Current Concepts in Clinical Treatment of Osteochondral Lesions of the Talus

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Abstract. Osteochondral lesions of the talus (OLTs) are common reason for the deep ankle pain and seriously affect patient's sports and the daily life. Managements of the OLTs including conservative treatment, cartilage repair surgery, cartilage replacement surgery and cartilage regeneration surgery. For asymptomatic, serendipitous, or acute OLTs with no displaced fragments, conservative treating is suitable to execute, including mainly including affected ankle immobilization with or without physical therapy, bone stimulation, or drugs used. For small OLTs, cartilage repair strategy like bone marrow stimulation technique (BMS) was recommended, and microfracture is the most commonly used surgical procedure. For larger OLTs, both cartilage replacement and cartilage regeneration could be considered including. Although there are many treatment options, each treatment option may have certain limitations and may not be applicable. With the continuous development of science and technology, the development of biological adjuvants and tissue engineering technology has been accelerated and promoted. The combined application of surgery and biological adjuvants and tissue engineering technology has gradually become a hot spot in clinical research. This work briefly introduced present strategies and advance in treatment of OLTs and discussed the potential application problems aiming to provide reference for the future treatment selection and research of OLTs.

Keywords: Osteochondral lesions; Cartilage; Talus; Treatment.

1. Introduction

Osteochondral lesions of the talus (OLTs) are common reason for the ankle pain, involving cartilage and subchondral bone. It has been reported in the literature that about 50%-70% of patients with acute ankle injury are associated with OLTs and young patients are more common [1]. Patients complaint deep ankle pain with stiffness, weakness, instability, noose, and swelling, and usually exacerbate with activity, seriously affecting mobility and quality of life. With the deteriorating and the cartilage further destroyed, it could deforminto traumatic arthritis [2]. Some physical examination can help doctors to diagnose OLTs, and commonly used clinical tests, such as MRI, CT, and arthroscopy, can assist diagnosis and guide treatments.

Cartilage is avascular composing by type II collagen and proteoglycans with poor repair ability so it is hard to heal after injury, which makes the treatment difficult. Effective cartilage repair can relieve symptoms and help patients to return to normal exercise and daily life. The management of OLTs can be roughly divided into the conservative treatment and the surgical treatment. Conservative treatment, mainly including affected ankle immobilization with or without physical therapy, bone stimulation, or drugs used, is an important method to relieve the symptoms of patients. If the effect is poor or the treatment fails, surgical treatment is still needed. There are three types of the surgical treatment in clinic: cartilage repair, cartilage replacement, and cartilage regeneration according to different therapeutic philosophies.

The selection of appropriate treatment modalities has a great impact on the outcome of OLTs. This work briefly introduced present strategies and advance in treatment of OLTs and discussed the potential application problems aiming to provide reference for the treatment selection and research of OLTs.

2. Treatment

2.1. Conservative management

Conservative treating method was recommended for acute OLTs with no displaced fragments. Asymptomatic and serendipitous OLTs were also appropriate for conservative management. Conservative treatments reduce the load on the lesions and bone edema, relieving symptoms such as pain, but it is hard to achieve cartilage healing since the special cartilage structure. 4-6 weeks immobilization was recognized for the optimal protocol with or without nonsteroidal anti-inflammatory drugs (NSAIDs), and physical therapy, bone stimulation, or bisphosphonate are also available modes. Studies have contrary results regarding the use of cast in immobilization. For example, Tol et al. found that success rate of OLTs patient with cast immobilization in conservative management was 41%, a worse results than the patient without cast as 59%, while Zengerink et al. compared the results of different studies concluded patients who used plaster had a higher success rate as 53% than the patients without cast as 45% [3,4]. Generally, conservative management of OLTs can be carried out for 3 months, and treatment beyond 6 months is not recommended, and the effective rate as their reported was around 40-60% [3-5].

As a minimally invasive treatment, extracorporeal shock wave therapy has been more and more widely used in clinic. Extracorporeal shock wave therapy can improve local blood circulation, promote tissue repair, and promote osteogenesis and can be combined with ankle arthroscopy, which play a role in the treatment of talus osteochondral injury.In a domestic clinical study, 54 cases of talus osteochondral injury with 60 talus were treated with divergent shock wave. The treatment scheme was energy 1.5~2.5 bar, 5 Hz, impact 2000~3000 times, 5 times as a course of treatment, a total of 3~4 courses of treatment. The patients were followed up at the 3, 6 and 12 months after the treatment. It was found that the VAS score of the patients decreased and the AOFAS score increased 3 months after treatment, which was statistically different from that before treatment ($P<0.05$). After 6 and 12 months of treatment, the pain of ankle joint of the patient was relieved continuously and the functional score was improved continuously ($P<0.01$); After treatment, the average injury area was significantly reduced ($P<0.01$), and the injury area of some patients could completely disappear. A retrospective study included 78 patients with OLT and these patients underwent the arthroscopic micro-fracture, anduse the visual analogue scale (VAS) and the American Association of Foot and Ankle Orthopedics (AOFAS) ankle-posterior scale scores to valuatetheefficacy, the average follow-up was 27.8 years. The results showed that after 12 weeks of using ESWT, the VAS scores showed very obvious improvement effect, also the AOFAS scores, which confirmed the efficacy of ESWT [6,7].

Biological products, such as Hyaluronate (HA), Platelet-Rich Plasma (PRP), andconcentrated Bone Marrow Aspirate(cBMA), have also been recommend as conservative treatment support [5]. Increasing the level of HA in synovial fluid was categorized to supple viscous component to reducing pain, and PRP preparations have selectively concentrated growth factor and might enhance healing response. Mei-Dan et al. carried out a randomized controlled trial about the PRP and HA in OLTs treatment [8]. They enrolled patients who had failed conservative treatment and were treated with intra-articular injections of PRP and HA at least 6 months and found VAS score decreased from 5.6 and 4.1 to 3.1 and 0.9 and Ankle-Hindfoot Scale increased from 66 and 68 to 78 and 92 respectively of patient. However, they included some patients who had previously had surgery and did not record patient's utilizing of painkillers. Generally, the present evidence to support biological products in the conservative management of OLTs is still insufficient.

Prognostic factors are an important consideration in deciding to continue conservative treatment. Klammer et al. found that the depth of OLTs, cystic lesion, and bone marrow edema were associated with pain level at a minimum of 2-year follow-up in a retrospective study[9]. In addition, age, body mass index(BMI), lesion size and location, and ankle instability are also prognostic factors that need attention[5]. Further surgery might be required for cases of failure of previous conservative treatment

2.2. Surgical Therapy

2.2.1 Cartilage repair strategy

Cartilage repair strategy was the most common method in current OLTs surgical treatment, including bone marrow stimulation technique(BMS), fixation, and debridement. Most cartilage repair operations can be performed under arthroscopy with simple procedures and less injury, and have been widely used in the clinical treatment of OLTs.

BMS was historically thought as the first-line treatment for small OLTs less than 15 mm in the diameter. Blood enters the defect by penetrate the subchondral bone plate and forms repair tissue forms, and stems cells promote the formation of fibrocartilage. Microfracture is one of the widely used BMS. Surgeons usually use microfracture cones with different angles to punch on the subchondral bone after lesion debridementarthroscopically. Clinical improvement has been widely reported in both short-term and long-term follow up. For example, Kim et al. followed up 70 OLTs patients after microfracture and found significant improvements in AOFAS from 63.1 to 91.0 and in VAS scores 6.2 to 1.2 at 2 years after surgery[10]. Another recent systematic review also reported satisfactory long-term clinical function score improvement post microfracture in OLTs patient at an around 13.0 years follow-up[11]. Subchondral drilling was another common BMS technique using rotating Kirschner wire drilling into the subchondral bone plate.Historically, it was thought with comparable efficacy to microfracture but had a poor access ability to the medial talus. However, recent studies have found better condition of subchondral bone after drilling facilitating the release of blood and cells in the lesion area than microfracture[12].Nowadays, doctorsalso focus on the combined use of biological products in BMS, and some researchedpreliminarily demonstrated good efficacy, however, the evidence that BMS combined with biologics have better clinical effects is still insufficient[13].

Fixation and debridement are also part of cartilage repair surgery. Fixation can preserve the original cartilage, but it has high requirements on the lesion: only large intact osteochondral fragment can be fixed[14]. Bone peg and bioabsorbable pin were both attainable fixed material. Arthroscopic debridement(AD) is simple and effective method, but conflicting results were reported in a recent study. Zhang et al. suggested that microfracture was better than AD in protecting ankle function, while Fermín et al. concluded same efficacy of AD and microfracture, and even a better subchondral bone integrity after AD [15,16].

2.2.2 Cartilage replacement

Cartilage replacement surgery is to replace damaged cartilage with normal hyalinecartilage tissue. According to the source of the grafts, the operation can be divided into autograft and allograft which are both current treatments for larger OLTs.

Autologous osteochondral transplantation (AOT) were thought for large OLTs, and graftswere usually obtained from the non-weight-bearing area of the ipsilateral knee joint. Conventional surgical procedures involve lesion exposure, debridement, and graft implantation, and malleolus osteotomy was always needed in treating some OLTs patients. A systematic review in 2022 showed a significant reduction in the level of clinical pain in patients after AOT[17]. In addition, a recent meta-analysis also found high rate of sports recovery in athletes after osteochondral autografts transplantation in 2021[18]. They reviewed nine studies involving 205 ankles and found that 81.3% of the athletes returned to their preinjury status. Despite favorable outcomes reported, surgical difficulties need to be addressed, including donor-site morbidity, and changing the source of the graft might be a solution. Wan et al. chose to select the graft attalar non-weight-bearing area and maintained a good clinical function score at mid-term follow-up[19]. Shi et al. selected osteoperiosteal grafts and concluded the same efficacy as AOT at 2 years of follow-up[20]. In addition, although the safety of osteotomy has been proven, less invasive surgical procedures are still worthy of investigation.

Osteochondral allografts transplantation (OAT) has a similar adaptation with AOT, and the allografts usually cameas fresh cadaver osteochondral tissue. OAT have no concern for donor-site morbidity and are more suitable for larger OLTs than AOT. A system review illustrated better

AOFAS and VAS scores postsurgery[21]. In this work, the survival rate of allograft was 86.6%. Chu et al. carried out a midterm follow-up research and also verified higher AOFAS and SF-36 scores[22]. Conventional OAT and AOT procedures are similar and osteotomy might be required. Arthroscopic OAT technology has been reported more and more studies in order to reduce injury. Particulated juvenile cartilage allografts are suitable for arthroscopic surgery which are from less than 13 years old donors, and have been reported with arthroscopic technique[23].

2.2.3Cartilage regeneration

Autologous chondrocyte implantation (ACI) is an important part in cartilage regeneration strategies, which is a simple operatio,and after the transplantation, it is mainly repaired with transparent cartilage without immune reaction. Chondrocytes still survive after operationand.And it is thought for large OLTs with or without previous surgery[22]. Healthy chondrocytes are firstly harvested in operation, and then implant into OLTs in next surgery after expanding. In addition, chondrocytes can be pre-seeded on scaffolds prior to transplantation, which is known as matrix-induced ACI (MACI). Both ACI and MACI reported satisfactory results[24]. However, there are still factors limit the application. For example, the activity of chondrocytes declines with age, resulting in poor outcomes in older patients. Besides, one step procedure is more attractive for both clinicians and patient than ACI or MACI, which limits the utilization of ACI and MCI.

3. Discussion

OLTs are strongly affect sport ability and daily life of patients, so the therapeutic interventions to OLTs are needed to relieve symptoms effectively and improve quality of life. Currently, many methods have been applied to the clinical treatment of OLTs, Doctors need to consider the patient's condition to choose the appropriate treatment.

Conservative management is an important method in treating OLTs. The optimal protocol is as immobilization, but there is still no agreement on the exact course of the reatment [3,4]. A standard and specific, more widely accepted non-surgical treatment model may be a future research direction. Biological productshave been recommended for the adjuvant therapy in OLTs patients with conservative treatment with research verifying effect. The variety of ingredients in biological products and the irregularity about their use might be reasons to limit further research. Although the evidence to support biological products in the conservative management is still insufficient, it is still a promising research direction. Nowadays, more than a few patients fail conservative treatment and require further surgical treatment.

Microfracture, as a routine BMS technique, is a simple cartilage repair strategy aiming to form fibrocartilage at the lesions. The quality of fibrocartilage is inferior to hyaluronic cartilage, and its degeneration is a concern. Although postoperative functional score improvement at short- and long-term postoperatively has been reported, there are few reports on the recovery of sports ability after microfracture surgery, which need further studies to prove its validity[10,11]. Another concern is the poor subchondral bone condition after microfracture, which may cause the subchondral bone collapse, block the bone pore and cysts formation. Studies of another BMS techniques to better protect the subchondral bone, such as drilling, may be another direction of future research[12]. Combination use of biological products is also a promising research direction. Establishing criteria for the composition and use of biologics is critical to validate their ability to improve surgical outcomes in BMS[13]. With the innovation of materials and instruments, the effectiveness of other cartilage repair procedures such as fixation and AD has been recognized, and recent studies have reported their surgical efficacy, which might be in conflict with previous studies[16].

Cartilage replacement surgery include AOT and OAT, which are recommend for larger OLTs. Pain relieve and high rate of sports recovery were reported to demonstrated the effect of AOT[17,18]. However, donor-site morbidity might lead surgical failure and has been a major concern of AOT. Some researcher try to alter the source of the graft as solutions, such as the graft from talar non-weight-bearing area and the iliac crest, and conclude similar results to the graft from the non-weight-

bearing area of the ipsilateral knee joint[19,20]. Grafts used in OAT come from the cadaver, which means it has no concern of donor site morbidity compared to AOT, and satisfactory results also published[21]. At present, the commonly used AOT and OAT for the treatment of OLTs in some parts require additional osteotomy, which is complicated and traumatic, and all-arthroscopic technology is a very promising direction. Although some studies have preliminarily reported the effectiveness of all-arthroscopic AOT and OAT, more studies are needed to explore the difference in efficacy between AA and traditional surgical methods, and put forward possible suggestions for improving surgical procedures[23].

ACI and MACI are important representations of cartilage regeneration strategies by implanting healthy and expanded chondrocytes with or without pre-seeded on scaffolds, and satisfactory results have also been published[24]. However, ACI and MACI require at least two surgeries, and they is difficult to guarantee surgical results in patients with low chondrocyte activity, which means increased treatment costs and limited use in patients with aging years. Optimizing the surgical procedure and improving the activity of chondrocytes may be further research direction in the future.

4. Conclusion

Currently, OLTs patients can receive conservative treatment, cartilage repair surgery, cartilage replacement surgery and cartilage regeneration surgery. Most clinicians focus more on surgical treatment of OLTs, but as an important symptom relief therapy, conservative treatment of OLTs deserves more attention. At present, there is no consensus on the conservative treatment mode of OLTs. The results of clinical studies are contradictory, and there is still a lack of evidence for combining biological products to improve the outcome of conservative treatment. As a routine cartilage repair procedure, microfracture surgery has proven to be effective, but there are few studies on motor recovery after microfracture surgery. In addition, microfracture failure has been reported, which may be related to poor subchondral bone status after surgery. Future research should focus on the recovery of exercise level after microfracture surgery, and the improvement of cartilage status after BMS surgery, including the innovation of surgical procedures or the application of biological products. Studies on cartilage replacement, such as OAT and AOT, focus on reducing surgical trauma and donor complications. Researchers are currently looking at endoscopic graft techniques and changing the source of the grafts as a solution. Although initial positive results have been reported, further studies are needed to demonstrate their effectiveness. Cartilage regeneration techniques such as ACI are promising treatments for OLTs, but their complex procedures limit their clinical application. In the future, developing a more practical one-step process is key to improving the clinical utilization of ACI.

In a word, although a variety of managements are available, choosing the right method is still a challenge. Guided by the characteristics of the disease and the needs of patients, personalized treatment is the leading idea of the disease management. According to the location, size, degree and individual condition of the injury, a reasonable treatment plan will be selected to treat the disease, and a good therapeutic effect will be achieved. Clinicians and researchers need to further study the applicable conditions of various treatments, optimize treatment procedures, and clarify the details of treatment.

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