Osteoarthritic Changes After Superior and Inferior Joint Space Injection of Hyaluronic Acid for the Treatment of Temporomandibular Joint Osteoarthritis With Anterior Disc Displacement Without Reduction: A Cone-Beam Computed Tomographic Evaluation

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Purpose: This study compared the effect of superior and inferior joint space injections of hyaluronic acid (HA) and evaluated osteoarthritic changes in patients diagnosed with temporomandibular joint (TMJ) anterior disc displacement without reduction (ADDw/oR) in association with osteoarthritis (OA) by cone-beam computed tomography (CBCT).

Materials and Methods: One hundred forty-one patients with research diagnostic criteria for ADDw/oR in association with TMJ OA were randomly assigned to 1 of 2 study groups that received superior or inferior joint space injection of HA. CBCT and clinical examination were performed before treatment and at 3 and 9 months after treatment.

Results: One hundred twenty-six patients returned for the 3-month evaluations, and 74 returned for the 9-month evaluations. Condylar remodeling and TMJ function showed improvement in most patients after treatment. At 3 months, remodeling scores in the superior and inferior groups were 2.14 ± 3.16 and 4.08 ± 3.82, respectively, and scores were 4.80 ± 3.36 and 7.47 ± 3.90 at 9 months. There were significant differences between the superior and inferior groups at 3 and 9 months after treatment (3-month, P = .002; 9-month, P = .002). The Helkimo index of the inferior group was significantly lower than that of superior group at 3 and 9 months (3-month, P = .008; 9-month, P = .028). There were no significant differences in maximal mouth opening between the 2 groups at 3 and 9 months (3-month, P = .82; 9-month, P = .20).

Conclusion: Superior and inferior joint space injections of HA are effective methods for the treatment of ADDw/oR in association with TMJ OA. The injection of HA within the inferior joint space appears to result in better condylar reparative remodeling and improvement in jaw function.

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Osteoarthritis (OA) is a common disease of the temporomandibular joint (TMJ), characterized by articular deterioration. OA is usually associated with disc displacement, especially anterior disc displacement without reduction (ADDw/oR) in TMJ. Pain, joint noise, limited mouth opening, and jaw movement disorders are major clinical signs and symptoms. In the treatment of TMJ OA, numerous studies have described the efficacy of hyaluronic acid (HA) in superior joint space injection. However, the treatment effect was evaluated only by the improvement of function and clinical symptoms rather than by the improvement of osseous remodeling of the TMJ. Few studies on bony changes after HA treatment have been reported. Bony changes play an important role in the final diagnosis of OA and the evaluation of treatment effect. With the wide use of cone-beam computed tomography (CBCT), some researchers have evaluated osteoarthritic changes in the TMJ by CBCT.

Previously, the authors reported a method to treat disc displacement without reduction of the TMJ by superior and inferior joint space injections of HA. The purpose of this study was to observe the TMJ condylar bony changes and joint function after injection of HA into the superior and inferior joint spaces using CBCT.

**Materials and Methods**

**PATIENT SELECTION**

Diagnosis of ADDw/oR in association with OA was based on the Research Diagnostic Criteria for Temporomandibular Disorders. The inclusion criteria were subjective pain, limited mouth opening, limited mandibular movement, and radiographic evidence (including CBCT, magnetic resonance imaging, and arthrography) of OA and ADDw/oR. Patients with systematic diseases, such as rheumatoid arthritis, or other connective tissue diseases, injections of corticosteroids, or any other kind of previous treatment were excluded. One hundred forty-one patients were included in this study and randomly assigned to 1 of 2 study groups: the superior or the inferior joint space injection group. Patients underwent a cycle of 3 injections (once every 2 weeks) of HA 1 mL (Shanghai Jianhua Fine Biological Products Co, Ltd, Shanghai, China) and 2 follow-up assessments after treatment (at 3 and 9 months). The injection method has been described elsewhere. The entry point of the needle was approximately 10 mm anterior to the tragus. For the superior joint space injection, patients were asked to open the mouth widely; then, the tip of the needle was directed to the glenoid fossa anteriorly, superiorly, and medially. For the inferior joint space injection, the needle was directed to the lateral pole of the condylar head, and patients were asked to open the mouth slightly; the tip of the needle was moved to the posterior slope of the condylar head. Patients were advised to perform mouth-opening exercise every day after injection. TMJ examinations with CBCT were obtained before treatment and at 3 and 9 months after treatment and were evaluated by 2 doctors independently. All patients were informed about the research purpose and consented, and this study was approved by the ethics committee of the School and Hospital of Stomatology, Wuhan University (Wuhan, Hubei, China).

**CBCT EVALUATION**

CBCT examinations of the TMJs were performed with a NewTom VG (QR srl, Verona, Italy) device. Two doctors were instructed to evaluate all images independently without knowledge of any information about the patients. If there was any disagreement, a second evaluation was performed by another doctor without knowledge of the preceding records. In this study, the scoring system used to evaluate the degree of condylar damage was based on the radiographic assessment of CT and CBCT in the literature. The damage index included flattening, erosion, osteophytes, sclerosis, and cysts in the sagittal and coronal views.

A point rating scale (0 to 3) was used to define the severity of flattening:

- 0 none (normal)
- 1 minor (slight flattening of the contour of the condylar head)
- 2 moderate (condylar head obviously flattened with a straight profile)
- 3 severe (large part of the condylar head severely flattened)

A point rating scale (0 to 3) was used to define the severity of erosion:

- 0 none (normal)
- 1 minor (cortical bone is discontinuous)
- 2 moderate (damage extending to the upper layer of subcortical bone)
- 3 severe (damage extending to the deeper layer of subcortical bone)

A point rating scale (0 to 3) was used to define the severity of osteophyte formation:

- 0 none (normal)
- 1 minor (osteophyte <1 mm)
- 2 moderate (osteophyte 1 to 2 mm)
- 3 severe (osteophyte >2 mm)

A point rating scale (0 to 2) was used to define the severity of sclerosis:

- 0 none (normal)
- 1 minor (sclerosis in cortical layer)
2 severe (sclerosis extending throughout most of the condylar head)

A point rating scale (0 to 2) was used to define the severity of cysts:

0 none (normal)
1 minor (a small cavity below the articular surface)
2 severe (>1 large cavity below the articular surface)

The entire condylar head was observed, including sagittal and coronal views on CBCT. Changes should be confirmed in at least 2 consecutive slices to avoid misinterpretation. Scores from the sagittal and coronal views were summed, thus providing possible total scores for flattening (0 to 6), erosion (0 to 6), osteophyte (0 to 6), sclerosis (0 to 4), cyst (0 to 4). The total damage score for the condyle was evaluated by summing the scores of different damage indices in the sagittal and coronal views; thus, the total score ranged from 0 to 26.

Based on previous damage to the condyle, remodeling changes of the damaged condyle were assessed at follow-ups. Remodeling changes of the condyle included the profile of the condyle, new bone formation, dissolution of osteophytes, and decrease of sclerosis and cysts.

A point rating scale (−1 to 3) was used to define the condylar profile:

−1 worse changes (more severe condylar flattening)
0 no change
1 minor changes (profile of condylar surface slightly rounded)
2 moderate changes (condyle obviously rounded without a smooth surface)
3 best changes (rounded condylar contour with a smooth surface)

A point rating scale (−1 to 3) was used to define the formation of new bone in the condyle:

−1 worse changes (more severe erosion of the condyle)
0 no change
1 minor changes (bony defects are partly repaired, cortical bone is discontinuous)
2 moderate changes (bony defects are totally repaired and cortical bone is discontinuous)
3 best changes (bony defects are totally repaired and cortical bone is continuous)

A point rating scale (−1 to 3) was used to define the dissolution of osteophyte in the condyle:

−1 worse changes (osteophyte larger than before treatment)
0 no change
1 minor changes (one third of osteophyte dissolved)
2 moderate changes (two thirds of osteophyte dissolved)
3 best changes (osteophyte completely dissolved)

A point rating scale (−1 to 2) was used to define the decrease of sclerosis in the condyle:

−1 worse changes (more severe sclerosis in condyle)
0 no change
1 minor changes (sclerosis slightly decreased)
2 best changes (sclerosis completely absent)

A point rating scale (−1 to 2) was used to define the decrease of cysts in the condyle:

−1 worse changes (more severe cysts in condyle)
0 no change
1 minor changes (decreased number and size of cysts)
2 best changes (cysts absent)

The treatment effect was assessed by remodeling after treatment. Slices matching those examined before treatment were selected for the evaluation of radiographic changes of OA. The total remodeling score was evaluated by summing the changes in the remodeling scores of the sagittal and coronal views (range, −10 to 26). A positive score (1 to 26) suggests reparative remodeling, whereas a negative score suggests continued degenerative changes.

<table>
<thead>
<tr>
<th>Table 1. COMPARISON OF THE 2 GROUPS IN BASELINE SCORES</th>
<th>Superior (n = 73)</th>
<th>Inferior (n = 68)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (yr)</td>
<td>31.42</td>
<td>34.12</td>
<td>.31</td>
</tr>
<tr>
<td>Female/male</td>
<td>62/11</td>
<td>62/6</td>
<td>.31</td>
</tr>
<tr>
<td>Left</td>
<td>30</td>
<td>31</td>
<td>.76</td>
</tr>
<tr>
<td>Right</td>
<td>43</td>
<td>37</td>
<td>.78</td>
</tr>
<tr>
<td>Damage score*</td>
<td>5.55 ± 2.64</td>
<td>5.56 ± 2.53</td>
<td>.98</td>
</tr>
<tr>
<td>MMO*</td>
<td>31.11 ± 7.88</td>
<td>30.00 ± 6.81</td>
<td>.37</td>
</tr>
<tr>
<td>Helkimo index*</td>
<td>7.40 ± 3.09</td>
<td>7.71 ± 3.32</td>
<td>.57</td>
</tr>
</tbody>
</table>

Abbreviation: MMO, maximal mouth opening.
* Differences between 2 groups were analyzed by analysis of variance.
† Differences between 2 groups were analyzed by χ² test.


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2 moderate changes (condyle obviously rounded without a smooth surface)
3 best changes (rounded condylar contour with a smooth surface)
TMJ FUNCTION

The Helkimo clinical dysfunction index was measured and recorded, including mandibular movement, maximal mouth opening (MMO), protrusive and lateral excursion, tenderness of masticatory muscles, TMJ tenderness, and TMJ noise. Treatment was considered valid with a decrease of the Helkimo index.

STATISTICS

Difference between the 2 groups with respect to radiographic evaluation and TMJ function were statistically analyzed with repeated-measures analysis of covariance or \( \chi^2 \) test using SPSS 20 (SPSS, Inc, Chicago, IL). A \( P \) value less than .05 was considered significant for all analyses.

Results

One hundred twenty-six patients returned for the 3-month follow-up (superior group, \( n = 65 \); inferior group, \( n = 61 \)). Seventy-four patients returned for the 9-month follow-up (superior group, \( n = 44 \); inferior group, \( n = 30 \)). No important difference between the 2 groups was observed for age, gender, treated side, score of CBCT assessments, and TMJ function before treatment (Table 1).

Approximately 89.36% of patients underwent the 3-month follow-up. Reparative remodeling of the condyle was observed in 44 and 51 patients in the superior and inferior groups, respectively. Severe degenerative changes were observed in 13 and 6 patients in the superior and inferior groups, respectively. Eight patients in the superior group and 4 in the inferior group showed no change. The remodeling score was significantly higher in the inferior group (\( P = .002 \); Table 2). TMJ function showed improvement in most patients at the 3-month follow-up, with improvement of mandibular movement, pain relief, and increase of MMO. The Helkimo index was significantly lower in the inferior group (\( P = .008 \); Table 3). The post-treatment values of MMO were 37.63 ± 6.51 and 37.89 ± 5.94 mm in the superior and inferior groups, respectively; there was no significant difference between the 2 groups (\( P = .82 \)).

At the 9-month follow-up, 52.48% of patients were present. Most patients had better condylar morphology than at the 3-month follow-up. The remodeling score was significantly higher in the inferior group (\( P = .002 \); Table 2). TMJ function showed improvement in most patients at the 9-month follow-up. The Helkimo index was significantly lower in the inferior group (\( P = .028 \); Table 3). The post-treatment values of MMO were 41.48 ± 6.38 and 39.57 ± 5.84 mm in the superior and inferior groups, respectively, and there was no significant difference between the 2 groups (\( P = .20 \)).

In this study, condylar remodeling was found in most patients at follow-up, as exhibited by the following

### Table 2. CONE-BEAM COMPUTED TOMOGRAPHIC ASSESSMENT AT 3- AND 9-MONTH FOLLOW-UPS

<table>
<thead>
<tr>
<th></th>
<th>3-mo Follow-Up</th>
<th>9-mo Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Damage Score</td>
</tr>
<tr>
<td>Superior group</td>
<td>65</td>
<td>5.71 ± 2.71</td>
</tr>
<tr>
<td>Inferior group</td>
<td>61</td>
<td>5.54 ± 2.59</td>
</tr>
</tbody>
</table>

* Damage score, 0 to 26; remodeling score, −10 to 26.
† \( P = .002 \), differences between 2 groups were analyzed by analysis of variance.
‡ \( P = .002 \), differences between 2 groups were analyzed by analysis of variance.

### Table 3. HELKIMO INDEX AT 3- AND 9-MONTH FOLLOW-UPS

<table>
<thead>
<tr>
<th></th>
<th>3-mo Follow-Up</th>
<th>9-mo Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Before Treatment</td>
</tr>
<tr>
<td>Superior group</td>
<td>65</td>
<td>7.34 ± 3.18</td>
</tr>
<tr>
<td>Inferior group</td>
<td>61</td>
<td>7.46 ± 3.30</td>
</tr>
</tbody>
</table>

* \( P = .008 \), differences between 2 groups were analyzed by analysis of variance.
† \( P = .028 \), differences between 2 groups were analyzed by analysis of variance.
indices: rounded contour of the condyle (Fig 1), formation of new bone (Fig 2), osteophyte dissolution (Fig 3), decrease of sclerosis (Fig 4), and decrease of cysts (Fig 5). CBCT assessment showed a better effect of osteoarthritic changes after inferior joint space injection (Figs 6, 7). The most common radiographic changes of the condyle in this study were new bone formation and osteophyte dissolution. Many patients had partial new bone formation at the 3-month follow-up, and cortical bone formation was observed in some patients at the 9-month follow-up. Interestingly, some patients with severe degenerative changes at 3 months exhibited reparative remodeling at 9 months (Fig 8).

FIGURE 1. Profile of condyle. A, Condyle flattening was observed before inferior joint space injection. B, At 3-month follow-up, there were some reparative progressive changes in the condyle. C, At 9-month follow-up, the profile of the condyle became rounded.

FIGURE 2. New bone formation. A, Condylar erosion was observed before inferior joint space injection. B, At 3-month follow-up, partial new bone formation was observed. C, At 9-month follow-up, partial new bone formation with discontinuous cortical bone was observed.

Discussion

This study showed improvements of radiographic bony changes and TMJ function after superior and inferior joint space injection of HA at the 3- and 9-month follow-ups. The results of bony changes and the Helkimo index were considerably better in the inferior group at 3 and 9 months.

Numerous studies have evaluated the efficacy of HA injection for the treatment of TMJ OA using clinical parameters.4-6,16 Only a few studies have compared the efficacy of HA injection for TMJ OA using radiology, which visualizes bony changes in the TMJ.15 However, improvement of clinical symptoms does not completely reflect improvement of osteoarthritic

FIGURE 3. Dissolution of osteophyte. A, A severe osteophyte was observed before superior joint space injection. B, At 3-month follow-up, the osteophyte was obviously smaller. C, At 9-month follow-up, the osteophyte was completely dissolved.

FIGURE 4. Dissolution of sclerosis. A, Severe sclerosis was observed before inferior joint space injection. B, At 3-month follow-up, the sclerosis was partially dissolved.


FIGURE 5. Dissolution of cyst. A, A severe cyst was observed before superior joint space injection. B, At 3-month follow-up, the cyst was obviously dissolved.

FIGURE 6. Obvious remodeling of the condyle in a patient in the superior group. A, C, Sagittal and coronal images of the condyle before injection depict severe erosion and flattening. B, D, At 9-month follow-up, partial new bone formation with discontinuous cortical bone was observed.

FIGURE 7. Obvious remodeling of the condyle in a patient in the inferior group. A, C, Sagittal and coronal images of the condyle before injection show severe erosion and flattening. B, D, At 9-month follow-up, partial new bone formation with continuous cortical bone was observed.

changes. Roh et al\(^1\) found that the prognosis of osteoarthritic changes may be independent of clinical signs and symptoms after 1-year follow-up with CT. Palconet et al\(^{17}\) found a poor correlation among condylar changes, pain, and other clinical symptoms in TMJ OA by CBCT. Clinical and CBCT examinations were used to evaluate HA efficacy in this study.

Recently, CBCT has been considered an alternative imaging technique for the diagnosis of degenerative changes of the TMJ.\(^{11,18}\) It is widely used for its high-resolution multiplanar images and lower radiation dose. Panoramic radiography is simple and relatively inexpensive. However, poor reliability and low sensitivity for detecting osseous changes have limited its widespread use in TMJ evaluation.\(^{14}\) Magnetic resonance imaging is often used to assess the soft tissue components.\(^{14,19}\) CT has been a valuable method in the evaluation of TMJ, but the high cost and relatively high radiation dose are limitations for radiographic evaluation of the TMJ.\(^{14,20}\) Honda et al\(^{9}\) reported that CBCT and conventional CT are very reliable for evaluation of the condyle based on autopsy specimens. The diagnostic efficacy of CBCT is as good as that of conventional CT.

It has been reported that patients with ADDw/oR have a higher incidence of degenerative changes. Erosion and osteophytes are extremely common in patients with ADDw/oR and the condyle can shrink during the follow-up period.\(^{2,21}\) These findings allowed researchers to infer that OA is associated with ADDw/oR because of the long-term disorder of the relation between the disc and the condyle. HA, which is produced by synoviocytes of the joints, becomes depolymerized, resulting in a decrease in molecular weight and viscoelasticity, making the cartilage susceptible to injury.\(^{22,23}\) HA has an important role in lubrication, buffering, nutrition, anti-inflammation, and cartilage repair. Injection of exogenous HA can stimulate endogenous HA, regulate the property of the synovial fluid, form a protective barrier on the joint surface, decrease the joint friction coefficient, and decrease the risk of damage. A previous study has reported that high-molecular-weight HA (hylan G-F 20) improves cartilage integrity and
decreases osteophyte formation in experimental OA. In this study, improvements of osteoarthritic abnormalities and TMJ function were found in most patients after treatment.

Interestingly, some patients with severe degenerative changes at 3 months had reparative remodeling at 9 months. This may be because the condyle remained at the early phases of remodeling in susceptible patients 3 months after treatment. In this study, the inferior group showed better effects by improvements in the Helkimo index and remodeling score. The authors supposed that because the inferior articular space injection reaches the damaged condylar surface more directly, exogenous HA in the inferior space would cover the cartilage to protect the cartilage against proteolytic enzymes and inflammatory cells, decrease friction, and provide nutrition for chondrocytes, promoting cartilage repair. Thus, the inferior injection may produce a better effect than the superior injection. Long et al found that patients with ADDw/oR had better improvement of clinical symptoms after inferior joint space injection. A systematic review proved that inferior space injection or double space injection was more effective in treating temporomandibular disorders than superior space injection.

During the follow-ups, 15 patients were lost at 3 months and 67 were lost at 9 months. The large loss of follow-up is the main limitation of this study and reasons for the loss are complex. The HA injection may be attributable to the relief of patients’ symptoms. In addition, most patients in the authors’ hospital came from the central region of China, which is economically underdeveloped, so poor compliance and financial problems are other reasons for the loss of patients. To decrease the impact of lost patients, the damage score and the Helkimo index before treatment at different periods were calculated and no major differences were found between the 2 groups at follow-up. Multicenter research is the authors’ future goal for this kind of study.

In general, this investigation suggested that inferior joint space injection of HA is a better method to treat TMJ OA with ADDw/oR owing to the obvious radiologic changes and improvement in TMJ function.

Acknowledgments

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References