Treatment of Thumb Carpometacarpal Joint Osteoarthritis

Subjects: Orthopedics

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Thumb carpometacarpal joint (CMCJ) arthritis is the second most common location for degenerative osteoarthritis in the wrist and hand and several surgical treatments have been proposed so far, from arthrodesis to motion sparing procedures —such as trapeziectomy alone or in combination with interposition of autograft, allograft and ligamentoplasty.

Keywords: fat grafting ; fat transfer ; carpometacarpal arthritis ; thumb arthritis

1. Introduction

The presence of mesenchymal stem cells in adipose tissue was first described in 2001 by Zuk et al. [1]. These cells have been characterized by strong regenerative properties and a multilineage differentiation potential comparable to bone marrow mesenchymal stem cells [1][2][3][4]. Since then, the regenerative capacity of adipose tissue along with its anti-inflammatory and immunomodulatory properties have been a constant field of research and clinical application. From pure macrofat and nanofat grafting to enzymatically isolated adipose derived stromal vascular fraction (SVF) and cultured stem cells, the adipose tissue has been studied in a wide range of degenerative diseases [5].

In particular, adipose-derived SVF is a popular product that has been clinically applied to joints with osteoarthritic changes [6][7][8][9]. It is isolated by enzymatic digestion and centrifugation of the harvested fat and consists of a heterogenous cell population of mesenchymal stem cells, pericytes, endothelial progenitor cells and immune cells, with strong regenerative capacity and a potential synergistic effect on immunomodulation, inflammation and angiogenesis [10]. Intra-articular injection of autologous SVF derived from lipoaspirate has been used for the symptomatic treatment of grade 3 and 4 knee osteoarthritis, with a significant clinical and radiological improvement at one year of follow-up [6][7]. In a large prospective and multicenter case control study which included a total of 1128 patients, intra-articular SVF injection was performed in patients with grade 2 to 4 osteoarthritis of large weight bearing joints (knee and hip) or other joints (shoulder, elbow, wrist, ankle and foot). Patient-reported symptoms were improved in 91% of patients 12 months after SVF cell therapy [8]. In a phase I/II clinical trial, intra-articular injection of high dose (1.0×10^8 cells) precultured adipose derived stem cells in osteoarthritic knees improved joint function and pain and also led to cartilage regeneration [9].

Despite the recent popularity of the application of fat tissue in the symptomatic treatment of knee and hip osteoarthritis, its high abundance within the body and its high surgical accessibility, there are limited data regarding its use in small joint arthritis.

Thumb carpometacarpal joint (CMCJ) arthritis is the second most common location for degenerative osteoarthritis in the wrist and hand and several surgical treatments have been proposed so far, from arthrodesis to motion sparing procedures —such as trapeziectomy alone or in combination with interposition of autograft, allograft and ligamentoplasty [11][12][13]. These techniques are mainly indicated for the treatment of the late stages of the disease (stage 3 and 4 according to Eaton classification) [14].

However, there is a great variety in surgeons' preferences and none of the available techniques show superiority over another [15]. Consequently, a less invasive procedure that could provide symptomatic relief or postpone surgery seems desirable.

2. Adipose Cell-Based Therapies for the Treatment of Thumb Carpometacarpal Joint Osteoarthritis

Despite the heterogeneity of patients among different studies, such as including patients with different stages of osteoarthritis (from stage I to stage IV), intra-articular injection of fat resulted in reduction in pain with subsequent

improvement in hand function, as reported by DASH and MHQ scores during a variable period of follow-up (from three months to two years). In terms of grip and pinch strength, the results were conflicting and ranged from no change to significant improvement. More specifically, in three studies no improvement in pinch and/or grip strength was reported [16][17][18]. In another trial, the grip strength was only subjectively evaluated before and after fat injection and objective measurement of grip strength with dynamometer was performed only postoperatively [17]. Therefore, direct comparison was not performed and the overall benefit could not be estimated. In general, all published studies proved the safety of fat grafting and the absence of major complications. Moreover, and when compared to resection arthroplasty, the technique was associated with a shorter operating time [19].

The fat processing technique, which is a very important step to reduce contaminants within the lipoaspirate—such as fluid, blood cell fragments and oil–and preserve adipocytes and stem cells, has been characterized by heterogeneity among the reviewed studies. There are three main types of fat processing that involve centrifugation, gravity separation and washing [20]. It was shown that washing preserves a greater number of adipose stem cells, while centrifugation can cause damage to the adipocytes and stem cells due to centrifugal forces [21]. However, results in cell yield after each fat processing technique differ and should be interpreted with caution because they vary greatly depending on the isolation protocol and the method of quantification [22]. In the reviewed articles, centrifugation was the most common method of choice, either alone or in combination with washing [23][24][19][25]. Mechanical homogenization, which was also frequently used, is a method of tissue fragmentation that can reduce the size of fat particles up to 400–600 μm. When it is processed by sequential passes through different Luer lock sizes, it gives a product known as nanofat.

The latter is rich in regenerative stromal cells and lacks mature adipocytes, which have been ruptured due to the shear forces [26]. In the studies where the lipoaspirate was mechanically homogenized, no sufficient data were reported regarding the size of the fragmented tissue and the content of the final product in viable cells [16][17][18].

In several human studies injection of mechanically or enzymatically isolated adipose-derived cellular products into knee joints with osteoarthritis can give promising results in terms of symptomatic relief of pain and improvement in joint function [6][7][27]. However, despite numerous studies investigating the effectiveness of adipose-derived products in knee osteoarthritis, there are limited data regarding their regenerative effect and clinical application on small joint arthritis, like thumb CMCJ arthritis. In a published study by Mayoly et al. [28], a mixture of fat and platelet-rich plasma (PRP) was developed as an advanced therapy medicinal product and it was injected intra-articularly in three patients suffering from grade 4 radiocarpal arthritis. The fat was harvested with a small cannula with holes of 1 mm and it was mixed with PRP. Three months following injection and up to one year thereafter, all patients reported a decrease in pain and improvement in hand function, but no significant improvement in grip strength and wrist motion was recorded.

In the reviewed articles, a symptomatic improvement was observed in all patients following fat injection but the mechanism of action of the injected cells is unknown.

Theories include a cushioning effect, due to the interposed adipose tissue, or a regenerative potential, due to the presence of stem and other progenitor cells within the fat. For this reason, randomized controlled trials comparing fat grafting with nanofat or SVF are imperative to discover the main mechanism of action. However, a double effect cannot be excluded. Strong evidence suggests that the regenerative capacity of these cells is based on their paracrine action and their ability to secrete active biomolecules, such as cytokines and growth factors. Prantl at al. [29] studied the “secretome” capacity of these cells following mechanical processing of the lipoaspirate, such as centrifugation and homogenization, and reported no significant change in secretome composition when compared to the unprocessed fat. Through this paracrine action, adipose regenerative cells have demonstrated angiogenic, anti-inflammatory and immunomodulatory capacity and are considered as a promising treatment for osteoarthritis [30]. Recently, the interest has been focused on adipose-derived exosomes, which are extracellular vesicles secreted by adipose stem cells and contain bioactive molecules, such as proteins, microRNAs, lncRNAs and mRNAs [31]. In one study, exosomes derived from adipose stem cells were shown to downregulate inflammation and oxidative stress and mediate antisenescence effects in osteoblasts obtained from patients’ knees with severe osteoarthritis [32].

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