

Combined Effect of Subchondral Microfracture & Platelet-rich Plasma in Small Full Thickness Articular Cartilage Lesions of the Knee Joint

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Abstract

Background

Knee chondral defects do not heal and if not treated may progress to degenerative joint changes. Treatment of full thickness knee chondral defects is a challenge with many available options for management. There is a trend towards biological and tissue engineering solutions. This is supported by the good results of numerous studies. However, study designs are mostly heterogenous and difficult to be compared. Some relatively simple and cheap cartilage repair procedures (as microfracture) have been mentioned sparsely in the literature, and claimed to yield good results when combined it with PRP injection.

Objectives

The aim of this study, was to analyze the clinical results of combined PRP injection and microfracture (which is the most common performed cartilage repair modality).

Patients and methods

A prospective study included Twenty patients with full thickness knee chondral defects were treated with microfracture (MF), combined with PRP injection in Sheikh Zayed specialized and Menofia university hospitals. The results were assessed at the end of follow up clinically using IKDC and MRI

Results

The maximum age incidence in this study was from $25 \leq 30$ (50%) and the least incidence was from $41 \leq 50$ (15%). The youngest patient in this study was 25 years old and the eldest was 47 years old. There were 17 males and only 3 females showing male predominance. There were 11 patients affected on the right side and 9 on the left side. 18 patients (90%) had associated injuries 10 patients had M.M tear, 3 patients had M.M tear and OCD, 2 patients had M.M tear and L.M tear, 2 patients had ACL tear and 1 patient had ACL tear and M.M tear. The predominant mechanism of injury is traumatic twisting injury in 16 patients and degenerative injury in 4 patients.

Conclusion

combined microfracture and PRP injection improve the outcome of chondral lesions at 3 and 6 months follow-up on international knee documentation score.

key words

microfracture, platelet-rich plasma, chondral lesion.

Introduction

Articular cartilage damage is common; cartilage can be injured by impact, repeated loading, tensional loading, joint misalignment and foreign bodies in the joint space. [1], *Studies suggest that 20%-60% of knee arthroscopies reveal focal chondral or osteochondral defects. There are Different articular cartilage repair procedures share the aim to restore articular cartilage structure and function.*

Conservative treatment: is considered in mild symptomatic cases or in cases with small lesions where surgery could do more harm than good.[1,2]

The purpose of surgery is regeneration of osteo-

chondral defects to ultra structural and biomechanical competence of hyaline cartilage like Abrasion arthroplasty, Osteochondral autografting (OATS): (Mosaicoplasty), Osteochondral allografting fresh or deep freeze Autologous chondrocyte implantation (ACI), Matrix-induced Autologous chondrocyte implantation (MACI) Microfracture

Microfracture is a single-stage procedure suited for small, well-contained, Outerbridge grade 3 to 4 cartilage lesions, can be performed on any size lesion, but Steadman et al. reported trends of better results with lesions smaller than 400 mm², It enhances chondral resurfacing by providing a suitable environment for new tissue formation and taking advantage of the body's own healing potential.[3]

Specially designed awls are used to make multiple perforations, or “microfractures,” into the subchondral bone plate. Perforations are made as close together as possible, but not so close that one breaks into another. Integrity of the subchondral bone plate must be maintained. The released marrow elements (including mesenchymal stem cells, growth factors, and other healing proteins) form a “super clot” which provides an enriched environment for new tissue formation. The rehabilitation program is crucial to optimize the results of the surgery. It promotes the ideal physical environment for the mesenchymal stem cells to differentiate into articular cartilage-like cells, leading to development of a durable repair cartilage that fills the original defect.[4]

Methods of augmentation of microfracture 7 Platelet-rich plasma

PRP is a procedure used in articular cartilage repair on a molecular level on chondrocytes and mesenchymal stem cells by increasing cell proliferation and synthesis of proteoglycans and collagen type 2.[5]

8. Injection of bone marrow aspirates:

The benefit from the osteochondral progenitor cells and mesenchymal stem cells which exist in bone marrow.

Patients and Methods

Patients

Twenty chondral ulcers in 20 patients had been treated by combined microfracture and 3 PRP injections at Menoufia university and Sheikh Zayed hospitals between October 2015 and October 2017.

The patients were followed for at least 6 months post-operatively. This study included arthroscopically evident chondral lesion measures $\leq 2.5 \text{ cm}^2$ in medial femoral condyle of femur grade III or IV (as scored by ICRS classification) with or without associated injury. All patients aged 25-50 years, and good knees stability, Patients with septic knee, advanced osteoarthritis, and knee malalignment were excluded from the study.

Methods

A joint exploration was carried out through standard arthroscopic portals in order to identify the chondral lesion and score it based on the ICRS arthroscopic system, and to evaluate the presence of eventual lesions affecting meniscus or ligaments. Treatment of

the defect included also a preliminary lesion debridement aimed at obtaining clear-cut edges and stable edges and removing the calcified cartilage by using a curette to avoid going too deep into the subchondral bone; once the bottom of the lesion was prepared, 3-4 mm-deep perforations were performed using a specific conical awls with an approximately 4 mm bone bridge between perforations. Furthermore, all patients were treated with PRP intraarticular infiltrations on the seventh, fourteenth and twenty-first day after surgery. Thirty to Forty-five milliliters whole blood was collected from the cubital vein into a 50mL syringe that contained 3mL sodium citrate. Then, samples were put in the centrifuge (Eppendorf, 5702 R, Germany). This device is a desktop-size with disposable cylinders for the blood.



Figure 1: Debridement strategies

- A: wash out
- B: shaving
- C: trimming the loose cartilage tags
- D: refining the edge to a perpendicular transition

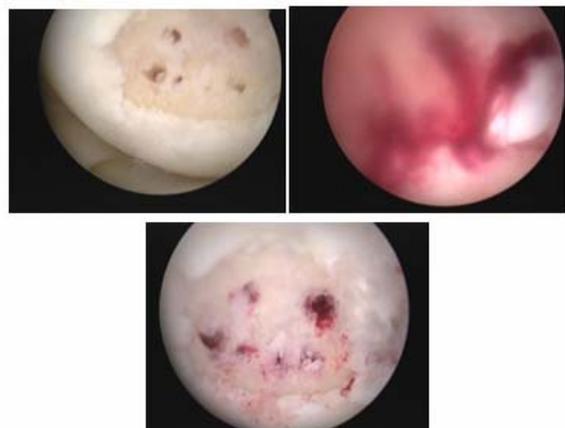


Figure 2: a. Microfracture 1st view with 50 mmHg inflow. b. Microfracture 2nd view with reduced inflow pressure. c. Microfracture 3rd view with the inflow pressure re-increased

The anticoagulated blood is centrifuged at 1,500 rpm for 10minutes then transfer of the upper layer with buffy coat to empty sterile tubes then second spin 3000rpm for 5minutes.

Approximately 5mL of PRP was obtained for each patient.

The platelet-rich plasma was then loaded into a 5-mL syringe with a 22-gauge needle.

Platelet-rich plasma then activated by 0.1% of the sample calcium gluconate.

The 5 mL PRP obtained were infiltrated into the knee previously treated by microfracture reparative surgery. All patients had a standard rehabilitation protocol, avoided weight-bearing on the treated knee for 6 weeks after the arthroscopy, closed kinetic chain exercises to increase stability and core-stability until return to normal day life activities in approximately 8 weeks.

Evaluation(results)

1. Clinical evaluation:

All patients previously evaluated during the preoperative phase were reassessed at three weeks, six weeks, three months and 6 months follow-up based on the international knee documentation committee (IKDC), the subjective knee function to perform both a clinical and functional evaluation.

Statistical analysis:

Data were collected, tabulated and statistically analyzed by an IBM compatible personal computer with SPSS statistical package version 20.

follow-up visits an improvement of all evaluation scores could be observed compared to the preoperative. Results more satisfactory were reported, both for what concerns pain symptomatology and functional recovery, in all 20 patients treated with reparative microfracture surgery and PRP injection. In this thesis 20 patients were examined arthroscopically for knee derangement. There were 17 males and 3 females with age ranged from 25 to 50 years old. Their complaint was pain with activity like climbing up or down stairs and squatting only in 7 patients, pain and locking in 10 patients, pain and giving way in 3 patients, effusion in 6 patients and synovitis in 2 patients.

There was evident history of trauma in 16 patients and no definite history of trauma in 4 patients.

Clinical examination revealed (+ve) McMurray test in all patients, 3 patients had (+ve) Lachman test, (+ve) anterior drawer test, (+ve) pivot shift test, All patients had (-ve) varus stress test and (-ve) valgus stress test, 15 patients had full range of motion before surgery while 5 patients were unable to completely flex the knee.

MRI shows M.M injury in 16 patients bucket handle

in 8 patients, radial tear in 3 patients, horizontal tear in 3 patients and root tear in 2 patients lateral meniscal injury in 1 patient's flab injury.

ACL complete tear in 3 patients, OCD injury in 3 patients and only chondral lesion in 2 patients.

Scopic examination revealed isolated chondral lesion in 2 patients, there was chondral lesion associated with meniscal injury in 17 patients, chondral lesion associated with torn ACL in 3 patients.

Chondral lesions grading according to ICRS classification was grade 3 in 7 patients, grade 4 in 13 patients.

All patients were managed by combined microfracture meniscal injuries: managed by partial meniscectomy in 13 cases subtotal meniscectomy in 4 cases.

ACL managed by ACL reconstruction by gracilis and semitendinosus muscles graft in 3 cases

PRP injection

Pre-operatively IKDC was 40.5150 + 8.76009

IKDC at 3 months 48.602000 + 12.83937 IKDC at 6 months 77.5350 + 10.97841

Discussion

Chondral and subchondral lesions are common and typically affect young athletic population failure to recognize these injuries can result in long term disability [4].

Chondral lesions accelerate degenerative changes, especially for large defects without vertical margins.

Articular cartilage has no ability to regenerate normal hyaline cartilage, mesenchymal tissue is converted into fibrocartilage which has decreased proteoglycan content compared to hyaline cartilage, fibrocartilage which has decreased proteoglycan content compared to hyaline cartilage, fibrocartilage is also less resilient with poor response to stress and therefore, continued trauma to the joint can lead to further degeneration [5]

If articular cartilage loses the ability to adapt to repetitive stresses, loss of patient performance may be followed by development of chondropenia and ultimately osteoarthritis [6]

In this study 20 patients with knee problem were examined, investigated and scoped for their lesions

The aim of our work was to know the effect of combined microfracture and PRP injection of chondral lesions .

In our study there is 2 patients had isolated chondral lesion 10%, there is 10 patients had associated medial meniscus tear with the chondral lesion 50%, there is 2 patients had associated medial and lateral meniscus tears with chondral lesions 10%, there is 3 patients had associated medial meniscus tear and OCD with chondral lesions 15% , there is 2 patients had associated ACL tear 10% ,there is 1 patient had associated ACL and medial meniscus tears with chondral lesion 5%.

These results correlate with that is reported by Curel et al.,[8]. Chondral lesion may occur alone or in association with meniscal injuries or ligamentous injuries and they also noticed that loss of meniscal integrity or ligamentous instability may increase the load on the chondral surface and may worsen existing defects and/or prevent successful repair.

Also our findings correlates with Scop et al.,[9] observation that meniscal tears with partial thickness articular cartilage defects are most common type of articular cartilage injury encountered in orthopedic surgical practice .

The main bulk of chondral lesions affect young patients below 40 years 80% in our study.

In this study chondral lesion was graded according to ICRS grade we found that grade 3 represented by 7 patients 35% and grade 4 represented by 13 patients 65%.

These results correlates with those reported by Scop et al that chondral and osteochondral injuries are common and typically affect young athletic population [9].

Also these results correlate with those of Curl et al in his review of 31000 patients with knee problem in all age groups and reported that articular cartilage damage was found in (63%) of patients with more than (60%) of patients with more than (60%) having grade 3 or grade 4 lesion, chondral lesion with no associated injury in (36%) of patients .

The main complain in this study was pain in (35%) of patients , pain and locking in (50%) of patients while (15%) of patients complain of pain and giving way, Curel et al and Moreno Morelli et al.,[7] that patients may be presented by painswelling ,locking , giving way i.e there is no specific complain for chondral lesion.

In this study most patients with duration of injury <4

months had chondral lesion of grade 3 and most patients with duration of injury \geq 4 months had chondral lesion grade 4.

The relation between chondral lesion severity and duration had been explained by that is said by scoop et al.,[9]

That loss of articular integrity through injury , deterioration over time the dose response curve showed that chondropenia and articular cartilage defects can no longer provide adequate response to loading [10]

This theory had been supported by Ros et al , [11] who reported that if articular cartilage loses the ability to adapt to repetitive stresses will lead to loss of athletic and will be followed by the development of chondropenia and ultimately osteoarthritis [12].

Also Depalma, Mitchel et al reported that continued trauma to injured cartilage can lead to further degeneration.

Travis et al [13] reported that loss of meniscal integrity or ligamentous instability increase the load on the chondral surface and may worsen the existing defect and prevent successful repair or restoration .

The significance of MRI in the diagnosis of associating injury to chondral lesion as torn ACL or M.M or L.M injury was evident in this study , these results also reported by Scopp et al that is MRI is important in the diagnosis of chondral lesion because it facilitates the diagnosis of concomitant injuries [14].

However MRI has limited role in the diagnosis of chondral lesion in this study this in contrast to Loullie et al., who reported that MRI improved dramatically in recent years and now play an important role in assessing articular cartilage structural integrity.

Investigators have applied a variety of magnetic resonance sequences to evaluate the appearance of articular cartilage demonstrates a multi laminar appearance but there is disagreement about the number of layers in normal articular cartilage and the histologic significance of of each layer [14].

On the other hand recent studies by Friemert [15] and Vassilios demonstrated that the role of MRI in diagnosis of chondral lesion is still controversy and it cannot replace arthroscope in diagnosis of chondral lesion [16], arthroscoperemains the gold standard of chondral lesions diagnosis [17] because of MRI low sensitivity and high specificity in diagnosis of chondral lesion, it can be useful in exclusion of chondral lesion [18].

In this study 3 patients had torn ACL with ICRS

grade 4 of chondral lesion, there were 10 patients had torn M.M 6 from them had chondral lesion ICRS grade 4 and 4 patients had chondral lesion grade 3, there were 2 patients had combined M.M and L.M tear one of them with chondral lesion grade 3 and the other grade 4, there were 3 patients with M.M and OCD 2 of them had grade 4 one of them had grade 3.

These results could be explained by what is said by Travis et al [13] who reported that loss of meniscal integrity or ligamentous instability increase the load on the chondral surface and may worsen the existing defect and prevent successful repair or restoration.

The technique adapted for treating patients in this thesis was for chondral lesion by (microfracture) management of any associated injuries in these patients was done as reconstruction of torn ACL or partial meniscectomy for meniscal injury this was done according to Travis et al., [13] that is management of associated conditions such as ligament insufficiency and or meniscal injury is essential for successful outcome of chondral repair.

This also reported by Dunn et al., [19] that unstable tibiofemoral joint leads to increase articular cartilage lesion.

Also Ceregor et al., [20] reported that is loss of only 30% of meniscus increases joint contact pressures by more 350.3%.

Also postoperative management according to Kevin Hong et al., [21]

Microfracture was done for 16 patients improvement occurred postoperatively in 12 patients and improvement in 4 patients later.

These results also correlate with Steadman et al., [22] in a study of 72 patients treated by microfracture and followed up for an average of 11 years, 80% of patients who were younger than 45 years old and had no ligamentous or meniscal injuries demonstrated good to excellent results, results seen with microfracture technique have led to a question of the durability of fibrocartilage repair in active individuals [23].

Gobbi ⁽²⁴⁾ et al., that in a study of 53 patients treated with microfracture (mean follow up 72 months) found that:

Through the first 2 years, 80% noted improvement but this decreased to 55% by final follow-up [24].

Gill [25] also reported that good short-term functional results with 86% of patients reporting that their knees felt normal or near normal.

The poor long-term results are less promising due to the poor resistance of fibrocartilage to the compressive loads and subsequent fissuring and fragmentation.

Marrow stimulating techniques are recommended by Brian et al., for smaller lesion (2cm²) in active patients with no more than moderate symptoms or for larger lesions than (2cm²) in lower demand patients with mild symptoms but less successful for larger defects. [26]

The effect of marrow stimulating techniques (microfracture) to form fibrocartilage repair was successful in relieving patients but failed in others was explained by Brian [12] et al., that regardless to the type of injury with intervention, there is no ability of articular cartilage to regenerate normal hyaline cartilage, violation of subchondral bone will however expose the damaged area to the progenitor cells residing within the subchondral there by leading to fibrocartilage repair but this tissue is biologically and biomechanically inferior to hyaline cartilage and demonstrates predominance of type 1 collagen rather than normally abundant type 2 collagen [13].

Also Depalma and Mitchel [15] et al explained the poor response in some patients treated by marrow stimulating technique that defects of articular cartilage do not heal with normal articular cartilage.

Mesenchymal tissue is converted into fibrocartilage has decreased proteoglycan content compared with hyaline cartilage [24].

Growth factors play an important role in maintaining the cartilage tissue and joint structures homeostasis as a whole [25] and thanks to their interaction they give a contribution to the increasing of chondral phenotype cells expression and proliferation, they stimulate the mesenchymal stem cells differentiation in a chondrogenic sense, they promote the matrix deposition and slow down the matrix catabolism, and they reduce the suppressive effect exerted by the inflammatory mediators on the proteoglycans synthesis. The biological rationale of PRP implementation in degenerative joint pathology is to obtain a local concentration of growth factors capable of promoting the maintenance of joint homeostasis [26] and preventing the joint damage. Several in vivo studies based on animal and clinical models showed the efficacy of PRP both for chondral lesions and in the early degenerative joint pathology. In the recent past the use of platelet concentration has been increasingly adopted. Sanchez and colleagues published a comparative study conducted on 60 patients affected by knee arthrosis: 30 were treated by PRP and 30 by hyaluronic acid (HA) infiltrations. The analysis of results showed that the group treated with

growth factors presented higher results, with a more effective control of pain and a more satisfactory recovery of joint excursion.[27] In addition, the Saegusa group reported a good pain symptomatology management and an improvement of joint functionality in a cohort of 261 patients treated with PRP implantation and evaluated at a 6-month follow-up.[28] Besides, Kon and colleagues reported clinical and functional results of patients with chondral lesions and first-stage arthrosis treated with infiltration cycles performed on a weekly basis. Results show a significant improvement at 6 and 12-month follow-up.[29] TGF- β 1, also known as the cartilage-inducing factor and the differentiation inhibitor factor, is a protein formed by two monomers of 120 amino acids amino acids joined by a disulphide bond with a cystine knot structure. Among the three TGF- β isoforms, the β 1 is the most abundant and it is secreted by almost all cells. There are several advantages deriving from the use of PRP. In the first place it is an easy to perform procedure, fast, inexpensive and one-step which acts on cells in the defect site. Unfortunately there is not an agreement in the literature on the quality of the tissue newly formed after the two-techniques combination. For instance, Milano et al. in a study performed on an ovine model combining the two techniques reported the absence of newly formed hyaline cartilage based on histological evaluations.[30]

Conclusions

An effective strategy to achieve this goal is represented by the combination of Stedman's surgery with PRP infiltrations; indeed PRP, thanks to the action exerted by several growth factors contained in platelets, may act as a great support both to rapidly resolve the inflammatory process and to promote chondral defects regeneration.

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