Return to Sports After Bone Marrow–Derived Cell Transplantation for Osteochondral Lesions of the Talus

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Abstract

Objective. Arthroscopic “one-step” technique based on bone marrow–derived cell transplantation (BMDCT) have achieved good results in repairing osteochondral lesions of the talus (OLT), overcoming important drawbacks of older techniques. It may be particularly adequate for the treatment of athletes in order to permit a safe and stable return to sports. The aim of this study was to report the results at 48 months of a series of athletes and the factors influencing the return to sports. **Design.** Case series. A total of 140 athletes underwent a “one-step” BMDCT repair of OLT. All the patients had the cells harvested from the iliac crest, condensed and loaded on a scaffold, and then implanted. Patients were evaluated clinically by the American Orthopaedic Foot and Ankle Society (AOFAS) scores and Halasi score. **Results.** AOFAS score improved from 58.7 ± 13.5 preoperatively to 90.6 ± 8.6 ($P < 0.005$) at 24 months, and to 90.9 ± 10.7 at 48 months. Halasi score was 6.88 ± 1.8 preinjury, 4.08 ± 1.7 preoperatively, and 5.56 ± 2.0 at final follow-up. At the final follow-up, all the patients (beside 1 failure and 3 lost) were able to return to activity and 72.8% were able to resume sports at preinjury level. **Conclusions.** “One-step” BMDCT repair of OLT had good clinical results that was durable over time in athletes, permitting a return to sports at preinjury level in the majority of patients. The preoperative presence of impingement and articular degeneration were the main negative prognostic factors.

Keywords

mesenchymal stem cells, articular cartilage, sports injury, ankle, cartilage repair

Background

Clinical results in athletes and the capability to return to activity at a preinjury level is a hot topic in ankle cartilage repair due to a remarkable diffusion in sport practice.^{1–4} Overtime various surgical options have been proposed to restore an adequate cartilaginous layer on the talar dome and overall good results were reported, but only few works have definitively focused on sportsmen.^{3–5} The ideal treatment for cartilage lesions in the athlete is controversial: an early return to sport is crucial, but a resilient, qualitative osteochondral tissue is required as well.^{3–17}

Microfractures are able to provide good results, especially in osteochondral lesions of the talus (OLT) treatment, with a good percentage of return to sports activities.¹¹ Moreover the rehabilitation and the return to sport require a quite short time (4 months), which is ideal for athletes.¹¹ Nevertheless, microfractures restore a fibrocartilage tissue; whereas other techniques like autologous chondrocyte implantation (ACI) or bone marrow–derived cell transplantation (BMDCT) regenerate good quality hyaline cartilage.^{1–17} These techniques imply a longer rehabilitation (12 months): moreover, ACI requires high costs and 2 operations.¹ “One-step” BMDCT

has been proposed as an effective treatment to repair the osteochondral lesions with hyaline cartilage, with the advantage of lower costs and a single surgical stage.^{1,11,14–16} Previously published series showed encouraging results on general population; still no exhaustive articles report the results of this technique on the athletes and its impact on the return to sports.^{1,11,14–16}

The aim of this study was to evaluate the return to sport of athletes with OLT, treated with one-step BMDCT procedure.

Methods

From October 2006 to June 2012, we enrolled 140 patients (mean age 30.3 ± 10.5 years) with focal OLT. All the patients regularly practiced sports: 3 of them were professional

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Table 1. Number of Patients Practicing Each Type of Sports Activity, Presence of Arthritis, Mean Lesions Size, Mean AOFAS Score Preoperatively, and Mean AOFAS Score at Last Follow-up.

Sport	Patients, n	Age, Years (Mean $\pm$ SD)	Defect Size, cm ² (Mean $\pm$ SD)	Patients With Arthritis (n)	AOFAS Score, Preoperatively (Mean $\pm$ SD)	AOFAS Score, at Last Follow-up (Mean $\pm$ SD)
Football	46	29.3 $\pm$ 8.6	2.0 $\pm$ 1.3	9	60.6 $\pm$ 15.5	93.0 $\pm$ 18.4
Running	27	36.3 $\pm$ 9.7	2.1 $\pm$ 1.7	6	58.7 $\pm$ 12.9	92.0 $\pm$ 8.8
Cycling	12	38.9 $\pm$ 8.5	2.4 $\pm$ 0.8	3	54.9 $\pm$ 9.1	86.3 $\pm$ 14.0
Fitness	9	31.7 $\pm$ 14.1	2.1 $\pm$ 0.5	2	55.7 $\pm$ 15.2	89.3 $\pm$ 11.6
Tennis	7	30.3 $\pm$ 10.8	1.9 $\pm$ 0.6	3	58.1 $\pm$ 11.6	82.3 $\pm$ 14.2
Swimming	7	22.1 $\pm$ 7.6	2.1 $\pm$ 0.6	1	58.1 $\pm$ 9.7	88.1 $\pm$ 6.0
Volley	6	20.2 $\pm$ 7.3	1.7 $\pm$ 0.4	2	64.5 $\pm$ 10.5	90.3 $\pm$ 9.2
Dancing	6	17.5 $\pm$ 2.8	1.5 $\pm$ 0.2	0	59.5 $\pm$ 12.4	86.3 $\pm$ 16.4
Other	20	28.5 $\pm$ 9.6	2.0 $\pm$ 0.7	1	56.1 $\pm$ 17.4	87.5 $\pm$ 11.2

AOFAS = American Orthopaedic Foot and Ankle Society.

full-time elite athletes, 28 were semiprofessional sportsmen, while 109 were amateur athletes. The different types of sports practiced are listed in **Table 1**.

The mean follow-up was 26 months (range 12-84 months).

All patients were treated with BMDCT using a “one-step” technique.¹⁴ The surgery was indicated for focal osteochondral lesions of the talar dome classified as chronic type II-IIA (>1.5 cm² in area, respectively <5 or >5 mm deep), according to the Giannini’s classification.¹⁷

Inclusion criteria were also age between 15 and 50 years and the compliance to the postoperative rehabilitation program. Joint degeneration grades 0, 1, or 2 of the van Dijk’s scale were considered eligible for the study.¹⁸

Patients with rheumatoid arthritis, hematological disorders, joint degeneration van Dijk’s grade 3 were excluded from this series.¹⁸ Inclusion and exclusion criteria were ensured by independent evaluation of the patients by the authors FV and LR.

The patients were 93 males and 47 females with mean body mass index (BMI) of 24 ± 3 kg/m². Mean lesion size was 2.0 ± 1.1 cm² and depth 5.1 ± 1.9 mm; the lesion was located laterally in 36 patients and medially in 101, and in 3 cases involved both medial and lateral aspects of the talar dome. Fifty-one (36.4%) patients had been treated previously by other cartilage repair techniques with unsuccessful result and recurrence of symptomatology. In 100 patients, the lesion had a clear posttraumatic origin and time elapsed between trauma and the treatment was 36 months (range 0-300 months). In 95 (69.3%) patients, anterior bony impingement was associated to the lesion, while 27 (19.7%) of them had OLT and concomitant II staged arthritic ankle.¹⁸

The ethical committee of our institution approved the protocol for this investigation. All investigations were conducted in conformity with ethical principles of research and written informed consent was signed by all the patients enrolled in this study.

Surgical Technique

The patient was placed in the prone position under general or spinal anesthesia. The bone marrow was harvested from the posterior iliac crest using sterile technique, described in previous articles.¹⁴⁻¹⁶ A total amount of 60 mL of bone marrow aspirate was collected and inserted into a concentrator-separator device (IORG1, Novagenit, Mezzolombardo, TN or BMaC, Harvest Technologies Corp, Plymouth, MA, USA). After a 15-minute working cycle the aspirate was reduced in volume in order to obtain 6 mL of bone marrow concentrate rich in nucleated cells. During the concentration process the patient was turned in a supine position and a standard ankle arthroscopy, or an anterior mini-arthrotomy, was performed. The lesion site was visualized and prepared until the healthy bone was reached. With the help of a millimetric probe, the lesion size was accurately measured. If the lesion was deeper than 7 mm, autologous cancellous bone was harvested from the proximal tibia as graft to fill the lesion. The composite to be implanted was prepared loading the scaffold with 2 mL of bone marrow concentrate. Because of changes in commercial availability over time, 3 different type of scaffolds were used in this series. Twenty-five patients received one-step procedure using collagen powder (Spongostan Powder; Johnson & Johnson Medical Ltd, Gargrave, Skipton, UK), which, once mixed with autologous cell concentrate and platelet gel, becomes a malleable paste, 70 received hyaluronic acid membrane (HYAFF-11; Fidia Advanced Biopolymers, Abano Terme, PD, Italy) while 45 received a collagen membrane (Biopad, Novagenit, Mezzolombardo, TN, Italy) as scaffold.

Using the same instrumentation previously described for the arthroscopic autologous chondrocyte implantation the composite was placed onto the lesion site.¹³ A layer of platelet-rich fibrin, collected from the autologous venous blood, was added in order to improve stability and cellular

proliferation.¹⁹ Multiple flexion-extension ankle movements were performed under direct/arthroscopic control to verify the stability of the implant.

Postoperative Protocol

Continuous passive motion (CPM) was started from the first day after surgery and gradually increased as tolerated. Partial weightbearing and swimming were advised at 6 weeks, increasing to complete weightbearing at 8 weeks.

Four months after surgery, all the patients were allowed to resume low-impact sport activities. Six months after surgery, running and progressive training for high-impact activities such as tennis and soccer were allowed.

Patient's Evaluation

A preoperative clinical and physical examination was completed for each patient. A history of possible ankle trauma and any previous treatment were investigated. Preoperatively, 2 different clinicians (FV and LR) examined the ankle for instability, malalignment and range of motion, and completed the American Orthopaedic Foot and Ankle Society (AOFAS) score.²⁰ A standard radiographic examination, including anteroposterior and lateral weightbearing views, and magnetic resonance imaging of the affected ankle were taken preoperatively.

Patients were examined at 6, 12, 18, 24, and every year after surgery up to 72 months and clinical evaluation by AOFAS and Halasi scores was performed in all cases.^{20,21} All the patients were evaluated at 24 months, 56 patients were seen at 48 months and 13 patients achieved the 72-month follow-up. Three patients were lost at follow-up between the 24- and 48-month follow-up since they did not come to the control visits and they did not answer phone calls.

Statistical Analysis

All continuous data were expressed in terms of the mean and standard deviation. Categorical variables were expressed as frequency and percentages. The Kolmogorov-Smirnov test was performed to test normality of continuous variables. The Levene test was performed to assess homoscedasticity. The repeated-measures general linear model (GLM) with Sidak test for multiple comparisons was performed to assess the differences of the clinical scores at different follow-up times. Analysis of variance followed by the Scheffé post hoc pairwise comparison was used to assess the among groups differences of continuous, normally distributed and homoscedastic data, the Kruskal-Wallis test followed by the Mann-Whitney test with Bonferroni correction for multiple comparison was used otherwise. Pearson chi-square test evaluated by exact

methods for small samples was performed to investigate the relationships between grouping or dichotomous variables. The Kaplan-Meier survival analysis with the log-rank test was performed to assess the influence of grouping variables on the return to sport of the observed patients. The Cox regression was used to assess the influence of continuous variables on the return to sport of the observed patients.

For all tests, $P < 0.05$ was considered significant.

All statistical analysis was performed using SPSS v.19.0 (IBM Corp, Armonk, NY, USA).

Results

No intraoperative complications were reported. Postoperatively, 1 patient had a superficial infection of the anteromedial arthroscopic portal, requiring a successful 1 week of oral antibiotic therapy.

All the patients were evaluated at 24 months, 56 patients were seen at 48 months, and 13 patients achieved the 72-month follow up (mean: 39 months). Three patients were lost at follow-up between the 24- and 48-month follow-up since they did not come to the control visits and they did not answer phone calls.

In 116 (83%) of the patients, the surgical treatment was performed completely arthroscopically and in 24 (17%) cases a mini-arthrotomic access was required; associated procedures such as screws removal, calcaneus osteotomy, hallux valgus correction, loose bodies removal, lateral ligament reconstruction and percutaneous Achilles' tendon lengthening were performed in 13 patients.

In 92 (66%) cases, the lesion was associated with lower degrees of ankle arthritis and in 45 (32%) ankles anterior impingement, confirmed arthroscopically or through direct visualization, was removed during surgery.

Overall the preoperative AOFAS score was 58.8 ± 13.5 . Postoperatively, a progressive improvement was observed up to 90.6 ± 8.6 ($P < 0.005$) at 24 months, with a percentage of the maximum possible improvement (calculated as $[\text{AOFAS score at the follow up} - \text{AOFAS preop}/100 - \text{AOFAS preop}] \times 100$) of $77.38\% \pm 20.91\%$. Only 56 patients arrived at 48 months but the score was maintained in this group (90.9 ± 10.7). A slight nonsignificant decrease in the mean clinical score was reported, with a final value of 86.9 ± 17.6 at 72 months (but only 13 patients achieved the longest follow-up of the series) (**Fig. 1**).

The Halasi score was rated 6.88 ± 1.8 preinjury (evaluated retrospectively), 4.08 ± 1.7 preoperatively, and 5.56 ± 2.0 at last follow-up of 36 months (range 12-84; **Fig. 2**).

All patients returned to complete weightbearing and regular walk at a mean of 2.48 ± 0.9 months, while they were able to resume their sports activity at 6.6 ± 4.8 months, requiring 18.52 ± 15.7 months to reach the preinjury level.

In detail, 12 months after surgery 32.1% (standard error [SE] 3.9%) of patients returned to the same level of sport, at

Figure 1. Graph showing the pattern of the mean American Orthopaedic Foot and Ankle Society (AOFAS) score evaluated at established follow-up up to 72 months.

Figure 2. Graph showing the pattern of Halasi score evaluated at pre-injury time, before surgery and at last follow-up.

2 years of follow-up 65.2 % (SE 4.2%), at 36 months 70.4% (SE 4.3%), and at 48 months 72.8% (SE 4.6%; **Fig. 3**). All

elite and semiprofessional players returned to their own sport activities, at the same level.

Figure 3. Graph showing the rate of patients and the time returning to the same level of sport activities.

Table 2. Patient Characteristics Based on Division Into “High-Impact Sport Activities” and “Low-Impact Sport Activities” Groups.

Sport	Patients (n)	Age, Years (Mean $\pm$ SD)	Defect Size, cm ² (Mean $\pm$ SD)	Patients With Arthritis (n)	AOFAS Score, Preoperatively (Mean $\pm$ SD)	AOFAS Score, at Last Follow-up (Mean $\pm$ SD)	Rate of Return to Sport (%)
High-impact sport activities	109	30.1 $\pm$ 9.6	2.1 $\pm$ 0.6	23	59.5 $\pm$ 14.9	91.8 $\pm$ 17.3	72.90
Low-impact sport activities	31	30.6 $\pm$ 14.6	2.1 $\pm$ 0.7	4	55.5 $\pm$ 11.6	86.4 $\pm$ 14.3	72.60

Grouping the patients basing on the type of sports practiced (low- or high-impact activities) no difference was reported in the capability to resume sports at the same level (Tables 1 and 2)

Sex, age, arthroscopic or arthrotomic approach, traumatic origin of the lesion, previous surgeries, associated surgeries and location of the lesion, time elapsed between trauma and surgery, lesion size, BMI, and preoperative AOFAS score did not significantly affect the return to sports.

The need of bone grafting in the bottom of the lesion (18 cases) showed a tendency to negatively affect the time to return to the same level of sports ($P = 0.16$). The presence of anterior bony impingement (95 patients) did negatively affect the return to sports at previous level ($P = 0.036$).

A similar report was noticed for early arthritis, since a lower number of patients with arthritis in their ankle resumed sports after surgery at same level of activity ($P = 0.024$; Fig. 4).

Discussion

Return to sport after cartilage procedure is a hot topic, but very few conclusions are currently available.^{4,7,9} Mithoefer *et al.*⁸⁻¹⁰ found that cartilage procedures on athletic knees are generally effective, with a mean of two-thirds of patients coming back to sport; Park and Lee¹¹ reported a good return to pre injury sports activities (87% at 3 years) following microfractures, with final results affected by patient age. Although higher rates of return to sport were reported for mosaicplasty, microfractures have been considered the best treatment in athletes, for good results and rapid return to sport.²⁻¹⁰

Return to sport after OLT treatment has not been adequately described. Few prognostic factors were identified: youth, lower body mass index, smaller OLT size, and physical and pharmacological treatments.^{2,4,11}

The current study is the first work completely focused on return to sport after a regenerative procedure for OLT. It showed that the “one-step” BMDCT technique achieved

Figure 4. Graph showing the rate of patients and the time returning to the same level of sport activities shared into 2 groups: athletes with and without arthritis. Lower number of patients with arthritis in their ankle resumed sports after surgery at same level of activity.

good and stable clinical results in a series of 140 professional or amateur athletes, with no complications reported, at 72-month follow-up.

A return to high-impact activity was achieved at a mean of 6.6 months. A good rate of return to sport activities at the same preinjury level was achieved after 12 months (32.1%), with a final result of 72.8% at 48 months. The sport practice (high- or low-impact activities) did not influence the final result. In fact, Halasi score showed no significant difference in the return to sports at previous level: athletes practicing either low- or high-impact sports activities were able to resume sports at previous level after surgery.

Moreover, AOFAS score did not correlate with the return to sport at previous level. This finding may be explained by motivational factors and increasing age of patients. Frequently, the patients experienced a fear of reinjury, which led the patients to lower the activity level despite of the satisfying AOFAS score.

In contrast with previous experiences in literature, the time elapsed between trauma and surgery, sex, age, traumatic origin of the lesion, previous surgeries, associated surgeries and location of the lesion, lesion size, BMI and preoperative AOFAS score showed no impact on the return to sports.^{2,4,8-11} Signs of moderate ankle osteoarthritis, impingement, and lesion depth influenced the return to sport in this case series, consistent with a previous report.⁵

It should be noted that a general significant deterioration of the clinical score was reported between 24 and 48 months in a previous general case series from the same authors, including a mixed population of nonsportsmen and athletes.¹⁵ Considering the stable outcomes in the series currently reported, it seems that strong motivation in athletes may play an important role to return to full activity. This is also in line with Hangody *et al.*⁶ who showed a faster and better clinical outcome in a population of professional athletes following mosaicplasty, possibly due to strong motivational factors.

A possible alternative treatment for OLT in athletes may be ACI, widely considered the gold standard in cartilage regeneration.^{3,7,13} Nevertheless, the need for 2 surgical operations, high costs resulting from cell expansion, and late return to activity are major drawbacks of this technique.¹ In a recent comparison of ACI and BMDCT for ankle OLT, the rate of return to sport appeared better in BMDCT than ACI, although non-statistically different results were achieved.¹

Whereas the timing of return to high impact sports for the BMDCT in the athletes seems shorter than in ACI, the timing is longer when compared with microfractures, even when an aggressive rehabilitation program is adopted.^{2,4,8-10} The main reason is related to the biological process taking place in BMDCT, which is largely similar in ACI repair.⁷

The authors believe that the higher quality of the repaired cartilage is worth the couple of additional rehabilitation months,

especially in professional athletes willing to extend their career perspective and in all the patients practicing recreational sports.

This study has some limitations. The main limitation is the retrospective design with absence of a control group. The 3 different scaffolds used as cell support during the surgical procedure are a consistent limitation of the study. Nevertheless, as it is stated in the current study and in previously published case series, the biomaterial did not statistically influence the final results.¹⁶

Conclusions

The arthroscopic “one-step” BMDCT reported highly satisfactory clinical midterm results, even more stable in athletes than in the general population. This technique avoids the major disadvantages of previously proposed procedures, such as the high costs and the need for multiple surgeries, allowing a safe and reasonably quick return to sport with a good regenerated osteochondral tissue.

The necessity of a single step surgery makes it particularly useful for those professional athletes who are ideally candidates for regenerative procedures but require a quite quick recovery, with the perspective to improve their sports career.

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

Ethical approval for this study was obtained from the ethical committee of our institution (29877).

Informed Consent

Written informed consent was obtained from all patients enrolled in the study.

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