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One-step cartilage repair in the knee: Collagen-covered microfracture and autologous bone marrow concentrate. A pilot study

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ABSTRACT

Background: Different single-stage surgical approaches are currently under evaluation to repair cartilage focal lesions. To date, only little is known on even short-term clinical follow-up and almost no knowledge exists on histological results of such treatments. The present paper aims to analyze the clinical and histological results of the collagen-covered microfracture and bone marrow concentrate (C-CMBMC) technique in the treatment of focal condylar lesions of knee articular cartilage.
Methods: Nine patients with focal lesions of the condylar articular cartilage were consecutively treated with arthroscopic microfractures (MFX) covered with a collagen membrane immersed in autologous bone marrow concentrate (BMC) from the iliac crest. Patients were retrospectively assessed using several standardized outcome assessment tools and MRI scans. Four patients consented to undergo second look arthroscopy and biopsy harvest.
Results: Every patient was arthroscopically treated for a focal condylar lesion (mean area 2.5 SD(0.4) cm^2). All the patients (mean age 43 SD(9) years) but one experienced a significant clinical improvement from the pre-operative condition to the latest follow-up (mean 29 SD(11) months). Cartilage macroscopic assessment at 12 months revealed that all the repairs appeared almost normal. Histological analysis showed a hyaline-like cartilage repair in one lesion, a fibrocartilaginous repair in two lesions and a mixture of both in one lesion.
Conclusions: The first clinical experience with single-stage C-CMBMC for focal cartilage defects in the knee suggests that it is safe, it improves the short-term knee function and that it has the potential to recreate hyaline-like cartilage.
Level of evidence: IV, case series.

1. Introduction

Focal cartilage defects are a common cause of knee symptoms and disability and may progress to osteoarthritis (OA) [1,2]. To be effective a cartilage repair procedure should recreate hyaline-like cartilage and ultimately prevent OA [3].

The limits of the microfracture (MFX) treatment with respect to lesion size and to long term functional improvements [3,4] and the high cost and the need for two operations of the autologous chondrocyte implantation (ACI) and ACI-related procedures [5] have prompted the search for new one-step cartilage repair methods. Autologous matrix-induced chondrogenesis (AMIC) has emerged as a new technique adopting a collagenic scaffold combined with microfractures [6]. Similar procedures have been developed, adopting synthetic polymers like polyglycolic acid (PGA)/hyaluronan in combination with microfracture and have shown the potential to restore hyaline-like cartilage [7–9]. In all these techniques microfracture should permit the migration of mesenchymal stem cells (MSCs) from the subchondral bone, and the scaffold should keep cells in situ and serve as support for tissue differentiation.

The intra-articular delivery of bone marrow concentrate (BMC) and marrow aspirate improved the outcomes of microfracture in full thickness cartilage defect in the horse model [10] and in the goat model [11] respectively. This observation may be possibly explained by the fact that the BMC from the iliac crest contains higher concentration of MSCs with respect to tibial or femoral bone marrow blood, and with greater doubling potential [12]. This observation has led to modifications to the original single-stage technique involving the addition of BMC to treat talar osteochondral lesions [13].

In the present study cartilage lesions have been treated with the association of MFX, BMC from the iliac crest and a collagenic coverage scaffold. The aim of this study was to analyze clinical and histological outcomes of collagen-covered microfracture and bone marrow concentrate (C-CMBMC) for the treatment of patients with full-thickness, focal, condylar knee cartilage defect.

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2. Materials and methods

2.1. Study design

From February 2008 to March 2011, nine consecutive patients with symptomatic chondral lesions of the knee underwent all-arthroscopic C-CMBMC. After ethical committee approval, full informed consent was obtained from each patient. Inclusion criteria were: lesion size $\geq 1.5\ cm^2$, age ≤ 60, chondral defect Outerbridge type III or IV, adherence to the rehabilitation protocol, full anagraphics available, signed consent, and full surgeon report available. Exclusion criteria were tibiofemoral or patellofemoral malalignment, knee instability, kissing lesions, advanced OA, rheumatic, metabolic or neoplastic diseases. Every patient, after informed consent, was asked to undergo a second look arthroscopy with biopsy for assessing the state of the repair at 12 month follow-up. Failure was defined as the need of a new surgical procedure to treat persisting pain or effusion in the previously operated knee. Patients were retrospectively analyzed with standardized assessment tools such as the International Knee Documentation Committee (IKDC) score, the Lysholm score the VAS and the Tegner activity scale. Patients were also evaluated with MRI scans at variable follow-up.

2.2. Surgical technique

The CMBMC surgical technique has been described in detail by Gigante et al. [14]. Briefly, a small area over the iliac crest donor site was draped. After diagnostic arthroscopy to confirm the indication for the procedure a 2.5 mm Jamshidi needle was inserted percutaneously into the iliac crest. Sixty milliliters of bone marrow blood were aspirated and processed with the MarrowStim Concentration kit (Biomet, Warsaw, IN) according to the manufacturer's instructions, obtaining 3–4 mL of BMC.

The chondral lesion was debrided and microfractures were performed using appropriate awls. The lesion main dimensions were measured and reported on a rubber template that was then adjusted to the exact shape of the defect. A Biocollagen MeRG® collagen membrane (Bioteck, Vicenza, Italy) was cut to match the defect shape and immersed in BMC until implantation.

The water flow was stopped and water was aspirated from the joint cavity. A 10:one mixture of 1–2 mL fibrin glue and BMC was laid on the lesion bed using a long needle. The membrane was inserted through the appropriate portal with a grasper and fitted into place with a probe. An additional 2–3 mL of the fibrin glue-BMC mixture was injected over the membrane and left to solidify for 2–3 min. Finally, the excess of the fibrin glue-BMC mixture was removed and the knee repeatedly flexed and extended to check membrane stability.

The patients started continuous passive motion on days 4–5 and partial weight-bearing at 3 weeks, progressing to full weight-bearing at 6 weeks. Isometric quadriceps and hamstrings training and straight leg raising were advised during the non-weight-bearing period. Light sports activities such as swimming, cycling or jogging on even soft ground were allowed at 6 months. Permission to participate in unrestricted sports activity was given after 12 months.

2.3. Second-look arthroscopy

Four patients consented to second-look arthroscopy and biopsy harvest. Biopsies were performed with a standard 2.5 mm diameter Jamshidi needle (Fig. 1a). The specimens were placed in 10% formalin and sent for histology processing. The quality of the implanted tissue was evaluated by the surgeon using the criteria of the International Cartilage Repair Society [15] Cartilage Repair Assessment (CRA) [15].

2.4. Histology

Histological and histochemical characteristics of the repair tissue were evaluated. Specimens were decalcified, paraffin-embedded and stained with Safranin-O to detect the presence of glycosaminoglycans. Polarized microscopy was used to discriminate between hyaline-like cartilage and fibrocartilage. The ICRS II Histology Scoring System [16] was used to evaluate the quality of the repair tissue. Histological evaluation was performed blindly by two different investigators and scores were averaged.

2.5. Statistical analysis

The Student *t*-test was performed for the IKDC score, the Lysholm score and the VAS to compare pre- and postoperative values. Data are expressed as means with standard deviations. The nonparametric Wilcoxon-signed rank test was performed for the Tegner activity scale to compare pre- and postoperative values. Data are expressed as medians and interquartile ranges. For all tests, $p < 0.05$ was considered significant. The statistical software SPSS (Version 17.0) was used for biometric analysis.

3. Results

3.1. Clinical outcome

No patient-related complications nor device-related complications were encountered. None of the patients was lost at follow-up. All patients followed the standardized rehabilitation protocol. Patients' characteristics and patient-reported outcomes are shown in Table 1. Associated intervention at the time of surgery was two (one partial meniscectomy and one synovectomy). A patient with an unshouldered cartilage defect required a mini-arthrotomy to fix the membrane with polar stitches.

A statistically significant improvement in the mean IKDC subjective score from 49 SD(11) to 82 SD(12), mean Lysholm score from 58 SD(13) to 88 SD(11) and mean VAS from 7.6 SD(1) to 2.3 SD(2.2) from preoperative values to the latest follow-up were obtained ($p < 0.05$) (see Table 1 for single values). The median Tegner activity scale showed no significant difference from pre-injury level of 4 (interquartile range 4–7) to post-operative level of 4 (interquartile range 3.5–6.5) at latest follow-up ($p > 0.05$) (see Table 1 for single values). On the other hand, a significant increase in the activity level from post-injury 2 (interquartile range 2–3) to post-operative was observed at latest follow-up ($p < 0.05$).

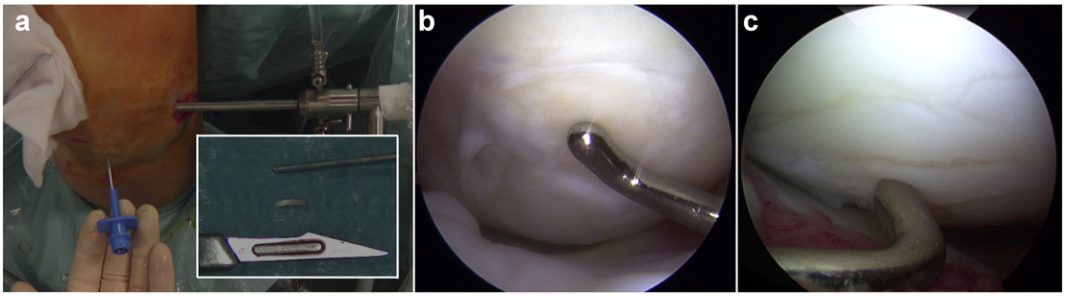

Fig. 1. Second-look arthroscopy and biopsy harvest. a) The Jamshidi needle is inserted from the appropriate portal and the bioptic cylinder is harvested. b) Second look biopsy showing a repair in level with the surrounding cartilage, completely integrated, with a smooth surface and a slightly fibrillated border. c) Repair in level, with a slightly demarcating border and minute fissurations.