Joints

Treatment of osteochondritis dissecans of the knee with a biomimetic scaffold. A prospective multicenter study

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Abstract

Purpose: the aim of the present study was to evaluate the clinical outcome of the treatment of osteochondritis dissecans (OCD) of the knee with a type-I collagen-hydroxyapatite nanostructural biomimetic osteochondral scaffold.

Methods: twenty-three patients affected by symptomatic knee OCD of the femoral condyles, grade 3 or 4 of the International Cartilage Repair Society (ICRS) scale, underwent biomimetic scaffold implantation. The site of the defect was the medial femoral condyle in 14 patients, whereas in 9 patients the lateral femoral condyle was involved. The average size of the defects was 3.5 ± 1.43 cm^2. All patients were clinically evaluated using the ICRS subjective score, the IKDC objective score, the EQ-VAS and the Tegner Activity Score. Minimum follow-up was two years. MRI was performed at 12 and 24 months after surgery and then every 12 months thereafter.

Results: the ICRS subjective score improved from the baseline value of 50.93 ± 20.6 to 76.44 ± 18.03 at the 12 months ($p < 0.0005$) and 82.23 ± 17.36 at the two-year follow-up ($p < 0.0005$). The IKDC objective score confirmed the results. The EQ-VAS showed a significant improvement from 3.15 ± 1.09 to 8.15 ± 1.04 ($p < 0.0005$) at two years of follow-up. The Tegner Activity Score improvement was statistically significant ($p < 0.0005$).

Conclusions: biomimetic scaffold implantation was a good procedure for treating grade 3 and 4 OCD, in which other classic techniques are burdened by different limitations. This open one-step surgery gave promising stable results at short-term follow-up.

Level of evidence: Level IV, therapeutic case series.

Key words: cartilage, knee, osteochondral lesions, ostechondritis dissecans, scaffold.

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Introduction

Chondral and osteochondral lesions are relatively common and are often caused by traumatic injury (1). In the past 20 years, there have been many studies dealing with cartilage restoration and, even though the quality of restored cartilage is now debated, a series of satisfying results have been reported in the literature (2-13). The treatment becomes increasingly challenging in the presence of larger defects and when there is involvement of the subchondral bone (8,14-18). Osteochondritis dissecans (OCD) is an acquired lesion of the subchondral bone that may result in separation and instability of the overlying articular cartilage (19,20). Among the multiple causes hypothesized, repetitive microtrauma correlated with a possible vascular insufficiency is the most credited theory (19). Whereas juvenile patients with small or stable lesions have a much better prognosis and the potential for healing by non-operative management, unstable lesions or OCD in skeletally mature individuals often do not respond to non-operative measures and require surgical intervention (19).

In large lesions of this kind, the use of autologous osteochondral transplantation and mosaic plasty is limited by donor site availability (21). Autologous chondrocyte implantation (ACI), on the other hand, is not limited by the size of the lesion and has been used successfully in the treatment of osteochondral lesions, adding the autogenous bone implant before the

implantation of autologous chondrocytes (14,15, 22-24). However, the technique involves two surgical procedures, performed several months apart, which implies long functional recovery times. Efforts to overcome these limitations have led to increasing use, with excellent results, of fresh allograft transplantation (25, 26). However, the management of this procedure is not straight forward and sometimes impossible, due to high costs, lack of donors and, in particular, the need to implant the allograft within 14 days.

To overcome these limitations, a cellular biphasic or triphasic scaffolds have recently been developed with the aim of promoting and inducing both subchondral bone and cartilage regeneration (16, 17, 27-32). Currently, only a few scaffolds have obtained the European Conformity (CE) certification and are available for clinical application in Europe (16, 17, 28, 29, 33, 34).

The aim of the present study was to evaluate the clinical outcome of the treatment of OCD of the knee with a type-I collagen-hydroxyapatite nanostructural biomimetic osteochondral scaffold.

Methods

Twenty-three consecutive patients affected by symptomatic knee OCD of the femoral condyles, grade 3 or 4 of the International Cartilage Repair Society (ICRS) scale, underwent implantation of a biomimetic osteochondral scaffold (MaioRegen; Fin-Ceramica Faenza SpA, Faenza, Italy) between 2009 and 2011 at three different centers highly specialized in the treatment of knee cartilage disorders.

MaioRegen is a three-dimensional matrix that mimics osteocartilaginous tissue. The scaffold consists of hydroxyapatite nanocrystals nucleated on type 1 collagen fibers present, in different concentrations, in three layers: the first layer consists entirely of type I collagen and has a smooth surface; the intermediate layer, which is thicker, is a combination of type I collagen (60%) and hydroxyapatite (40%); the third layer, which is thinner, consists of a mineralized blend of type I collagen (30%) and hydroxyapatite (70%) and it mimics the subchondral bone (**Fig. 1**).

All the patients gave their informed consent prior to their inclusion in the study, which had ethics committee approval and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its subsequent amendments. Exclusion
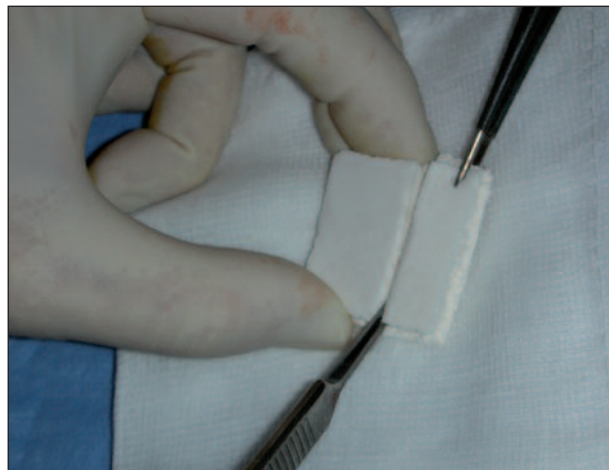

Fig. 1. MaioRegen scaffold.

criteria were: non-corrected axial malalignment (considered as above 5° from the normal axis), evaluated clinically and via radiographic examination, and the presence of co-morbidities such as: infectious, neoplastic, metabolic, and systemic inflammatory disorders.

The patients included 19 men and 4 women, with a mean age of 25.5±7.7 years. The site of the defects was the medial femoral condyle in 14 patients, whereas in 9 patients the lateral femoral condyle was involved. The average size of the defects was 3.5±1.43 cm^2.

Surgical procedure

The surgery was performed under spinal or limb anesthesia. A tourniquet was positioned on the thigh with the patient in a supine position. After an arthroscopic evaluation of the knee, the lesion was exposed through a lateral or medial parapatellar approach and was prepared with a drill specific for this purpose. The sclerotic subchondral bone was eliminated and an area approximately 9 mm in depth with a stable base was created to house the scaffold, which was then implanted press fit into the area (**Fig. 2**). The stability of the transplant was tested by cyclic flexion-extension of the knee while the graft was visualized, both before and after tourniquet removal. On the second postoperative day, mobilization of the knee was started. Early isometric and isotonic exercises and controlled mechanical compression were performed. Muscular voluntary contraction and neuromuscular electrical stimulation were prescribed and could be started at patient dis-
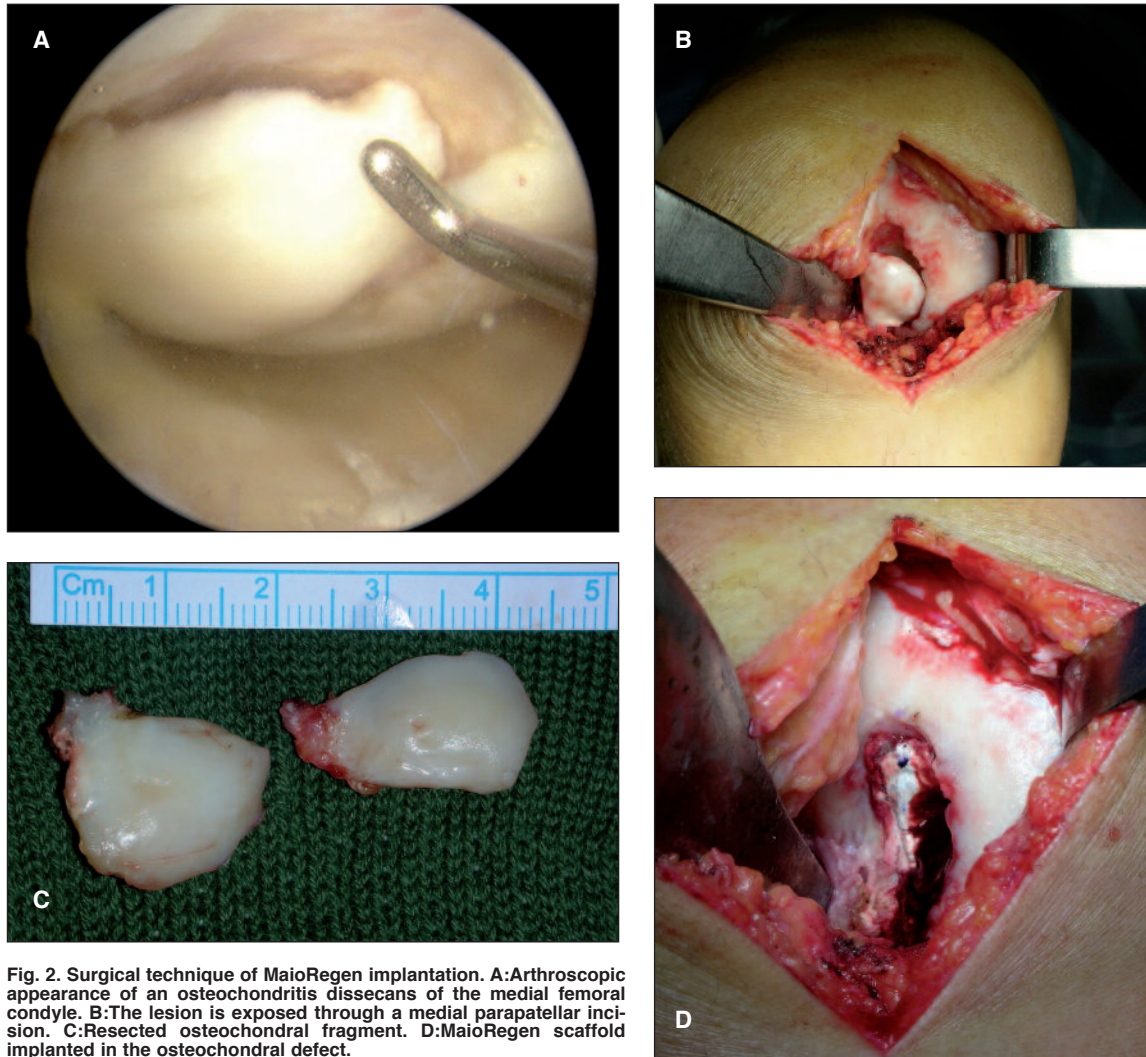
Fig. 2. Surgical technique of MaioRegen implantation. A:Arthroscopic appearance of an osteochondritis dissecans of the medial femoral condyle. B:The lesion is exposed through a medial parapatellar incision. C:Resected osteochondral fragment. D:MaioRegen scaffold implanted in the osteochondral defect.

charge. In the third or fourth week, weight touchdown with crutches was allowed, and the patient could then move progressively toward full weight-bearing, which was achieved within six to eight weeks of the surgery.

Outcome measurement
The clinical outcome in all the patients was assessed using the ICRS subjective score and the International Knee Documentation Committee (IKDC) score at 12 and at 24 months after the operation, and every 12 months thereafter.
Improvement in quality of life was measured using the EQ-VAS score and resumption of sporting activity

using the Tegner Activity Score. The patients underwent magnetic resonance imaging (MRI) preoperatively, at 12 and at 24 months after the operation, and every 12 months thereafter.

Statistical analysis
All the statistical analyses were carried out using the SPSS (Statistical Package of Social Sciences, Chicago, IL, USA) for Windows software program version 13.0. A p value of less than 0.05 was considered statistically significant. The results were expressed as mean values ± SD. The Kolmogorov-Smirnov test was performed to assess the normal data distribution. The paired T

test for normally distributed data, or the Wilcoxon test for non-normally distributed data, were used to test for significant differences between the baseline and various follow-up measurements.

Results

No patients were lost at follow-up. Statistically significant increases were recorded in all the assessment scores at the 12-month and 24-month follow-ups. In two cases the treatment failed, one on the lateral femoral condyle and one on the medial femoral condyle, with these patients continuing to experience pain and functional limitation of the joint.

Improvements were recorded in the ICRS subjective score, which increased from the baseline value of 50.93±20.6 to 76.44±18.03 at the 12-month follow-up (p<0.0005) and 82.23±17.36 at the 2-year follow-up.

Before surgery, more than 50% of the patients perceived abnormal or very abnormal knee sensations (IKDC objective C and D grade), due to moderate or severe swelling of the knee.

Assessment of the patients at the first follow-up (one year after surgery) revealed an improvement, and at two years the following scores were recorded: A, 11 patients; B, 7 patients; C, 2 patients, D, only 1 patient.

The EQ-VAS score also showed a significant increase, from 3.15±1.09 to 8.15±1.04 (p<0.0005) at the 2-year follow-up, with satisfaction recorded in 85% of the patients.

The Tegner Activity Score showed a significant increase (from 2.34±0.64 to 5.60±1.72 at the two-year follow-up), even though it did not reach the pre-injury level (6.04±1.89).

High-resolution MRI scans were performed in all the patients and showed complete filling of the defect in 80% of the lesions; in 70% of cases the repair tissue was isointense in relation to the adjacent cartilage. In all cases, the scaffold was still detectable at the level of the subchondral bone at the two-year follow, producing a different signal with respect to the adjacent subchondral bone.

Nevertheless, no case showed signs of subchondral bone impairment (such as subchondral edema) (**Fig. 3**).

Discussion

The present study suggests that MaioRegen collagen-hydroxyapatite osteochondral scaffold can be used to treat knee OCD with good clinical results at 2-year follow-up.

Osteochondral lesions are particularly difficult to treat as they involve two types of tissue that show different biomechanical features and healing capacity (19, 20). One of the approaches proposed for the treatment for deep osteochondral defects of the knee is staged open or arthroscopic bone grafting followed by ACI 4-9 months later (10, 11). The clinical outcome of such a procedure has not yet been reported; however, the need for three surgical procedures after the diagnosis poses a significant burden to the patient.

Minas and Peterson (24) and Peterson et al. (35, 36) have advocated the ACI "sandwich technique" as an alternative. Unfortunately, the outcome has been reported in only 7 patients. With the advent of the so-called "second-generation" ACI to overcome the limitations and the problems related to the "first-generation" ACI, a two-step procedure was proposed by different authors for the treatment for osteochondral lesions (22, 23). Bartlett et al. (2), Ochs et al. (12) and recently Filardo et al. (7) analyzed the clinical outcome in patients affected by OCD with the use of second-generation ACI associated with bone grafting harvested from different site (iliac crest, tibial cancellous bone), obtaining satisfactory results.

Despite the good results reported in the literature, these techniques present a number of problems: first of all, the bone grafting site (proximal tibia, iliac crest) is a source of post-operative pain and morbidity, which are directly proportional to the surgical exposure; in addition, the need for two surgical steps makes for longer recovery times.

In the United States, a different treatment option has been developed; fresh osteochondral allografting has been used to treat large osteochondral lesions of the knee (post-traumatic, vascular or idiopathic) and given excellent results in cases of OCD of the femoral condyle (25,26). However, this technique is burdened by high costs and difficult management due to the need to implant the graft within 14 days. For these reasons, many authors have turned their attention to the use of biphasic biomaterials with the capacity to promote joint surface regeneration by exploiting the differentiation (induced by the properties of the scaf-

Fig. 3. Postoperative imaging of MaioRegen implantation. A-B: MRI follow-up at one year. It is possible to note the scaffold *in situ* and the ongoing differentiation process. C-D: MRI follow-up at two years. The scaffold is still recognizable at subchondral level, but the cartilage layer appears continuous and the subchondral bone shows no signs of edema.

fold itself) of bone marrow stem cells (31, 32). Various experimental studies, both *in vitro* and *in vivo*, have been published (27,30), but in our experience only two scaffolds are available in clinical practice for the treatment of osteochondral lesions. The first is a biopolymercomposite of poly (D,L-lactide-co-glycol-ide), polyglycolic acid and calcium sulfate (TruFit; Smith&Nephew, Andover, Ma). The results obtained following implantation of this osteochondral substitute are discordant (33,34).

The second is MaioRegen. This has given promising results in animals and patients (16-18, 20, 28, 29).

Joints

Our study confirmed these results. The ICRS subjective score was found to be significantly increased, both at the 12-month and the 24-month follow-up. The Tegner Activity Score increased significantly and almost reached the pre-injury level. We had 13 patients who were athletes before symptom onset and 11 of them returned to the previous level of sports activity between one and two years after the operation. In conclusion, the MaioRegen biomimetic scaffold is an off-the-shelf, cell-free and cost-effective implant that can regenerate cartilage and osteochondral defects. Its implantation is a one-step procedure that can be used for difficult pathologies such as ostechondral lesions and OCD, in which other regenerative treatments have proved to be burdened by several limitations. However, the results are certainly to be confirmed at longer term follow-up.

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