Original Article With Video Illustration

Follow-up of a New Arthroscopic Technique for Implantation of Matrix-Encapsulated Autologous Chondrocytes in the Knee

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Purpose: The purpose of this study was to evaluate the clinical and sequential imaging follow-up results at a mean of 36 months after an arthroscopic technique for implantation of matrix-encapsulated autologous chondrocytes for the treatment of articular cartilage lesions on the femoral condyles. **Methods:** Ten patients underwent arthroscopic implantation of autologous chondrocytes seeded onto a bioabsorbable scaffold. The patients were evaluated clinically using a visual analog scale (VAS) for pain and International Knee Documentation Committee (IKDC), Lysholm, and Tegner scores. Magnetic resonance imaging (MRI) T2-mapping and magnetic resonance observation of cartilage repair tissue (MOCART) evaluations were also performed. Second-look arthroscopic evaluation using the International Cartilage Repair Society (ICRS) grading classification was performed at 12 months. **Results:** Compared with their preoperative values, at 36 months mean values ± standard deviation for the VAS scale for pain were 6.0 ± 1.5 to 0.3 ± 0.4. Improvement in clinical scores between preoperative values and 36-month follow-up values in subjective IKDC scores was 46.9 ± 18.5 to 77.2 ± 12.8; in Lysholm scores, it was 51.8 ± 25.1 to 87.9 ± 6.5, and in the Tegner activity scale it was 2.9 ± 1.7 to 5.9 ± 1.9. Mean T2 mapping and MOCART scores improved over time to 38.1 ± 4.4 ms and 72.5 ± 10, respectively. Mean ICRS score by second-look arthroscopy at 1 year was 10.4 ± 0.1. **Conclusions:** All clinical scores improved over time compared with the preoperative values. Clinical results are comparable with MRI T2 mapping and ICRS evaluations, suggesting that this arthroscopic technique for cell-based cartilage repair is efficacious and reproducible at a mean of 36 months of follow-up. **Level of Evidence:** Level IV, therapeutic case series.

Articular cartilage lesions are present in more than 60% of knee arthroscopic procedures, and they have been shown to affect the quality of life.[1,2] Regenerative techniques for cartilage repair based on cultured autologous chondrocytes offer hyaline-like cartilage repair, in comparison with reparative procedures that lead to fibrous tissue of inferior quality and less durability.[3-5] These cell-based approaches may also produce less morbidity at the donor site compared with osteochondral autografts, which are frequently used for bigger lesions.[6]

In the original technique described for autologous chondrocyte implantation (ACI), a flap of periosteum was sutured over the cartilage lesion, and chondrocytes in suspension were injected under the periosteal flap through an open approach. To minimize complications associated with open ACI, research has been focused on better options to deliver and ensure the permanence of chondrocytes at the repair site.[7-9] Matrix-seeded autologous chondrocyte implantation (MACI) and similar techniques address some of the potential limiting factors of ACI. By using an absorbable scaffold to allow cells to adhere and produce extracellular matrix, permanence of cells at the repair site could be obtained and complications related to the periosteal patch could be reduced.[10,11]

Several methods of cell-scaffold fixation have been reported. Erggelet et al.[12] used transosseous sutures. Herbort et al.[13] tested a biodegradable polylactide pin

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that requires precise perpendicular insertion on the subchondral bone. Others have used fixation using fibrin glue or self-adherence of the cell scaffold to the subchondral bone.[12-17]

The advent of new procedures for articular cartilage repair has increased the need for accurate noninvasive methods for objective evaluation of the repair. Magnetic resonance imaging (MRI) is currently being used for structural evaluation of cartilage repair.[18] Normal articular hyaline cartilage shows a predictable spatial variation in T2 relaxation time with depth at MRI, with an increase in T2 values from the subchondral bone to the articular surface. This normally correlates with the microscopic collagen organization and orientation seen in normal articular cartilage. Increased T2 values are most commonly associated with cartilage damage.[18] MRI T2 mapping values of the repair tissue compared with the surrounding normal cartilage can be used to determine the integrity and quality of the treatment. The MOCART scoring system is a qualitative measuring tool widely used for cartilage repair. This method evaluates the degree of defect filling, integration, quality, structure, signal, subchondral lamina, and subchondral bone as well as the presence of complications after cartilage repair.[19]

The purpose of this study is to evaluate the clinical and sequential imaging follow-up results at a mean of 36 months after an arthroscopic technique for implantation of matrix-encapsulated autologous chondrocytes to treat articular cartilage lesions in the knee.

We hypothesized that arthroscopic implantation of matrix-encapsulated autologous chondrocytes can result in significant improvement in clinical and MRI evaluation by T2 mapping and MOCART and close-to-normal cartilage formation seen at second-look arthroscopy after treatment of articular cartilage lesions on the femoral condyles, maintaining a stable improvement over time.

Methods

After institutional review board evaluation and approval of this pilot study, patients with a symptomatic full-thickness cartilage lesion on either femoral condyle, patients scheduled for arthroscopic anterior cruciate ligament (ACL) reconstruction or treatment of a meniscal lesion who were between 18 and 50 years of age were considered to be candidates for the study. Exclusion criteria included any type of arthritis, previous total meniscectomy, previous treatment of the chondral lesions, treatment for competitive athletes, and failure to adhere to a strict rehabilitation protocol. The patients signed an informed consent before surgery and were included when a full-thickness cartilage lesion was identified during arthroscopy. Patients underwent an index surgical procedure during which ACL or meniscal lesions were treated and osteochondral biopsy samples were obtained for chondrocyte isolation. A conventional rehabilitation program for the index procedure was conducted. During this time, cells were isolated and expanded in culture in a laboratory at the National Institute of Rehabilitation. A second surgical procedure was performed between 6 and 8 weeks after the first operation.

By this time, patients had no pain, had mild swelling, and had recovered full extension and more than 110° of knee flexion. Arthroscopic cell-polymer scaffold implantation was performed followed by a strict rehabilitation protocol. Clinical evaluation was performed preoperatively at 3, 6, 12, 18, 24, and 36 months, as was MRI evaluation using T2 mapping and MOCART scores. Second-look arthroscopy was performed at 12 months for ICRS classification. No biopsy specimens were obtained at this time.

Surgical Technique

Index Procedure and Cartilage Biopsy

Patients included in the study were those with preoperative full-thickness articular cartilage lesions diagnosed by MRI or patients with ACL or meniscal injuries in whom full-thickness articular cartilage lesions were identified during the index procedure and who had previously signed an informed consent. In either case, during the first surgical procedure, the full-thickness articular cartilage lesion was assessed and measured with an arthroscopic probe. Three 4 × 10 mm osteochondral cylinder biopsy specimens were obtained from a non–weight-bearing area adjacent to the intercondylar notch using an osteochondral graft harvester (COR; DePuy Mitek, Raynham, MA). The osteochondral cylinders were placed in a sterile container with transport media containing antibiotics/antimycotic agents and sent out for chondrocyte isolation, in vitro expansion, and cell-polymer scaffold formation as described previously.[9]

Chondrocyte Isolation, in Vitro Expansion, and Cell-Scaffold Construct Preparation. The 3 4-mm–diameter osteochondral cylinders obtained during the index or first surgical procedure were transported to a good manufacturing practice laboratory facility located in the surgical area of the National Institute of Rehabilitation. There, under sterile conditions in a laminar flow hood, cartilage was separated from bone by sharp dissection. Cartilage fragments were then digested in class I collagenase, cells were counted, and viability was assessed. Chondrocytes were then seeded onto a T-75 culture flask at a minimum density of 300,000 cells per 100 mg with culture medium (Dulbecco's Modified Eagle Medium-F12 GIBCO, Grand Island, NY) and 1% antibiotic-antimycotic agents and supplemented with 10% autologous patient serum. A sample of the cell suspension was sent to a laboratory in a different institution for microbiological evaluation (bacteria,