One-Year Outcomes of Intraarticular Fat Transplantation for Thumb Carpometacarpal Joint Osteoarthritis: Case Review of 99 Joints

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THERAPEUTIC 4

Background: This study aims to present a new therapeutic option for the treatment of thumb carpometacarpal joint osteoarthritis. Knowing that autologous fat may be beneficial for osteoarthritis through antiinflammatory and chondroprotective effects, the authors transplanted autologous adipose fat into the thumb carpometacarpal joint with the objective of postponing definite resection arthroplasty surgery.

Methods: In this pilot study, the authors performed surgery on 99 joints. The study population consisted of patients with symptomatic and radiologically confirmed osteoarthritis of the thumb carpometacarpal joint. After harvesting abdominal adipose tissue, 1 to 2 ml of fat without physical or enzymatic manipulation were transplanted into the thumb carpometacarpal joint. Surgical outcome was quantified by use of the Michigan Hand Outcomes Questionnaire in addition to strength and pain measurements during a 12-month follow-up consultation. We conducted Friedman's analysis of variance to gauge the differences over time regarding Michigan Hand Outcomes Questionnaire and pain under stress.

Results: From 2 weeks on, there was pain relief, both under stress and at rest. Friedman's analysis of variance revealed a significant change in pain under stress [chi-square (5) = 68.52; $p < 0.001$]. Postoperative Michigan Hand Outcomes Questionnaire Scores improved significantly over 12 months [chi-square (5) = 90.56; $p < 0.001$].

Conclusion: The authors' preliminary findings suggest that intraarticular autologous fat transplantation is a promising alternative treatment of carpometacarpal joint osteoarthritis of the thumb. (*Plast. Reconstr. Surg.* 145: 151, 2020.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, IV.

Osteoarthritis is a common degenerative problem encountered especially in the elderly population. Conservative therapy methods result in only temporary success. When nonoperative treatments fail, several types of surgical interventions with varying degrees of success are available. Surgical options range from denervation, through implants, to hemiresection or total resection of the trapezium with or without an arthroscopic approach.[1–5] None of the conservative methods so far results in long-term pain relief. Therefore, an interim solution is needed to reduce the pain for a longer period, to postpone definitive surgery, and to improve quality of daily life.

Our preliminary results in a comparative study comparing autologous fat grafting to cortisone injection showed promising results.[6] The hypotheses regarding success range from a simple placebo

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effect, through a cushioning effect, through scarring, to a regenerative effect of included adipose-derived stem cells. Several previous studies[7,8] have described the potential role of mesenchymal stem cells, which are currently a prime focus of research regarding regenerative medicine.[9] Studies have been conducted in both animal and human joints.[10,11] Clinical trials published in recent years[12–14] have shown pain reduction and improved function (e.g., knee osteoarthritis), with the authors reporting cartilage regeneration.[12–14] Potential risks of injecting mesenchymal stem cells into joints were invalidated by the findings of Davatchi et al.,[15] who emphasized the safety of this method in a study with a 5-year follow-up period. There were no reports of malignant transformations.

Based on the knowledge of the antiinflammatory capabilities of adipose tissue,[16–18] the main idea of this study was to harvest abdominal fat before injecting it into the destroyed joint, without prior enzymatic modification. Thus, our aim was to provide short-term clinical results of autologous fat grafting in thumb carpometacarpal joint osteoarthritis, which is a well-defined model for osteoarthritis.

PATIENTS AND METHODS

We enrolled both male and female patients with painful and radiographically confirmed osteoarthritis stage 1 to 3 according to the Eaton-Littler classification. Patients were included if they presented a visual analogue scale score under stress of at least 40 of 100 mm, pain for more than 1 year, and conservative treatments having been exhausted. Patients were excluded if they presented themselves with arthritis or prior surgery of the scaphotrapeziotrapezoid joint.

We collected sociodemographic variables and asked the patients to describe their "activity level." Level 1 is equivalent to someone who, during work, is not so much dependent on the function of the hand (e.g., teacher, telephone operator); level 2 describes someone whose works consists of 50 percent manual and 50 percent cognitive tasks (e.g., shop assistant, doctor); and level 3 refers to someone who is absolutely dependent on the function of the hand (e.g., physiotherapist, musician, cook). Furthermore, we asked the subjects which hand and whether the dominant or nondominant hand was affected.

Technique

In all patients, we have harvested the fat tissue from the abdominal region in local anesthesia using the LipiVage 200-5 single-use system (Genesis Biosystems, Lewisville, Texas). The lower abdomen was accessed through a single umbilical incision, before infiltrating approximately 50 ml of tumescent solution (1000 ml of saline solution, 1 ml of 1:200,000 adrenaline, and 600 mg of lidocaine). The adipose tissue was automatically separated from oils and fluids by an integrated filter in the syringe. The fat was mechanically homogenized with two syringes that were connected to a three-way valve (Fig. 1). Subsequently, while using a disposable 20-gauge needle and a 3-ml Luer-Lok (BD Medical, Franklin Lakes, N.J.) syringe, between 1 and 2 ml of lipoaspirate was injected into the thumb carpometacarpal joint under fluoroscopic radiographic guidance (Fig. 2). [**See Video (online)**, which shows the injection of the lipoaspirate under fluoroscopic radiographic guidance.] The operative technique used in this study has previously been described in detail by Haas et al.[6] After wound closure and application of dressings, a plaster cast was applied for 7 days. Patients received no physiotherapy, and presented themselves for follow-up examinations after 2, 6, and 12 weeks and after 6 and 12 months postoperatively.

Assessment

Preoperative and postoperative outcomes were measured by one observer using the Michigan Hand Outcomes Questionnaire, visual analogue scale (pain at rest and pain under stress), pinch strength (Pinch Gauge Dynamometer; model no. PG-30; B+L Engineering, Tuscin, Calif.), and grip strength [Jamar Dynamometer (Jamar

Fig. 1. Technique of mechanical homogenization of fat before injection.

Fig. 2. Injection of the lipoaspirate (20-gauge needle and a 3-ml Luer-Lok syringe) under fluoroscopic radiographic guidance.

Technologies, Hatfield, Pa.); and Saehan DHD-1 Digital Hand Dynamometer (Gyeongsangnam-do, Republic of Korea)]. We asked the patients about their subjective opinion of the procedure 6 months postoperatively. The possible answers when compared to the preoperative situation included "major difference," "little difference," or "no difference." The second question was whether they would recommend the operation to a friend and whether they would undergo the procedure again, independent from the result.

Our primary outcome endpoint constituted postoperative pain relief under stress. The secondary outcome was determined as the quality of daily life, measured by using the Michigan Hand Outcomes Questionnaire. In the early stages of our study, we quantified range of motion and Kapandji score.[19] However, because there was no change in the first 30 patients, we did not continue with these measurements.

Data of patients who decided not to undergo the follow-up examinations were analyzed until they quit. This included a total of six patients who were subsequently listed as "lost to follow-up," reportedly because of a lack of improvement after treatment.

Data Analysis

We performed descriptive analyses of all sociodemographic and clinical variables including pain under stress (primary outcome) and the Michigan Hand Outcomes Questionnaire score (secondary outcome). To account for missing values, we conducted multiple imputations of the primary and secondary outcome variables. Cases missing more than three of six time points in the two respective outcome variables were excluded from imputation and further analyses. We imputed five times using linear and logistic regression models.

To analyze change over time in pain under stress and the Michigan Hand Outcomes Questionnaire score, we performed Friedman's analysis of variance. To prevent inflation of the alpha level when performing two Friedman's analyses of variance, the level of significance was set at $p < 0.025$ instead of $p < 0.05$ (Bonferroni correction).

We conducted Dunn-Bonferroni post hoc tests to track significant changes. All analyses were carried out using IBM SPSS Version 25 (IBM Corp., Armonk, N.Y.).

Ethical Approval

The study was performed according to the principles of the Declaration of Helsinki 1996. All relevant study materials were approved by the ethics committee of the Ludwig-Maximilians-Universität München, Germany (reference number 81-14).

RESULTS

Objective Findings

Descriptive analyses indicated that pinch and grip strength decreased initially and then returned to the preinjury state by 6 weeks, with no change at 12 months.

Subjective Findings

We operated on 89 patients with symptomatically and radiographically diagnosed thumb carpometacarpal osteoarthritic joints from January of 2014 to August of 2016. Ten of the included subjects underwent bilateral procedures—seven of them in a single operation—resulting in a total of 99 treated thumb carpometacarpal joints, of whom we have full data on 57. The mean age was 61 ± 9.7 years (range, 21 to 79 years). There were 69 women (69.7 percent) and 30 men (30.3 percent). The demographics of the patient cohort are listed in Table 1. Clinical variables over the course of time are given in Table 2 and plotted in Figures 3 through 5. It must be noted that the sample sizes varied at the different time points (Figs. 3 through 5).

Nineteen cases had more than three missing baseline or follow-up values for pain under stress,

Table 1. Sociodemographic Variables and Baseline Clinical Information

Characteristic	No. (%)
Gender	99*
Male	30 (30.3)
Female	69 (69.7)
Handedness	90*
Both	5 (5.6)
Left	4 (4.4)
Right	81 (90.0)
Operated side	99*
Left	57 (57.6)
Right	42 (42.4)
Affected hand	90*
Nondominant	48 (53.3)
Dominant	42 (46.7)
Activity level	57*
Low	3 (5.3)
Moderate	27 (47.4)
High	27 (47.4)
Eaton-Littler classification	93*
1	8 (8.6)
2	27 (29.0)
3	58 (62.4)

*No. of valid cases.

and 25 cases had more than three missing values for the Michigan Hand Outcomes Questionnaire score. These cases were excluded from analysis with Friedman's analysis of variance, resulting in $n = 80$ for the primary outcome and $n = 74$ for the secondary outcome.

Friedman's analysis of variance revealed a significant change in pain under stress [chi-square (5) = 668.52; $p < 0.001$] in addition to the Michigan Hand Outcomes Questionnaire score [chi-square (5) = 690.56; $p < 0.001$] over time. Post hoc tests revealed that pain under stress at 2 and 6 weeks and at 3, 6, and 12 months was significantly lower than at baseline ($p < 0.001$ for all comparisons). Similarly, compared to baseline, Michigan Hand Outcomes Questionnaire scores were significantly higher at 6 weeks ($p < 0.01$), 3 months ($p < 0.001$), 6 months ($p < 0.001$), and 12 months ($p < 0.001$), indicating improvement. Compared to 2 weeks, there was significant improvement ($p < 0.001$) of Michigan Hand Outcomes Questionnaire scores at 3, 6, and 12 months.

Ten patients received bilateral treatment, with the respective joints being included in our results. The individual results of these cases were as follows: four patients reported major improvement of both hands, another four of them noticed no difference after treatment, and two patients reported pain reduction in only one of the joints.

Subjective Patient Evaluation

In addition, we asked the patients about their subjective opinion regarding the difference when comparing their preoperative and postoperative situation. Sixty-one percent answered that they felt a major difference after 6 months, 12 percent felt a little difference, and 27 percent felt no difference ($n = 56$). Regarding the question of whether they would undergo the same treatment procedure again, 73 percent answered affirmatively, whereas 51 (84 percent) answered that they would recommend this new therapeutic option to a friend.

Side Effects

No severe side effects were observed. One hematoma after liposuction occurred. One patient suffered from extreme pain and subsequently received intravenous analgesics and stayed in the hospital for 3 days. After discharge, the pain was treated with oral medication and stopped 3 weeks postoperatively. In this case, no swelling, no local infection, and no laboratory-chemical infection were observed. So far, two of the included patients (2 percent) needed further surgery before follow-up examination could be conducted.

DISCUSSION

Our results show that this therapy option has a significant effect regarding improvement of pain and quality of life. Furthermore, the results are comparable to those of the few clinical studies that were recently published regarding the same topic, which all show a positive influence of autologous

Table 2. Clinical Variables over the Course of Time

	Preoperatively		2 Wk		6 Wk		3 Mo		6 Mo		12 Mo	
	Valid No.	Mean ± SD	Valid No.	Mean ± SD	Valid No.	Mean ± SD	Valid No.	Mean ± SD	Valid No.	Mean ± SD	Valid No.	Mean ± SD
Pain under stress*	97	66.1 ± 18.1	74	49.1 ± 21.7	61	48.5 ± 23.8	57	42.5 ± 24.5	47	40.0 ± 24.3	57	37.0 ± 23.7
Pain at rest*	98	20.8 ± 20.0	75	8.4 ± 16.1	62	12.1 ± 20.7	58	7.4 ± 14.0	48	8.3 ± 15.5	57	8.4 ± 17.8
Pinchmeter score†	80	5.6 ± 2.0	68	4.8 ± 2.0	57	5.0 ± 1.9	55	5.3 ± 2.0	44	5.3 ± 1.7	40	5.8 ± 1.8
Dynamometer score†	91	25.8 ± 10.7	71	23.1 ± 10.3	60	23.3 ± 9.4	56	24.9 ± 9.1	44	24.5 ± 9.0	40	25.8 ± 7.4
MHQ score†	72	56.6 ± 15.4	70	56.5 ± 18.3	63	62.9 ± 18.0	58	70.3 ± 17.9	46	72.9 ± 17.3	49	72.9 ± 17.6

MHQ, Michigan Hand Outcomes Questionnaire.
*Lower means indicate lower pain.
†Higher means indicate better scores; scores of the operated side.

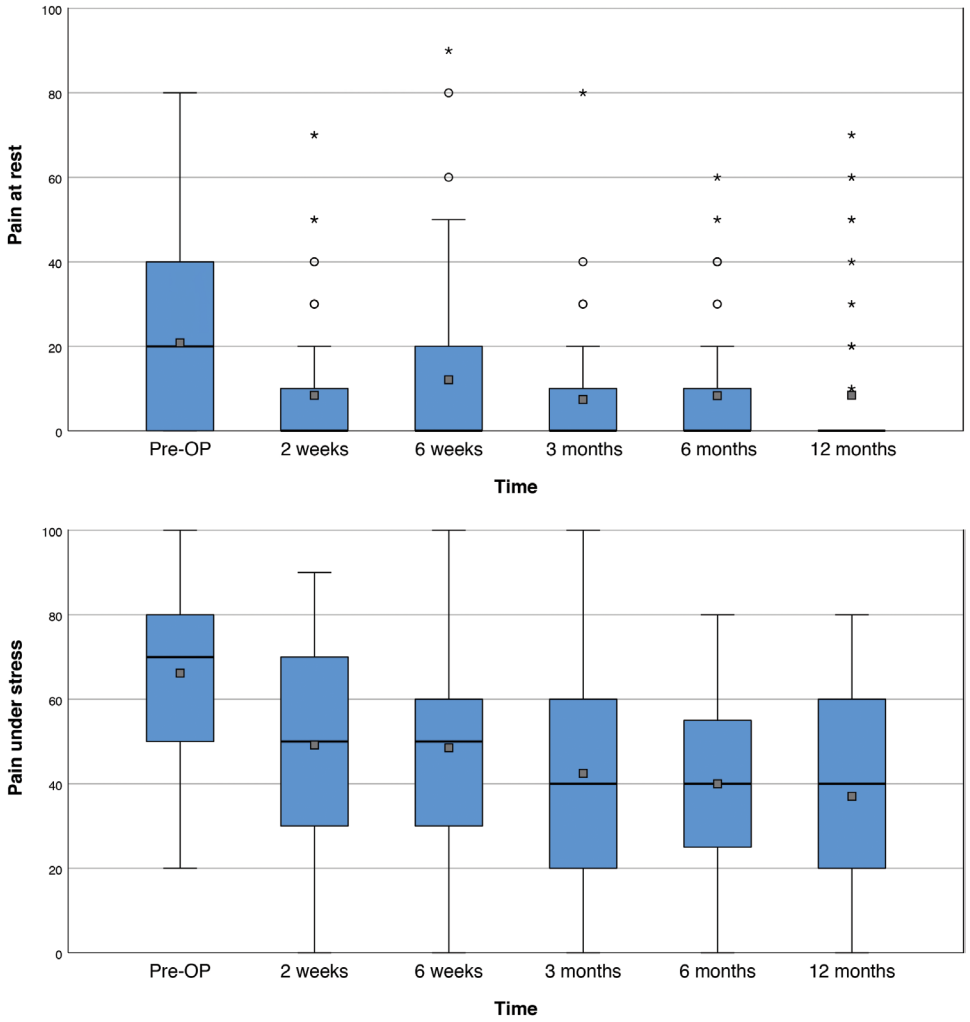

Fig. 3. Box plots of (*above*) pain at rest and (*below*) pain under stress (visual analogue scale values in millimeters) per follow-up (valid number). Lower values indicate lower pain. *Squares* represent mean values.

fat transplantation into the thumb carpometacarpal joint.

In a first pilot study in 2014, Herold et al. described an improvement of pain after 3 months following autologous fat transplantation in the thumb carpometacarpal joint.[20] In 2017, the same authors published their follow-up results for 50 patients while observing a significant pain reduction of 53 mm on the visual analogue scale (under stress) 12 months after the intervention. In contrast to our results, Herold et al. have seen better results, especially in the early stage of osteoarthritis (Eaton-Littler stage 2).[21]

Erne et al. compared the clinical results of Lundborg arthroplasty with the sole use of fat injection. They compared two completely different procedures that have the same goal: to reduce pain in everyday life.[22] The authors concluded that after 1 year, both interventions showed a significant ($p < 0.05$) comparable pain level (resection group, 10 of 100 mm visual analogue scale score; fat group, 29 of 100 mm visual analogue scale score). A similar outcome regarding pain was validated by an almost equal Disabilities of the Arm, Shoulder and Hand outcome measure in both groups. Although group sizes were rather small (12 patients versus nine patients), there was a significant advantage of the fat injection intervention in terms of shorter time to return to work after surgery.

In a recent pilot study published from Haas et al., a comparison between autologous fat and corticosteroid injection was performed with follow-up examinations performed for 3 months after injection.[6] These findings also showed a significant advantage in the group with autologous fat

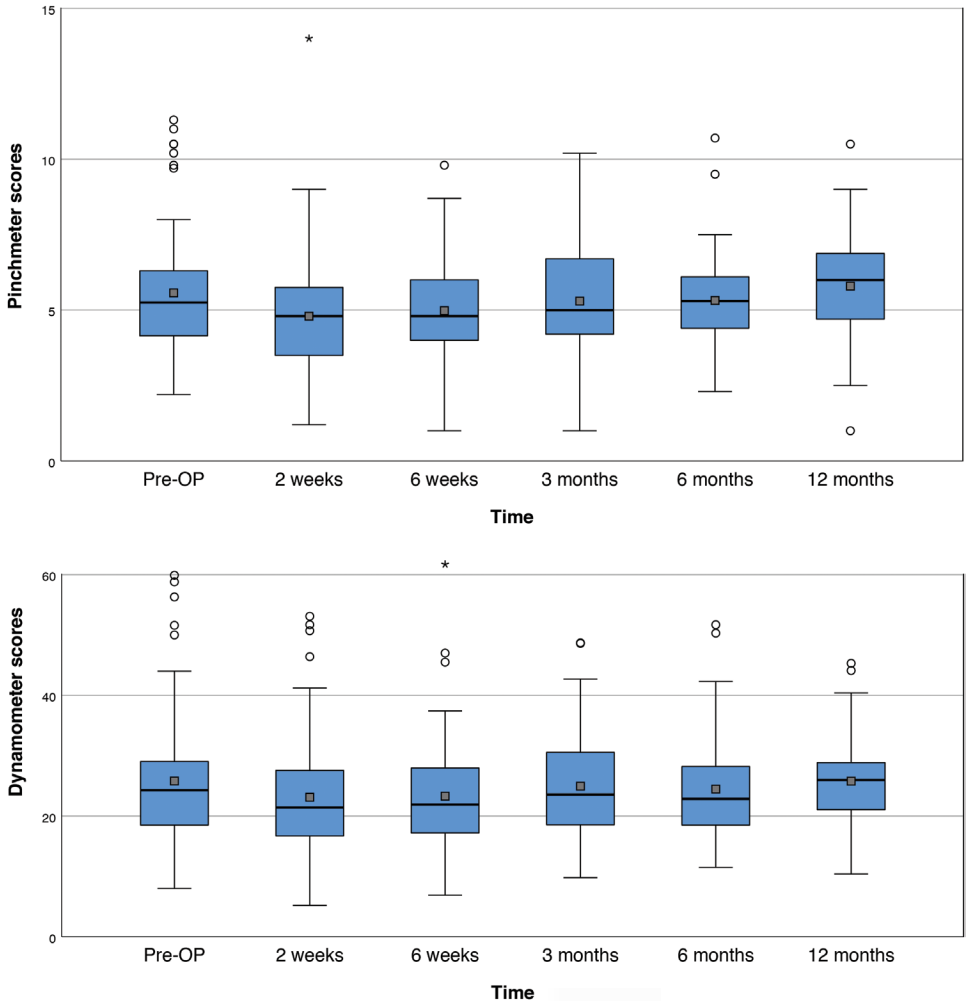

Fig. 4. Box plots of (*above*) Pinchmeter and (b) Jamar Dynamometer scores in kilograms per follow-up (valid number). Higher values indicate better scores. *Squares* represent mean values.

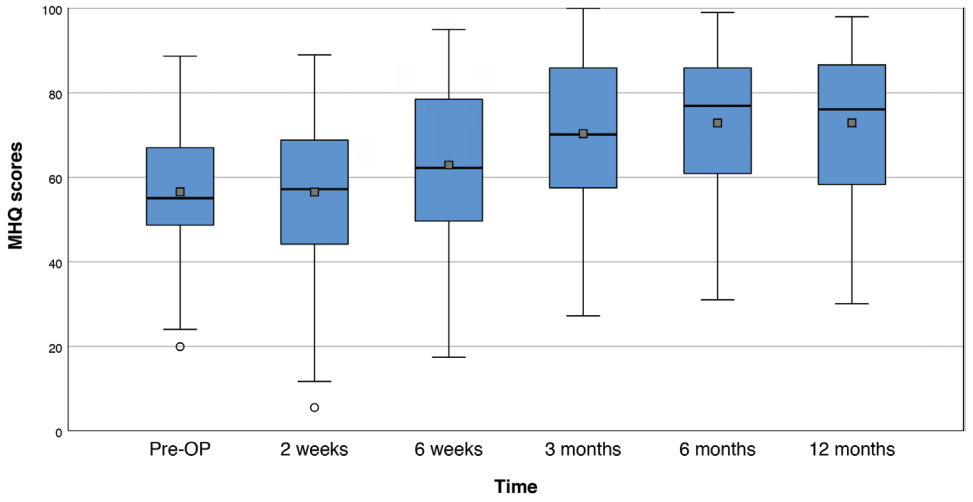

Fig. 5. Box plots of Michigan Hand Outcomes Questionnaire scores per follow-up (valid number). Higher values indicate better scores. *Squares* represent mean values.

transplantation compared to cortisone injection in terms of reduction of pain at rest and under stress. Visual analogue scale score for pain at rest was reduced by 23 mm, and that for pain under stress was reduced by 34 mm in the group receiving fat injections. These results were statistically significant when compared with pretherapy values (visual analogue scale score for rest, $p = 0.007$; visual analogue scale score for stress, $p = 0.001$). Furthermore, the results showed a significant improvement of quality of life and function as measured by the Disabilities of the Arm, Shoulder and Hand outcome measure and the Michigan Hand Outcomes Questionnaire in the autologous fat transplantation group. This positive effect indicates a prolonged reduction in pain in everyday life, compared with a single cortisone injection.

Schomacher concludes that if patients had at baseline a pain level of at least 40 of 100 mm on the visual analogue scale, an improvement of at least 20 of 100 could be considered clinically relevant.[23] Our descriptive results implied a reduction of pain under stress of 29 mm on average, starting with 66 mm at the baseline. Thus, the results are significant and clinically relevant. At lower initial values of resting pain, as in this study, a reduction of 10 mm is already clinically relevant according to Haas et al.[24] Our descriptive analyses revealed an average reduction of pain at rest of 13 mm on the visual analogue scale comparing preoperative (21 mm) and 12-month postoperative (8 mm) results.

Our findings indicate a positive therapeutic effect of the transplantation of autologous fat into thumb carpometacarpal joints with degenerative osteoarthritis. The questionnaires confirmed a significant improvement ($p < 0.001$). The greatest benefit for the patient was the pain relief both at rest and under stress. We found a significant reduction in pain under stress. We analyzed pain and quality of life at different time points after the intervention. The significance was given from the first follow-up examination after 2 weeks ($p < 0.001$) and showed the same significance after 1 year, except for the 6-week follow-up. The significantly improved results that support the success of the treatment are all subjective outcome parameters. None of the diagnostic and thus objective parameters (grip and pinch force, range of motion) showed any change. Erne et al. also described no radiologically observed change after 1-year follow-up, although there was a significant reduction of pain.[22]

Sixty-one percent of the patients felt a "major difference" after 6 months after treatment compared with their preoperative situation. Moreover, a high willingness to recommend the therapy to others suggests that the procedure is not associated with pain or discomfort for the patients. Furthermore, these patients' perceptions underline the promising statistically significant results measured with the method outlined above.

However, the underlying mechanisms for the clinical success are still not fully understood and require further research. We can only hypothesize regarding the reasons for pain relief, because it was not possible to analyze the joints histologically after the procedure.

There are a lot of potential hypotheses for the therapeutic effect. One aspect could be that the transplanted autologous fat tissue acts as a filling material and thus has a kind of buffer or cushioning function or a gliding effect during movement. A further possible hypothesis could be that adipose-derived stem cells that are included in the lipoaspirate[7] mediate regenerative processes. Stem cells can be immunomodulatory and reduce inflammatory reactions.[16–18] It has also been shown in clinical and experimental studies that human stem cells are used for the regeneration of tissue, even from adipose tissue. After injection of these cells into a target tissue, it has been hypothesized that these cells will undergo tissue-specific differentiation into local cells. Studies have analyzed further capabilities of adipose-derived stem cells and also describe a chondroprotective effect with the possibility of regeneration of the arthritic chondrocytes.[13] The possibility of differentiation of stem cells into chondrocytes is well known, but currently no method is available to verify the potential reparation process driven by stem cell–derived chondrocytes.[17,25,26]

The transplantation of autologous fat may also have a reparative function. Bosetti et al. have analyzed in vitro the effect of autologous fat and cartilage. They showed that cultured clusters of lipoaspirate induced a spontaneous outgrowth of cells with the typical differentiation potential, which was then shown to repopulate fragments of damaged cartilage.[27] It may not be only the cartilage that is of importance. Synovitis causes pain, and 50 percent of patients with osteoarthritis have synovitis,[28] whereas it is also known that synovitis aggravates osteoarthritis.[29] Synovitis exhibits the following pathognomonic findings: proinflammatory cytokines, such as interleukin-1β and tumor necrosis factor-α, which are released by activated macrophages of the synovia.[30,31] There are a lot of in vitro studies currently ongoing that are investigating the influence of

antiinflammatory cytokines on osteoarthritis.[32] Therefore, a possible explanation for the positive effect of the fat transplantation may also be the release of cytokines that subsequently reduce the degree of arthritis because of an immunosuppressive effect. However, a regenerative effect mediated by adipose-derived stem cells is also possible but not proven.

Limitations

This study has some limitations. For example, the study was not designed as a randomized controlled trial and was not blinded. Thus, we cannot measure the magnitude of a placebo effect. However, the long-lasting pain relief over 12 months suggests minimal impact. Nevertheless, the results of our pilot study open up a new promising alternative treatment option that needs further investigation in a larger randomized controlled trial and a longer follow-up. As the first carpometacarpal joint is a useful model for osteoarthritis research, our promising results could possibly be transferred to other human arthritic joints.

CONCLUSIONS

The findings of our study showed that autologous fat grafting is a safe procedure and provided appreciable benefit in 61 percent of studied cases 12 months postoperatively. It does not preclude the necessity of subsequent and more invasive surgery such as trapeziectomy, but may allow some patients to avoid such a course of action. However, data collected over a longer period are needed to establish the method's role in the treatment of thumb carpometacarpal joint osteoarthritis, and further research is essential to better understand the treatment effect.

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