Update on the Use of Microfragmented Adipose Tissue (MFAT) in Knee Osteoarthritis

Prof. Reha N. Tandogan, M.D.

Senior Surgeon, Çankaya Orthopedics, Ankara, Türkiye
Chair, Dept. of Orthopedics & Traumatology, Halic University Istanbul, Türkiye
RMOS Board Member
Past Chair, European Knee Associates Section of ESSKA

Adipose tissue is a rich source of mesenchymal stem cells (also known as Medicinal Signaling Cells), Adipose Derived Stem Cells (ADSC)) located in the Stromal Vascular Fraction (SVF). Previously these cells were obtained enzymatically from lipoaspirates or expanded in cell cultures, leading to regulatory problems or the need for expensive GMP laboratories if cells needed to be cultured. Enzymatically processed lipoaspirate contains ADSCs, endothelial precursor cells (EPCs), endothelial cells (ECs), macrophages, smooth muscle cells, lymphocytes, pericytes, as well as pre-adipocytes, collectively named the SVF (1). SVF has been shown to be effective in the symptomatic treatment of OA. A recent meta-analysis of 79 RCTs with 8761 patients were comparing the intra-articular injection of autologous conditioned serum (ACS), bone marrow aspirate concentrate (BMAC), botulinum toxin, corticosteroids (CS), hyaluronic acid (HA), mesenchymal stem cells (MSC), ozone, saline placebo, platelet-rich plasma (PRP), plasma rich in growth factor (PRGF), and stromal vascular fraction (SVF) demonstrated that SVF injections resulted in the greatest improvement in pain and functional outcomes in patients with knee OA at up to 1 year (2).

Regulatory issues have led to the development of microfragmented adipose tissue techniques with minimal manipulation; here autologous cells are harvested, processed and used at the point of care without expansion/enzymatic treatment (3). Subcutaneous fat may be harvested from the abdomen or thigh using dedicated lipoaspiration cannulae and mechanically processed using filtration/fragmentation, centrifugation and lavage. The final product usually called Microfragmented Adipose Tissue (MFAT). This process results in the removal of blood elements and maintenance of tissue structure and stromal cell populations (4). MFAT contains varying amounts of stromal cells exhibiting the phenotype of ADSC's (such as CD73, CD90 and CD105) as well as CD44 and CD146 found in pericytes. MFAT has similar regenerative, angiogenic, anti-fibrotic and immunomodulatory properties to its enzymatically digested counterpart (1, 5) and has recently been used for the symptomatic treatment of osteoarthritis (OA). Compared to BMAC, adipose tissue has a higher percentage of nucleated cells (0.001–0.01% vs 15-30%) and is less likely to be affected by the patient's age (6). Cell viability has been reported be around 80% for various point of care mechanical processing techniques of lipoaspirate (7).

The mechanical processing method, cell number, viability and characterization of MFAT is not standardized, leading to difficulty in comparing the outcomes of different devices. A recent review by Liu et al., identified 13 unique devices/systems for the mechanical processing of adipose tissue and found that when cell concentration, cell viability and MSC immuno-phenotypic analysis was considered, the most effective manual devices/systems were ones using filtration and cutting/mincing (7). However no definite conclusions on clinical effectiveness could be reached due to heterogeneity of the data (7).

A systematic review of 12 clinical trials using different techniques of processing adipose tissue, has found improvement is pain and functional scores of patients with knee OA up to 2-years (8). Unfortunately, most of the studies were low-quality only two were prospective randomized controlled trials. Most studies on MFAT injections report improvements up to 2-years, with decreasing effectiveness over time. However, the expected duration of symptomatic improvement with MFAT treatment is not clear, some studies report deteriorating outcomes after one year (9).

Although generally indicated for mild to moderate OA, MFAT has also been used for advanced knee OA, with acceptable outcomes. An international multi-centric study of 75 patients found the best outcomes were in K-L 2 patients, although patients with K-L 4 arthritis and previous surgeries also benefited from MFAT injections (10). In another prospective series of 20 patients with K-L 4 OA, conversion to total knee arthroplasty was 15% at 12 months (11). Another 4-year follow-up study with MFAT injection demonstrated a 68% effectiveness regardless of cartilage status, although patients with synovitis had a 75% failure rate (12). These outcomes have led to the proposal of MFAT injections as a low-morbidity alternative biological treatment to delay the need for total knee replacement in suitable patients (13).

The addition of MFAT to microfracture has been shown to provide superior cartilage restoration compared microfracture alone in focal chondral defects in humans (14). However, no structural change cartilage morphology in follow-up MRI's have been conclusively demonstrated in isolated intra-articular MFAT injections in patients with OA. A recent study with d-GEMRIC MRI at 2 years after MFAT injection in patients with knee OA has shown increased GAG content, but further studies are needed to prove the disease modifying effect of MFAT on OA (15).

Microfragmented adipose tissue may also be used in combination with other treatments such as PRP and arthroscopic debridement. Duscher has coined the term Lipoarthroplasty for this combination treatment although long term outcomes are lacking (16). A randomized multicenter study of 302 patients found superior outcomes with combined MFAT+arthroscopy compared to HA+arthroscopy at 2-years (17). Similarly another prospective study of 78 patients found superior outcomes in patients with arthroscopic debridement + MFAT compared to debridement alone at 29 months (18).

The superiority of MFAT procedures to other injectable orthobiologics has not been established. Three RCT's comparing MFAT with PRP have found similar improvements in pain and function with both treatments in patients with mild to moderate OA. (19, 20, 21). Two studies comparing BMAC vs. MFAT have found similar improvements in patient reported outcomes and function at 6 months & 1 year respectively (22, 23). Although a protocol for RCT has been published (24), there are no studies comparing the efficacy of enzymatically digested vs mechanically fragmented adipose tissue.

In conclusion MFAT injection is a safe and effective symptomatic treatment alternative for mild to moderate knee OA. There are a variety of processing techniques resulting in different cell counts, viability and cell phenotypes, making comparison between techniques difficult. The quality of published studies has increased in recent years, and this will lead to a better understanding of efficacy and patient selection. Disease modifying effect of MFAT on OA has not been conclusively demonstrated. The superiority of MFAT treatment to other injectable orthobiologics has not been established and further studies are needed to define subtle differences in outcomes.

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