

Outcomes after Micronized Fat Adipose Transfer for Glenohumeral Joint Arthritis and Rotator Cuff Pathology: a Case Series of 18 Shoulders

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SUMMARY

Background. This study aimed to evaluate the safety and clinical outcomes of patients treated with micro-fragmented adipose tissue for shoulder pain secondary to glenohumeral osteoarthritis and rotator cuff pathology.

Methods. 16 patients (18 shoulders) who had failed previous conservative therapies and received a single injection of micro-fragmented adipose tissue for shoulder pathology. Outcomes including pain, disability, and safety were assessed at minimum of six months.

Results. Significant improvements in visual analog scale scores ($p < 0.001$) and pain disability index scores ($p = 0.02$) with no major adverse events were observed at six months.

Conclusions. Micro-fragmented adipose tissue may be helpful to improve pain and function in a subset of patients with chronic glenohumeral osteoarthritis and rotator cuff tears. No major complications were identified in our case series.

KEY WORDS

Medicinal signaling cells; MFAT; orthobiologics; regenerative medicine; shoulder.

INTRODUCTION

Shoulder pain is a common debilitating condition with an estimated annual prevalence ranging from 4.7-46.7% (1). In 2008, nearly 19 million adults (>8% of the US adult population) reported chronic shoulder pain (2). Rotator cuff disorders and glenohumeral osteoarthritis are two of the most common etiologies (3,4). Patients frequently continue to suffer with pain despite treatment, with 40-50% having continuous or recurrent pain complaints at one year (5). Direct costs in 2000 for treating shoulder pain in the United States totaled \$7 billion (3).

Early in the clinical course of shoulder disorders typical treatments offered include activity modification, physical therapy, oral anti-inflammatories and corticosteroid injections (4). The long-term use of corticosteroid is becoming

increasingly controversial, as there are concerns regarding tendon and chondral toxicity (6). Until recently, the next step in treatment was often surgical with rotator cuff repair or shoulder arthroplasty. Not all patients are candidates for repair secondary to a variety of patient and lesion factors, and post-operative recovery for arthroplasty has significant downtime (7,8). Newer injection options such as platelet rich plasma and mesenchymal signaling cells (MSCs), the latter of which are typically obtained from autologous bone marrow or adipose tissue are now being increasingly used (9). MSCs are cells with the perceived capability to differentiate into cells that regenerate tissue functionality following injury (10). Numerous mechanisms have been proposed to explain how MSCs may support tissue repair and relieve pain. Secretion of cytokines and growth factors through a

paracrine mechanism likely plays a large role (11). This paracrine activity is thought to stimulate angiogenesis and have anti-inflammatory properties (12). Secondary to its abundant vasculature, adipose is an excellent medium for MSC harvest. The procurement procedure consists of a minimally invasive harvest with higher cell concentration per unit volume compared to bone marrow concentrate (13). Complex regulations limit utility of culture expansion techniques and enzymatic digestion to obtain stromal vascular fraction. Mechanical treatment with micro-fragmentation provides an effective means of obtaining minimally manipulated adipose tissue known as micro-fragmented adipose tissue (MFAT) for therapeutic use (14).

Limited literature is available on the outcomes of patients treated with MFAT for shoulder pain. Continued clinical use necessitates continued analysis of outcomes of the procedure. In the present study, we report the functional and pain outcomes of 16 patients (18 shoulders) treated with MFAT injections for glenohumeral osteoarthritis and rotator cuff tears.

METHODS

Participants

All patients with glenohumeral osteoarthritis or rotator cuff tears treated with adipose-derived stromal cells from November 2017 to May 2019 at a single outpatient sports medicine clinic were evaluated for inclusion. Diagnosis was obtained through history, examination, and imaging.

Inclusion criteria were: (1) primary diagnosis of glenohumeral osteoarthritis or rotator cuff tear, (2) pathology present on magnetic resonance imaging or plain radiography, (3) pain duration greater than 6 months, and (4) failed conservative management with any combination of physical therapy, corticosteroid injection, visco-supplementation, platelet rich plasma, or arthroscopy. Exclusion criteria were corticosteroid injection within 3 months of MFAT procedure, malignancy, active infection, or auto-immune arthritis.

Sixteen patients (18 shoulders) met criteria and were analyzed. Seventeen shoulders had pathology confirmed through MRI, and in one case severe glenohumeral osteoarthritis was confirmed with plain radiography.

Procedure

The Lipogems® procedural kit was used in all patients. This kit provides the necessary resources for the harvest, processing, and transfer of MFAT. Mild mechanical forces are employed to reduce adipose tissue cluster size and eliminate proinflammatory oil and blood residues (15). The resultant

product is neither enzymatically treated nor culture expanded. All injections were performed by two experienced physiatrists using ultrasound guidance (CE, JBS). The following standardized procedural protocol was used:

Harvest site was determined in the standing position. The patient was subsequently placed supine or prone for flank and thigh harvest sites, respectively, and the skin overlying the harvest site was cleansed with chlorhexidine. After injection of local anesthetic, an 18-gauge needle tip was used to create a small incision. The site was infiltrated with tumescent anesthesia (500 mL Normal Saline, 1 mL of 1:1000 Epinephrine, 50 mL of 1% Lidocaine/25mL of 2% Lidocaine, 5 mL of 8.4% Sodium Bicarbonate) using the 17-gauge Lipogems® blunt anesthesia tip connected to a 60 mL syringe. The cannula was advanced laterally to medially to disperse the tumescent anesthesia. At least 20 minutes post completion of tumescent anesthesia, the lipoaspiration was started. Fat was harvested using a 13-gauge lipoaspirate cannula connected to a 20 mL VacLok syringe. Care was taken to avoid any air being introduced to the syringe. The lipoaspirate syringes were placed in a sterile cup to decant and subsequently transferred to the Lipogems® device for processing. The final product was placed in 3mL syringes for the treatment. As the lipoaspirate was being washed, excess tumescent was expressed from the harvest site and the puncture site was dressed in steri-strips and a sterile gauze, which was then covered by Tegaderm. Tape was placed along the harvest site to minimize swelling, bruising, and post-procedure pain. Ultrasound guidance with a curvilinear probe for the glenohumeral joint and linear probe for rotator cuff lesions was used for tissue transfer with an in-plane needle approach. Under sterile conditions, the final adipose aspirate was injected into the target site using a 18g 3.5-inch needle. Average MFAT injectate volume was 4.9 ± 1.4 mL for glenohumeral arthritis and 1.4 ± 0.6 mL for rotator cuff pathology. After completion of the procedure, the patient was monitored for 15-20 minutes and provided the post-procedure instructions, which were reviewed in-person.

Assessments

Approval was obtained from our institution's quality improvement advisory board; IRB approval was thereby waived by the institution. This study meets the ethical standards of the journal (16). Data was collected during routine clinic follow-up visits. The following outcomes were collected: visual analog scale (VAS), pain disability index (PDI), and percent global improvement. The primary outcome was VAS and PDI score changes from baseline at 6-month follow-up. All patients presented for their 6-month follow-up, with most having additional visits before and after.

The VAS is an 11-point scale with 0 being no pain and 10 being worst possible pain. The PDI is comprised of 7 questions assessing the impact of chronic pain on activities such as recreation, self-care, and occupation. Scores range from 0 (no disability from pain) to 70 (worst disability from pain) (17). Percent global improvement scores ranged from 0% (no improvement) to 100% (maximum possible improvement).

STATISTICAL ANALYSIS

Descriptive statistics were used to evaluate variable frequencies. Within participant changes were evaluated using paired two-tailed Student's t-tests to calculate differences between baseline, 6-month, and greater than one-year VAS and PDI scores. Mean and standard deviations or percentages are reported for the full cohort. Threshold of significance was set at $P < 0.05$. A minimal clinically important difference

(MCID) value of 1.4-point change was used for VAS and 9.5-point change for PDI (18,19). Descriptive values of proportion of participants meeting MCID are presented.

RESULTS

Demographics and clinical characteristics are depicted in **table I**. Most patients' (72%) procedure was in the shoulder of the dominant arm and on average duration of symptoms was approaching 6 years. Follow-up was obtained in all participants for minimum of 6 months (average follow-up was 12.1 ± 5.6 months). Diagnostic imaging identified severe glenohumeral joint osteoarthritis and partial supraspinatus tears as the most prevalent pathologies, seen in 50% and 33% of shoulders, respectively (**table II**).

At baseline, mean VAS was 6.1 ± 2.1 and mean PDI was 21.4 ± 9.2 . There was significant improvement between baseline and 6-month follow up VAS ($p < 0.001$) and PDI ($p = 0.02$) (**figures 1,2**). For the 10 shoulders with greater than one-year follow-up, significant improvement in VAS ($p < 0.001$) and PDI ($p = 0.03$) was observed. At 6 months, the MCID was met for 14 (78%) of shoulders for VAS and 9 (50%) of shoulders for PDI. At final follow-up, global improvement averaged 70% (range 20-100%). One minor complication was reported of transient contact dermatitis from the dressing applied to the harvest site. No other complications were observed or reported.

Table I. Demographic and Clinical Characteristics (N = 16 Patients). Values are mean and standard deviation or percentages. BMI: body mass index; PRP: platelet-rich plasma; MRI: magnetic resonance imaging.

N = 16 Patients	
Age	65.1 \pm 9.6
BMI	28.5 \pm 6.1
Laterality	
Right	11 (68.7%)
Left	3 (18.8%)
Bilateral	2 (12.5%)
Dominant Arm	
Right	16 (100%)
Symptom Duration (m)	65.7 \pm 59.9
Follow-up (m)	12.1 \pm 5.6
Sex	
Male	9 (56%)
Female	7 (44%)
Previous Treatments	
Physical Therapy	16 (100%)
Steroid Injection	15 (94%)
PRP Injection	10 (63%)
Imaging	
Plain Radiograph	16 (100%)
MRI	15 (94%)

Table II. Pathology on Imaging (N = 18 Shoulders).

N = 18 Shoulders		
Glenohumeral Osteoarthritis		
Moderate	4	22,20%
Severe	9	50%
Rotator Cuff Pathology		
Supraspinatus		
Tendinosis	2	11,10%
Partial Tear	6	33,30%
Full tear	2	11,10%
Acromioclavicular Osteoarthritis	5	27,80%
Infraspinatus		
Tendinosis	2	11,10%
Partial Tear	2	11,10%
Subscapularis		
Partial Tear	1	5,60%

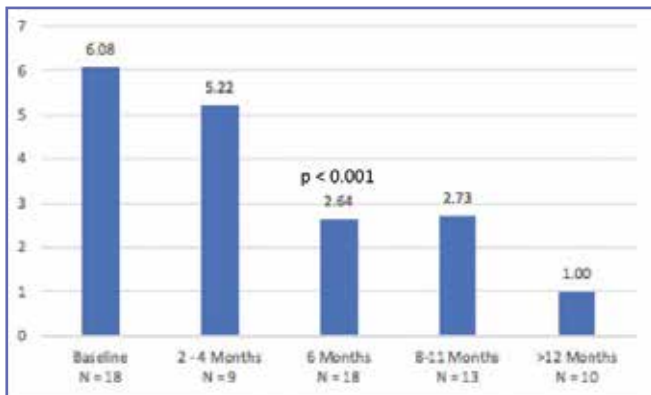


Figure 1. Visual Analog Scale Score Changes. Depicted are mean scores with corresponding number of patients for each follow-up time point.

DISCUSSION

Recalcitrant shoulder pain from osteoarthritis and rotator cuff pathology remains a common problem encountered in clinical practice. In this population of 15 patients, a majority reported significant improvements in pain and/or disability at six months using MCID criteria and no major adverse events were reported. These findings are notable as all patients had failed multiple prior conservative interventions, were not candidates or not ready for surgery, and reported pain and functional limitations for many months. The findings suggest MFAT may be successful in a portion of patients with shoulder pain from GHJ arthritis or RTC disease, with benefits measured 6 months from procedure. Current literature on MFAT use for shoulder pain remains limited. Striano *et al.* reported results on 18 patients with chronic shoulder pain treated with MFAT (20). Patients were followed for one year and significant improvement was noted for pain reduction and functional improvement using the Numeric Pain Scale and American Shoulder and Elbow Surgeons Score. Pain scores decreased from a baseline of 7.5 to 3.6 at one year. In the present study, we observed similar improvement in pain and disability. While statistical analyses could not be completed for after 6 months in our study, seven patients had follow-up times greater than 10 months with average point decreases of 4.2 and 4.6 in VAS and PDI, respectively, from baseline. A case report of a T10 complete paraplegic wheelchair user with chronic shoulder pain found improved pain and functional outcomes one-year post Lipogems[®] procedure (21). This allowed him to maintain independence and resume activities of daily living. Two studies report stromal vascular fraction (SVF) outcomes on shoulder pain via arthroscopy. Jo *et al.* treated 19 patients with varying doses of culture expanded SVF at the time

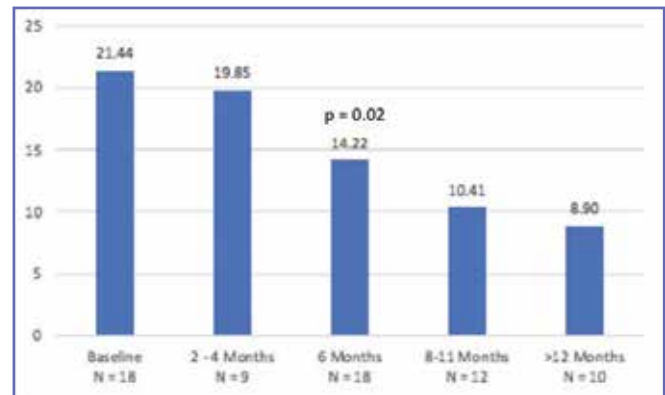


Figure 2. Pain Disability Index Score Changes. Depicted are mean scores with corresponding number of patients for each follow-up time point.

of an arthroscopic examination (22). Significant improvement was found at six months for the mid and high dose groups. The SVF used in this study was obtained through enzymatic digestion. Notably, culture-expanded cells are not approved for use in the United States as they violate the Federal Drug Administration's minimal manipulation regulations for MSCs. Kim *et al.* compared outcomes of surgical repair alone for rotator cuff tears against repair coupled with injection of adipose-derived MSCs loaded in fibrin glue. They found decreased re-tear rates in the surgery plus adipose-derived MSC group, but no significant differences in pain outcomes (23).

Multiple mechanisms have been proposed for how adipose-derived signaling cells may improve pain and function for shoulder pathology. Immunomodulatory and anti-inflammatory properties secondary to a paracrine secretion of growth factors and cytokines likely contributes (11). In MFAT, these trophic properties can be attributed to the undifferentiated cells which are isolated from adult harvested adipose tissue (24). Additionally, tendon needling when treating rotator cuff tears invariably occurs and can have pain relieving properties (25).

While the findings are encouraging, results of this large case series should be interpreted with caution. Case series retrospective design is limited by sample size, low level of evidence (IV) and absence of a control group which precludes comparing outcomes amongst other treatment options. Selection bias of participants may influence results (including choice of procedure and out of pocket expense). MFAT is not a covered benefit under most commercial and government insurers in the United States, and out of pocket expense varies depending on which particular MFAT kit is used as well as overhead and demographics of the practice location. Often this amounts to a couple thousand US dollars.

Notably no patients studied had received visco-supplementation with hyaluronic acid (HA) prior to their MFAT procedure. *In vitro* studies have demonstrated HA to potentially enhance tendon cell viability and proliferation (26). Additionally, in a review of 11 clinical studies, HA was found to improve pain and function in shoulders with rotator cuff tears (27). While often not covered by insurers in the United States, HA is typically a cheaper treatment option that can be considered prior to MFAT. The degree of osteoarthritis and rotator cuff tear severity may also influence results and was not controlled for in this study. Follow-up was obtained for a subset of patients to 6 months, and clinical results are often reported at time points 12 months after the procedure (28,29). However, this report adds to the limited literature

using Lipogems® and suggests further investigations using rigorous methodology (randomization, blinding, and larger sample sizes with more homogenous degree of pathology) would help understand the benefits of this procedure. In conclusion, our results suggest MFAT may be helpful to improve pain and function in a subset of patients with chronic glenohumeral osteoarthritis and rotator cuff tears. No major complications were identified in our case series. Additional studies ideally prospective with a control group are needed for further evaluation of this treatment.

CONFLICTS OF INTERESTS

The author declare that they have no conflict of interests.

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