the ankle. Osteoarthritis Cartilage 1999; 7: 474-9.

van Valburg A A, van Roermund P M, Marijnissen A C, Wenting M J, Verbout A J, Lafeber F P, Bijlsma J W. Joint distraction in treatment of osteoarthritis (II): effects on cartilage in a canine model. Osteoarthritis Cartilage 2000; 8: 1-8.

Yoshimi T, Kikuchi T, Obara T, Yamaguchi T, Sakakibara Y, Itoh H, Iwata H, Miura T. Effects of high-molecular-weight sodium hyaluronate on experimental osteoarthrosis induced by the resection of rabbit anterior cruciate ligament. Clin Orthop 1994; (298): 296-304.