■ SPECIALTY UPDATE: FOOT AND ANKLE

Osteochondral lesions of the talus

ASPECTS OF CURRENT MANAGEMENT

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Osteochondral lesions (OCLs) occur in up to 70% of sprains and fractures involving the ankle. Atraumatic aetiologies have also been described. Techniques such as microfracture, and replacement strategies such as autologous osteochondral transplantation, or autologous chondrocyte implantation are the major forms of surgical treatment. Current literature suggests that microfracture is indicated for lesions up to 15 mm in diameter, with replacement strategies indicated for larger or cystic lesions. Short- and medium-term results have been reported, where concerns over potential deterioration of fibrocartilage leads to a need for long-term evaluation.

Biological augmentation may also be used in the treatment of OCLs, as they potentially enhance the biological environment for a natural healing response. Further research is required to establish the critical size of defect, beyond which replacement strategies should be used, as well as the most appropriate use of biological augmentation. This paper reviews the current evidence for surgical management and use of biological adjuncts for treatment of osteochondral lesions of the talus.

Cite this article: *Bone Joint J* 2014;96-B:164–71.

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doi:10.1302/0301-620X.96B2.31637 $2.00

Bone Joint J 2014;96-B:164–71.

Osteochondral lesions (OCLs) of the talus are commonly associated with injuries of the ankle, occurring in up to 70% of acute sprains and fractures.[1] The recognition of these lesions and how to treat them has developed gradually over the past 200 years and continues to evolve. Trauma is the predominant aetiology of OCLs of the ankle.[2-4] Examining more than 500 patients, Flick and Gould[2] found evidence of trauma in 98% of lateral lesions and 70% of medial lesions. Although this is the most common cause of OCLs, a number of non-traumatic causes have also been proposed, including congenital factors, ligamentous laxity, spontaneous necrosis, steroid treatment, embolic disease and endocrine abnormalities.[4-6] The significantly higher incidence of OCLs in siblings as well as the prevalence of bilateral lesions suggests a congenital or hereditary cause.[7,8] Tissue necrosis has also been shown to have an important role in their development.[9] Zengerink et al[10] suggested necrosis as a secondary event rather than a cause of OCLs, and proposed that microtrauma caused by repetitive articular cartilage surface loading or excessive stress leads to cellular death via disruption of collagen fibrils and thickening of the subchondral bone.

In recent years, the goals of treatment of OCLs of the talus have been debated. Although pain relief and return of function are the immediate goals of any procedure, the long-term effectiveness of any treatment must also be considered. In this review we describe the current concepts of surgical treatment, outcomes, and the potential use of biological augmentation for OCLs of the talus.

Non-operative treatment

Non-operative treatment may be indicated for asymptomatic lesions, with patients being advised to limit athletic activities and to take non-steroidal anti-inflammatory drugs (NSAIDs). In a systematic review, Zengerink et al[11] found seven studies describing non-operative treatment, with many dating back > 20 years, when surgical options were limited. They describe a total of 169 patients, who were treated non-operatively, with a success rate of 49.1%. However, success was determined solely on symptomatology, and not on the physiological healing of the OCL. Although non-operative treatment may relieve symptoms in the short term, they often recur due to inadequate healing of the lesion.[12]

Surgical treatment

Conventionally, treatment has either been reparative with bone marrow stimulation, or replacement with tissue transplantation, with

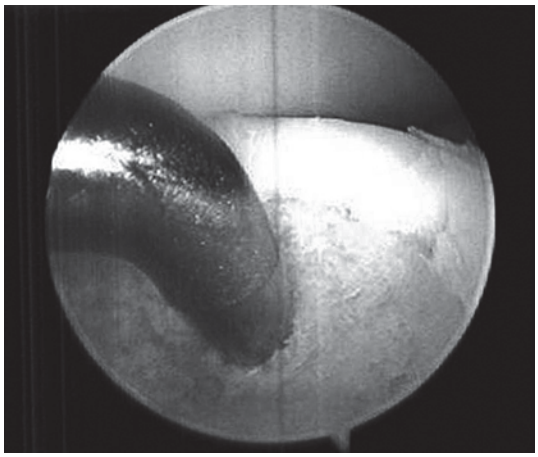

Fig. 1a

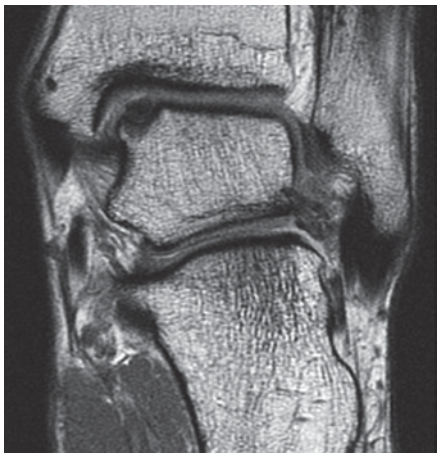

Fig. 1b

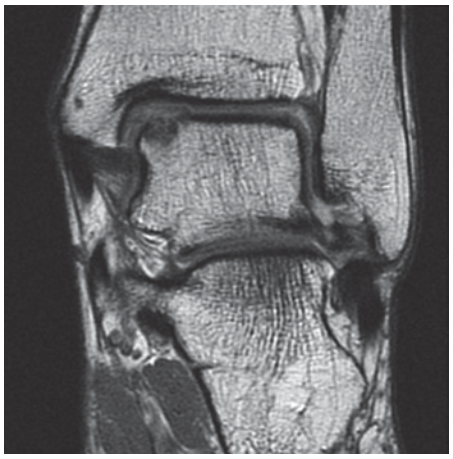

Fig. 1c

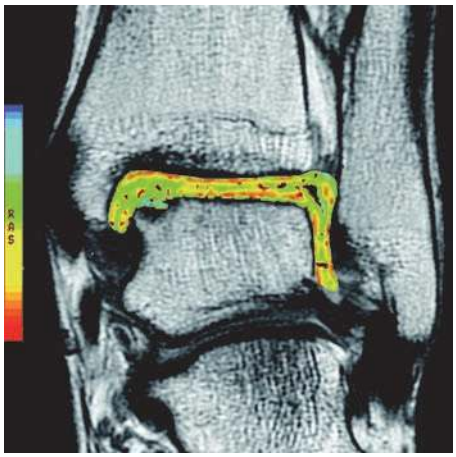

Fig. 1d

Figure 1a – arthroscopic image showing microfracture of an osteochondral lesion following curettage and debridement. Figures 1b and 1c – coronal cartilage-sensitive fast-spin MRI scans of the ankle joint taken b) before bone marrow stimulation and c) at one year after the procedure. Figure 1d – coronal T_2 mapping image showing normal stratification of the graft and adjacent native articular cartilage.

the decision to either repair or replace being based primarily on the size of the lesion.[11,13] However, other factors, such as the failure of previous treatment and the presence or absence of a cyst in the talus, must also be taken into account and considered accordingly.

Reparative strategies

Microfracture. Microfracture is widely used for lesions up to 15 mm in diameter.[11,13-19] Multiple holes are created in the subchondral plate at 3 mm to 4 mm intervals, stimulating the release of mesenchymal stem cells (MSCs) and growth factors (Fig. 1).[20] The inflammatory response results in the formation of a fibrin clot that leads to the eventual formation of fibrocartilaginous repair tissue, consisting of primarily type-I collagen. In contrast to native articular hyaline cartilage composed primarily of type-II collagen, type-I collagen has inherently different biological and mechanical properties that are likely to degenerate over time.[21]

Although there have been no level I randomised controlled trials (RCTs) comparing microfracture with other cartilage repair strategies, there have been several retrospective and prospective reports on the short-term results, including a level II randomised trial. Chuckpaiwong et al[15] reported good to excellent results in 100% of patients with lesions < 15 mm in diameter (n = 73) at 32 months' follow-up. However, they found that all but one of the 32 patients with lesions > 15 mm in diameter had a poor outcome. They also concluded that age, body mass index (BMI), duration of symptoms, history of trauma and the presence of osteophytes were significantly associated with a poor outcome. The effect of the size of the lesion on the clinical outcome was further assessed by Choi et al[13] in a series of 117 patients followed for a mean of 44.5 months (12 to 81). Of the 25 patients with lesions > 15 mm in diameter, 80% had a poor outcome.

Although many authors have reported good short-term results, several have reported poorer outcomes. Hunt and Sherman[22] reported only 46% good or excellent outcomes in 28 patients at a mean follow-up of 66 months (six to 169) after microfracture using the Berndt and Harty scale.[22,23] A study by Ferkel et al[17] of 50 patients with

chronic OCLs of the talus treated with microfracture reported 72% excellent or good results at a mean follow-up of 71 months (24 to 152). Becher et al[24] found that, in 25 patients at 3.6 to 9.6 years after microfracture, all had evidence of surface fibrillation and fissuring on MRI, raising concern for the durability of the repair tissue and the deterioration of outcome with the passage of time.[24] Other authors have reported similar findings.[17,24,25] Choi et al[26] also found that patients with uncontained OCLs of both the medial and lateral shoulders of the talus had worse clinical outcomes than those with contained lesions, even when adjusting for size. Clinical and radiographic results with the longest follow-up after microfracture were recently published by van Bergen et al.[27] At a mean follow-up of 141 months (101 to 242), 74% of patients (n = 37) rated their ankle as good or excellent according to the Berndt and Harty scale, whereas 33% of patients had progression of osteoarthritis by one grade[22,23] compared with the preoperative radiographs. They also found that size, location, classification of the defect,[23] age, BMI, duration of symptoms and traumatic aetiology were not associated with the clinical or radiological outcome.

Although the results of microfracture in the short to medium term are good, there is no consensus on the rehabilitation programme to be used after the procedure. Periods of non-weight-bearing ranging from one week to three months have been suggested, to protect the repair tissue.[28] A recent study by Lee et al[29] compared early (two weeks) with delayed (eight weeks) weight-bearing after microfracture for small to mid-sized OCLs of the talus (mean 1.0 cm^2 (0.6 cm^2 to 1.8 cm^2)) and found no difference in functional outcomes at a mean follow-up of 37 months (24 to 76). This suggests that smaller lesions may not require delayed weight-bearing, but larger lesions with greater edge loading may need to be protected for longer.

There is only one long-term study on microfracture with promising clinical results; however, medium-term studies that show repair with fibrocartilage may not be durable. At present we are not aware of any studies that specifically report the results of repeat microfracture in these patients. Savva et al[30] reported a good outcome after a repeat debridement procedure, but these results have not been supported by additional research; it is the only study of its kind. It is the experience of the senior authors (JDFC, JGK) that patients are unlikely to agree to undergo a second microfracture procedure after failure of the first. As concluded in a Cochrane review of the treatment of OCLs of the talus, high-quality level I RCTs comparing microfracture with other forms of surgical treatment are required to establish treatment guidelines based on the size of lesions that maintain good long-term functional and radiographic outcomes.[31]

Replacement strategies

Autologous osteochondral transplantation. Autologous osteochondral transplantation, or mosaicplasty, is a cartilage replacement technique intended for large primary, cystic or failed secondary lesions.[11,32-35] It involves harvesting one or more cylindrical osteochondral grafts, most commonly from the periphery of the ipsilateral knee, and transplanting them into the prepared site of the defect on the talus. The goal is to replace damaged cartilage and subchondral bone with an autologous graft that has similar biological and mechanical properties to the native hyaline articular cartilage (Fig. 2).

The majority of studies on autologous osteochondral transplantation are retrospective case series with only one prospective randomised study to date.[36] Successful clinical outcomes have been reported, particularly assessing whether the procedure allows for a return to athletic activity. Hangody et al[37] reported a large series of patients treated in this way. At a mean follow-up of seven years, 93% of patients (n = 13) had good to excellent results. At second-look arthroscopy, biopsy of the graft revealed similar proteoglycan content to articular cartilage and type II collagen. Good results were reported by Paul et al[38] in a series of 131 patients followed for a mean of 60 months (24 to 141). They found that most patients were able to return to their sporting activities. However, the mean activity level of the patients according to the Tegner Activity Scale[39] and the Activity Rating Scale[40] had decreased significantly. A recent second-look arthroscopy study by Kim et al[41] evaluated factors associated with clinical outcomes after mosaicplasty and found that soft-tissue impingement, the amount of uncovered area around the graft and BMI affected the clinical outcome. A systematic review by Zengerink et al[11] reported 87% good to excellent results following autologous osteochondral transplantation in 243 patients, with some studies reporting 100% success.

Despite successful outcome scores, there are several concerns about mosaicplasty. The amount of physiological loading and fluid ingress the cartilage of the knee can withstand when implanted to the talar dome has not been established. Several studies have shown that the articular cartilage of the ankle has a lower water content and higher glycosaminoglycan content than the cartilage of the knee, which may contribute to the reduced incidence of degenerative changes in the ankle (21%) compared with the knee (66%).[42,43] Other concerns include donor site morbidity, reported in between 2% and 50% of cases, incongruence between the graft and the surrounding cartilage, the potential need for an osteotomy, and cyst formation.[33,35,37,44,45]

Congruent as opposed to incongruent grafts placed within a range of 1 mm sunk to 0.5 mm proud have been shown to partially restore the contact mechanics of the ankle, highlighting the need for accurate placement of osteochondral grafts.[46] Imhoff et al[32] reported clinical and MRI outcomes at follow up of seven years on 26 OCLs in 25 patients. They found that patients with either minor incongruity or complete congruity of the grafts had significantly better American Orthopedic Foot and Ankle Society (AOFAS) scores[47] than patients with major incongruency. The potential complications resulting from a medial

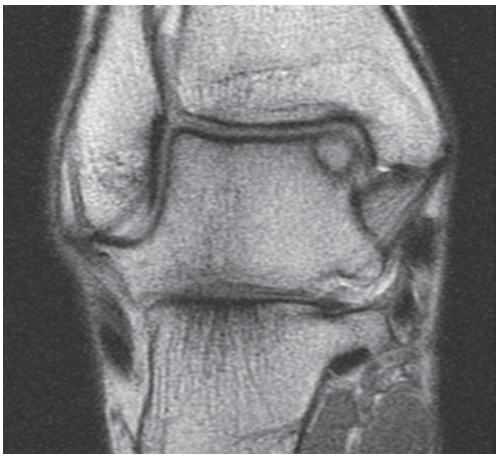

Fig. 2a

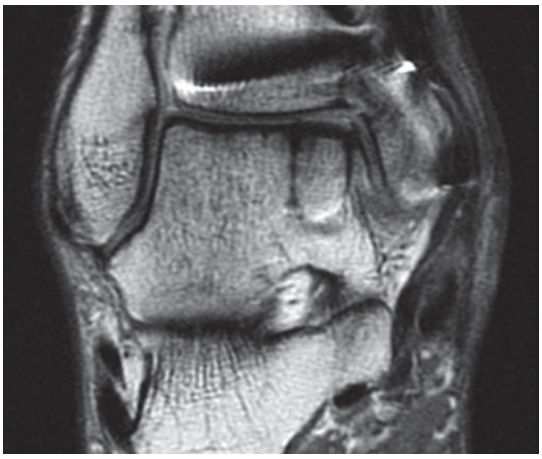

Fig. 2b

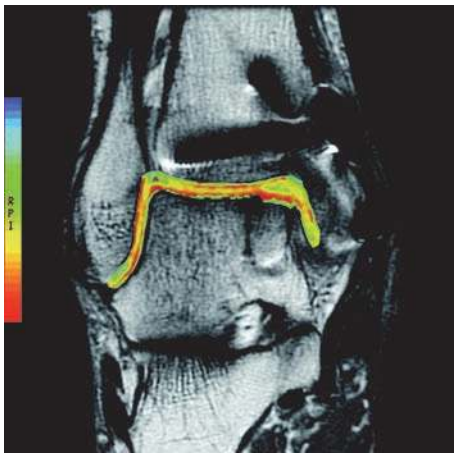

Fig. 2c

Figures 2a and 2b – coronal cartilage-sensitive fast-spin MRI of the ankle joint a) before autologous osteochondral transplantation and b) at one year after the procedure. Figure 2c – coronal T_2 mapping image showing normal stratification of the graft and adjacent native articular cartilage.

malleolar osteotomy have been addressed by Lamb et al[48] who found that only 5% of their 62 patients had pain, and that almost all had satisfactory healing and fixation with fibrocartilaginous tissue evident on MRI evaluation. Cyst formation following the procedure was highlighted by Valderrabano et al[45] in a series of 12 patients at a mean follow-up of 72 months (43 to 91). The authors reported good to excellent satisfaction in 92% of patients. However, there were several radiological anomalies of the graft site at follow-up, including evidence of cyst formation on MRI in 75% of patients.

Autologous osteochondral transplantation provides good functional outcome scores in the short and medium term. Reports suggest these scores do not significantly deteriorate with the passage of time when the procedure is performed properly, ensuring congruency of the graft and surrounding cartilage.[33]

Osteochondral allograft transplantation. Osteochondral allograft transplantation is a similar replacement technique in which a graft of viable cartilage and bone is taken from a cadaver and shaped to fit the size, depth and orientation of an OCL. The advantages of this procedure are its ability to replicate the anatomy of the joint after debridement of the defect, the need for only one graft for larger lesions, and the avoidance of donor site morbidity.[49] Although both fresh and frozen allografts can be used, declining viability of chondrocytes has been described following the use of frozen grafts.[50,51] Although fresh grafts should be harvested within seven days of the death of the donor, it has been reported that 78% of chondrocytes are viable at four weeks.[52,53] Immune rejection, disease transmission, limited availability and high costs are limitations of this procedure.

There are few studies reporting the results of osteochondral allografts in the talus, and most are small prospective

and retrospective case series. However, most report good outcomes in between 73% and 100% of patients.[54-56] A retrospective study by El-Rashidy et al[49] of 38 patients reported excellent or good outcomes in 28 patients at a mean follow-up of 37.7 months (6 to 72). The mean AOFAS scores increased from 52 pre-operatively to 79 post-operatively, with significant improvements in the mean visual analogue score (VAS) for pain. The MRI results also showed good congruency of the grafts and stability in most (66.7%) patients, but poor incorporation of the graft in 80%. Raikin[57] reported similar results in a prospective study following 15 patients at a mean 44 months after osteochondral allograft transplantation for cystic lesions > 30 mm in diameter. Clinical outcome scores improved and the mean AOFAS increased from 38 pre-operatively to 83 post-operatively. However, there was radiological evidence of collapse or resorption of the graft in 67% of patients, and narrowing of the joint space in 60%. Two patients (13%) required arthrodesis of the ankle.

The limited evidence in the literature suggests that osteochondral allografts are effective in the short term, particularly for large lesions that may not be amenable to other forms of treatment.

Autologous chondrocyte implantation/transplantation (ACI/-T). ACI in the knee joint was first developed in an attempt to regenerate damaged cartilage with hyaline-like tissue.[58] The two-step procedure was modified and described in the ankle for the treatment of larger lesions and those without associated osteoarthritic changes.[59] During the first stage of the procedure, a region of healthy native articular cartilage is identified, biopsied and enzymatically digested, and the chondrocytes isolated by filtration and cultured for 11 to 21 days. A second procedure is required for chondrocyte implantation. The major limitation is the need for two procedures, which increases both cost and the potential for morbidity. It is also still unknown how many cells are required for repair of a defect, and there is concern regarding an uneven distribution of cells during the procedure. Bentley and Greer[60] also suggested that freezing and storing chondrocytes may reduce their chondrogenic potential owing to de-differentiation.

A prospective study of ACI performed by Nam, Ferkel and Applegate[61] evaluated 11 patients. Arthroscopy at a mean of 14.2 months found that all patients had full cover of the defect, and at 38 months the mean AOFAS score had improved by 35 points. Post-operative periosteal hypertrophy was noted in 20% of patients. Battaglia et al[62] in a study of 20 patients assessed at a mean follow-up of five years after ACI, found that the mean AOFAS score improved from 59 pre-operatively to 84 post-operatively. On MRI, a T_2 map value consistent with normal hyaline cartilage was found in all patients. A recent meta-analysis of studies on ACI in the treatment of OCLs of the talus by Niemeyer et al[63] reported a clinical success rate of 89.9% in 213 patients. Furthermore, Gobbi et al[36] compared outcomes in 33 similarly sized OCLs treated with chondroplasty, microfracture and autologous osteochondral transplantation and found no differences in the mean AOFAS scores. Although this is the only RCT (Level II evidence) on the treatment of OCLs of the talus to date, it is important to note that the trial only evaluated anterior and lateral lesions, and the study was underpowered in its statistical analysis.

Matrix-induced autologous chondrocyte implantation (MACI). This is also a two-stage reparative technique, except that the chondrocytes are embedded in a matrix, several types of which have been described, including type I/III collagen, hyaluronan and polyglycolic/polylactic acid.[11,64,65] Benefits of MACI include the fact that the matrix may be secured to the defect with a fibrin sealant, not requiring fixation with sutures. It has also been reported that more viable cells are delivered to the lesion, which may lead to better long-term results.[66]

Giannini et al[67] reported the results of MACI using a hyaluronan-based scaffold in 46 patients, with excellent clinical outcome scores and histological results at a mean of 36 months post-operatively. The mean AOFAS score improved from 57.2 points to 89.5 post-operatively. Second-look arthroscopy in three patients, at a mean of 18 months post-operatively, confirmed the regeneration of hyaline-like cartilage. The clinical outcome following MACI was further assessed by Giza et al[64] in ten patients followed for two years. The mean AOFAS scores improved 13 points after one year, and this improvement was maintained after two years.

Wiewiorski et al[68-70] have published several studies on the use of autologous matrix-induced chondrogenesis (AMIC) in combination with a collagen I/III membrane called Chondro-Gide (Geistlich Pharma AG, Wolhusen, Switzerland). Chondro-Gide provides a porcine collagen matrix that stimulates chondrogenesis in MSCs of cancellous bone, leading to the production of type II collagen and glycosaminoglycans. In a recent study involving 26 patients, they reported that the mean AOFAS scores improved by 29 points at a mean of 31 months (24 to 54) post-operatively. On MRI, nine patients (35%) had complete filling of the defect and 22 (84%) had normal or near-normal signal intensity of the repair tissue compared with the adjacent native cartilage.[69]

Metallic implantation. Van Bergen et al[71,72] were the first to describe the use of a contoured metallic implant for the treatment of OCLs of the medial talar dome. In a cadaveric study, they demonstrated that the implant was safe for clinical use, while preventing excessive loading of the implant.[71] They reported the first clinical outcome in a case report, with the patient returning to full activity by one year.[72] They recommend the use of this implant for large lesions of the medial talar dome (> 20 mm in diameter) after failed primary procedures, but these guidelines must be substantiated with further evidence and long-term results before this procedure can be used clinically.

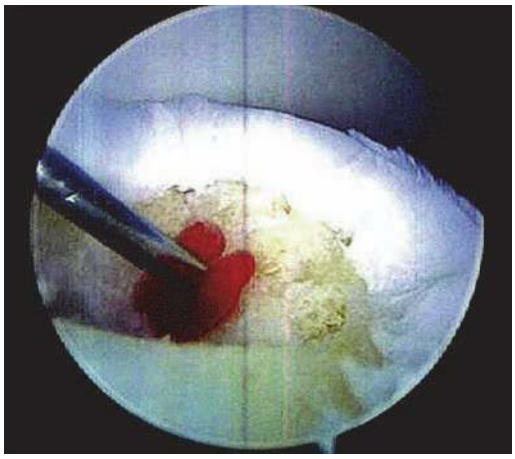

Fig. 3

Arthroscopic image of the intra-articular administration of platelet-rich plasma following microfracture.

Particulated juvenile articular cartilage allograft transplantation. The use of particulated juvenile articular cartilage grafts in cartilage repair is in its infancy, with the first reported series in the patella in 2007.[73] Several *in vivo* and *in vitro* studies have produced promising results and shown the ability of the transplanted chondrocytes to migrate, multiply, and form new hyaline cartilage that integrates well with the surrounding tissue.[74-76] A further advantage of juvenile chondrocytes is their high cellular density and ability to produce extracellular matrix. The largest study to date by Coetzee et al[77] involved 24 ankles and found that the procedure resulted in good to excellent AOFAS functional outcomes in 78% of patients with a mean defect size of 125 mm^2 at a mean follow-up of 16.2 months (10.5 to 25.6).

Biological augmentation

Concentrated bone marrow aspirate. Bone marrow aspirate contains a variety of bioactive cytokines, including MSCs, which have been investigated as a means of improving cartilage repair. The bone marrow is harvested using a simple one-step aspiration technique, at which time one of several commercially available centrifugation systems can be used to concentrate the mononuclear MSC-containing cell layer. MSCs are, however, only a small fraction of total nucleated cells in the aspirate, or approximately 0.001% to 0.01% of mononuclear cells after density gradient centrifugation.[78,79]

Although the use of bone marrow aspirate has been described[33] for the treatment of OCLs, there have been no human clinical studies demonstrating improved effectiveness over standard surgical techniques. Fortier et al[80] investigated the use of concentrated bone marrow aspirate (cBMA) as an adjunct to microfracture in an equine model. They created bilateral 15-mm defects on the lateral trochlear ridge of the stifle joint and randomly administered one of two treatments: cBMA and microfracture, or microfracture alone. At eight months post-operatively the macroscopic and histological scores of repair tissue were significantly improved in the cBMA group, and histological data demonstrated greater type-II collagen, proteoglycan and glycosaminoglycan content in this group. MRI evaluation demonstrated more normal collagen architecture, and second-look arthroscopy revealed improved integration of the repair tissue in the cBMA group.

Platelet-rich plasma. Platelet-rich plasma (PRP) is an autologous blood product defined as a twofold or more increase in the concentration of platelets above the baseline value, or > 1.1×10^6 platelets/μl.[81] Platelets are a rich source of growth factors, including epidermal growth factor, fibroblast growth factor, platelet-derived growth factor, transforming growth factor-β and vascular endothelial-derived growth factor,[82,83] which may promote cartilage repair (Fig. 3).

Although no studies have reported on the use of PRP as an adjunct to surgical treatment, Mei-Dan et al[84] recently performed a prospective quasi-randomised controlled clinical trial comparing PRP with hyaluronic acid (HA) injection for the treatment of osteochondral lesions of the talus. In 32 patients with a six-month follow-up, the outcome was assessed using the AOFAS Ankle–Hindfoot score,[47] VAS scores for pain, stiffness and function, subjective global function and disability. There was a significantly better clinical improvement after PRP treatment than after HA injection in all categories except the VAS pain score.

Conclusions

OCLs of the talus present a challenge and their treatment remains controversial. It is important to stress the need for high-level evidence and the need to enrol patients in clinical trials to establish the most effective treatment for these lesions. However, in the absence of this evidence, both reparative and replacement strategies may be considered. Currently, microfracture is the preferred primary treatment for small lesions, whereas autologous osteochondral transplantation may be considered for larger or cystic lesions. In the event of a failed primary procedure, cell-based techniques and allograft transplantation may provide a solution. Basic scientific evidence for biological augmentation is promising; however, well-designed clinical trials, which are difficult to set up, are needed to extrapolate these findings to a clinical setting.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

This article was primary edited by J. Scott and first-proof edited by D. Rowley.

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