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Original Article

Surgical treatment of chondral knee defects using a collagen membrane – autologus matrix-induced chondrogenesis☆

Diego Costa Astur, Jonathas Costas Lopes, Marcelo Abdulklech Santos, Camila Cohen Kaleka, Joicemar Tarouco Amaro, Moises Cohen*

Departamento de Ortopedia e Traumatologia, Escola Paulista de Medicina (EPM), Universidade Federal de São Paulo (UNIFESP), São Paulo, SP, Brazil

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ABSTRACT

Objectives: To evaluate the clinical and functional results of patients diagnosed with full-thickness chondral defects on symptomatic knees who underwent a biological repair technique using autologous matrix-induced chondrogenesis.

Methods: Seven patients who underwent surgical treatment due to chondral lesions in the knee by autologous matrix-induced chondrogenesis were evaluated. The Lysholm, Kujala and visual analog scale of pain questionnaires were applied before and 12 months after the surgery. Nuclear magnetic resonance images were evaluated 12 months after surgery according to MOCART (magnetic resonance observation of cartilage repair tissue) cartilage repair tissue score.

Results: Of the seven patients evaluated, three presented defects classified as grade III and four as grade IV according to the International Cartilage Repair Society classification. Chondral defects were located in the medial femoral condyle ($n = 2$), patella ($n = 2$), and trochlea ($n = 3$). The mean age of the patients (six men and one woman) was 37.2 years (24–54 years). The mean chondral defect size was 2.11 cm^2 (1.0–4.6 cm^2). After 12 months, post-operative nuclear magnetic resonance showed resurfacing of the lesion site with scar tissue less thick than normal cartilage in all patients. The mean MOCART score was 66.42 points. A significant decrease in pain and an improvement in the Lysholm and Kujala scores were observed.

Conclusion: The use of the collagen I/III porcine membrane was favorable for the treatment of chondral and osteochondral lesions of the knee when assessing the results using the VAS, Lysholm, and Kujala scores 1 year after surgery, as well as when assessing the magnetic resonance image of the lesion 6 months after surgery.

☆ Study conducted at Departamento de Ortopedia e Traumatologia, Escola Paulista de Medicina (EPM), Universidade Federal de São Paulo (Unifesp), São Paulo, SP, Brazil.

* *Corresponding author.*
E-mail: marceloabdul@me.com (M.A. Santos).

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Tratamento cirúrgico das lesões condrais do joelho com o uso da membrana de colágeno – condrogênese autóloga induzida por matriz

Palavras-chave:
Artroplastia subcondral
Cartilagem articular
Condrogênese
Colágeno
Traumatismos do joelho

RESUMO

Objetivos: Avaliar os resultados clínicos e funcionais dos pacientes com diagnóstico de lesões condrais de espessura total em joelhos sintomáticos submetidos a um método de reparação biológica por meio da técnica de condrogênese autóloga induzida por matriz.

Métodos: Foram avaliados sete pacientes submetidos a tratamento cirúrgico devido a lesões condrais no joelho pela técnica de condrogênese autóloga induzida por matriz. Foram usados os questionários Lysholm e Kujala e a escala visual analógica da dor antes e após um ano de cirurgia. As imagens de ressonância nuclear magnética foram avaliadas após 12 meses de acordo com os critérios de reparo cartilaginoso de Mocart (*magnetic resonance observation of cartilage repair tissue*).

Resultados: Dos sete pacientes avaliados, três apresentavam defeitos classificados como grau III e quatro como grau IV, de acordo com a classificação da *International Cartilage Repair Society*. Os defeitos condrais estavam no côndilo femoral medial (n = 2), na patela (n = 2) e na tróclea (n = 3). A média de idade dos sete pacientes (seis homens e uma mulher) foi de 37,2 anos (24 a 54). O tamanho médio dos defeitos condrais foi de 2,11 cm^2 (1,0 a 4,6 cm^2). Após 12 meses, a ressonância nuclear magnética pós-operatória mostrou preenchimento do local da lesão com tecido cicatricial menos espesso do que a cartilagem normal em todos os pacientes. O valor médio do questionário de Mocart após 12 meses foi de 66,42 pontos. Observou-se diminuição importante na dor e melhoria da avaliação dos questionários de Lysholm e Kujala.

Conclusão: O uso da membrana de colágeno I/III de origem porcina se mostrou favorável no tratamento de lesões condrais e osteocondrais do joelho quando se avaliaram os resultados obtidos com a escala visual analógica da dor e o questionário de Lysholme Kujala um ano após a cirurgia, bem como quando se avaliou a imagem da lesão na ressonância magnética seis meses após a cirurgia.

Introduction

The articular cartilage is an avascular tissue with a low mitotic potential, composed mainly of proteoglycans and rich in type 2 collagen; chondrocytes account for only 5% of its weight. Its oxygen and nutrient supply comes from the synovial fluid through the diffusion process, which is facilitated by cyclic compressive loads through a pumping mechanism during joint movements.[1]

One of the major challenges for orthopedic surgeons is the treatment of chondral injuries.[2] Due to the poor healing potential of human articular cartilage and the degree of discomfort caused by these lesions, surgical intervention has been widely used in attempts to resurface cartilage defects.[3] Several techniques have been used, such as microperforations, autologous and heterologous osteochondral grafting, and autologous chondrocyte implantation.[4]

Periosteal flaps had long been used to cover cartilage defects after microperforations; however, the use of the periosteum showed some restrictions, first for affecting the donor area, and a particular problem was the hypertrophy of the implanted tissue, which led to receptor area morbidity.[5] Thus, there has been a growing interest in the development of resorbable biological tissues that could replace the periosteum previously used to cover the lesions. One of the tissues developed is the collagen membrane, which serves as a support and cover for the mesenchymal cells originating from the subchondral bone that migrate after the microperforations.

The present study is aimed at clinically and radiologically evaluating patients with chondral lesions who underwent surgery with the microperforation technique and collagen membrane implant in cartilage defects of the knee.

Material and methods

After approval by the ethics committee, an observational case series study of patients with knee cartilage lesions was conducted between 2015 and 2016.

Nine patients (eight males and one female) with chondral lesions of the patella, trochlea, and femoral condyle underwent surgical treatment with microperforations, followed by the application of collagen membrane at the lesion site.

The inclusion criteria were patients under 60-years-of-age, who had pain originating from the patellofemoral and tibiofemoral joints, and whose lesions were classified as grades III or IV (according to the classification of the International Society of Cartilage Repair) and had a minimum

diameter of 1 cm. The criteria for non-inclusion were patients who presented poor lower limb alignment (without prior surgical correction), high or low patella, abnormal patellar tilt, anterior cruciate ligament injury requiring surgical reconstruction, meniscal tears, need for surgery in the injured knee for previous treatment of a cartilaginous lesion, joint infection, or systemic inflammatory diseases. The exclusion criteria comprised patients who were lost to outpatient follow-up or did not agree to participate.

Preoperative assessment

Patients with knee pain and history and physical examination suggestive of chondral lesion of the patellofemoral or tibiofemoral joints underwent imaging tests capable of detecting and identifying the lesion. Radiographic exams were performed to identify the bone anatomy and limb alignment, as well as magnetic resonance imaging (MRI) capable of identifying the type and size of the chondral lesion. Thus, the study included the patients who fulfilled the previously outlined criteria.

Surgical procedure

The first step in the surgical procedure is a knee arthroscopy through the anterolateral and anteromedial portals. After the lesion is located, the arthroscopy is interrupted; then, a longitudinal parapatellar approach is made according to the side of the lesion.

The non-viable margins are resected; then, curettage of the cartilage surface is performed in order to remove the calcified layer of damaged cartilage.

A metal template is used to define the precise size of the defect to be covered; this template is then used to cut the membrane after immersing it in saline. Subsequently, microperforations spaced 2–4 mm apart and approximately 4 mm in depth are made. When the lesion is prepared to receive the cover, a porcine I/III collagen membrane (Chondrogide, Geistlich Pharma AG, Wolhusen, Switzerland) is placed on the lesion. Care is taken to ensure that the most porous part of the membrane is in contact with the subchondral bone, and it is temporarily secured with two needles. Finally, the membrane is sutured to the articular cartilage with five to six stitches of absorbable monocryl 5.0 sutures and supplemented with fibrin glue on the edges of the membrane.[6,7]

Rehabilitation

All patients remained immobilized for 3 weeks with a functional brace without weight-bearing.

From the third to the fifth week, the treatment is aimed at decreasing inflammation, increasing knee range of motion, and achieving quadriceps muscle control. Patients in whom the lesion affected the weight-bearing area (medial femoral condyle) remained without weight-bearing. In patients with patellar or trochlear lesions, partial weight-bearing was initiated.

Between 5 and 8 weeks, all patients are encouraged to walk without the orthosis. This is conducted progressively and increased, so that gait without support can be authorized by the end of the period. Hydrotherapy and stationary bike exercises are progressively encouraged. After 4–6 months, the patient is released to run, as well as to perform pivot and jump movements. Finally, between 6 and 8 months, the patient is authorized to practice contact sports.

Clinical, functional, and imaging evaluation

The following data on the lesion were recorded: location, affected side, and lesion size. Moreover, the lesion was identified by magnetic resonance imaging through the nine MOCART criteria 12 months after surgery.[8] The Lynsholm and Kujala knee function questionnaires were used, as well as the preoperative visual analogue scale and also after 12 months of surgery.[9–11]

Statistical analysis

Due to the small number of cases, a level of significance of 10% was adopted. Non-parametric Wilcoxon tests were used to compare different moments for each analyzed score. To compare the topography of the lesion, the nonparametric Kruskal–Wallis test was used. Finally, Spearman correlation was used to measure the relationship between age and area with the different scores used.

Results

Of the nine patients included in the study, two were excluded for not following the treatment, so seven patients were studied, six males and one female. The mean age was 37.2 years (24–54); four cases presented lesion in the right knee and three cases, in the left knee.

The lesions affected the femoral trochlea in three cases, the femoral condyle in two, and the patella in two others. Lesion size ranged from 1.0 to 4.6 cm^2 (mean of 2.11 cm^2; Table 1).

By the Lynsholm questionnaire, the patients presented a mean of 59.3 points (±6.1) before surgery and 81.3 points (±10) 12 months after the surgical procedure. When analyzed separately by topography, this average was higher in the postoperative period for trochlear lesions, but no statistically significant difference when compared to lesions in other knee regions ($p > 0.05$).

By the Kujala questionnaire, patients presented a mean of 64 points (±8.9) before surgery and 86.9 points (±6.5) 12 months after the surgical procedure. When analyzed

Table 1 – Region and size of identified and treated lesions of the seven patients included in the present sample who completed treatment.

Patient	Region	Side	Size (cm^2)
1	Trochlea	L	1.98
2	MFC	R	0.8
3	MFC	R	1.65
4	Trochlea	L	1.56
5	Trochlea	R	1.56
6	Patella	L	4.68
7	Patella	R	2.34

Table 2 – Evaluation of the questionnaires applied preoperatively and 1 year after surgery. It was observed that for the Lysholm and Kujala questionnaires and the VAS, the results were statistically better.

Variable	Mean	Median	*p*-Value
Lysholm			
Preoperative	59.3	61	0.018
Postoperative	81.3	85	
Kujala			
Preoperative	64	65	0.028
Postoperative	86.9	86	
VAS			
Preoperative	7.4	7	0.017
Postoperative	3.5	3	

separately by topography, this average was also higher in the postoperative period for trochlear lesions, but there was no significant difference when compared to lesions in the other regions of the knee ($p > 0.05$).

When the VAS was analyzed, patients presented a mean of 7.4 points (±1) before surgery and 3.5 points (±1.5) 12 months after the surgical procedure. When analyzed separately by topography, this average was lower in the postoperative period for patellar lesions, but no statistically significant difference when compared to lesions in other knee regions ($p > 0.05$; Table 2).

The relationship between the patient's age and lesion size with the results of the questionnaires before and after the surgery were also assessed. No correlation was observed between these parameters, suggesting that the patient's recovery and the complaints associated with this lesion are not related to age, nor to the size of the lesion when the present inclusion criteria are considered ($p > 0.05$).

Preoperative MRI showed three grade III lesions and four grade IV lesions, ranging from 1 to 4.68 cm^2 (mean: 2.11 cm^2; median: 1.58 cm^2). In all cases, the presence of joint effusion was observed, in addition to at least a subchondral edema in the topography of the lesion. The results obtained from the MRI showed that the subchondral edema persisted throughout the follow-up period; it also indicated the resurfacing of the area of the osteochondral lesion with good integration at the edges in all cases evaluated 12 months after surgery. The mean MOCART[8] score after 12 months was 66.42 points, ranging from 55 to 85 points.

In one case, the patient developed articular blockage, requiring an arthroscopic joint release. In that case, it was observed that the lesion was partially covered by a fibrocartilaginous tissue of lower thickness than the adjacent articular cartilage (Figs. 1 and 2).

Discussion

Collagen membranes were developed to improve the results obtained with the microfracture technique. Despite presenting good results when well indicated for the treatment of chondral knee injuries, it is known that 25% of athletes do not return to sports practice and those who return are usually unable to obtain the same performance level as before the injury.[12] *In vitro* studies have shown that a membrane composed of collagen can retain cartilage repair cells, such as mesenchymal cells from the subchondral bone.[13] In a series of 147 cases of chondral lesions in the acetabulum (Outerbridge grades 3 and 4), the authors concluded that the short-term clinical outcome is satisfactory in patients with chondral lesions who underwent microfracture treatment with or without the membrane. However, the group in which the collagen membrane was used presented a more substantial and lasting improvement, particularly in patients with large lesions (>4 cm^2).[14]

In the present study, it was observed that all patients treated with this technique presented pain improvement; in a subjective assessment, 85% of the patients reported being very satisfied with the treatment. This result is in agreement with several other studies previously described in the literature.[14–19] Patients started treatment with a mean of 7.4 points on the VAS and, after 6 and 12 months, the mean was 3.3 and 3.5 points, respectively, which indicates a significant clinical improvement ($p < 0.05$).

Gile et al.[16,17] concluded that 87% of patients treated with collagen membrane were highly satisfied 1 year after the surgery. In their series, the mean Lynsholm score was 36 (±21) before surgery. After 12 months, the mean score was 67 points (±24), reaching 76 points (±28) 2 years after surgery. Although the present case series presented the results obtained before and 12 months after surgery, the Lysholm and Kujala questionnaires presented similar results, with a significant improvement in their score ($p < 0.05$) for both. Nonetheless, the results were still higher than those obtained in the study by Gile et al.[17]

Two of the present patients underwent simultaneous treatments; one was submitted to valgizing tibial osteotomy and another to extensor mechanism realignment. However, there was no significant difference between the scores of these patients and of those who were submitted exclusively to the chondral lesion treatment. Correction of the femorotibial axis or patellofemoral alignment is essential for the success of the technique. The chondral lesion is usually a consequence of an overload or increased pressure of one bone on another. Correcting the cause of the cartilage damage is paramount.

Kusano et al.[19] also analyzed the difference between the presence of a chondral and an osteochondral lesion. In their study, patients were divided into three groups: chondral lesions on the femoral condyle, osteochondral lesions on the femoral condyle, and chondral lesions on the patella. In their series of patients, those authors came to the conclusion that patients treated for osteochondral lesions presented worse functional results when compared with the other groups.[16] Although the present study did not analyze separately the differences between the types of lesion, the authors believe that osteochondral lesions have a potential for worse results due to the characteristics of the lesion, which often result not only in bone and cartilage lesions but also in subchondral edema and infiltration of synovial fluid with inflammatory characteristics.

Postoperative MRI does not show remission of lesion characteristics at the same pace as on clinical examination. Nonetheless, it was possible to observe differences of great importance in the analyzed patients, as it shows the quality of

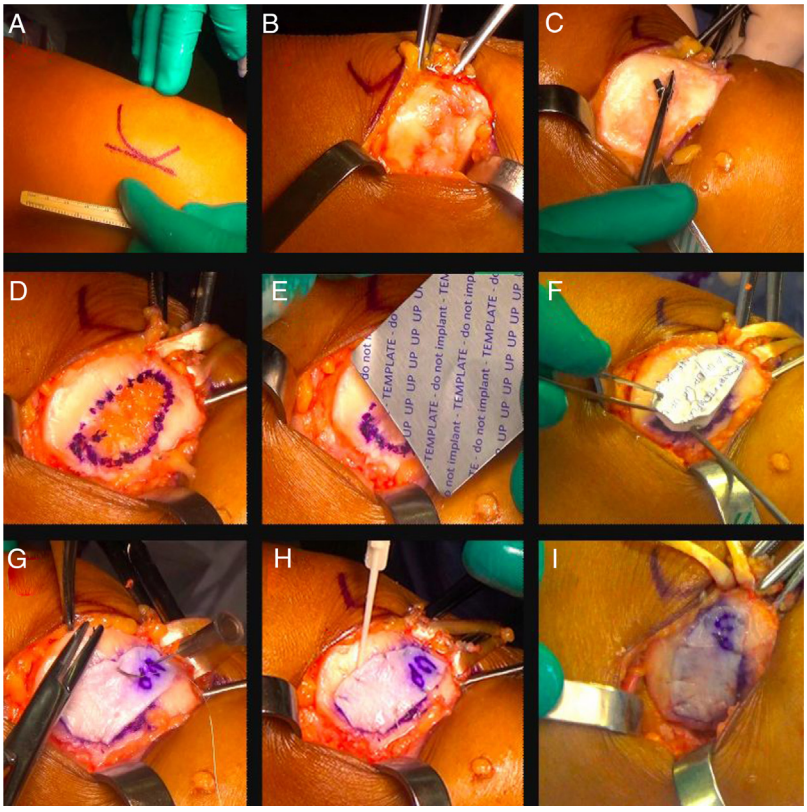

Fig. 1 – Intraoperative images of the surgical technique showing a collagen membrane in a chondral patellar lesion. (A) Incision site and medial parapatellar arthrotomy. (B) Kirschner wire used as a 'joystick' to evert the patella. (C) Identification and debridement of the chondral lesion. (D) Debrided and microperforated receptor area. (E) Metallic template used to measure the dimension of the lesion. (F) Metal mold cut, together with the membrane. (G) Membrane suture in the cartilage with absorbable No. 5.0 suture. (H) Fibrin glue used at the edges of the lesion. (I) A final view of the procedure showing the osteochondral defect covered and secured by the collagen membrane.

the repair tissue obtained after the procedure.[20] Kusano et al.[19] found inconsistent results in their series, as some patients presented good resurfacing of defects, while others presented no resurfacing or hypertrophy. Integration into the border zone was generally good, but the subchondral bone and adjacent abnormalities were common. Almost all patients presented an increased signal in the repaired tissue. In another study, three typical alterations of bone marrow lesions were found, such as effusion and bone hypertrophy beneath the repaired tissue. Most patients ($n = 10$) presented a resurfacing defect greater than 50%.[21]

Dhollander et al. followed-up a group of patients who underwent repair surgery of the patellofemoral joint and found that the clinical evolution of the patients was in disagreement with the radiological evolution; they observed poor integration at the edges of the membrane and osteophyte formation at the lesion site in 30% of patients after 24 months postoperatively.[21]

The present authors believe that MRI may be used as an indication of failure of the surgical treatment, but not as an indication of short-term success. A longer follow-up allows a more careful evaluation of the results obtained with the use of the collagen membrane on a chondral lesion. In the present study, after 12 months, satisfactory results were observed on the MOCART score.[8]

This is a series of cases with a small number of patients evaluated in different regions of the knee. This was the main limitation of the present study; however, it was possible to elucidate the characteristics of the lesion and the evolution of the patient's treatment until the time considered appropriate for the return to sports activity. This is the first series analyzed in Brazil.

The repair of symptomatic chondral lesions continues to be a challenge, especially in cases of young patients suffering from a painful, full thickness lesion that may potentially result in a functionally limited, degenerated knee. The use of collagen membrane-induced chondrogenesis has been shown to be a suitable option for the treatment of severe chondral lesions in the knee, with favorable results. No donor area is required to remove osteochondral plugs or to culture and differentiate chondrogenic cells to implant at the lesion site; therefore, the treatment is effectively less costly and can be done in a single surgical procedure.

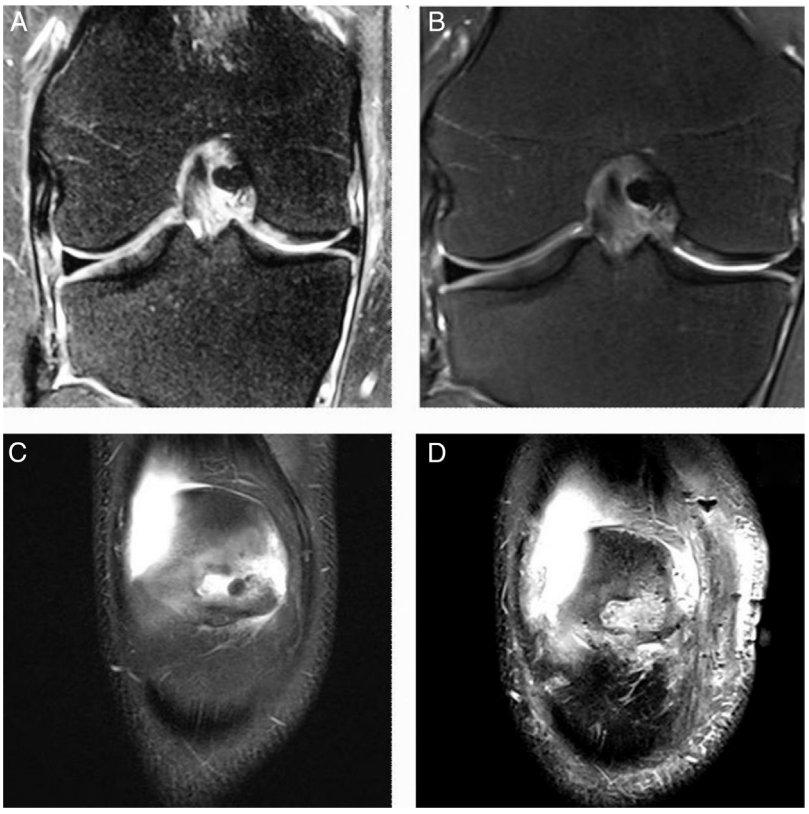

Fig. 2 – Magnetic resonance imaging of two patients who underwent surgical treatment, preoperatively and 1 year postoperatively. (A) A T2-weighted coronal section showing a chondral lesion on the inner side of the medial femoral condyle. (B) A postoperative image showing the resurfacing of the previous cartilaginous lesion. (C) A coronal image of the patella, showing the lesion area on the medial facet. (D) Area resurfaced by the collagen membrane.

Conclusion

The use of the porcine I/III collagen membrane was favorable in the treatment of osteochondral lesions of the knee when evaluating the results obtained with the VAS, Lysholm questionnaire, Kujala questionnaire, and MRI after 12 months of surgery.

Conflicts of interest

The authors declare no conflicts of interest.

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