



Review Article

Current treatment concepts for osteochondral lesions of the talus

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ABSTRACT

Osteochondral lesions of the talus (OLT) are a well-known cause of ankle joint pain and can sometimes lead to instability. These lesions are not only confined to articular hyaline cartilage, they can also affect the subchondral bone at the weight-bearing aspect of the talar dome. Nonoperative treatment is the preferred option for small lesions, however surgical intervention is recommended for large lesions or those for which conservative treatment has failed. Microfracture, abrasion arthroplasty and multiple drilling are all classified as bone marrow stimulation procedures; they are used to try to recruit precursor cells for cartilage regeneration and are especially suitable for small OLT lesions. For large lesions, osteochondral autografting and allografting are better options to reconstruct the articular defect, as they have better contours and mechanical strength. When there is limited subchondral bone involvement in large lesions, cell-based therapies such as autogenous chondrocyte implantation, potentially combined with a biomaterial matrix, are a promising option and acceptable functional outcomes have been reported. To provide evidence-based recommendations for clinicians, this article evaluates the currently available treatment strategies for OLT and their evolution over the past few decades.

KEYWORDS: *Microfracture, Osteochondral lesion, Talus*

INTRODUCTION

Osteochondral lesion of the talus (OLT) is an injury involving the articular cartilage and subchondral bone. Kappis first described OLT in 1922 and named it osteochondritis dissecans [1]. Traumatic injuries such as an ankle sprain were frequently combined with OLT and patients often have chronic ankle instability with repetitive sprains. However, 24% of patients cannot recall any cause of the injury [2]. Unlike ankle ligament injuries, the pain is deeper, with intermittent ankle swelling and a limited range of motion in the ankle despite a period of conservative treatment. Previously, the terms of osteochondritis dissecans or osteochondral defect have been used to describe this clinical observation. Nowadays, however, OLT is used since the lesion is not only due to traumatic events, but also cystic lesions or other pathological factors. In daily practice, six imaging characteristics are used to describe OLT lesions [Figure 1]. (1) There are several different types of lesion, including chondral, osteochondral, subchondral, and cystic. (2) Lesions can then subsequently be subclassified as nondisplaced or displaced and (3) stable or unstable using De Smet's criteria [3]. (4) Location is also a very important category which can be subdivided into anterior, central and posterior in the sagittal plane, and combined with medial, central and lateral in the coronal plane, formulated as a tic-tac-toe scheme [4]. (5) Whether the lesion is

contained or uncontained is a useful descriptive feature, especially during surgery. (6) Finally, lesion size is crucial for the treatment choice, as if the lesion diameter is larger than 15 mm, it should be considered a large lesion and the grafting technique can have favorable outcomes. Although the descriptive characteristics of OLT lesions can help with choosing the treatment strategy, they cannot forecast the therapeutic result. Most patients who suffer from ankle pain correlated to OLTs can be treated nonoperatively. Surgical intervention is often reserved for those patients for which conservative treatment fails. At present, there are several surgical procedures available for managing symptomatic OLTs. For smaller lesions, marrow stimulation is a possible treatment modality, including multiple drilling, microfracture, and abrasion arthroplasty. However, a pitfall of this method is that the newly regenerative tissue is fibrocartilage, which possesses less mechanical strength than hyaline cartilage and is easily degraded and damaged over a short period of time [5,6]. When considering the treatment of large OLT lesions, osteochondral autografts or allografts are favorable choices for restoration of the whole articular


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surface of the talus. Mosaicplasty or Mega-OAT is used in accordance with the lesion size. Autologous chondrocyte implantation (ACI) has been described in recent decades and has the potential to regenerate the hyaline cartilage. However, this results in fibrocartilage and hyaline cartilage tissues being interspersed, and there is a need for two surgical procedures, and there is less mechanical strength, which are all concerning disadvantages of this method [7]. This review paper evaluates the current treatment strategies and recent advances for the treatment of OLT.

CLASSIFICATION

Previously, the most widely used classification system for OLT lesions was introduced by Berndt and Harty [Table 1] [8]. The assessment of the lesion is based on its appearance on plain radiographs and is divided into four stages. Anderson established a magnetic resonance imaging (MRI)-based classification system which was modified from Berndt and Harty's system and this has become the most popular classification system in recent times [Table 2] [9]. Anderson added stage IIa representing a cystic lesion. Hepple also used MRI to evaluate the staging and assigned cyst lesions as stage V [10]. Arthroscopic classification was believed to be the most accurate method for evaluating OLT since direct visualization was possible with a probe during surgery. Pritsch was the first to describe an arthroscopic classification system based on the condition of the chondral injury [11]. Ferkel further modified this classification system to include cystic lesions and displaced osteochondral lesions [Table 3] [12]. Despite the possible existence of good inter- and intra-observer reliability in all of these classification systems, MRI classification is still the best image modality for helping in clinical decision-making. The correlation between the description of a lesion from arthroscopic findings and image reporting is directly proportional. MRI examination can coincide with the arthroscopic grading up to 81%–83% [13,14].

CONSERVATIVE TREATMENT

For nondisplaced or minimally displaced OLTs, most studies recommend treatment with conservative management [9,15-18]. Displaced OLTs with acute pain and limited ankle range of motion should be considered for treatment with surgical intervention. Loose body removal and fragment fixation internally are both reasonable options. Conservative treatment includes casting immobilization, a walking boot used with non-weightbearing protection, physical therapy, bone stimulation, and even a bisphosphonate prescription. Several retrospective studies have shown good results with conservative treatment for non-displaced OLTs [17,19,20]. One meta-analysis reported a 45% success rate using conservative treatment [2]. Nonetheless, patients who receive nonoperative management seldom recover to their previous level of sports activity. Furthermore, early ankle osteoarthritic changes were reported in patients who were treated nonoperatively [15,20]. The current general consensus is that surgical intervention should be performed when conservative treatment fails and there is persistent symptomatic OLT.

Table 1: Berndt and Harty radiographic classification

Stage	Definition
I	Subchondral compression fracture with intact cartilage
II	Partial detachment of osteochondral fragment
III	Complete detached fragment without displacement
IV	Detached and displacement fragment

Table 2: Anderson magnetic resonance imaging classification

Grade	Definition
1	Subchondral trabecular compression, MRI: Bone marrow edema, normal plain radiographs, positive bone scan
2a	Subchondral cyst
2b	Incomplete separation of osteochondral fragment
3	Completely detached, nondisplaced fragment with surrounding synovial fluid
4	Displaced osteochondral fragment

MRI: Magnetic resonance imaging

Table 3: Ferkel arthroscopic staging system

Grade	Definition
A	Smooth, intact, but soft cartilage
B	Rough cartilage
C	Fibrillations or fissures
D	Flap present or bone exposed
E	Loose, nondisplaced fragment
F	Displaced fragment

Bone marrow stimulation method

To date, many surgical options for OLT have been described, including multiple drilling, microfracture, abrasion arthroplasty, autogenous osteochondral grafting, allograft talus transplantation and ACI [21]. Multiple drilling, microfracture, and abrasion arthroplasty are all bone marrow stimulation methods and have an optimal functional outcome. The purpose of bone marrow stimulation methods is to penetrate the subchondral bone, which leads to the release of bone marrow precursor cells and growth factors. The healthy bone marrow precursor cells and related cytokines may contribute to articular cartilage regeneration for the OLT lesions. Initially, these techniques were developed to treat OLT lesions for all grades and sizes. However, at present, bone marrow stimulation is generally only performed for lesions smaller than 150 mm² or 15 mm in diameter, and has favorable outcomes for early to mid-term follow-up [22,23]. Arthroscopic debridement is performed before the marrow is stimulated and all the unstable osteochondral fragments should be removed until a healthy cartilage rim is observed. In cases where the articular cartilage is intact and only the subchondral area was involved, retrograde drilling may be indicated [24]. Thermal injury is a danger during multiple drilling and abrasion arthroplasty as the nearby cartilage and subchondral bone may be damaged and its healing potential will thus be decreased. Microfracture should be a better technique as there is no risk of thermal damage during subchondral bone picking [Figure 2]. However, like other bone marrow stimulating techniques, the newly regenerated cartilage is fibrocartilage or fibrous tissue. The major component of fibrocartilage is Type I collagen [6].

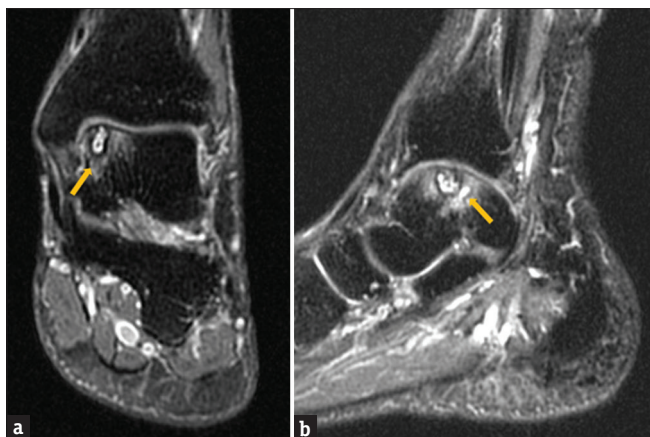


Figure 1: MRI examination revealed an Anderson IIB lesion over left medial talar dome (arrow). (a) AP view of the lesion. (b) lateral view of the lesion

Fibrocartilage has been demonstrated to have reduced resilience, lower stiffness, and early wear properties compared with hyaline cartilage [25]. That being said, numerous retrospective studies have reported optimal results for bone marrow stimulation techniques for treating OLTs [24,26-30]. The size of the lesions treated using this technique were very varied and ranged from 0.25 to 4 cm², while the treatment results ranged from 39% to 96%. A study by Chuckpaiwong *et al.* reported on 105 patients who received arthroscopic microfracture treatment. They defined the operational treatment as successful if the functional results fitted 3 of the 4 following criteria: (1) >50% improvement in the visual analog scale (VAS) score during exercise, (2) >50% improvement in the VAS score for pain in daily activity, (3) an American Orthopaedic Foot and Ankle Society (AOFAS) hindfoot score improvement of >30 points, and (4) a Roles and Maudsley score of 1 or 2. They reported the a cut off size of 15 mm in diameter for successful arthroscopic microfracture treatment, as 73 lesions out of the 105 ankles treated had a successful outcome and all of the 32 unsuccessful lesions had a diameter larger than 15 mm except one [22]. Choi designed a study based on the lesion size in a two-dimensional plane. A total of 120 OLT lesions underwent microfracture treatment and they found that lesions smaller than 150 mm² were more likely to achieve a favorable outcome [31]. Based on the results of these two studies, most surgeons only perform bone marrow stimulation techniques for lesions <150 mm² or 15 mm in diameter. However, a meta-analysis study recently reported that a more-suitable lesion cut off size for the bone marrow stimulation technique should be <10.2 mm in diameter or 107.4 mm² [32]. Furthermore, in a recent study, it was demonstrated that South Eastern Chinese individuals have a smaller talus than Caucasian individuals [33]. The average central trochlea tali width is only 20.3 mm in Asian people. As a consequence, a lesion 15 mm in diameter or 150 mm² in area would extend over half the width of the talar trochlea, which is a relatively large lesion and may lead to poor surgical outcomes [34]. Based on anatomic proportionality, 100 mm² or 10 mm in diameter should be considered as the lesion cut-off size for bone marrow stimulation in Asian populations.

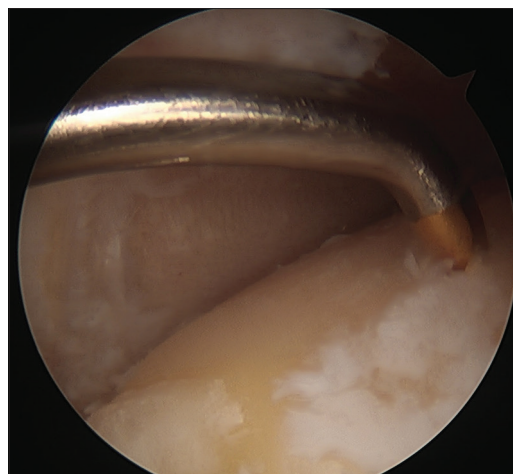


Figure 2: The osteochondral lesion was debrided and treated with microfracture technique. Microfracture was performed by chondral pick

A systematic review reported that patients with OLT lesions <150 mm² had good to excellent functional outcomes at short-and mid-term follow-up after microfracture treatment [35]. However, at long-term follow-up, the results were less predictable. Ferkel reported that 35% of patients (17/50) had deteriorated results at 5 years' follow-up [12]. Nevertheless, one 8–12 years' long-term follow-up study revealed that functional outcomes were maintained over time [36] and the AOFAS hindfoot score still had an average 88 points (range: 64–100). However, radiographic evaluation revealed that 33% of patients had progressive osteoarthritis. The discrepancy between later osteoarthritic changes and surgical outcomes is discernible. Lee also reported a 2nd look arthroscopic finding at postoperative 12 months after microfracture treatment [37]. According to the International Cartilage Repair Society (ICRS) score, 60% of OLT lesions healed, while only 30% of the lesions were fully integrated within the circumference of the healthy cartilage. In spite of this, 90% of patients reported good or excellent AOFAS hindfoot scores of over 80 points. Consequently, in the bone marrow stimulation method, newly regenerated fibrocartilage with less mechanical strength is still a crucial factor and is correlated with long-term outcomes. Moreover, this kind of treatment is limited in smaller lesions. Persistent pain and progressive cartilage deterioration are the most common complication.

Osteochondral autografting

Osteochondral autografting has been developed to treat large OLT lesions. Restoration of the articular defect with hyaline cartilage and good bony ingrowth into the surrounding recipient site are the potential advantages of this treatment modality. The autografting procedure is also used as a salvage surgery for failed bone marrow stimulation therapy. Donor sites are often harvested from the peripheral femoral condyle of the knee. Whether a cylindrical strut graft or multiple plugs (mosaicplasty) are used is dependent on the OLT lesion size. A periarticular osteotomy, such as a medial malleolar osteotomy, transfibular osteotomy, or anterolateral tibial plafond osteotomy are often carried out to help ensure there is adequate visualization of the lesion and graft fixation [38-40].

The incidence of delayed union or nonunion is about 0%–2% [41-44]. A 6–8-week period of non-weight bearing and cast immobilization is recommended, which means it has a longer recovery time than the bone marrow stimulation method.

Several retrospective studies have reported favorable results for osteochondral autografting. Kennedy reported significant short-term improvements in mean foot and ankle outcome scores and SF-12 scores in 72 patients. A total of 42 patients recovered to the same level of sports activity as they were prior to injury [45]. Scranton showed that cystic lesions in 45 out of 50 patients treated with autologous osteochondral grafts had good or excellent results at a mean 36 months follow-up [46]. Hangody published a 17-year prospective study and revealed 92% good to excellent results following treatment with talar mosaicplasty [47]. Another recent study performed a second look arthroscopy and compared it with MRI evaluation [48]. Arthroscopic findings revealed that 9 ankles (36%) were not completely healed according to the ICRS grading system. The postoperative MOCART score was 67.8 (range, 30–95), with good functional outcomes. Interestingly, 6 patients (24%) had a mismatch finding between their second-look arthroscopic findings and their MRIs.

Donor site morbidity remains a concern during autograft harvesting. Reddy *et al.* reported that 4 out of 11 patients had significant knee discomfort and donor site morbidity [49]. About 37% of patients had poor postoperative outcomes and the most commonly mentioned problem was knee instability during daily activities. LaPrade and Botker also reported that two cases suffered severe donor site morbidity with hypertrophic fibrocartilage at the graft harvest sites, which led to knee pain as well as locking [50]. In contrast, Hangody and Fuels reported donor site morbidity rates as low as 3% in a long-term follow-up study which included 831 patients treated with mosaicplasty [51]. Kennedy recently unveiled similar low donor site morbidity after treating 72 patients [45]. Three patients (4%) had painful donor site discomfort in the knee joint but 2 were pain free after intra-articular steroid injections. One patient needed an arthroscopic debridement for the scar tissue incarcerated in the knee joint. This study advised to fill the donor site with synthetic bone as a void filler to help with new tissue regeneration and this may have contributed to the low percentage of donor site morbidity. The limitation of osteochondral autografting is the not suitable for mega-sized talar lesion and donor site morbidity is the major concern.

Osteochondral allografting

Osteochondral allograft transplantation fills the defect with a size matched graft and is performed for deep and large OLT lesions [Figures 3-5]. A major advantage is that there is no donor site morbidity. The use of a single graft also reduces potential fibrocartilage ingrowth in comparison with multiple plug mosaicplasty [34,52]. Although osteochondral autografting provides excellent outcomes, and provides numerous viable chondrocytes, allografting is more suitable for larger OLT lesions, shoulder non-contained defects and failed multiple mosaicplasties.

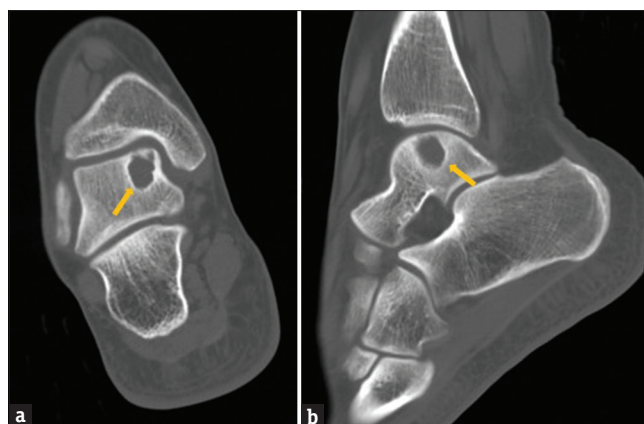


Figure 3: CT examination revealed a large cyst lesion over medial talar dome (arrow). (a) AP view and (b) lateral view depicted a Raikin zone 4 lesion

Gross first proposed this talar osteochondral allografting technique in 2001 for 9 patients [53]. The 12 years' follow-up revealed that the average allograft survival time was 9 years. Gortz treated 12 patients with lesions larger than 170 cm² by filling in the defect with fresh osteochondral allografting [54]. The allograft survival rate was 83%. The author reported that 60% of the patients had improved function, 80% had reduced pain, and 90% were satisfied with their functional recovery. Raikin reported on 15 ankles with large-volume cystic lesions that >300 mm³ and had a mean follow-up time of 54 months. The AOFAS scores improved an average of 45 points and 11 patients had good or excellent functional results [55]. El-Rashidy recently published a large study on the treatment of OLT using fresh osteochondral allograft transplantation and this has shown favorable short-term outcomes [56].

Although one of the negative factors associated with osteochondral allografting is the potential for infection transmission, several improvements have been proposed in a previous literature review [34,56,57]. First, in comparison with osteochondral autograft, lesion size is not an important issue even if the area is >300 mm² [52]. Precise size matching for the configuration of the lesion is advantageous [34]. Furthermore, only one strut of osteochondral allograft is necessary for filling the OLT lesion, which mitigates potential fibrocartilage ingrowth and leads to higher mechanical properties [58]. The biggest advantage of osteochondral allografts is that the interface between multiple osteochondral allograft plugs in large lesions is eliminated. This is important because poor cartilage integration between plugs can contribute to reduced durability of the osteochondral graft [32]. Allograft availability and lower healing rate than autograft are the limitation and may be complicated with graft subsidence and disease transmission.

Cell-based therapy

ACI was proposed as a treatment option in the past two decades and favorable clinical outcomes have been reported. Brittberg first developed ACI for the treatment of full-thickness chondral defects in the knee joint [59]. ACI is a 2-stage procedure; the first step is to harvest cartilage from a non-weightbearing site on the lateral or medial femoral condyle. After the cartilage is minced into small pieces and

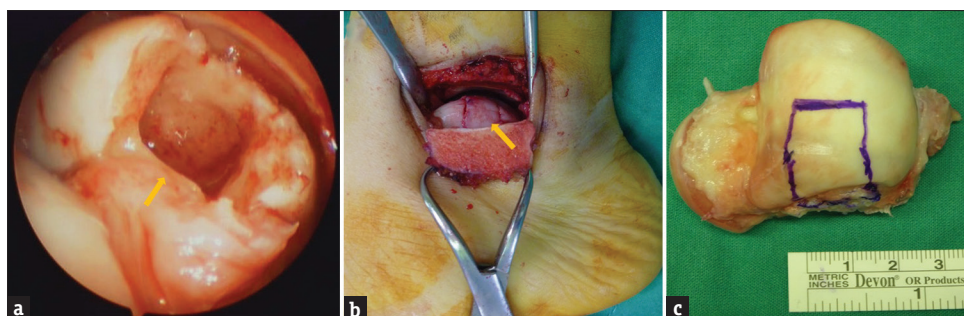


Figure 4: Arthroscopic examination revealed (a) a large medial talar dome cystic lesion with diameter >1 cm (arrow) (b) a matched size allograft was fitted into the osteochondral defect (arrow) (c) talus allograft

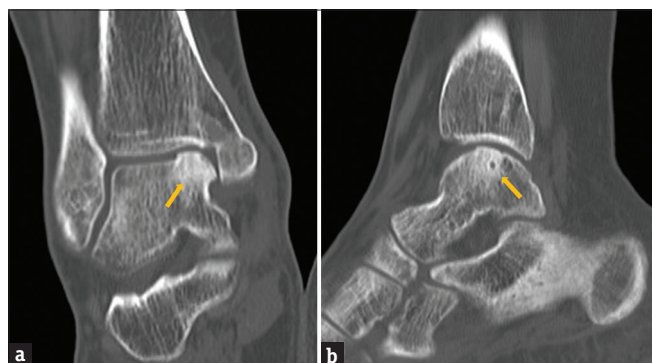


Figure 5: Postoperative 1 year CT revealed adequate bone and cartilage integration (arrow) in (a) AP view and (b) lateral view

digested by collagenase, the cell suspension is centrifuged and the cell pellet is cropped. The cell pellet is then resuspended in culture medium and cell expansion occurs for 2 weeks. Adequate amounts of chondrocytes are subsequently implanted into the chondral defect and sealed with a periosteum. Fourteen of the 16 patients with femoral condylar chondral lesions had good-to-excellent results at 2 years' follow-up [59]. Several studies have also shown positive outcomes following its clinical usage in talar lesions [60-62]. Giannini reported favorable results for 8/8 patients (100%) at a mean follow-up of 26 months [60]. The preoperative AOFAS score was 32 points and this improved to an average of 91 points postoperatively. The 2nd look arthroscopy revealed good cartilage-like tissue regeneration in the recipient site and the histological staining demonstrated adequate type II collagen expression and abundant proteoglycan secretion in the extracellular matrix. Battaglia *et al.* also reported a similar result as evaluated by AOFAS scores at 5 ± 1 years' follow-up [62]. T2 mapping MRIs also showed values comparable with normal hyaline cartilage in all cases after ACI treatment.

However, newly regenerated hyaline cartilage and fibrocartilage interposition, the poor rebuilding of the subchondral defect, requirement of 2-stage procedures, were the mentioned pitfalls. Since the newly regenerated fibrocartilage has poor mechanical strength and resilience, joint degeneration will progress with time. Another issue of concern is the graft hypertrophy when periosteum is used as Brittberg originally proposed. This hypertrophy may be due to the cambium layer of periosteum possessed progenitor cells, which stimulate cell overgrowth. To overcome this sequelae, a collagen I/III

membrane has been used for the coverage flap. Gooding published a study comparing the effectiveness of these two types of covering membrane [63]. The periosteum group had 20% graft hypertrophy compared with 2.9% in the collagen membrane group. Thus, collagen membranes have become the favorable covering material for sealing chondrocytes in the cartilage defect.

Matrix-associated chondrocyte implantation (MACI) is a new treatment method based on tissue engineering technology. Chondrocyte/matrix scaffold constructs have been developed for cartilage regeneration in recent decades [64,65]. Currently available matrices are often composed of collagen or hyaluronic acid-based biodegradable materials. 3D scaffolds provide cells a biomimetic environment similar to the human body. Advantages of this method include maintenance of the cell phenotype in the matrices, even distribution of cells in the scaffold and matching size implants. Recent studies have shown promising results when using MACI for the treatment of OLTs [66-69]. Magnan reported a positive result when 30 OLTs were treated with chondrocyte/collagen matrices using the MACI technique. At an average nearly 4 years' follow-up time, the mean preoperative AOFAS score was 36.9 which improved to an average of 83.9 postoperatively. Good to excellent results were observed in 28 of 30 patients [66]. Giannini treated 46 patients with the MACI method using a hyaluronic acid matrix and the mean AOFAS score improved from 57.2 preoperative to 86.8 at 12-month follow-up. The 36-month follow-up showed a persistent result with an average score of 89.5 points. Thirty-eight out of 46 patients reported excellent or good results and only 5% reported poor results. Richter and Zech reported using bone marrow stem cells/collagen I/III matrix to treat OLT in 124 OLTs [69]. The VAS FA score was improved from 45.2 preoperative to 84.4 postoperative with an optimal outcome. Recently, an expandable biomimetic scaffold was reported and revealed optimal hyaline cartilage regeneration both in *in vitro* and *in vivo* animal model [64,65]. The character of higher biocompatibility of the organized scaffold maybe a better choice for tissue engineered cartilage in the future. However, ACI and MACI technique still have some drawback. Regenerated fibrous tissue, fibrocartilage, and hyaline cartilage interposition with less mechanical strength may procure the limited results. High economic cost and donor site morbidity remain potential barriers.

CONCLUSION

The treatment for osteochondral lesions of talus has evolved over the past few decades and a lot of new treatment options have been described. Nonoperative treatment is a good primary treatment option. Although positive results such as pain relief and functional status improvement are reported, poor healing potential of the articular hyaline cartilage is the inherent limitation. Surgical intervention, including bone marrow stimulation techniques, osteochondral autografting or allografting, and cell-based therapies all play important roles as treatment strategies in accordance with the lesion size and defect depth. However, all current surgical methods have limitations. With the increase in bionic implants found in translational medicine, tissue engineered cartilage regeneration technology such as MACI or other new biotechnology for the treatment of osteochondral lesions of talus will most likely play a promising role in its future treatment.

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