**(A Prospective controlled clinical trial comparing surgical and conservative treatment in patients with irreducible anterior displacement of the temporomandibular joint disc).**

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Abstract

To compare the effects of surgical and conservative treatment on the recovery of joint function in adult patients with anterior disc displacement without reduction (ADDMoR Remodeling of articular disc and condyle and influence of the psychological state. The project plans to include adult ADDWoR patients who need surgical and conservative treatment and divide them into a surgical and conservative treatment group. During the operation, surgical treatment and conservative treatment are used, respectively. MRI was performed at the time of initial diagnosis, 1 month, 6 months, 12 months, and 24 months after treatment; small field CBCT was performed at the time of initial diagnosis, 6 months, 12 months, and 24 months after treatment, and temporomandibular joint function assessment, bite force, masticatory efficiency, electromyography, and mental health assessment were performed at the time of initial diagnosis, 3 months, 6 months, 12 months and 24 months after treatment.

**MAIN OUTCOME MEASURES:** ① Changes in temporomandibular joint function; ② Morphological changes of the articular disc; Secondary outcome measures: ① condylar reconstruction; ② Changes in mental state.

**Keywords:** irreducible anterior displacement of temporomandibular joint disc, surgical treatment, conservative treatment, prospective controlled trial

## 1、 Research background

The incidence of temporomandibular disorders (TMD) in adults is as high as 8% - 35%. Anterior disc displacement without reduction (ADDWoR) is the main type of late TMD lesions. The main symptoms include pain in the joint area and surrounding muscle tissues and restricted mouth opening, accompanied by tinnitus, hearing loss, migraine, and other symptoms. In severe cases, there may be perforation of the joint disc, bone absorption of the condyle and other structural changes, and even dental and maxillofacial deformities; it dramatically impacts patients' quality of life.

Currently, there are many treatment methods for ADDWoR, including conservative treatment focusing on joint cavity injection, cushion closing, blending, and physiotherapy, and surgical treatment focusing on joint disc reduction and reconstruction. The evaluation of different treatment methods is helpful to explore a perfect clinical diagnosis and treatment sequence of the disease, reduce or even avoid patient illness delay and over-treatment, and also helps to achieve the goal of personalized treatment of precision medicine. However, the number of ADDWoR patients in China is enormous, and the lack of clinical diagnosis and treatment standards leads to patients cannot accept unified and standardized treatment, which increases the psychological and economic burden of patients; At the same time, the differences in treatment concepts also lead patients to delay their illness treatment and therefore, need for excessive medical treatment increasing the social responsibility. Thus, China, as a large country with ADDWoR, starts from the long-term reconstruction of the temporomandibular joint disc and condyle under different treatment modes, further explores the indications of other treatment methods for the irreducible anterior displacement of the temporomandibular joint disc, establishes the clinical diagnosis and treatment sequence of irreducible anterior displacement of the temporomandibular joint, and standardizes the clinical diagnosis and treatment procedures, which will significantly improve the pertinence and effectiveness of our clinicians in the diagnosis and treatment of this disease.

## 2． Research purpose

1. To systematically explore the effect of surgical and conservative treatment on the recovery of temporomandibular joint function in adult ADDWoR patients through a large sample prospective controlled trial;

2. To explore the influence of surgical and conservative treatment on the shape and position of the temporomandibular joint disc, the remodeling of joint disc and condyle, and the psychological state of adult ADDWoR patients, and then establish the clinical diagnosis and treatment system of ADDWoR.

## 3． Research methods

### （1） Diagnostic criteria

Patients clinically diagnosed with anterior displacement without reduction received surgical treatment (reduction and anchorage of the temporomandibular joint disc) or conservative treatment.

### （2） Case selection

1. Inclusion criteria

① Patients aged 18-45;

② Patients with MRI confirming irreducible anterior displacement of temporomandibular joint disc, along with the small field of view CBCT;

③ Patients with a history of more than 3 months, including joint pain, murmur, or abnormal mandibular movement;

④ The patient informed and agreed to be included in the study;

**2. Exclusion criteria**

① Patients who have been treated for temporomandibular joint disorders;

② Patients with infection, tumor, trauma, and other diseases;

③ Patients with jaw deformity, dentition defect, inability to form stable occlusion, and severe occlusion disorder;

④ The disc is seriously deformed and perforated, and the operation of the articular disc cannot be performed;

⑤ Patients with Immune system disease suffering from rheumatoid arthritis.

**3. Conditions for withdrawal or termination of the study**

**(1) Patient withdrawal:**

① The patient asked to withdraw from the clinical study;

② The patient cannot complete relevant examinations as required, which affects the data collector;

③ Patients privately accepted other joint treatment schemes during the trial;

④ The patient has other diseases or serious complications during the trial and needs treatment or rescue, which may affect the study plan.

**(2) Termination of the study**

① In the study, it was found that there was a major mistake in the clinical plan, and it was difficult to evaluate the therapeutic effect;

② In the process of implementation, it is difficult to assess the therapeutic effect if the research plan is found to have important deviations and then continues to be carried out;

**4. Case abscission criteria**

(1) Definition of abscission: the subjects who have filled in the informed consent form and screened for qualified entry into the trial are all abscission cases whenever and for any reason, as long as they have not completed the prescribed treatment cycle.

The causes of shedding cases may be as follows:

① The study subjects could not complete relevant examinations as required or accept other treatment schemes privately during the treatment;

② During the observation process, those who were naturally separated and lost to follow-up, including those who were successful in surgery but could not complete the whole course of treatment, so the clinical data collection was incomplete, which affected the efficacy evaluation;

③ Cases with serious adverse reactions or adverse events and complications unsuitable for clinical trial treatment are suspended from the study.

**(2) Management of shedding cases**

① When the case falls off, the researcher should contact the patient as much as possible using visiting the door, making an appointment for follow-up and calling, asking the reason for the fall off and the patient's condition, and completing the evaluation items that can be completed;

② For the cases withdrawn due to adverse reactions or complications, corresponding treatment measures should be taken according to the actual situation;

③ Relevant application data should be kept appropriately for shedding cases and on file for comprehensive analysis and statistics.

## （3） Treatment plan

This project is a prospective controlled study, including patients with ADDWoR who have received conservative and surgical treatment.

1. Treatment specification:

**(1) Norms of conservative treatment:**

① Treatment specification of sodium hyaluronate injection: upper and lower joint cavity injection. After the injection treatment, the patient is instructed to open and close the mouth to distribute the drug in the joint cavity evenly. During the treatment, the patient will be instructed to perform mouth-opening training 100 times daily and bite hard objects. Inject once every 1-2 weeks, 4-5 times in total;

② Specification for treatment of stable jaw pads: use transparent resin materials to make stable jaw pads, and the maxillary full compression line shall be covered. The jaw plane shall be kept flat. During the median occlusion, the functional tip of the mandibular teeth shall be in uniform contact with the occlusal surface of the jaw pad, and there is no crisscross relationship between the cusp and the fossa. The patient wears the occlusal plate for 24 hours and carries out re-examination and grinding every 2 to 4 weeks. After adaptation, the patient can return once a month. After the occlusion is stable, the occlusal plate is removed for 6 months.

③ Accommodation treatment specification: use red and blue occlusal paper with different thicknesses to determine occlusal interference points by allowing patients to occlude in the middle, laterally and protrusively, repeatedly confirm the interference points, finally determine occlusal interference points, adjust and grind occlusal interference points, and restore uniform and non-interference contact of the whole mouth.

**(2) Surgical treatment specification:**

The temporomandibular joint disc was operated through a small incision in front of the ear. During the operation, the anterior attachment of the joint disc was fully released, and the

disc was corrected above the condyle with anchor screws. The soft jaw pad shall be worn for 2-3 weeks immediately after the operation.

**2. Diagnosis and treatment process:**

(1) Conservative treatment group

① At the initial diagnosis, MRI and bilateral CBCT small field examination were taken to assess the temporomandibular joint function, bite force, masticatory efficiency, EMG, and mental health

② Conservative treatment (occlusive therapy or/and adjustment of the teeth or/and joint cavity injection therapy) within 1 month after diagnosis

③ MRI was performed at 1 month, 6 months, 12 months, and 24 months after treatment

④ CBCT examination of the small bilateral field was performed 6 months, 12 months, and 24 months after treatment

⑤ The temporomandibular joint function assessment, bite force, masticatory efficiency, EMG, and mental health assessment were performed at 3, 6, 12, and 24 months after treatment

**(2) Surgical treatment group**

① At the initial diagnosis, MRI and CBCT were taken for bilateral small field examination, and temporomandibular joint function assessment, bite force, masticatory efficiency, EMG, and mental health assessment were performed

② Reduction and anchorage of the temporomandibular joint disc within 2 months after diagnosis

③ MRI was performed at 1 month, 6 months, 12 months, and 24 months after the operation

④ CBCT examination of the small bilateral field was performed 6 months, 12 months, and 24 months after the operation

⑤ The temporomandibular joint function, occlusal force, masticatory efficiency, EMG, and mental health were evaluated at 3, 6, 12, and 24 months after the operation

**3. Evaluation index**

(1) Evaluation indexes of temporomandibular joint function:

The functional symptom indexes of the temporomandibular joint were evaluated before and after conservative treatment and surgical treatment:

① Mandibular movement: including mouth opening degree, mouth opening type, forward extension, and lateral movement;

② Joint murmur: including bounce and friction sound;

③ Joint area tenderness: including the lateral joint capsule, the posterior condyle area, and the condyle going backward through the external auditory canal;

④ Masticatory tenderness: overhead area, anterior part of the temporal muscle, the middle part of the temporal muscle, posterior part of the temporal muscle, anterior part of the masticatory muscle, deep part of the masticatory muscle, the lower part of the masticatory muscle, posterior part of the digastric muscle, medial pterygoid muscle, the upper part of the sternocleidomastoid muscle, the middle part of the sternocleidomastoid muscle, the lower part of the sternocleidomastoid muscle, the upper part of the trapezius muscle, the lower part of trapezius muscle;

⑤ Resting and occlusal pain: VAS scores were used for all patients. Resting pain was the joint pain when the patient was in the mandibular position; The occlusal pain was evaluated after chewing gum for 20 seconds.

**(2) Morphological analysis of articular disc:** MRI was used to reconstruct the articular disc before and after conservative treatment and surgical treatment, and the morphological changes were digitally analyzed:

① MRI examination specification: before scanning, the patient should fill in the informed consent form for scanning, and the doctor should check the patient's information; GE Signa

1.5T magnetic resonance imaging equipment, T2WI and PDWI sequences, matrix: 288 × 256, the field of vision 14cm × 12.6cm; At the time of examination, the patient was in the supine position, the midpoint of the connecting line between the two external auditory meatuses was at the center, the midsagittal plane of the face was vertical to the ground plane, and the orbital ear plane was vertical to the ground; Scan the oblique sagittal and oblique coronal positions of the left and right joint closures and the largest openings;

② **Segmentation threshold of temporomandibular joint disc:** MRI imaging DICOM data of 50 patients were obtained, the data was imported into Mimics 20.0 software, and an attending physician and a chief physician independently divided the temporomandibular joint disc (Edit Mask function). The controversial part was discussed and decided by two physicians. After 100 sides of the joint discs of 50 patients were divided, the gray value of the joint disc was measured; the average gray value of the temporomandibular joint disc is 0-235 (this work has been completed in the previous work);

③ **Reconstruction of temporomandibular joint disc:** import the patient's temporomandibular joint MRI data into 20.0 software. First, use threshold segmentation (the threshold range is 0-235) to obtain the preliminary segmentation image of the temporomandibular joint disc. Because the threshold values of the temporomandibular joint disc and the articular tubercle, fossa, and condylar bone are similar, it is necessary to further manually separate the temporomandibular joint disc from the surrounding tissues after the preliminary segmentation (Edit Mask function), Each side of the articular disc shall be divided for three times, and the results of the three times shall be compared. The final result shall be the two times with similar results. If the three times are different, the superior physician shall determine the segmentation operation through discussion. Perform the same segmentation operation on each layer of each side of the articular disc (the image of one side of the disc is>5 layers). After the segmentation operation, complete the three-dimensional reconstruction (Calculate part) based on the temporomandibular joint disc mask;

④ **Morphological analysis of temporomandibular joint condyles:** The volume, total surface area, maximum length, and maximum width were measured based on the three-dimensional model of the temporomandibular joint disc; Sagittal section and coronal section were performed on the three-dimensional model of the temporomandibular joint disc; Measure the maximum length of the section where the maximum longitudinal section area is located, then the average thickness of the section the maximum longitudinal section area/the maximum length of the section.

(3) Analysis of condylar reconstruction: compare the joint CBCT before and after conservative treatment and surgical treatment, reconstruct the condyle and conduct digital analysis of bone remodeling:

① CBCT inspection specification; Before scanning, the patient shall fill in the scanning informed consent form, and the doctor shall check the patient's information; Morita 3D Accuitomo (Morita, Japan) CBCT equipment was used for scanning; At the time of examination, the patient was supine and occluded at the cusp intersection;

② Three-dimensional reconstruction of the condyle: import DICOM data (T1, T2, T3) of the patient's joint CBCT into ITK-SNAP (www.itksnap. org) software, use Segmentation Mode to segment the condyle, then import the condyle segmentation into 3D Slicer (www.slicer. org) software, and reconstruct the three-dimensional model of the condyle (Model Maker) based on the condyle segmentation.

③ Measurement of condylar reconstruction: because the condyle has an irregular surface, the condyle is artificially divided into five surfaces: front, back, medial, lateral, and upper, and the reconstruction of each surface is analyzed separately. The analysis of condylar remodeling is based on the registration technique. Currently, the commonly used registration technologies include landmark-based, surface-based, and voxel-based registration. Considering the imaging characteristics of this study, the surface-based registration method with high accuracy is selected. In addition, to improve the stability and accuracy of registration results, regions without reconstruction (coronoid process, sigmoid notch, posterior edge of ascending branch) are selected as registration regions. Specific steps: 3D models of T1, T2, and T3 condyles (based on Mesh) → registration of selected

areas → average mesh by SPHARM-PDM shape analysis module → select five faces of T1 condyle by Pick and Paint module → map the selected areas to the exact positions of T2 and T3 condyles → analyze the average distance between each face of T1, T2 and T3 condyles by Mesh statistical module, This distance is a quantitative indicator of condylar remodeling (positive and negative values represent bone deposition and bone absorption on the surface of the condyle, respectively).

(4) Psychological evaluation: The psychological status was evaluated with the SCL-90 scale of a mental health test.

### （4） Risks and benefits

The surgical and conservative treatment received by the subject was routine treatment operations; therefore, any possible post-treatment risks are considered routine too. The department had corresponding prevention and rescue measures. If the surgical treatment patient causes an allergic reaction and rejection reaction of the subject, which leads to wound infection and does not heal, the anchor nail shall be taken out by surgery. Subjects may receive surgical treatment to shorten the treatment time and obtain higher satisfaction. Whether the subject enters the surgical or conservative treatment group after joining, this study will subsidize 500 yuan for each subject participating in and completing this clinical study.

### （5） Research quality control and assurance

Patients participating in this trial will be treated by physicians with rich surgical experience. The imaging data and reconstruction model will simultaneously be done before and after treatment and handed over to two doctors who can operate the software skillfully for measurement. Before the statistical analysis of the research data, the monitoring committee will also review the clinical data to ensure it is correct.

### （6） Ethical requirements

This experiment will fully comply with the ethical principles of the Helsinki Declaration and the International Ethics Guide for Biomedical Research issued by the International Committee of Medical Science Organizations, respect personality and fairness, strive to maximize the benefits of the subjects, and avoid harm as much as possible. Furthermore, we will inform all patients and their families of the relevant issues of this trial in detail before the trial, and they will also keep a copy of the informed consent form.

## 4. Safety evaluation

This experiment will compare the prospective control study on the disc condyle remodeling of patients with irreducible anterior displacement of the temporomandibular joint disc under different clinical treatment modes. The treatment methods are the mainstream methods in China, and the consent form will be signed before the treatment of relevant risks, which will not increase the additional risks to the subjects.