A Single Intra-Articular Injection of Autologous Micro-Fragmented Adipose Tissue Results in Clinically Significant Improvement in Knee Pain and Function in Patients with Diffuse Degenerative Knee Osteoarthritis

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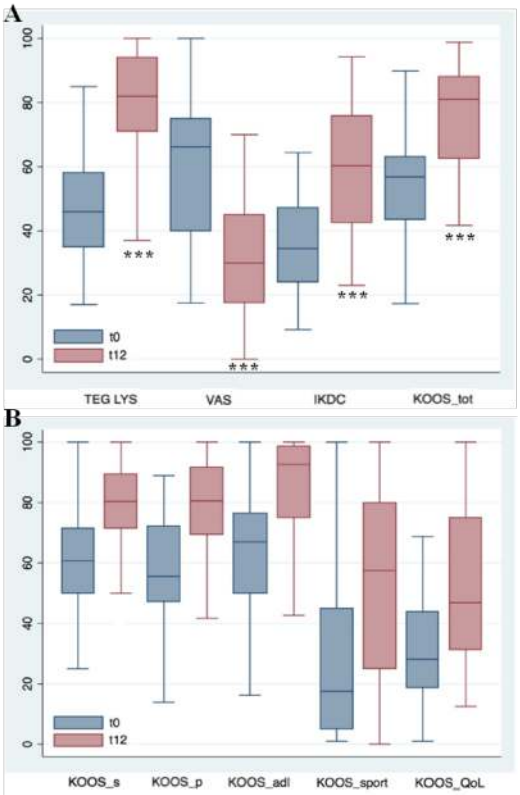
Disclosures: A. Russo: 2; Lipogems. V. Condello: None. V. Madonna: None. M. Guerriero: None. S. Bruder: 3B and 4; Lipogems. C. Zorsi: None.

INTRODUCTION: Knee chondropathy represents a challenge for orthopaedic surgeons because of the limited regenerative properties of the cartilage tissue. While a variety of novel treatments have been proposed in the last few decades, they have been limited to only focal cartilage lesions. For diffuse degenerative chondral lesions, no adequate biological treatments are currently available. New therapeutic approaches, such as the use of mesenchymal stem cells (MSCs) have shown promising results when applied in the context of joint degeneration. MSCs are able to activate and influence the microenvironment via trophic, mitogenic, immunomodulatory and anti-microbial actions. Adipose-derived MSCs have been shown to be a good source of these naturally occurring cells. However, to date, the methods of extracting and expanding adipose-derived MSCs have been expensive, and involved multi-step processes and the use of scaffolds, cells, and growth factors. Based on these considerations, we utilized a commercially available system (the Lipogems® processing kit) that intra-operatively provides micro-fragmented, minimally manipulated adipose tissue in a short time without cellular expansion or enzymatic treatment. The aim of this retrospective study was to evaluate the 1-year outcome of a single intra-articular injection of autologous, micro-fragmented adipose tissue (referred to as Lipogems), using the Lipogems kit, in patients with degenerative chondral lesions.

METHODS: Thirty patients were treated with autologous, micro-fragmented adipose tissue (Lipogems). Inclusion criteria included diffuse degenerative chondral lesions of grade >II (ICRS classification), constant pain (VAS pain scale ≥ 50), resistant to NSAIDS, and failure of conservative treatments (physiokinesitherapy, hyaluronic acid, platelet-rich plasma, corticosteroids) for at least 12 months. Of these 30 patients, twenty-four (80%) had also an associated surgery (ACL/LCL reconstruction, high tibial osteotomy, meniscectomy), while six (20%) underwent arthroscopy alone. Fifteen patients (50%) underwent previous surgeries more than one year prior to the current study. Pre-operatively and 12 months after the procedure all the patients were clinically evaluated with direct medical examination, standard X-rays and MRI. Knee Injury and Osteoarthritis Outcome Score (KOOS), International Knee Documentation Committee (IKDC)-subjective, Tegner Lysholm Knee, and Visual Analogue Scale (VAS) pain questionnaires were also collected. A level of at least 10 points of improvement in the scores was selected as a cut-off representing a clinically significant difference. The lower or lateral abdomen was chosen as donor site for adipose tissue harvesting. Harvested fat was immediately processed in the Lipogems processing kit. The entire process, carried out in one surgical step, was performed in complete immersion in physiological solution minimizing any trauma to the cells. Micro-fragmented fat (10 cc) was injected intra-articularly after the arthroscopic procedure. For statistical comparisons, the Shapiro-Wilk test was used to test the normal distribution of continuous variables and the Wilcoxon Signed-Rank Test was employed to compare the mean of two paired groups (baseline and 12 months). All analyses were performed with STATA ver. 14 (StataCorp, 4905 Lakeway Dr, College Station, TX 77845, USA). A $p<0.05$ was considered statistically significant. Since the micro-fragmented fat is autologous, minimally manipulated and widely used in other surgical fields (i.e. lipofilling), safety was assessed by evaluating local adverse events, such as fever, infection, and excessive swelling of the knee. The study was approved by the Ethics Committee of Verona and Rovigo, Italy (protocol # 10227, March 1st, 2016). All procedures mentioned in this study were carried on in accordance with the ethical standards and with the Helsinki Declaration of 1975, as revised in 2000.



*** p<0.0001 for 12 Months versus Time Zero

RESULTS SECTION: At 12 months follow-up (t12 in Figures), an improvement of at least 10 points in the IKDC-subjective and total KOOS was observed in 70% and 67% of the patients, respectively. The total median improvement was 20 points both in IKDC-subjective and in total KOOS [(interquartile range (IQR) 8-36 and 4-36, respectively, $p<0.0001$; Figure A)]. A higher percentage of success was found in VAS pain and Tegner Lysholm Knee, where 83% and 87% of the patients, respectively, showed an improvement of at least 10 points compared to the pre-operative values, with a total median improvement of 24 (IQR 37-13, $p<0.0001$) in VAS pain and 31 (IQR 14-46, $p<0.0001$; Figure A) in Tegner Lysholm Knee. In general, we observed improvements of more than 20 points in more than 50% of the patients and more than 50% of the patients improved at least 30 points in VAS pain scale. Considering the five KOOS subscales, the observed median improvement was 21 points (IQR 1-32) in symptoms, 19 (IQR 4-41) in pain, 17 (IQR 3-33) in activity daily living, 15 (IQR 0-50) in sport, and 13 (IQR 0-38) in the quality of life (Figure B). Only three adverse events were recorded, which required no additional treatment, and no cases of post-operative infection, post-arthroscopic algodystrophy or stiffness were recorded.

DISCUSSION: The main finding of this retrospective study is that autologous, micro-fragmented adipose tissue graft is a safe adjuvant for the treatment of diffused degenerative chondral lesions. Indeed, no major complications were observed, either at the knee or at the harvested site and no patient worsened compared to the pre-operative condition. Twelve months after the injection, a substantial proportion of patients experienced a clinically significant improvement (≥ 10 point change) in IKDC-subjective, total KOOS scores and VAS pain, while improvements of more than 20 and 30 points were seen in some patients. Furthermore, clinical improvement was evident in each of the five KOOS subscales. The Lipogems processing kit, as used in this study, overcomes many of the challenges of extracting and expanding adipose-derived MSCs embedded in other methods. While these data provide promising clinical outcomes, additional larger randomized and controlled trials are needed to more fully investigate the long-term safety and efficacy.

SIGNIFICANCE/CLINICAL RELEVANCE: The results of this study demonstrate the safety and efficacy of autologous micro-fragmented adipose tissue injection using the Lipogems processing kit for the treatment of diffuse degenerative knee chondropathy. Clinical improvement was evident in a substantial proportion of patients. The single-step procedure is easy, economic, quick, minimally invasive, and is associated with a low percentage of adverse events.