The Use of an Acellular Collagen Matrix ChondroFiller® Liquid for Trapeziometacarpal Osteoarthritis

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Received: 07-February-2023; Manuscript No jahs-23-88862; **Editor assigned**: 18- February -2023, Pre QC No. jahs-23-88862 (PQ); **Reviewed**: -25-February -2023, QC No jahs-23-88862 ; (Q); **Revised:** 27-February-2023, Manuscript No. jahs-23-88862 (R); **Published:** 28-February-2023, doi: 2684-124X .2023.12. (1).10001.

Abstract

Rhizoarthrosis is a disabling disease of the hand that causes pain, stiffness and weakness of the thumb, resulting in impaired function and strength of the hand. Non-surgical treatment mostly consists of activity modifications, NSAID intake, splinting and corticosteroid intrarticular injections. After the failure of conservative treatment, various surgical options exist.

The acellular matrix ChondroFiller Liquid® is a resorbable filler based on type I collagen and a neutralizing solution, used to form a protective layer around the cartilage defect while stimulating the growth of chondrocytes and the consequent induction of cartilage regeneration.

Our study was aimed at the infiltration of ChondroFiller Liquid® on 43 patients, divided in two cohorts according to the Eaton-Littler classification (group A stage 1-2; group B stage 3-4). The objectives of the study were: evaluation of any adverse events; assessment of the Numeric Rate Scale (NRS); possible improvement of the grip strength evaluated with Jamar test and pinch test; possible improvement of the Disability of the Arm, Shoulder and Hand questionnaire (DASH score); evaluation of any modification of the cartilage component analyzed by serial MRI studies. The patients were assessed on an outpatient basis and recruited according to the inclusion criteria with x-ray and, only for group A, also with MRI. All patients were clinically evaluated with the Jamar test, Pinch test, NRS and DASH score. Subsequently, a single infiltration of ChondroFiller Liquid® under fluoroscopic guidance was performed, followed by a clinical re-evaluation 30 days after infiltration with the administration of DASH score and NRS. At 6 months all the patients were re-evaluated with Jamar test, Pinch test, NRS, DASH score and only the patients of group A underwent further MRI. The results of the study show that there was an improvement in pain symptoms, associated with an increase in force in the pincer and grip movements evaluated with clinical tests. MRI imaging showed a change in the joint profile in patients subjected to infiltration, in some patients with reduction of bone oedema and periarticular effusion. With this case, we wanted to emphasize that despite the developing technology, physical examination and clinical history are still the basic and low-cost diagnostic methods.

Keywords: Rizarthrosis ● Osteoarthritis ● Thumb ● Carpometacarpal ●Regenarative ● Joint Infiltration ● Cartilage

Introduction

Osteoarthritis of trapezius-metacarpal joint (TMJ), also called Rhizarthrosis, is a degenerative joint disease of the hand which affects the articulation between I metacarpal bone and trapezium. It is the second most common degenerative disease of the hand in term of frequency, after the distal interphalangeal joint osteoarthritis [1]. Its frequency rises markedly with age: its prevalence reaches around 30% in postmenopausal women [2] up to 91% of prevalence in patients over 80 [3]. The exact causes of the higher prevalence among women than men are not completely clear: anatomical, heritable, hormonal (major ligament laxity) factors are suspected [4].

Nevertheless, only in the minority of the patients this condition evolves in symptomatic disease determining pain, swelling, loss of function, with a considerable impact on the quality of life in final stages [5]. According to the European League Against Rheumatism (EULAR), the first approach is conservative at the beginning of the symptomatology, including physiotherapy, NSAIDs, ultrasounds, use of a brace during the activities stressing the joint. Therefore, it is common to provide early individualized treatment based on the patient's clinic [6]. If pain persists after this treatment and radiological findings progresses, infiltration therapy with Hyaluronic Acid (HA) or Corticosteroids can be considered, even if the efficacy of this kind of treatment is still under debate [7]. Some authors support the superiority of HA than corticosteroids in term of pain release and benefit duration [8], especially in the early stage of the disease [9]. On the other hand, corticosteroid intraarticular injection may result in short term relief of symptoms reducing inflammatory reaction [10].

If conservative treatment was not effective, in case of advanced osteoarthritis in symptomatic patients, a surgical procedure can be considered. Many surgical techniques have been developed, including: trapeziectomy with or without ligament reconstruction and tendon interposition (LRTI), trapezius-metacarpal arthrodesis, arthroplasty, arthroscopic debridement (TMA) [11].

Regarding the surgical technique to choose, there is no superiority over each other in terms of function improvement, pain relief, range of motion increase [12].

The most commonly used radiographic classification system for TMJ osteoarthritis was proposed in 1973 by Richard Eaton and William Littler [13]. This classification needs an antero-posterior radiography and lateral radiograph of the TMJ of the thumb with the sesamoid bones superimposed on one another but not always is preformed correctly [14]. The Eaton-Littler classification divides radiological findings in four stages: stage I with normal radiographical findings but patients syntomatic in TMJ stressing activities; stage II characterized by joint space narrowing with less than 2mm osteophites and at least 1/3 carpal-metacarpal joint subluxation; stage III with a marked reduction of joint space, a subluxation of the joint greater than 1/3 and osteophites greater than 2mm (the scapho-trapezial joint is not involved in this stage); stage IV with deterioration of TMJ, subluxation involving the scapho-trapezial joint with sclerotic morphological changes and joint space narrowing.

ChondroFiller Liquid® (Meidrix biomedicals GmbH®, Esslingen, Germany) is a cell free 2 component collagen type I solution. It is characterized by the potential to induce the creation of a protective layer on cartilage defect and to stimulate its regeneration. It is isolated by acid extraction from rat tail tendons subjected to rigorous veterinary supervision. ChondroFiller Liquid® assumes its final form once applied in situ, beginning the gelling process that causes the collagen-based solution to consolidate within the defect. As shown in animal studies, due to the biological properties of the implant, chondrocytes from the surrounding tissue have the opportunity to grow in the gel, where they synthesize collagen type two. Currently, ChondroFiller Liquid® is used in knee, shoulder, hip ad ankle joint with a cartilage defect lesser than 3 cm^2.

The purpose of our study was to evaluate the treatment of cartilage lesion in the TMJ using a cell free matrix hydrogel, i.e. ChondroFiller Liquid® by a percutaneous intraarticular infiltration.

Methods

Our study involved 43 patients who were voluntarily enrolled during an initial outpatient clinical evaluation during the period June-September 2021 (time 0 -T0). All patients were adults with unilateral or bilateral Eaton-Littler-classified rhizarthrosis diagnosed on radiographs taken in the last year. The criterion of laterality or dominance of the limb to be treated for enrolment was not considered binding and participation in the study required the signature of an informed consent. Patients were stratified into two groups (A and B) according to Eaton-Littler: group A included patients with grade 1 and 2 rhizarthrosis; group B those with grade 3-4 rhizarthrosis. The exclusion criteria were as follows: patients who have undergone cortisone and/or hyaluronic acid infiltrations in the last 6 months; patients with traumatic outcomes involving TMJ; history of rheumatological pathologies; under 18 years old; current pregnancy; patients with metabolic disorders (e.g. diabetes). The main assumption defined for the participants in the study was the non-exclusion, in case of therapeutic failure found at the evaluation carried out 6 months after the. infiltration of ChondroFiller Liquid®, of a possible subsequent surgical intervention. The study abandonment criteria were defined with the withdrawal of informed consent.

The objectives of the study were defined as follows: evaluation of any adverse events related to the infiltrative treatment with ChondroFiller Liquid®, such as an allergic reaction to the product or a post-injection infection (e.g., septic arthritis); evaluation of a possible reduction of pain in the treated subjects defined by the Numeric Rating Scale (NRS) [15]; evaluation of a possible improvement in grip strength (detectable by Jamar test and Pinch tests) [16,17] and in the ability to carry out daily activities, detectable by administering the Disability of the Arm, Shoulder and Hand questionnaire (DASH score) [18]; evaluation of the TMJ in patients belonging to group A, by comparing an Magnetic Resonance Imaging (MRI) performed at the time of enrollment and one 6 months after surgery (patients with initial and intermediate degrees of rhizarthrosis).

All patients enrolled for the study underwent ChondroFiller Liquid® injection in operating sessions of 10-12 patients each in the period October 2021-January 2022 (time 1 – T1). In the same session before the infiltration, the Jamar test and the three Pinch tests (key grip, bi-digital grip, three-point grip) were performed, the subjective pain was defined according to the NRS and the investigation questionnaire of the DASH score was administered. The infiltration was performed in an outpatient operating room in a sterile environment. No local anaesthesia was administered in order to not potentially interfere with the active effect of the product, the procedure was comparable to a classic intra-articular infiltration. The infiltration was performed by the same operator under constant fluoroscopic control and subsequently a dressing was made with a fiberglass palm to thumb brace, modelling on the anatomy of the patient's hand. The position brace was removed on an outpatient basis after three weeks.

Subsequently, a follow-up visit was performed 30 days after the infiltration procedure (time 2 - T2), with further assessment of joint pain by means of new administration of the DASH and NRS questionnaire and detection of any occurrence of adverse events. 6 months after the infiltration, all the patients were re-evaluated on an outpatient basis (time 3 - T3): the Jamar Test and Pinch tests were performed again; NRS and DASH scores were assessed for all patients; for patients belonging to group A, a second MRI was performed to identify any TMJ alterations. The results of the MRI comparison were analyzed by attributing dichotomous variables to five different items: morphological progression of the osteoarthritic alterations; decrease in signal intensity in the STIR sequence (indicator of bone edema); reduction of joint effusion; overall radiological progression of degeneration; general radiological improvement. Pre- and post-treatment MRI analysis was conducted by the same expert radiologist to minimize inter-individual variability.

Statistical Analysis

All demographic and clinical data of the analyzed cohort were summarized using descriptive statistical methods. In particular, the mean values and standard deviations were used for the symmetrically distributed continuous variables, the median and the interquartile range for the asymmetrically distributed continuous variables, and the frequency distributions for the categorical variables.

The absolute and relative frequencies of treatment-related adverse events recorded during the study period were calculated.

Pre/post-treatment differences in grip strength were assessed separately in the two study groups using Student's t-test directly for paired data or after log transformation if a non-normal distribution was present. Differences between pain scores and ability to carry out activities of daily living measured at visits 1, 2, and 3 were assessed separately in the two study groups using the nonparametric Friedman's test. The homogeneity of the values detected in the tests of strength, NRS and DASH-score in the two groups was studied by applying the t-test for independent samples if homoskedastic variables or the non-parametric Mann-Whitney test if heteroskedastic variables.

On the subjects belonging to group A, the percentages of difference in the pre- and post-treatment MRIs relating to the five items analysed, were qualitatively calculated. These data, being dummy variables, only inform of this difference without any further indicative score. To test the association of this information, Fisher's exact test was used (given the small number it was not possible to use the Chi-squared test) for each of the 10 combinations. Finally, multivariate linear regression models were tested for each clinical outcome measure at 6 months (T3), considering gender, age in years and the degree of rhizarthrosis as predictors. In particular, two new dummy variables for stages II and III were constructed in the model, with stage I as the level of comparison.

When appropriate, results were presented with their respective 95% confidence intervals. All statistical tests were performed considering a significance level of 5%.

Result

No adverse events were detected during the surgical procedure which was well tolerated for all patients and conducted without local anesthesia. The amount of infiltrated filler was approximately 0.6-0.8 ml, depending on the pain feedback expressed by the patient. During the procedure, an enlargement of the joint space of the TMJ was detected radiographically in all patients.

No local alteration was detected, no patient developed signs or symptoms of local superinfection at the site of infiltration.

Periodic outpatient evaluations were performed according to the study protocol by the same operator, measuring the NRS, the DASH-score and evaluating joint function with strength tests. MR imaging checks were performed as per protocol by all patients except one who did not show up for follow-up.

The data extracted from the questionnaires and strength tests were summarized in a digital database. A second database was created to collect data detected during radiological examinations. All the results were noted on the patient's medical record, filed at the Hand Surgery Unit, University Hospital of Verona - Italy.

The study population consisted of patients with grade I (4.65%), II (48.84%) and III (46.51%) rhizarthrosis sec. Eaton-Littler. Laterality was distributed as follows: 37.21% right hand; 62.79 left hand. Group A consisted of 22 patients (51.16%) and group B of 21 patients (48.84%).

The results of the observations conducted on the NRS, DASH score, Jamar and Pinch tests are summarized in Table 1

Table 1. Values found in outpatient evaluations with mean, standard deviation and extremes. In particular, the lines highlighted in grey refer to non-normally distributed variables, for which the medians and interquartile differences have been considered (95% confidence interval).

Variable	Mean/Median	Stdandard Deviation / Interquartile Difference	Min	Max
NRS	4.56	2.89	0	10
DASH score	74.43	22.38	34	130
JAMAR	18.72	9.62	2	49
PINCH – key grip	3	3	2.5	4
PINCH – bi-digital grip	1.5	1.5	1	2
PINCH – three-point grip	2.97	1.71	0.5	6
NRS	4.16	2.94	0	10
DASH score	75.5	25.44	31	138
NRS	1.5	3	1	2.86
DASH score	59.5	43	47.29	76.86
JAMAR	20	9	18	22
PINCH – key grip	4.08	2	1	10
PINCH – bi-digital grip	2.63	1.47	0.5	5
PINCH – three-point grip	3.83	2.01	0.5	8

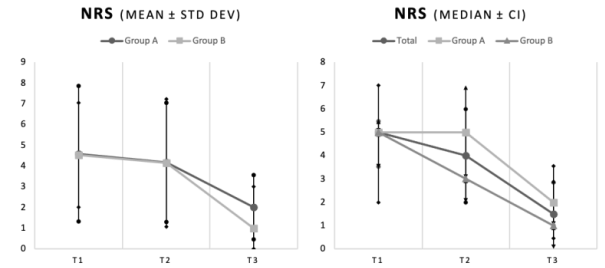

Figure 1 NRS values detected at clinical controls expressed as mean ± standard deviation and median ± confidence interval. STD DEV: standard deviation; CI: confidence interval.

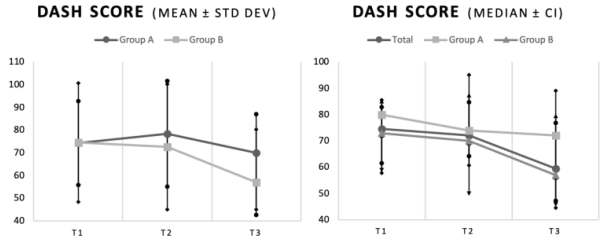

Figure 2 DASH score values detected at clinical controls expressed as mean ± standard deviation and median ± confidence interval.
STD DEV: standard deviation; CI: confidence interval

Paired tests conducted on pre- and post-treatment strength tests are summarized in Table 2.

Table 2. Paired tests conducted on pre- and post-treatment strength tests at T1 and T3. The lines highlighted in grey refer to non-normally distributed variables, therefore a logarithmic transformation (log-normal distribution) was applied. Statistically significant relationships are highlighted in bold (p-value < 0.05).

		T1		T3		T3 - T1			
		Mean / Geom. Mean	Std Dev	Mean / Geom. Mean	Std Dev	Mean / Geo Mean Ratio	Lower CI	Upper CI	p-value
JAMAR	**Total**	18.21	9.14	20.64	9.61	2.43	0.49	4.37	0.016
	A	18.33	11.05	20.14	11.13	1.81	-1.73	5.35	0.299
	B	18.1	7.02	21.14	8.06	3.05	1.1	5	0.004
PINCH - key grip	**Total**	3.46	1.93	4.08	2	0.62	0.12	1.12	0.016
	A	3.14	1.94	4.1	2.15	0.95	0.2	1.71	0.016
	B	3.79	1.91	4.07	1.9	0.29	-0.39	0.96	0.389
PINCH - bi-digital grip	**Total**	1.55		2.2		1.42	1.16	1.73	0
	A	1.73		1.86		1.08	0.84	1.39	0.54
	B	1.4		2.56		1.8	1.36	2.41	0
PINCH – three-point grip	**Total**	2.89	1.66	3.83	2.01	0.94	0.49	1.39	1.00 E-04
	A	2.69	1.77	3.52	2.16	0.83	0.27	1.39	0.006
	B	3.1	1.55	4.14	1.84	1.05	0.29	1.8	0.009

A: Group A; B: Group B; Geom. Mean: Geometric Mean; Geo Mean Ratio: Geometric Mean Ratio; Std Dev: Standard Deviation CI: 95% confidence interval

For the Jamar test variable, it was possible to apply the paired t-test since the variable is normally distributed. A statistically significant positive difference was recorded in the pre-post treatment difference both overall (p-value 0.0155) and in group B (p-value 0.0039): mean and 95% Confidence Interval (CI) of the difference between the variable at T3 and at T1 are 2.43 (0.49; 4.37) overall, 1.81 (-1.73; 5.35) in group A and 3.05 (1.1; 5) in group B. In particular, the Jamar test at T3 is overall 2.43 higher than at T1.

Similarly, for the Pinch - key grip variable, a statistically significant positive difference was recorded in the pre-post treatment difference both overall (p-value 0.0157) and in group A (0.0159): mean and 95% CI of the difference between variable a T3 and at T1 are 0.62 (0.12; 1.12) overall, 0.95 (0.20; 1.71) in group A and 0.29 (-0.39; 0.96) in group B; this variable at T3 is overall 0.62 higher than at T1.

Also for the Pinch - bi-digital grip variable, a statistically significant positive difference was recorded in the pre-post treatment difference both overall (p-value 0.0001) and in detail by groups: mean and 95% CI of the difference between the variable at T3 and at T1 are 0.94 (0.49; 1.39) overall, 0.83 (0.27; 1.39) in group A and 1.05 (0.29; 1.80) in group B: this variable at T3 is overall higher by 0.94 compared to T1.

Finally, a logarithmic transformation was performed for the Pinch - three-point grip variable because the starting variable was not normally distributed. On the transformed (log-normal distribution), it was possible to apply the t-test for paired data. Considering this distribution, the data are presented in terms of ratio of geometric means. A statistically significant positive relationship was recorded in the pre-post treatment difference both overall (p-value 0.0013) and in group B (0.0003): the geometric mean ratio at T3 and at T1 associated with the relative 95% CI was respectively 1.42 (1.16; 1.73) overall, 1.08 (0.84; 1.39) in group A and 1.80 (1.36; 2.41) in group B; this variable at T3 is overall 42% more than at T1.

Friedman's repeated measures test was applied to the NRS and DASH score values. In particular for the NRS, both overall and separately in the two groups under study, there is a statistically significant relationship between pain score and time, with a decrease during outpatient visits particularly recognizable at T3 (Figure 1). The upper confidence interval is less than the median at T2, while at T2 the values overlap with those at T1. In the comparisons made with Bonferroni's correction, a statistically significant variation between the NRS at T1 and at T3 is observed in all groups (stronger overall and in group B, weaker but still clearly significant in group A), while the relationship between the value at T2 and T3 is not statistically significant in group A (Table 3). Also for the DASH score, both overall and separately in the two groups under study, there is a statistically significant relationship between the reduction in disability and time, with a median decrease over visits and very wide confidence intervals (Figure 2). In comparisons made with Bonferroni's correction, a statistically significant change between the DASH score at T2 and at T3 was observed only overall and not separately by group (Table 3).

Table 3 Comparison between the NRS and DASH score values detected at clinical controls. Statistically significant relationships are highlighted in bold (p-value < 0.05).

Total		Group A		Group B	
Comparison	**p-value**	**Comparison**	**p-value**	**Comparison**	**p-value**
NRS1-NRS2	0.4731	NRS1-NRS2	0.8036	NRS1-NRS2	0.6072
NRS1-NRS3	**0**	NRS1-NRS3	**0.0023**	NRS1-NRS3	**0.0001**
NRS2-NRS3	**0**	NRS2-NRS3	0.1185	NRS2-NRS3	**0**
DASH1-DASH2	0.4296	DASH1-DASH2	1	DASH1-DASH2	0.2632
DASH1-DASH3	0.0385	DASH1-DASH3	0.2632	DASH1-DASH3	0.1153
DASH2-DASH3	**0.0029**	DASH2-DASH3	0.0784	DASH2-DASH3	0.0266

Furthermore, comparison tests of the data associated with the different variables were performed. These turned out to be homogeneous, with differences in distribution within the same variable that were not statistically significant. Only for the two-digital pinch test results, on the log transform, a statistically significant association was found: the geometric mean ratio between group A and group B was 0.60, with a CI of 0.41 to 0, 87 and a p-value of 0.008.

The MRIs performed at T1 and T3 were compared on patients belonging to group A (Figure 3).

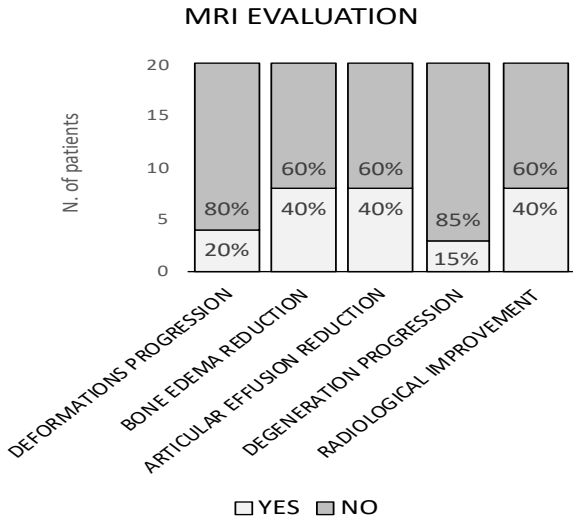

Figure 3 Comparison in patients belonging to group A of MRIs performed at T1 and T3, expressed as a dichotomous variable according to five items.

Two patients did not undergo T3 MRI and therefore were considered as dropouts. In 80% non-progression of the joint deformation was observed, in 40% reduction of bone edema, in 40% reduction of joint effusion, in 40% non-progression of joint degeneration in 85% and global radiological improvement in 40%. In particular, a statistically significant relationship was found in the following comparisons: morphological progression of the arthritic changes compared to the overall radiological progression of the degeneration (p-value 0.004); reduction of bone edema intensity compared to reduction of joint effusion (p-value <0.001); reduction in bone edema intensity compared to overall radiological improvement (p-value <0.001); reduction in joint effusion compared to overall radiological improvement (p-value <0.001).

By applying the multivariate linear regression models to the surveys carried out at T3, for the variables NRS, DASH score, Pinch test - key grip, Pinch test - bi-digital grip and Pinch test - three-point grip, no variability described by the tested models was found. Therefore, gender, age and degree of rhizarthrosis do not seem to help explain the distributions of these variables. Instead, for the Jamar test variable a statistically significant relationship is observed with the sex variable alone: females have a value 14.03 times lower than males at the control at T3.

Discussion

Our study allowed to evaluate the infiltration with ChondroFiller Liquid® in the TMJ in patients affected by rhizarthrosis at different stages. It is important to underline that several analyzed patients suffered from bilateral rhizarthrosis, often with different stage and different impact in terms of pain and limitation in daily activities. During the design phase of the study protocol it was decided to not report a comparison with the contralateral limb in order not to add a further bias. The choice of the limb to be treated was made in agreement with the patient, according to the criterion of treating the most debilitating side. The analyzed cohort was homogeneous between Group A and B, all patients completed the proposed clinical follow-up with the exception of two patients belonging to Group A who did not perform control MRI at T3. The high compliance demonstrated by the enrolled patients can be interpreted as a strong interest in improving a pathological condition with remarkable repercussions in terms of pain and functionality.

This study allowed to confirm the potential use of ChondroFiller Liquid® also in the field of small joints, expanding the classic indication as a filler in osteochondral lesions of large joints (e.g. knee, hip and ankle). The execution of the infiltrations under constant fluoroscopic control has highlighted the dilatation of the joint space secondary to the injection, even in patients with rhizarthrosis in an advanced stage. Since the procedure was performed without local anesthesia, the appearance of pain during the infiltration and therefore during the distraction of the TMJ allowed us to quantify the exact volume of filler, based on pain response.

Statistical processing showed that the cohort within the two groups considered was homogeneously distributed with respect to the variables considered, regardless of whether the patients evaluated belonged to group A or B.
The NRS data showed a significant improvement in pain. It is interesting to underline how the difference between the data detected at T1 and T2 is lower than that detected at T2 and T3. Clinical control carried out at T2 showed that several patients complained of little benefit in terms of pain, contrary to the benefit reported at T3. Probably the steric hindrance of the filler in the joint compartment narrowed by the pathology caused a tension of the capsule with the onset of pain. At the T3 control, the improvement is attributable both to the disappearance of the "capsular distraction pain" and to the mechanical decompression of the articular surfaces of the TMJ. The data relating to the DASH score showed a similar trend to that relating to the NRS, with an overall improvement statistically significant in terms of functionality. Again, no effective benefit was found at T2, probably secondary to the discomfort caused by the infiltration and the fiberglass brace placed after the procedure. However, for these two variables, the analysis of differentials between the times does not always show statistical significance (Table 3). The strongest data is the NRS for both group A and group B, while the DASH score is significant only considering the difference at T2 and T3 in the whole cohort. Probably, this evidence falls within the statistical limits of a numerically small cohort subjected to questionnaire assessments (ie the DASH score) with high intrinsic variability. Moreover, as already explained, the further bias of discomfort secondary to infiltration has been added to this. It is therefore optimal to consider the trend of these variables globally, having verified the almost homogeneity in the two distinct groups.

The data relating to the resistance tests showed a statistically significant improvement in almost all the analysed variables. In particular, the Jamar was significant both globally and in group B, while the Pinch tests were significant in all groups considered (the only exception was for the Pinch - key grip in group B). Therefore, the improvement in strength was more significant for patients with advanced osteoarthritis. This finding could be justified by the remarkable recovery observed in patients with TMJ mobility severely limited by advanced osteoarthritis, who rapidly recover over a greater range of strength than patients with minor stage osteoarthritis. It should be emphasized that a considerable variability was also found for the resistance tests, in consideration of the numerous intrinsic biases of the measuring devices. Despite this, the statistical significance assumes an even more decisive importance in describing the objective improvement following the infiltration.

The improvement in strength, pain, and function was detected to be in line with other studies evaluating corticosteroid or hyaluronic acid injection into

the TMJ [7]. However, the results we found at T3 are prospectively favorable for hypothesizing a longer duration of benefit compared to the infiltratives currently in use. Limiting ourselves to the adopted protocol follow-up, our study is not inferior to the currently adopted gold standard, with the addition of the chondrogenic potential of the infiltrated filler. ChondroFiller Liquid® could in fact gives a more regenerative contribution compared to corticosteroids or hyaluronic acid, with a benefit on the cartilage strongly damaged by the degenerative pathology. In the future, it is hoped that further studies will be conducted to confirm the long-term regenerative potential of ChondroFiller Liquid® also in the context of small joints.

With reference to the comparison between the MRI performed at T1 and that performed at T3 in the patients belonging to group A, considering the most represented variables, no progression of the deformation or joint degeneration was found. The reduction of bone edema, the reduction of joint effusion and an overall radiological improvement were not detected in most of the patients, instead found in just under half of the treated patients. This contrasts with the clinical improvement observed globally and in individual groups. Probably, a limitation of the study protocol was the timing of the MRI check: perhaps a more deferred evaluation would have shown a radiographic improvement also for these last variables. Further studies will be needed to confirm this hypothesis. In addition, the small number of patients evaluated radiographically likely further limited the finding of joint compartment improvement on MRI. The statistical analysis was limited to the evaluation of the relationship between the variables, which proved to be homogeneous in the two previously exposed trends. In the future, the implementation of a more accurate radiological descriptive protocol could constitute a decisive aspect in the statistically significant detection of the variables considered.

Finally, applying multivariate linear regression models, a statistically significant relationship was found between the Jamar variable and female sex. This data is particularly interesting: despite the intrinsic biases of our protocol, the limited number of the patient cohort and the short observation period, it was possible to detect a known correlation between TMJ osteoarthritis and the female sex, more affected by this pathology as noted above. In particular, in such patients there is a greater increase in grip strength (e.g. Jamar) than in the general population. In addition to the more advanced states, the female sex would be the ideal target for the use of ChondroFiller Liquid® in the treatment of rhizarthrosis.

Therefore, the use of ChondroFiller Liquid® to infiltrate the TMJ has the potential to improve pain symptoms, functional deficit and improve the use of the affected hand in daily activities. The direct consequence is the procrastination of the surgical approach, which can be deferred especially in the advanced stages. Indeed, in the latter, patients frequently present advanced age, an increased risk of anesthesia and sometimes a reluctance to undergo surgery. From this point of view, ChondroFiller Liquid® represents a valid alternative to slow down the course of the pathology and give relief to the patient, without precluding a subsequent surgical time.

In further studies it would therefore be interesting to evaluate a comparison with the contralateral limb, increase the period of observation and the size of the cohort, to reinforce what was detected in our study. It is not yet defined how long the treatment performed can bring benefits to the patient, as the long-term follow-up is still ongoing. Given current valuations, the benefit is likely to be long-term.

Conclusion

ChondroFiller Liquid® has proven to be a valid alternative to the surgical approach, at least to slow down the progression of painful symptoms and functional limitation. In particular, an improvement in grip strength was found especially in patients with advanced osteoarthritis of the TMJ, while pain and increased functionality were more significant in the entire cohort of treated patients. MRI provided a non-progressive assessment of osteoarthritis degeneration and joint deformation, showing a reduction of bone edema and inflammation. The clinical improvement would therefore justify a less invasive and faster recovery infiltrative approach anticipating the possible subsequent surgical approach.

Acknowledgment

All authors played a key role in the study. MC designed and directed the study, reviewed the data and supervised the drafting of the paper; FZ performed the infiltration and reviewed the data; MG, LG, EI, UL contributed to data collection at outpatient follow-up visits and to writing of the paper; VB performed the statistical elaborations; UL managed the paper's writing and publication.

Funding

ChondroFiller Liquid® prefilled syringes were kindly provided by Meidrix biomedicals GmbH®, Esslingen, Germany. No financial contributions supported this study.

Competing Interests

All authors declare that they have no conflicts of interest for this study.

Abbreviations

TMJ: trapezius-metacarpal joint
NRS: Numeric Rating Scale
DASH score: Disability of the Arm, Shoulder and Hand questionnaire
MRI: Magnetic Resonance Imaging
T1/2/3: time 1/2/3
CI: Confidence Interval

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