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# 전산화 단층촬영을 바탕으로 한 턱관절 골관절염 변화에 관한 종적 연구

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2021년 8 월

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**ABSTRACT**

# A Longitudinal Investigation of Temporomandibular Joint Osteoarthritis on Computed Tomography and Related Clinical Factors

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This study aimed to analyze long-term changes of temporomandibular joint (TMJ) condylar osteoarthritis (OA) based on computed tomography (CT) and to identify its correlation with clinical features of TMJ OA.

Eighty-nine patients (76 female and 13 male; 152 morbid joints and 26 healthy joints) who had taken follow-up CTs at least once in addition to their initial evaluation were selected. The mean follow-up period was 21.47±10.86 months and mean age was 33.17±17.65 years. Cross-sectional clinical data including age, gender, range of motion, pain, joint noise, centric occlusion/centric relation discrepancy, disc displacement, occlusal splint therapy, intraarticular injection, nonsteroidal anti-inflammatory drug (NSAID) medication, and longitudinal CT

images were collected and statistically analyzed with analysis of variance and logistic regression. To evaluate the extent of destruction from TMJ OA, destructive change index (DCI) was set as the number of TMJ condyle sections in which destructive changes including erosion and subchondral bone cyst among 9-imagenery sections could be observed.

Overall mean DCI decreased from 1.56 to 0.66 which reflects improvement of destructive change of TMJ OA in general. 93 joints (93/152, 61.2%) showed improvement, 27 joints (27/152, 17.8%) worsened and 32 joints (32/152, 21.1%) no change. Initial and final DCI were both significantly higher in the pain positive group compared to the pain negative group (p=0.04). Occlusal stabilization splint and NSAID therapy showed a significantly positive effect on the prognosis of TMJ OA (OR 1.63, p= 0.015; OR 4.34, p=0.011, respectively).

In conclusion, TMJ OA showed improvement in the majority of cases long-term. The prognosis of TMJ OA accompanied by pain was unfavorable showing additional bone destruction. Restoration by regaining cortical intactness in TMJ OA could be observed in approximately 2 years on average and occlusal stabilization splint and/or nonsteroidal anti-inflammatory drug treatment was beneficial on TMJ OA prognosis. Initially mild destructive bone changes may worsen so periodic follow-up imaging is essential.

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**Keywords**: temporomandibular disorders, temporomandibular joint, osteoarthritis, computed tomography, long-term prognosis

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# I. INTRODUTION

Osteoarthritis (OA) is a chronic degenerative disease accompanying inflammation and bone changes in joints.[1,2] Mechanical irritation causing tissue destruction may lead to expression of inflammatory mediators originating from the synovium, eventually resulting in defective cartilage metabolism. Catabolic processes overpowering the anabolic capacity of chondrocytes tilts the homeostatic balance causing progressive cartilage destruction.[1,3,4]

Signs and symptoms of temporomandibular joint (TMJ) OA include pain, limited movement, tenderness on palpation, and joint sounds. The most critical characteristics of TMJ OA is joint deformity identified radiographically such as flattening, osteophyte, sclerosis, erosion, joint mice and subchondral bone cysts. Destruction of the TMJ condyle such as erosion can cause malocclusion and skeletal facial deformity mainly in the form of retrognathism, anterior open bite, and facial asymmetry.

Because TMJ condyles are surrounded by a variety of adjacent anatomical structures, plain radiographs have limitations in determining the accurate osteoarthritic status of the joint. Computed tomography (CT) allows visualization of the bony structure in multiple dimensions offering superior reliability and accuracy compared to conventional radiographs and tomography.[5,6]

There are several studies reporting the disagreement between the degree of clinical symptoms and radiologic findings in TMJ OA patients. Wiese et al. concluded that pain-related variables have no correlation with an increased prevalence of degenerative changes in TMJ tomograms.[7] Bony changes of the condyle on cone-beam CT (CBCT) showed poor correlation with patients' clinical signs and symptoms including pain.[8] On the other hand some studies state that non pain-related factors such as age and sex are more closely associated with TMJ OA prognosis.[7,9]

By evaluating long-term clinical and radiographic data longitudinally one could gain a more practical and accurate understanding of TMJ OA prognosis compared to a cross-sectional study. Currently the guideline for effective intervention on TMJ OA is insufficient and related

longitudinal studies on TMJ OA considering clinical factors are in high demand.

In this study, clinical features of TMJ OA, longitudinal osseous changes of the TMJ condyle on CT and their inter-relationship were analyzed to verify factors that improve TMJ OA long-term.

# II. REVIEW OF LITERATURE

## 1. Anatomy and physiology of the temporomandibular joint

The TMJ is a complex joint that shows two very characteristic movements: hinge/rotation and translation. The TMJ is consisted of two bones, the mandibular condyle with a width of 18-23 mms medial to lateral and 8-10 mms anterior to posterior and the articular fossa of the temporal bone. Between the two bones lies the articulating disc of dense fibrous connective tissue, devoid of nerves or vessels and surrounded by collateral ligaments attached to the condyle permitting rotation of the disc when the condyle is engaged.[10]

The articular surface of the TMJ condyle is lined with dense fibrocartilage rather than hyaline cartilage as with other synovial joints and this allows the articular surface to endure the constant forces generated during mandibular motion.[11] Just below the surface, there is an area called the proliferative zone that acts as a cell reservoir for undifferentiated mesenchymal cell distribution.[12] Mesenchymal cells act as chondrocyte precursors for underlying zones[13], which is closely related to reactive proliferation of joint cartilage with functional demands during loading.[14]

The third area is the fibrocartilaginous zone, where fibrocartilage is arranged in a three-dimensional network structure enabling resistance to compressive and shear forces biomechanically. The fibrocartilaginous zone contains flat fibroblast-like cells with endoplasmic reticulum surrounded by a dense intercellular matrix of collagen fibrils and proteoglycans.[15] Proteoglycans embedded in the network of collage fibrils also play a role in

resisting compressive forces against joint surface.[16,17] Proteoglycans are composed of a protein core and glycosaminoglycan chains that consist a matrix. Hyaluronic acid is connected to proteoglycans creating proteoglycan aggregates. Proteoglycan is interlaced through the collagen network, preventing complete swelling of proteoglycan aggregates. Mechanical pressure from loading during normal function stays in equilibrium with pressure from the internal cartilage. The proteoglycans make maintain the collagen network under persistent tension with the articular cartilage gaining its physical properties in this way.[16]

The fourth layer is the calcified cartilage zone, consisting of chondrocytes and chondroblasts. Chondrocytes actively produce collagen, proteoglycan, glycoproteins, and enzymes.[18] In this region, chondrocytes become bloated and destroyed, leaving the cytoplasm to form osteoblasts from within the myeloid cavity.[19]

Synovial fluid covers articular surface and has an essential role in joint lubrication and nutrition. Articular cartilage is avascular so nourishment of the structures depends on synovial fluid. Therefore, a change in the synovial membrane results in change in the composition of synovial fluid, which in turn causes alterations in cartilage metabolism.[20] Hyaluronic acid present in synovial fluid is believed to have a pivotal function in joint lubrication.[21]

## 2. Pathophysiology of temporomandibular joint osteoarthritis

Continuous functional loading on the TMJ resulting in biomechanical changes of the cartilage has a main role in the development of OA as with other synovial joints.[22,23] TMJ OA is primarily attributed to overloading caused by conditions such as severe malocclusion, skeletal asymmetry, and parafunctional habits with muscle overuse. Increasing attention is being paid to the role of inflammation of the subchondral bone.[23-25]

Increase of intraarticular pressure causes partial hypoxia in the tissue. Hypoxia induces transcription factor-1(HITF-1) which causes expression of vascular endothelial growth factor

(VEGF).[26] VEGF in charge of the migration of osteoclasts and expression of several genes involving tissue remodeling including MMP contributes to the occurrence of OA.[27-29] Matrix metalloproteinase (MMP)-1, -3, -9 expression was significantly higher in the synovial fluid of pathological joints.[30] Substrate degradation enzymes such as MMP and aggrecanase, which occur when continuous loading is applied to the joint cartilage, play an essential role in the decomposition and loss of collagen and proteoglycan.[31,32]

Hypoxia also drives intracellular metabolism to depend on anaerobic glycolysis. When loading is lifted, blood flow is increased resulting in the generation of reactive oxygen species (ROS) such as superoxide anions.[33] ROS causes denaturation and decomposition of hyaluronic acid, which plays a major role in intraarticular lubrication,[33-35] leaving the joint surface vulnerable to friction and loading along with an increase in MMP.[36]

The importance of inflammation in the development of TMJ OA is drawing attention. In an experimental study of induced chronic inflammation in rodent TMJ models, the expression of IL-1β and TNF-α increased.[37] When the synovial fluid of TMJs diagnosed as capsulitis/synovitis were analyzed, the mean TNF-α level was significantly higher in the pain side compared to the contralateral non-pain side.[38] According to a study which analyzed the synovial fluids of TMJ OA patients, concentrations of carboxy-terminal telopeptides I and II (CTX-I and CTX-II), serum cartilage oligomeric matrix protein, and prostaglandin E2 (PGE 2) were higher compared to knee OA patients.[39] However, the levels of those in the synovial fluid of TMJ OA patients were not significantly higher compared to healthy controls in another previous report.[40]

The subchondral bone of TMJ is considered to have another important role in the progression of TMJ OA. Recently researchers suggested that the initiation or progression of TMJ OA is due to the increased turnover of subchondral bone.[41-43] Chondrocytes of the degraded cartilage may modulate osteoclastogenesis by increasing the ratio between receptor activator of nuclear factor (NF)–κB ligand (RANKL) and osteoprotegerin (OPG).[42] Upregulation of osteoclastic

activity and increased RANKL/OPG ratio likely contributes to increased subchondral bone turnover during early stages of TMJ OA.[41] The effect of subchondral bone remodeling is commonly observed in the early stages of TMJ OA, however the role of subchondral bone turnover in TMJ OA etiology still requires further investigation.[44]

## 3. Epidemiological features of temporomandibular joint osteoarthritis

There are large variations in epidemiologic findings related to the age and gender distribution of TMJ OA in previous literature. According to Heloe et al., 11% of TMD patients have osteoarthritis,[45] while Brooks et al. reported that 35% of the asymptomatic joints showed flattening based on magnetic resonance imaging (MRI).[46] An autopsy-based research showed that bone changes of the condylar surface of TMJ could be found in 22–40% of the subjects.[47-49] Although previous studies do not show consistent results regardless of the presence of clinical symptoms, it is known that subclinical or destructive bone changes can be observed in 30 to 60% of TMD patients. Among them, clinical symptoms or destructive bone changes can be detected in 8-12% of the subjects.[50]

Another interesting point is that the linear correlation between age and OA commonly observed seen in other joints cannot be found in the TMJ. According to a study that investigated the age distribution of patient diagnosed as TMJ OA, there are only a few patients in their 20-30s, the largest number in their 40s, and the number of older patients is smaller,[51] suggesting that bony changes in the TMJ can begin at a relatively early age.[52]

In terms of gender distribution, it is also generally accepted that women are more susceptible as in other joints. It is true that there are several studies to support that statement,[53,54] but there are also reports that report no difference[46,48] or male predominance.[49,55]

This inconsistency in epidemiological study results may come from the uncertainty of whether radiographic bone changes unaccompanied by clinical signs or symptoms and also cases showing non-destructive changes maintaining an intact cortical bone lining as with

flattening, sclerosis and osteophyte should be considered as a pathologic condition. Also it could be due to the differences in the sensitivity of radiographic evaluation methods. Therefore, it may be necessary to limit the meaning of OA to bony changes accompanied by clinical symptoms such as pain or dysfunction or bony changes recognized as destructive based on radiologic tests.

## 4. Radiographic assessment of temporomandibular joint osteoarthritis

For the diagnosis of OA, it is necessary to identify bony changes observed on radiographs. The most commonly and traditionally used radiographs are panorama and transcranial radiograph.[56-58] Panoramic radiographic imaging mainly reflects the medial part of the condyle and transcranial view mainly reflects the lateral part. Therefore, the two images show different sites of the condyle, so the possibility of osteoarthritis should be suspected when degenerative changes are observed in any one of the images.

However, despite its easy-to-use advantage in clinical practice transcranial or panoramic imaging has limitations as a screening tool in evaluating osteoarthritic changes in the TMJ.[6,59-63] Earlier Ludlow et al.[63] stated that biplanar tomography was significantly more accurate in assessing condylar lesions compared to biplanar panoramic images ($p = 0.007$) in a comparative study to evaluate diagnostic accuracy. According to Ahmad et al.,[6] the reliability of TMJ OA diagnosis among three different examiners was poor for panoramic radiography ($k = 0.16$), fair for MRI ($k = 0.46$), and near excellent for CT ($k = 0.71$) and positive percent agreement for diagnosing OA was highest with CT (84%) followed by MRI (59%) and panoramic radiography (19%).

To diagnose TMJ OA accurately, CT is recognized as the gold standard, and MRI, which has the highest reliability regarding soft tissue and articular disc pathologies, is also considered reliable in the diagnosis of osteoarthritis, but less superior than CT.[6, 59] Recently, cone beam CT, which is gaining popularity in the dental field, has also been reported to be very useful in

diagnosing OA and its utilization for this purpose is showing an increase.[5,8,9,64]

The 2014 Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) consensus set the diagnostic criteria for TMJ OA as history of TMJ noise during function or movement at examination or within the past 30 days reported by the patient and crepitus noise at movement detected by palpation. The sensitivity and specificity following such criteria is 0.55 and 0.61, respectively. Therefore, imaging is required for definite diagnosis with CT being the preferred choice and at least one of the following should be positive, subchondral cyst; cavitation below the articular surface, erosion; discontinuity of articular cortical lining, generalized sclerosis; unclear trabecular orientation with no delineation between the cortical and trabecular bone throughout the condylar head, or osteophyte; exophytic formation of bony tissue of the surface. Flattening and/or sclerosis may represent variation of normal structure, aging, adaptive remodeling, or could be a precursor to destructive degenerative joint disease (DJD).[6,65]

## 5. Management of temporomandibular joint osteoarthritis

The treatment of TMJ OA is not fundamentally different from that for other subgroups of TMDs, as its clinical symptoms are also not distinct from it. Based on the known pathophysiology of TMJ OA until now, treatment should be centered on reducing mechanical overload.[10,50]

Conservative treatments including patient education, behavior control, physical therapy, medication, and occlusal stabilization splint therapy should be prioritized in a way that reduces the functional load on the TMJ and increases physiological tolerance for a sufficient period of time, and surgical procedures such as intraarticular injection, arthroscopy, and arthroplasty should be considered step by step for symptoms that do not respond to conservative treatments.[50]

The effectiveness of these treatments in reducing clinical symptoms of OA is supported by numerous reports,[16,66-69] but information on the correlation between improvements of clinical

symptoms and actual bone change in osteoarthritis not much known.

### 1) Physical therapy

Physical therapy is a common adjuvant therapy which is well recognized as an effective treatment approach for TMD.[70,71] Although physical therapy helps reduce symptoms of TMD and restore normal function, evidence until now does not support a particular type of therapy. Conventional physical therapy for TMD symptoms includes thermal, ultrasound, and electrostimulation therapy.

Thermotherapy is based on the principle that heat improves blood circulation in areas where it is applied.[72] A heated moist towel can be placed on the symptomatic TMJ area for 10 to 15 minutes. Coolant therapy is also known as a simple and effective way to promptly reduce pain.[73] The most commonly used coolant therapy on TMJs is a vapor coolant spray based on ethyl chloride or fluoromethane.[74] Vapor coolant is sprayed for about 5 seconds from a distance of 1-2 feet, and can be repeatedly sprayed after warming the tissue again.[10]

Ultrasound therapy affects deeply situated tissue by increasing the temperature inside the tissue compared to surface thermotherapy.[75] Ultrasound therapy increases deep tissue blood flow and separates collagen fibers, improving flexibility of the tissue.[70] Transcutaneous electrical nerve stimulation (TENS) therapy applies persistent stimulation to the cutaneous nerve fibers at a subthreshold level of pain.[76] If the TENS stimulation is applied in a painful area, the electrical activity may reduce pain nociception.[77]

### 2) Medication

Pharmacological treatment can be an effective way to control TMD symptoms. The most common drugs used are analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, anti-anxiety drugs, muscle relaxants, antidepressants, and glucosamine.

**Nonsteroidal Anti-inflammatory Drugs (NSAIDs)**

NSAIDs are very useful for most cases of TMD pain. This drug is effective for mild to moderate inflammatory conditions including TMJ OA.[78] When tissue damage occurs, certain chemical intermediates are released, one of which is prostaglandin. Prostaglandins mediate inflammation, vasodilatation and sensitization of afferent C-fiber. Arachidonic acid is changed into prostaglandins by the enzyme cyclo-oxygenase (COX).[78]

NSAIDs can suppress the inflammatory pathway by inhibiting COX production. The induction of COX-2 is activated by pro-inflammatory cytokines including IL-1 and TNF-α.[79] Nonselective inhibition of COX can increase the risk of side effects, mainly gastropathy.[79,80]

**Corticosteroids**

Corticosteroids are potent anti-inflammatory drugs that are rarely prescribed for the treatment of TMD due to side effects except for acute and severely painful joint inflammation.[81] TMJ intraarticular injection of corticosteroids such as triamcinolone or dexamethasone has been recommended in cases of severe pain with unsuccessful conservative treatment. Although there have been concerns regarding long-term adverse effects such as progression of joint destruction, the long-term prognosis appears to be good for alleviating TMJ pain and dysfunction with no or minimal increase in radiographically visible degenerative changes.[82-84]

**Benzodiazepines**

Benzodiazepines are antianxiety agents that can be administered to patients with chronic pain. Although there is concern about drug dependency and potential of worsening depression in chronic pain patients,[85] several studies demonstrated their efficacy in treating muscle pain of TMD.[86,87] Benzodiazepines are not preferred for the treatment of OA it is prescribed for TMJ OA with chronic muscle pain involved central sensitization.

**Muscle relaxants**

Muscle relaxants are helpful in preventing increased muscle activity associated with TMD.[88] Tizanidine proved to be effective for the treatment of chronic daily headaches.[89] Cyclobenzaprine was found to be statistically superior to either placebo or clonazepam in

reducing mandibular pain on awakening.[90] Evidence of the efficacy of muscle relaxants for TMD treatment does not include osteoarthritis recommends combination with other drugs or conservative management.[81]

**Glucosamine**

Glucosamine is an aminomonosaccharide occurring naturally from the human body. It is a constituent of proteoglycans which is a crucial component of the articular cartilage.[91] Glucosamine was first introduced as a potential therapeutic agent for OA in 1969.[92] In the early 1980s, several authors reported that pain of knee OA patients reduced gradually and progressively and the range of motion improved with the administration of glucosamine sulfate compared to placebo.[93-96] According to a study to compare glucosamine sulfate and ibuprofen in TMJ OA patients, TMJ pain on function improved with both glucosamine and ibuprofen, with a 20% decrease in primary outcome and the number of patients with favorable results did not show a statistically difference between groups ($p = 0.73$).[97] Although there is not enough evidence on the effectiveness of glucosamine as an adjunctive medication for osteoarthritis, various related researches including tissue, animal and human studies are being conducted.[92,93,97,98]

## 3) Occlusal stabilization splint

Occlusal stabilization splints have been frequently used in the treatment of TMD for a long time including TMJ OA. Occlusal splints have many uses, but one of them is to temporarily provide a state of engagement in which the TMJ is placed in the most stable position. It can also be used to enhance normal muscle function while reducing abnormal muscle activity by creating optimal conditions for reconstructing myofascial reflexes. Occlusal splints are also used to protect teeth and support structures from abnormal loading that can cause tooth fracture or attrition.[10]

A number of studies have suggested good results with occlusal splints in TMD treatment

compared to placebo,[99,100] including TMJ OA.[101,102] In arthrogenous TMD patients, occlusal splint therapy resulting in a changed condylar position provided relief of symptoms compared to no treatment.[99] Occlusal splints also have been used to reduce microtrauma due to parafunctional habits[103] and decrease loading on the condyle.[10] Occlusal splint therapy was likely to reduce nocturnal muscle activity levels in patients depending on the severity of symptoms.[103]

Earlier Okeson et al.[104] reported a significant decrease in total mean pain scores and significant increase in the range of mouth opening compared to relaxation treatment group. Kuttila et al.[105] reported that stabilization splints improved symptoms of severe arthralgia, and Al-ani et al.[106] reported its positive effect of alleviating TMD related pain. Although the efficacy of occlusal splints in TMD treatment has been supported by several studies,[99,102,107] Forssell et al. questioned its benefit in his systematic review.[108]

### 4) Intraarticular injection

Intraarticular injection have been applied to manage TMD.[109,110] The procedure is known to result in reduced intraarticular pressure and pain, and improved function.[14,111-116]

Researches into the effectiveness of intraarticular injection during the past 20 years have generally shown satisfactory results.[14,111-113,116] To further reduce invasiveness a 1-needle technique[117] and a single-puncture technique with a 2-needle device[112,118] have been introduced recently.

Hyaluronic acid is a natural polysaccharide and sodium hyaluronate is the salt of purified natural sodium hyaluronic acid. Hyaluronic acid controls the viscosity of synovial fluid supporting its lubricating and buffering properties.[119] In a systematic review on knee osteoarthritis intraarticular injection with hyaluronic acid resulted in modest improvement of symptoms. However, the results from studies on the use of hyaluronate for TMD were equivocal. For TMJ OA, the outcome of intraarticular injection was not different between

sodium hyaluronate and saline groups.[119] The study concluded that effect of hyaluronate injection in pain improvement was not significantly different compared to corticosteroid and better than placebo.[120]

Intraarticular injection of corticosteroids has been applied as a treatment for osteoarthritis, and its effectiveness has been shown through a number of researches. Intraarticular injection with corticosteroids relived the clinical symptoms of TMJ OA for up to 1 to 2 years in a randomized controlled double-blind trial.[82] Pain and other symptoms of TMJ OA were significantly reduced by a single intraarticular injection of methylprednisolone for 4 to 6 weeks.[121] Repeated glucocorticoid injections on TMJ OA resulted in a positive response after the initial injection but minimal responses to subsequent injections.[122]

Meanwhile, intraarticular injection of corticosteroids has been reported to worsen bone destruction and its application requires caution. Earlier Toller et al.[123] reported 'chemical condylectomy' phenomenon in the TMJ due to repeated intraarticular corticosteroid injections which increases the risk of intracapsular infection and accelerates articular cartilage destruction, suggesting a single articular injection of up to 40 mg of prednisolone trymethylacetate.

### 5) Surgical interventions

Clinical signs and symptoms of TMD are mostly well-controlled with conservative treatments. But when noninvasive approaches fail surgical treatment including arthrocentesis, arthroscopy, and arthroplasty could be effective.

Arthrocentesis on 38 joints with TMJ OA recalcitrant to non-surgical treatment was effective in restoring functional capacity with a 20-month follow-up,[124] suggesting that arthrocentesis is a safe procedure for TMJ OA. According to Goudot et al.[111] both arthroscopy and arthrocentesis were effective in improving function and decreasing pain.

Arthroplasty is a surgical procedure reshaping the condyle to eliminate osteophytes, erosion, and other osseous irregularities. Arthroplasty was first described in 1966 by Dingman and Grab

as a procedure applied to refractory osteoarthritis.[125] While this technique was reported to relieve pain, important concerns about the resulting mandibular dysfunction, malocclusion, facial asymmetry, and further articular destruction, disc displacement, and ankylosis have been raised.[23]

Surgical procedures, although often successful, comes with surgical risks and potential long-term side effects that might require additional surgery. Thus surgery should be considered only based on sufficient medical evidence.

## 6. Prognosis of temporomandibular joint osteoarthritis

Although the effectiveness of the above mentioned treatments on clinical symptoms of TMJ OA has been supported by various reports, there is not enough research on the correlation between improvement of clinical symptoms and actual osteoarthritic bone change.[66-69,126] Longitudinal comparisons of patients with TMDs and controls over 30 years have shown that conservative treatment, limiting mandibular movement, and physiotherapy, improved radiographic bone changes and clinical symptoms including mouth opening range, joint noise, and pain.[126,127] Lee et al. showed that clinical signs and symptoms of 30 TMJ OA patients improved at 74.1% within at about 7 months, but bone change on CT showed no difference in frequency between improved and unchanged and deteriorated groups over a year.[69] These results imply that the prognosis of OA changes may be independent of clinical signs and symptoms.

A study to investigate the longitudinal changes of erosive TMJ bone changes in adolescents treated with non-surgical methods showed that baseline erosions improved in 9/12 (75%) right and 14/15 (93%) left TMJs and approximately half of the joints developed an intact cortical outline.[128] According to a study to determine the effect of anterior repositioning splint (ARS) therapy on condylar bone change in adolescents/young adults, condylar repair and regeneration was significantly more frequent with ARS (78.1% of joints) compared to control (48.6% of

joints).[129] Ok et al.[130,131] assessed the improvement of TMJ OA after stabilization splint treatment based on CBCT images with an interval of 10.9±4.4 months and Liu et al.[132] evaluated osseous changes accompanying anterior repositioning splint therapy using CBCT after 6 months and reported double-contour images of the condyle that could be regarded as regenerative remodeling appeared in 80% of subjects.

# III. MATERIALS AND METHODS

## 1. Subjects

The patients who visited the Orofacial Pain Clinic of Seoul National University Dental Hospital complaining of TMD symptoms and showing bone change of the TMJ condyle on CT from January, 2010 to January, 2015 were evaluated. Among the initial subjects, those who had follow-up CTs 1≥ were selected, which were 89 patients in total. The number of afflicted joints was 152 joints with 26 joints not showing any bone change on CT images. The mean interval of CT assessment was 12.55±3.15 months. Exclusion criteria was subjects who had a history of orthodontic treatment, orthognathic surgery, macrotrauma, fracture, and systemic diseases that could involve joint deformity. The Institutional Research Board of Seoul National University Dental Hospital approved the study. IRB authorized exemption of informed consent (#ERI18009).

## 2. Clinical evaluation

Clinical parameters (mouth opening range, subjective pain level, joint noise, centric occlusion [CO]-centric relation [CR] discrepancy, and disc displacement) were assessed by two orofacial pain specialists.

Disc displacement was diagnosed based on research diagnostic criteria for TMD (RDC/TMD)

guidelines[133]; 0, no disc displacement and 1, disc displacement. Mouth opening range was the shortest distance at the midline between the upper and lower incisors (mm). Maximum mouth opening (MMO) was the amount of spontaneous opening range regardless of the presence of pain and comfortable mouth opening (CMO) was the maximum amount of painless spontaneous mouth opening. MMO < 38 mms was considered as mouth opening limitation (MOL). Those with TMJ pain at rest and/or on functioning were in the subjective pain positive group. Joint sounds (clicking and crepitus) during movement were recorded. CO/CR sliding distance when guided was also measured. A distance > 2 mms in any direction (antero-posteriorly and laterally) was regarded as positive CO/CR discrepancy.

Selected treatment modalities in this study were medication (non-steroidal anti-inflammatory drugs [NSAIDs]), occlusal stabilization splint, and intraarticular injections (hyaluronic acid and/or triamcinolone). The full-coverage type splint was made of hard acrylic resin with even bilateral occlusal contact in CR position with a 2 mm thickness in the molar area. The mean duration of splint therapy was 17.48±8.62 months. Intraarticular injection was done with a single needle inserted into the upper joint space followed by lavage and injection of hyaluronic acid (Shin Pung Pharm., Korea) and/or triamcinolone (Shin Pung Pharm., Korea).[117] The prescribed NSAIDs was diclofenac sodium per oral and mean prescription duration was 2.06±1.41 months.

## 3. Computed tomography

### 1) CT images

CT images with 0.75 mm slice collimation were taken with SOMATOM Sensation 10 (Siemens, Germany). Images were acquired in supine position and corrected sagittal, coronal, and axial images were reconstructed along the true axes of the mandibular condyle at 1-2 mm slice thickness.

## 2) Cross-sectional assessment

TMJ OA was diagnosed when typical OA changes of the TMJ condyle were identified on CT images. One orofacial pain specialist evaluated the following imaging characteristics: (1) flattening, loss of the rounded contour of the articular surface; (2) erosion, loss of continuity of the articular cortical bone; (3) osteophytes, marginal bony outgrowths of the condyle; (4) sclerosis, increased thickness of the cortical plate; and (5) subchondral cyst, cavity formation below the articular surface deviated from normal bone marrow pattern.[134,135]

Erosion and subchondral bone cyst formation were considered as destructive while flattening, sclerosis, and osteophyte formation not accompanied by erosion or subchondral cysts were considered undestructive TMJ OA. The extent of bone destruction of the condyle surface was assessed by dividing the surface into 3 sections antero-posteriorly between the tangent line of the most anterior and posterior point of the condyle. The condyle was again divided into 3 sections medio-laterally between the tangent line of the most medial and lateral point of the condyle on coronal views, resulting in 9 sections of the entire condyle surface (Figure 1).[69] Destructive change index (DCI) was the number of sections with destructive change (erosion or subchondral cyst formation).

## 3) Longitudinal assessment of TMJ OA

Longitudinal bone change was the change of DCI between the first and follow-up CT images. TMJ OA prognosis was grouped as follows: no change group, no change in DCI; improved group, decrease in DCI; worsened group, increase in DCI (Figure 2). The remodeling group (total bone recovery) was DCI 0 on the final CT image from DCI $\geq 1$ on the previous CT image.[69] The CT examiner was blind to any other clinical information of the subject. Prognosis was grouped according to the change between the initial and final DCI in subjects who had $\geq 3$ follow up CTs.

### 4. Statistical analysis

Demographic and clinical data were analyzed by Chi-square test. Changes of DCI according to clinical parameters were analyzed by repeated-measures ANOVA. Significant factors influencing TMJ OA prognosis were analyzed with logistic regression analysis. All statistical analysis was done with SPSS 21.0 (SPSS Inc., USA). Results were considered statistically significant at $P<0.05$.

# IV. RESULTS

### 1. Demographic and clinical characteristics

Total 76 women and 13 men (152 morbid joints) were enrolled in the subject group (age: 33.17±17.65 yrs). TMJ OA was most prevalent in the 20s age group followed by teens, 30s, 60s, 40s and 50s. The follow-up period was 21.49 ± 10.86 months. CMO and MMO value was 39.43±10.55 and 43.22±9.05 mms respectively. 25 subjects (26.97%) were categorized as MOL (MMO<38mm) group. Fifty subjects reported subjective pain (56.18%). Objective joint noise on mouth opening was recorded in 26 patients (29.21%). CO/CR discrepancy was observed in 32 patients (35.96%). Fifty-two patients (34.21%) were diagnosed with disc displacement. Stabilization splint therapy was done in 72 patients (80.90%) for 17.48±8.62 months. Twenty-one patients (23.60%) had intraarticular injection with hyaluronic acid and/or corticosteroids. NSAIDs were prescribed in 45 patients (50.56%) for 2.06±1.41 months. Results are described in table 1.

### 2. CT assessment of TMJ OA

The initial and final mean DCI was 1.56 and 0.66 respectively. Osteoarthritic bone changes of the TMJ improved in 93 joints (93/152, 61.2%), worsened in 27 joints (27/152, 17.8%), and did not change in 32 joints (32/152, 21.1%). The mean DCI decreased from 2.30 to 0.54 in the improved group and increased from 0.33 to 1.37 in the worsened group as shown in table 2.

Initial DCI of the improved group was significantly higher than the worsened group (p=0.004) (Figure3).

Changes between initial and final mean DCI values according to various clinical characteristics are shown in table 1 and figure 4. According to presence/absence of subjective pain, the change of DCI was significantly different (p=0.040). Both initial and final DCI were significantly higher with pain. Other investigated variables did not show a significant difference in the change of DCI.

### 3. Factors influencing TMJ OA prognosis

Favorable prognosis of TMJ OA was influenced significantly by clinical factors including initial DCI (OR 7.25, 95% CI 3.20-16.42, p=0.000), CO/CR discrepancy > 2 mms (OR 1.33, 95% CI 1.08-1.76, p=0.032), stabilization splint therapy (OR 1.63, 95% CI 1.09-2.42, p=0.015), and administration of NSAIDs (OR 4.34, 95% CI 0.97-19.50, p=0.011) by logistic regression analysis as presented in table 1. Intraarticular injection showed borderline significance (OR 1.49, 95% CI 0.99-2.23, p=0.057) while other variables were not significant. Nagelkerke $R^2$, an estimation of total log likelihood, was 0.627.

### 4. TMJ condyle remodeling

Sixty-four joints (42%) recovered from the destructive change totally showing complete remodeling (previous DCI score ≥1 and final DCI score 0). The follow-up duration was 21.55±9.71 months. Age, sex, stabilization splint therapy, NSAIDs, subjective pain, and CO/CR discrepancy >2 mms did not show any significant influence on TMJ remodeling through regression analysis.

Although most patients showed a fixed tendency of worsening or improvement, the DCI of 9 patients decreased and increased again afterwards.

# V. DISCUSSION

TMJ OA is relatively common and can be found not only in TMD patients but also can be identified during the course of any routine dental check-up. As development of imaging modalities including CT, deformity of the TMJ condyle due to OA can be easily confirmed with radiography and diagnosis is becoming more effective. However, considering the fact that osseous changes of TMJ OA can eventually lead to irreversible changes in occlusion and facial morphology, information supporting clinical decisions for proper intervention is still insufficient.

OA is generally regarded as a female predominant and age-related disease.[51,53,136] However, interestingly the linear correlation between osteoarthritic change and age seen in other joints is not correspondent in the TMJ. TMDs is known most prevalent in young adults in their 20s to 40s and TMJ OA may begin at a very early age.[51,52,137,138] Previous clinical and histopathological study showed that the mean age of TMJ OA occurrence was 34 years, which is in line with the results of this study.[139] The age and gender distribution of this study did not differ from previous studies on TMJ OA, thus allowing the generalization of our results.

In this study, various cross-sectional demographic and clinical data was analyzed with longitudinal serial CT image sets of TMJ OA. The mean follow-up period was 644.58 ± 325.71 days, which is long enough to allow sufficient assessment of TMJ OA prognosis in a longitudinal manner. Follow-up periods of most other longitudinal studies investigating the osseous prognosis of TMJ OA range from 6 months to 1 year approximately.[69,130-132] Due to the relatively longer follow-up period of this study, resolution of the destructive changes in the TMJ condyle could be observed in many cases (42% of total evaluated joints). Lei et al. reported a 62.7% (42/67) regeneration rate of the TMJ condyle in young adults with early stage OA; 78.1% of the anterior repositioning splint treatment group (25/32) and 48.6% of the control group (17/35).[129] Abrahamsson et al. reported that base line erosion of TMJ in adolescents improved in 9/12 (95%) of right condyle and 14/15 (93%) of left condyle with

non-surgical treatments and half of joints developed intact cortical outline.[128] Such results show that TMJ condyles with erosive surfaces can gradually recover and regain intact cortical lining over a long period of time which generally appears as sclerosis and flattening of the condyle morphology on radiographic imaging. Such processes may be called undestructive remodeling of the TMJ condyle. Without surface erosion or existing subchondral bone cysts, the TMJ condyle can be expected to endure loading that occurs during daily jaw functioning without progressive inflammation.[6]

Various terms have been applied to defining the condition of osseous changes of the TMJ condyle observed on radiographs accompanied by common signs and symptoms of TMDs such as pain and dysfunction. According to RDC/TMD guidelines[133] osteoarthrosis and osteoarthritis are both a subtype of degenerative joint disease only distinguished by the presence of pain and dysfunction. However, such differentiation is not well noted in medical literature and both terms have been used interchangeably.[6] Earlier Toller et al. also published results on degenerative joint disorder or arthrosis as a type of temporomandibular arthropathy.[51] A number of published studies at that time had used osteoarthrosis synonymously with degenerative joint disease of TMJ. However degenerative joint disorder or osteoarthritis is more commonly used nowadays. In this study we used osteoarthritis in the same vein embracing degenerative joint disease, osteoarthritis and osteoarthrosis. The remodeling group would be in a state more similar to osteoarthrosis defined by RDC/TMD, however the presence of pain was not considered in the differentiation.

The mean period for remodeling to take place in our patients was 21.55 ± 9.71 months. This value is the first to be suggested in literature and could be considered in the clinical evaluation and treatment planning of TMJ OA. However, the fact that the true initiation and termination of OA could not be determined should be considered when implicating the results of this study. The duration of treatment provided in this study was based on the patient's visit rather a true termination of TMD treatment and many factors may have influenced the treatment period of

each patient. Clinically, the 2-year period of this study could be long enough to provide practical insight by presenting how osteoarthritic joints undergo osseous changes during that period.

Bone changes of the TMJ condyle were qualitatively measured based on visual evaluation of 9 sections of the TMJ condyle. Cevidanes et al.[140,141] suggested a 3 dimensional quantification condylar resorption model technique and Ok et al. used superimposition with 6-imaginary sections to assess the longitudinal bone change in TMJ OA.[131] Although both methods are also suitable to assess TMJ OA, the method applied in this study was proper to highlight the importance of cortical bone intactness and also more simple allowing less room for error.[69,142] To represent the extent of destructive osseous changes occurring due to TMJ OA, DCI was calculated by counting the sections with destructive changes among the 9 sections of the TMJ condyle. Since we divided the condyle surface into sections and assessed the intactness of each section separately, DCI could accurately reflect the overall extent of destruction better than indirect superimpositioning.

The intactness of the cortical bone lining may be more important in sustaining the overall health of the TMJ condyle and may reflect the stage of the disease more precisely rather than morphological changes occurring as a consequence of bony destruction. Ko et al. reported that thickening of the cortex is presumably a response of the subchondral bone to a nonpathological level of pressure.[143] Bony changes in the cortical area may be considered as a radiographic index of the level of pathologic mechanical overloading occurring in the TMJ condyle that may be improved through treatments such as occlusal splints. A condyle with sound cortical surfaces can bear overloading better and not undergo a chronic inflammatory process.[6]

Lee et al. first introduced the 9-imaginery section method and its reliability was proven in a previous study.[132,142] In this study the landmarks of Lee's method were modified to enhance practicality by using tangent lines to the most prominent point in the contour of the condyle instead of the squamotympanic fissure and the apex of the eminence. The squamotympanic

fissure can easily be skipped on tomographic images according to slice thickness and the location of the apex of the eminence also can be affected by erosive bone changes occurring with OA. A preliminary study was conducted to verify the reliability of this modified method. CT images were evaluated for TMJ OA based on the modified method three times with a two-week interval by a single examiner who is a trained TMDs and orofacial pain specialist with more than 7 years of clinical experience. The reader was blind to all other clinical data. The Cohen's kappa value was 0.739 ($p < 0.005$ in all comparison among the 3 readings) showing substantial reliability.

The TMJ condyle showed recovery in the majority of subjects and the mean extent of destructive change decreased during the total follow-up period. TMJ OA is known as a self-limiting disease that shows spontaneous recovery. This process is mediated through the body's immune system and the duration of progress can be shortened through optimal intervention.[11,68,127] The results of this study showed that the initial extent of bone change was more severe in the improved group (initial DCI 2.32) compared to the worsened group (initial DCI 0.33). This implies that severe destruction of the TMJ condyle observed on initial radiographic imaging does not necessarily reflect more aggressive disease activity or severe stage of disease and even relatively severe destructions may show improvement while initially mild osteoarthritic changes can progressively worsen. Logistic regression analysis also showed that high initial DCI value is a significant index for prediction of better TMJ OA prognosis. Untreated TMJ OA may have a natural course of disease with a predetermined time of progression and the subjects of the worsened group may have been examined in the early stage of disease while the joints in the improved group were examined around the peak of the disease progression.[69]

The fact that a TMJ condyle which initially shows normal to mild OA change can later show more bony destruction warrants periodic follow-up CT imaging even with a patient receiving regular treatment. Although limited by the retrospective nature of this study, according to the

results a 2-year follow-up period for TMJ OA may be suggested and considered in treatment planning as it took 21.55 ± 9.71 months to observe no further destructive change in OA severity. Considering OA as a structural re-adaptation process to enable normal function with certain discrepancies between functional loading and the natural shape of the TMJ condyle, structural change may recommence unless contributing factors causing excessive loading are eliminated. So behavioral therapy to control unfavorable contributing factors must be persistently applied to ensure the successful management of TMJ OA.

Most demographic and clinical factors, such as age, gender, range of mouth opening, presence of joint noise and accompanying disc displacement showed no significant relationship with osseous changes in TMJ OA through repeated measures ANOVA which is in line with other previous studies.[7,8,69,140-143] While other studies state that factors such as age and gender are closely related to TMJ OA prognosis.[7,9]

The results of this study showed that disc displacement did not have a significant effect on TMJ OA prognosis and there was no significant difference in the change of DCI. There have been a number of arguments related to the relationship between disc displacement and TMJ OA reflecting the close relationship between the two conditions.[66,68,144] However, the data until now does not directly support causality and the sequential or causal relationship of disc displacement with the TMJ OA is yet to be established. The discrepancy of the results of this study from others may have resulted from the difference in diagnostic approaches or definitions of disc displacement. Disc displacement was judged clinically following RDC/TMD guidelines.[133] Unfortunately, the diagnosis of disc displacement of TMD not based on MRI is known to have insufficient reliability.[65] One point to consider is that the subtype of disc displacement (disc displacement with/without reduction with/without limited mouth opening) was not distinguished in this study. Also to enhance reliability, MRI characteristics should be evaluated in a longitudinal manner rather than cross-sectionally in comparing results with comparable studies. Another point to consider in reading the results of this study is that

there is possible interaction in the factors regarded as independent variables in regression analysis such as joint noise and disc displacement. However, there was no difference in results when regression analysis was done without disc displacement as an independent variable.

Only the presence of subjective pain at the initial examination showed a significant relationship with the difference in change of DCI between groups in this study. In the pain positive group, both initial and final DCI were significantly higher compared to the pain negative group. Patients with TMJ OA accompanied by pain may show additional osseous destruction so the pain level must always be evaluated at the initial diagnostic process and those with subjective pain should be treated more intensively from the beginning of treatment to gain favorable results. The mechanism in which subjective pain is related to destructive bone change is yet to be elucidated, however active interventions to control initial pain should be considered. Inflammatory cytokines that are known to directly evoke pain may also contribute to the additional osseous changes of the TMJ condyle sharing a common pathway between pain transmission and bone resorption.[145-146] Cevidanes et al. also revealed that the extent of resorptive changes in the TMJ OA condyle were closely related to pain severity and duration.[141]

Meanwhile, it is interesting that CO/CR discrepancy was another significant factor that influences TMJ OA prognosis. The subjects with CO/CR discrepancy showed a favorable prognosis with their osseous changes accompanied by more active remodeling. The relationship between CO/CR discrepancy and TMDs has been a controversial issue until now. Some suggested CO/CR discrepancy could lead to TMJ arthralgia, myalgia, disc displacement, and even TMJ OA.[147-150] And others have contended that an association between CO/CR discrepancy and TMDs could not be established.[151-155] Though CO/CR discrepancy appears to be a statistically significant factor that influences the prognosis of TMJ OA, this does not directly support a cause-and-effect relationship between CO/CR discrepancy and TMJ OA. The initial DCI of the improved group was significantly higher so occlusal disharmony or

CO/CR discrepancy may have been a mere consequence of this state.[147]

Several treatment modalities including behavioral modification, physical therapy, medication, occlusal splint therapy, intraarticular injection, and surgical procedures have been applied for the management of TMJ OA. Their treatment efficacy in improving signs and symptoms of TMDs have been sought through previous studies.[104-106,127,131,156-160] However, studies looking into the treatment efficacy focusing on bone changes of TMJ OA are scarce. This study revealed that occlusal stabilization splint therapy and NSAIDs had a significant influence on TMJ OA prognosis by logistic regression. Both modalities are currently the treatment of choice for TMJ OA and the results support their continued application.

Though intraarticular injection did not show a statistically significant effect on TMJ OA prognosis the significance level was relatively high (OR 1.49, p=0.057). Intraarticular injections are known to be effective in controlling pain of TMJ OA.[160] Lavage with intraarticular injections are beneficial by removing inflammatory cytokines associated with not only pain but also osseous changes, thus resulting in favorable TMJ OA prognosis.[111,112] However, the timing of the injection itself may be a crucial factor in determining the effects of the treatment and further well controlled prospective studies are necessary to establish a guideline. The fact that intraarticular injection was applied to those complaining of refractory pain and not responding to conservative treatment including occlusal stabilization splint and medication in this study may have influenced the results. For further investigations, injection count and type of drugs injected should be controlled though the efficacy between hyaluronic acid and corticosteroid on TMJ OA showed no significant differences.[161] The patients who had intra-articular injections were also less in number than those with occlusal stabilization splint or administration of NSAIDs, meaning non-homogeneity with other OA treatment groups.

Reducing general inflammation level by NSAIDs could relieve symptoms of TMJ OA and may consequently improve osseous changes by reducing prostaglandin level, an important mediator of inflammation.[145,146,159] Diclofenac sodium which was the only NSAIDs prescribed

in this study has been known for its effectiveness in the management of TMDs symptoms from arthrogenous origin.[163] Further studies to establish a guideline including dosage and administration regimen of NSAIDs in TMJ OA is warranted. Occlusal splints are known to relieve mechanical overloading and guard the condyle from recurrent hypoxia.[103] Favorable treatment outcomes have been verified in TMJ OA.[99,102,129,130,159,163] By combining the 2 treatment modalities it could be possible to physically reduce excessive loading on the condyle and chemically remove inflammatory mediators leading to efficient improvement of inflammatory condition and bony changes in the TMJ condyle.

There are several limitations of this study to consider in the understanding of the results derived. This study was a retrospective study and did not have a control group. Consequently, it was impossible to control various confounding factors and multiple biases could have occurred. In particular, the treatment protocol was not identical in all patients and many patients could have received multiple types of treatment making it hard to consider the effect of a single treatment modality on TMJ OA. Also variables considered as independent in regression analysis, such as disc displacement and noise, as well as treatment variables, are not completely independent from each other, which could have been a cause of statistical biases. To gain a more accurate insight into the true prognosis of TMJ OA and its related factors, a better-designed prospective controlled study will be needed in the future. Nevertheless, the results of this study may hold clinical significance as the number of subjects was not small and the duration of follow-up was relatively long.

Osteoarthritic changes of the TMJ condyle were evaluated in a longitudinal manner showing that destructive changes of the TMJ condyle due to TMJ OA improved in the majority of cases. Restoration of bony structure by regaining cortical intactness in TMJ OA could be observed in approximately 2 years on average and occlusal splint therapy and/or NSAIDs appeared to be beneficial. Initially mild destructive bone changes may progress more destructively so periodic follow-up imaging is necessary. TMJ OA accompanied by pain showed unfavorable osseous

prognosis. Such findings should be considered in the diagnosis and personalized treatment planning of TMJ OA.

Understanding the long-term osseous change in TMJ OA and assessing factors that may influence this process leads to information that may assist the selection of appropriate intervention methods and treatment timing that will eventually result in better prognosis of TMJ OA.

# VI. CONCLUSIONS

Osteoarthritic changes of the TMJ condyle were evaluated in a longitudinal manner showing that destructive changes of the TMJ condyle due to TMJ OA improved in the majority of cases. Restoration by regaining cortical intactness in TMJ OA could be observed in approximately 2 years on average and occlusal splint therapy and/or NSAIDs were beneficial. Initially mild destructive bone changes may worsen so periodic follow-up imaging is essential. TMJ OA accompanied by pain showed unfavorable osseous prognosis. Such findings should be considered in the diagnosis of TMJ OA for personalized treatment planning.

# REFERENCES


**1.** Mohit Kappor NNM. Osteoarthritis. Switzerland: *Springer International Publishing*; 2015.

**2.** Pereira D, Peleteiro B, Araujo J, Branco J, Santos RA, Ramos E. The effect of osteoarthritis definition on prevalence and incidence estimates: a systematic review. *Osteoarthritis Cartilage.* 2011;19:1270-1285.

**3.** Brandt KD, Radin EL, Dieppe PA, van de Putte L. Yet more evidence that osteoarthritis is not a cartilage disease. *Ann Rheum Dis.* 2006;65:1261-1264.

**4.** Buckwalter JA, Mankin HJ, Grodzinsky AJ. Articular cartilage and osteoarthritis. *Instr Course Lect.* 2005;54:465-480.

**5.** Honey OB, Scarfe WC, Hilgers MJ, et al. Accuracy of cone-beam computed tomography imaging of the temporomandibular joint: comparisons with panoramic radiology and linear tomography. *Am J Orthod Dentofacial Orthop.* 2007;132:429-438.

**6.** Ahmad M, Hollender L, Anderson Q, et al. Research diagnostic criteria for temporomandibular disorders (RDC/TMD): development of image analysis criteria and examiner reliability for image analysis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2009;107:844-860.

**7.** Wiese M, Svensson P, Bakke M, et al. Association between temporomandibular joint symptoms, signs, and clinical diagnosis using the RDC/TMD and radiographic findings in temporomandibular joint tomograms. *J Orofac Pain.* 2008;22:239-251.

**8.** Palconet G, Ludlow JB, Tyndall DA, Lim PF. Correlating cone beam CT results with temporomandibular joint pain of osteoarthritic origin. *Dentomaxillofac Radiol.* 2012;41:126-130.

**9.** Alexiou K, Stamatakis H, Tsiklakis K. Evaluation of the severity of temporomandibular joint osteoarthritic changes related to age using cone beam computed tomography. *Dentomaxillofac Radiol.* 2009;38:141-147.

**10.** Okeson JP. Management of Temporomandibular Disorders and Occlusion, ed 5. St Luise: *Mosby*; 2003.

**11.** Rasmussen OC. Temporomandibular arthropathy. Clinical, radiologic, and therapeutic aspects, with emphasis on diagnosis. *Int J Oral Surg.* 1983;12:365-397.

**12.** Kuroda S, Tanimoto K, Izawa T, Fujihara S, Koolstra JH, Tanaka E. Biomechanical and biochemical characteristics of the mandibular condylar cartilage. *Osteoarthritis Cartilage.* 2009;17:1408-1415.

**13.** Bibb CA, Pullinger AG, Baldioceda F. The relationship of undifferentiated mesenchymal cells to TMJ articular tissue thickness. *J Dent Res.* 1992;71:1816-1821.

**14.** Alpaslan C, Dolwick MF, Heft MW. Five-year retrospective evaluation of temporomandibular joint arthrocentesis. *Int J Oral Maxillofac Surg.* 2003;32:263-267.

**15.** Klinge RF. The structure of the mandibular condyle in the monkey (Macaca mulatta). *Micron.* 1996;27:381-387.

**16.** Stegenga B, de Bont LG, Boering G, van Willigen JD. Tissue responses to degenerative changes in the temporomandibular joint: a review. *J Oral Maxillofac Surg.* 1991;49:1079-1088.

**17.** Mao JJ, Rahemtulla F, Scott PG. Proteoglycan expression in the rat temporomandibular joint in response to unilateral bite raise. *J Dent Res.* 1998;77:1520-1528.

**18.** de Bont LG, Boering G, Havinga P, Liem RS. Spatial arrangement of collagen fibrils in the articular cartilage of the mandibular condyle: a light microscopic and scanning electron microscopic study. *J Oral Maxillofac Surg.* 1984;42:306-313.

**19.** Cohen B KI. Scientific foundations of dentistry. *Heineman Medical*; 1976.

**20.** de Bont LG, B stegenga. Pathology of temporomandibular joint internal derangement and osteoarthrosis. *J Oral Maxillofac Surg*. 1993;22:71-74.

**21.** Smith MM, Ghosh P. The synthesis of hyaluronic acid by human synovial fibroblasts

is influenced by the nature of the hyaluronate in the extracellular environment. *Rheumatol Int.* 1987;7:113-122.

**22.** Nitzan DW. The process of lubrication impairment and its involvement in temporomandibular joint disc displacement: a theoretical concept. *J Oral Maxillofac Surg.* 2001;59:36-45.

**23.** Tanaka E, Detamore MS, Mercuri LG. Degenerative disorders of the temporomandibular joint: etiology, diagnosis, and treatment. *J Dent Res.* 2008;87:296-307.

**24.** Krisjane Z, Urtane I, Krumina G, Neimane L, Ragovska I. The prevalence of TMJ osteoarthritis in asymptomatic patients with dentofacial deformities: a cone-beam CT study. *Int J Oral Maxillofac Surg.* 2012;41:690-695.

**25.** Matsumoto R, Ioi H, Goto TK, et al. Relationship between the unilateral TMJ osteoarthritis/osteoarthrosis, mandibular asymmetry and the EMG activity of the masticatory muscles: a retrospective study. *J Oral Rehabil.* 2010;37:85-92.

**26.** Pufe T, Lemke A, Kurz B, et al. Mechanical overload induces VEGF in cartilage discs via hypoxia-inducible factor. *Am J Pathol.* 2004;164:185-192.

**27.** Engsig MT, Chen QJ, Vu TH, et al. Matrix metalloproteinase 9 and vascular endothelial growth factor are essential for osteoclast recruitment into developing long bones. *J Cell Biol.* 2000;151:879-889.

**28.** Niida S, Kaku M, Amano H, et al. Vascular endothelial growth factor can substitute for macrophage colony-stimulating factor in the support of osteoclastic bone resorption. *J Exp Med.* 1999;190:293-298.

**29.** Tanaka E, Aoyama J, Miyauchi M, et al. Vascular endothelial growth factor plays an important autocrine/paracrine role in the progression of osteoarthritis. *Histochem Cell Biol.* 2005;123:275-281.

**30.** Tanaka S, Hamanishi C, Kikuchi H, Fukuda K. Factors related to degradation of

articular cartilage in osteoarthritis: a review. *Semin Arthritis Rheum.* 1998;27:392-399.

**31.** Huang K, Wu LD. Suppression of aggrecanase: a novel protective mechanism of dehydroepiandrosterone in osteoarthritis? *Mol Biol Rep.* 2010;37:1241-1245.

**32.** Abramson SB, Attur M, Yazici Y. Prospects for disease modification in osteoarthritis. *Nat Clin Pract Rheumatol.* 2006;2:304-312.

**33.** Grootveld M, Henderson EB, Farrell A, Blake DR, Parkes HG, Haycock P. Oxidative damage to hyaluronate and glucose in synovial fluid during exercise of the inflamed rheumatoid joint. Detection of abnormal low-molecular-mass metabolites by proton-n.m.r. spectroscopy. *Biochem J.* 1991;273(Pt 2):459-467.

**34.** Tanaka E, Detamore MS, Tanimoto K, Kawai N. Lubrication of the temporomandibular joint. *Ann Biomed Eng.* 2008;36:14-29.

**35.** Greenwald RA. Effects of oxygen-derived free radicals on connective tissue macromolecules: inhibition by copper-penicillamine complex. *J Rheumatol Suppl.* 1981;7:9-13.

**36.** Ohno-Nakahara M, Honda K, Tanimoto K, et al. Induction of CD44 and MMP expression by hyaluronidase treatment of articular chondrocytes. *J Biochem.* 2004;135:567-575.

**37.** Wang XD, Cui SJ, Liu Y, et al. Deterioration of mechanical properties of discs in chronically inflamed TMJ. *J Dent Res.* 2014;93:1170-1176.

**38.** Emshoff R, Puffer P, Rudisch A, Gassner R. Temporomandibular joint pain: relationship to internal derangement type, osteoarthrosis, and synovial fluid mediator level of tumor necrosis factor-alpha. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2000;90:442-449.

**39.** Vos LM, Kuijer R, Huddleston Slater JJ, Bulstra SK, Stegenga B. Inflammation is more distinct in temporomandibular joint osteoarthritis compared to the knee joint. *J Oral Maxillofac Surg.* 2014;72:35-40.

**40.** Vos LM, Kuijer R, Huddleston Slater JJ, Stegenga B. Alteration of cartilage degeneration and inflammation markers in temporomandibular joint osteoarthritis occurs proportionally. *J Oral Maxillofac Surg.* 2013;71:1659-1664.

**41.** Embree M, Ono M, Kilts T, et al. Role of subchondral bone during early-stage experimental TMJ osteoarthritis. *J Dent Res.* 2011;90:1331-1338.

**42.** Jiao K, Niu LN, Wang MQ, et al. Subchondral bone loss following orthodontically induced cartilage degradation in the mandibular condyles of rats. *Bone.* 2011;48:362-371.

**43.** Wang XD, Kou XX, He DQ, et al. Progression of cartilage degradation, bone resorption and pain in rat temporomandibular joint osteoarthritis induced by injection of iodoacetate. *PLoS One.* 2012;7:e45036.

**44.** Wang XD, Zhang JN, Gan YH, Zhou YH. Current understanding of pathogenesis and treatment of TMJ osteoarthritis. *J Dent Res.* 2015;94:666-673.

**45.** Helöe B, Helöe LA. Characteristics of a group of patients with temporomandibular joint disorders. *Community Dent Oral Epidemiol.* 1975;3:72-79.

**46.** Brooks SL, Westesson PL, Eriksson L, Hansson LG, Barsotti JB. Prevalence of osseous changes in the temporomandibular joint of asymptomatic persons without internal derangement. *Oral Surg Oral Med Oral Pathol.* 1992;73:118-122.

**47.** Axelsson S. Human and experimental osteoarthrosis of the temporomandibular joint. Morphological and biochemical studies. *Swed Dent J Suppl.* 1993;92:1-45.

**48.** Widmalm SE, Westesson PL, Kim IK, Pereira FJ, Lundh H, Tasaki MM. Temporomandibular joint pathosis related to sex, age, and dentition in autopsy material. *Oral Surg Oral Med Oral Pathol.* 1994;78:416-425.

**49.** Magnusson C, Ernberg M, Magnusson T. A description of a contemporary human skull material in respect of age, gender, temporomandibular joint changes, and some dental variables. *Swed Dent J.* 2008;32:69-81.

**50.** Lee JY. Osteoarthritis of the temporomandibular joint. *Journal of oral medicine and pain.* 2013;38:87-95.

**51.** Toller PA. Osteoarthrosis of the mandibular condyle. *Br Dent J.* 1973;134:223-231.

**52.** Dibbets JM, van der Weele LT. Prevalence of structural bony change in the mandibular condyle. *J Craniomandib Disord.* 1992;6:254-259.

**53.** Rasmussen OC. Description of population and progress of symptoms in a longitudinal study of temporomandibular arthropathy. *Scand J Dent Res.* 1981;89:196-203.

**54.** Kamelchuk LS, Major PW. Degenerative disease of the temporomandibular joint. *J Orofac Pain.* 1995;9:168-180.

**55.** Richards LC. Degenerative changes in the temporomandibular joint in two Australian aboriginal populations. *J Dent Res.* 1988;67:1529-1533.

**56.** Wilson BB. Panoramic and transcranial radiology in orthodontics and craniomandibular disorders. *J Gen Orthod.* 1996;7:12-20.

**57.** Alattar MM, Baughman RA, Collett WK. A survey of panoramic radiographs for evaluation of normal and pathologic findings. *Oral Surg Oral Med Oral Pathol.* 1980;50:472-478.

**58.** Bledsoe WS. The transcranial radiograph. The diagnostic difference between 'corrected' vs 'uncorrected' films. *Funct Orthod.* 1989;6:14-26.

**59.** Look JO, Schiffman EL, Truelove EL, Ahmad M. Reliability and validity of Axis I of the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) with proposed revisions. *J Oral Rehabil.* 2010;37:744-759.

**60.** Hussain AM, Packota G, Major PW, Flores-Mir C. Role of different imaging modalities in assessment of temporomandibular joint erosions and osteophytes: a systematic review. *Dentomaxillofac Radiol.* 2008;37:63-71.

**61.** Reiter S. The use of the panoramic radiograph for diagnosis of temporomandibular joint disorders (TMD)--comparison to other imaging techniques. *Refuat Hapeh*

*Vehashinayim (1993)*. 2007;24:22-29, 54.

**62.** Schmitter M, Gabbert O, Ohlmann B, et al. Assessment of the reliability and validity of panoramic imaging for assessment of mandibular condyle morphology using both MRI and clinical examination as the gold standard. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2006;102:220-224.

**63.** Ludlow JB, Davies KL, Tyndall DA. Temporomandibular joint imaging: a comparative study of diagnostic accuracy for the detection of bone change with biplanar multidirectional tomography and panoramic images. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1995;80:735-743.

**64.** Tsiklakis K. Cone beam computed tomographic findings in temporomandibular joint disorders. *Alpha Omegan.* 2010;103:68-78.

**65.** Schiffman E, Ohrbach R, Truelove E, et al. Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for Clinical and Research Applications: recommendations of the International RDC/TMD Consortium Network* and Orofacial Pain Special Interest Groupdagger. *J Oral Facial Pain Headache.* 2014;28:6-27.

**66.** de Bont LG, Dijkgraaf LC, Stegenga B. Epidemiology and natural progression of articular temporomandibular disorders. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1997;83:72-76.

**67.** de Leeuw R, Boering G, Stegenga B, de Bont LG. Radiographic signs of temporomandibular joint osteoarthrosis and internal derangement 30 years after nonsurgical treatment. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1995;79:382-392.

**68.** Stegenga B, de Bont LG, Boering G. Osteoarthrosis as the cause of craniomandibular pain and dysfunction: a unifying concept. *J Oral Maxillofac Surg.* 1989;47:249-256.

**69.** Lee JY, Kim DJ, Lee SG, Chung JW. A longitudinal study on the osteoarthritic change of the temporomandibular joint based on 1-year follow-up computed tomography. *J*

*Craniomaxillofac Surg.* 2012;40:e223-228.

**70.** Gray RJ, Quayle AA, Hall CA, Schofield MA. Physiotherapy in the treatment of temporomandibular joint disorders: a comparative study of four treatment methods. *Br Dent J.* 1994;176:257-261.

**71.** Di Fabio RP. Physical therapy for patients with TMD: a descriptive study of treatment, disability, and health status. *J Orofac Pain.* 1998;12:124-135.

**72.** Nelson SJ, Ash MM. An evaluation of a moist heating pad for the treatment of TMJ/muscle pain dysfunction. *Cranio.* 1988;6:355-359.

**73.** Burgess JA, Sommers EE, Truelove EL, Dworkin SF. Short-term effect of two therapeutic methods on myofascial pain and dysfunction of the masticatory system. *J Prosthet Dent.* 1988;60:606-610.

**74.** Travell J. Ethyl chloride spray for painful muscle spasm. *Arch Phys Med Rehabil.* 1952;33:291-298.

**75.** Esposito CJ, Veal SJ, Farman AG. Alleviation of myofascial pain with ultrasonic therapy. *J Prosthet Dent.* 1984;51:106-108.

**76.** Kane K, Taub A. A history of local electrical analgesia. *Pain.* 1975;1:125-138.

**77.** Long DM, Hagfors N. Electrical stimulation in the nervous system: the current status of electrical stimulation of the nervous system for relief of pain. *Pain.* 1975;1:109-123.

**78.** Rang HP DM, Ritter JM. Anti-inflammatory and immunosupressant drugs. In Pharmacology. Edinbug: *Churchill Livingstone*; 2001.

**79.** Vane JR BR. Overview-mechanisms of action of anti-inflammatory drugs. London: *Kluwer Academic Publishers*; 1996.

**80.** Sidenius K, Rasmussen NK, Boesen EM, Pedersen H. The contraceptive habits of women applying for termination of pregnancy. *Ugeskr Laeger.* 1983;145:3721-3724.

**81.** Leeuw Rd. Orofacial pain : guidlines for assessment, diagnosis, and management. 4th ed. USA: *Quintessence Publishing Co, Inc*; 2008.

**82.** Kopp S, Carlsson GE, Haraldson T, Wenneberg B. Long-term effect of intra-articular injections of sodium hyaluronate and corticosteroid on temporomandibular joint arthritis. *J Oral Maxillofac Surg.* 1987;45:929-935.

**83.** Vallon D, Akerman S, Nilner M, Petersson A. Long-term follow-up of intra-articular injections into the temporomandibular joint in patients with rheumatoid arthritis. *Swed Dent J.* 2002;26:149-158.

**84.** Wenneberg B, Kopp S, Gröndahl HG. Long-term effect of intra-articular injections of a glucocorticosteroid into the TMJ: a clinical and radiographic 8-year follow-up. *J Craniomandib Disord.* 1991;5:11-18.

**85.** Dionne R. Pharmacological Approaches. Chicago: *Quintessence*; 2006.

**86.** Singer E, Dionne R. A controlled evaluation of ibuprofen and diazepam for chronic orofacial muscle pain. *J Orofac Pain.* 1997;11:139-146.

**87.** Harkins S, Linford J, Cohen J, Kramer T, Cueva L. Administration of clonazepam in the treatment of TMD and associated myofascial pain: a double-blind pilot study. *J Craniomandib Disord.* 1991;5:179-186.

**88.** Stanko JR. Review of oral skeletal muscle relaxants for the craniomandibular disorder (CMD) practitioner. *Cranio.* 1990;8:234-243.

**89.** Saper JR, Lake AE, Cantrell DT, Winner PK, White JR. Chronic daily headache prophylaxis with tizanidine: a double-blind, placebo-controlled, multicenter outcome study. *Headache.* 2002;42:470-482.

**90.** Herman CR, Schiffman EL, Look JO, Rindal DB. The effectiveness of adding pharmacologic treatment with clonazepam or cyclobenzaprine to patient education and self-care for the treatment of jaw pain upon awakening: a randomized clinical trial. *J Orofac Pain.* 2002;16:64-70.

**91.** AL L. Biochemistry. New York: *Worth Publisher*; 1975.

**92.** Bohne W. Glucosamines in the conservative treatment of arthrosis. *Med Welt.*

1969;30:1668-1671.

**93.** Crolle G, D'Este E. Glucosamine sulphate for the management of arthrosis: a controlled clinical investigation. *Curr Med Res Opin.* 1980;7:104-109.

**94.** D'Ambrosio E, Casa B, Bompani R, Scali G, Scali M. Glucosamine sulphate: a controlled clinical investigation in arthrosis. *Pharmatherapeutica.* 1981;2:504-508.

**95.** Drovanti A, Bignamini AA, Rovati AL. Therapeutic activity of oral glucosamine sulfate in osteoarthrosis: a placebo-controlled double-blind investigation. *Clin Ther.* 1980;3:260-272.

**96.** Pujalte JM, Llavore EP, Ylescupidez FR. Double-blind clinical evaluation of oral glucosamine sulphate in the basic treatment of osteoarthrosis. *Curr Med Res Opin.* 1980;7:110-114.

**97.** Thie NM, Prasad NG, Major PW. Evaluation of glucosamine sulfate compared to ibuprofen for the treatment of temporomandibular joint osteoarthritis: a randomized double blind controlled 3 month clinical trial. *J Rheumatol.* 2001;28:1347-1355.

**98.** de Souza RF, Lovato da Silva CH, Nasser M, Fedorowicz Z, Al-Muharraqi MA. Interventions for the management of temporomandibular joint osteoarthritis. *Cochrane Database Syst Rev.* 2012:CD007261.

**99.** Ekberg EC, Sabet ME, Petersson A, Nilner M. Occlusal appliance therapy in a short-term perspective in patients with temporomandibular disorders correlated to condyle position. *Int J Prosthodont.* 1998;11:263-268.

**100.** Major PW, Nebbe B. Use and effectiveness of splint appliance therapy: review of literature. *Cranio.* 1997;15:159-166.

**101.** Mejersjo C, Hollender L. TMJ pain and dysfunction: relation between clinical and radiographic findings in the short and long-term. *Scand J Dent Res.* 1984;92:241-248.

**102.** Sato H, Fujii T, Yamada N, Kitamori H. Temporomandibular joint osteoarthritis: a comparative clinical and tomographic study pre- and post-treatment. *J Oral Rehabil.*

1994;21:383-395.

**103.** Clark GT, Beemsterboer PL, Solberg WK, Rugh JD. Nocturnal electromyographic evaluation of myofascial pain dysfunction in patients undergoing occlusal splint therapy. *J Am Dent Assoc.* 1979;99:607-611.

**104.** Okeson JP, Moody PM, Kemper JT, Haley JV. Evaluation of occlusal splint therapy and relaxation procedures in patients with temporomandibular disorders. *J Am Dent Assoc.* 1983;107:420-424.

**105.** Kuttila M, Le Bell Y, Savolainen-Niemi E, Kuttila S, Alanen P. Efficiency of occlusal appliance therapy in secondary otalgia and temporomandibular disorders. *Acta Odontol Scand.* 2002;60:248-254.

**106.** Al-Ani MZ, Davies SJ, Gray RJ, Sloan P, Glenny AM. Stabilisation splint therapy for temporomandibular pain dysfunction syndrome. *Cochrane Database Syst Rev.* 2004:CD002778.

**107.** Mejersjo C. Therapeutic and prognostic considerations in TMJ osteoarthrosis: a literature review and a long-term study in 11 subjects. *Cranio.* 1987;5:69-78.

**108.** Forssell H, Kalso E. Application of principles of evidence-based medicine to occlusal treatment for temporomandibular disorders: are there lessons to be learned? *J Orofac Pain.* 2004;18:9-32.

**109.** Murakami KI, Iizuka T, Matsuki M, Ono T. Recapturing the persistent anteriorly displaced disk by mandibular manipulation after pumping and hydraulic pressure to the upper joint cavity of the temporomandibular joint. *Cranio.* 1987;5:17-24.

**110.** Sanders B. Management of internal derangements of the temporomandibular joint. *Semin Orthod.* 1995;1:244-257.

**111.** Goudot P, Jaquinet AR, Hugonnet S, Haefliger W, Richter M. Improvement of pain and function after arthroscopy and arthrocentesis of the temporomandibular joint: a comparative study. *J Craniomaxillofac Surg.* 2000;28:39-43.

**112.** Nitzan DW, Dolwick MF, Martinez GA. Temporomandibular joint arthrocentesis: a simplified treatment for severe, limited mouth opening. *J Oral Maxillofac Surg.* 1991;49:1163-1170.

**113.** Carvajal WA, Laskin DM. Long-term evaluation of arthrocentesis for the treatment of internal derangements of the temporomandibular joint. *J Oral Maxillofac Surg.* 2000;58:852-857.

**114.** Nishimura M, Segami N, Kaneyama K, Suzuki T. Prognostic factors in arthrocentesis of the temporomandibular joint: evaluation of 100 patients with internal derangement. *J Oral Maxillofac Surg.* 2001;59:874-878.

**115.** Alpaslan GH, Alpaslan C. Efficacy of temporomandibular joint arthrocentesis with and without injection of sodium hyaluronate in treatment of internal derangements. *J Oral Maxillofac Surg.* 2001;59:613-619.

**116.** Fridrich KL, Wise JM, Zeitler DL. Prospective comparison of arthroscopy and arthrocentesis for temporomandibular joint disorders. *J Oral Maxillofac Surg.* 1996;54:816-821.

**117.** Guarda-Nardini L, Manfredini D, Ferronato G. Arthrocentesis of the temporomandibular joint: a proposal for a single-needle technique. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2008;106:483-486.

**118.** Rahal A, Poirier J, Ahmarani C. Single-puncture arthrocentesis--introducing a new technique and a novel device. *J Oral Maxillofac Surg.* 2009;67:1771-1773.

**119.** Bertolami CN, Gay T, Clark GT, et al. Use of sodium hyaluronate in treating temporomandibular joint disorders: a randomized, double-blind, placebo-controlled clinical trial. *J Oral Maxillofac Surg.* 1993;51:232-242.

**120.** Moldez MA, Camones VR, Ramos GE, Padilla M, Enciso R. Effectiveness of Intra-Articular Injections of Sodium Hyaluronate or Corticosteroids for Intracapsular Temporomandibular Disorders: A Systematic Review and Meta-Analysis. *J Oral*

*Facial Pain Headache.* 2018;32:53–66.

**121.** Alstergren P, Appelgren A, Appelgren B, Kopp S, Lundeberg T, Theodorsson E. The effect on joint fluid concentration of neuropeptide Y by intra-articular injection of glucocorticoid in temporomandibular joint arthritis. *Acta Odontol Scand.* 1996;54:1-7.

**122.** Ringold S, Torgerson TR, Egbert MA, Wallace CA. Intraarticular corticosteroid injections of the temporomandibular joint in juvenile idiopathic arthritis. *J Rheumatol.* 2008;35:1157-1164.

**123.** Toller PA. Use and misuse of intra-articular corticosteroids in treatment of temporomandibular joint pain. *Proc R Soc Med.* 1977;70:461-463.

**124.** Nitzan DW, Price A. The use of arthrocentesis for the treatment of osteoarthritic temporomandibular joints. *J Oral Maxillofac Surg.* 2001;59:1154-1160.

**125.** Dingman RO, Grabb WC. Intracapsular temporomandibular joint arthroplasty. *Plast Reconstr Surg.* 1966;38:179-185.

**126.** Bieniaszewski L, Staessen JA, Byttebier G, De Leeuw P, Van Hedent T, Fagard R. Trough-to-peak versus surface ratio in the assessment of antihypertensive agents. APTH Investigators. Ambulatory Blood Pressure and Treatment of Hypertension. *Blood Press.* 1995;4:350-357.

**127.** de Leeuw R, Boering G, Stegenga B, de Bont LG. Symptoms of temporomandibular joint osteoarthrosis and internal derangement 30 years after non-surgical treatment. *Cranio.* 1995;13:81-88.

**128.** Abrahamsson AK, Arvidsson LZ, Småstuen MC, Larheim TA. Improvement of bone-erosive temporomandibular joint (TMJ) abnormalities in adolescents undergoing non-surgical treatment: a longitudinal study. *Dentomaxillofac Radiol.* 2020;49:20190338.

**129.** Lei J, Yap AU, Liu MQ, Fu KY. Condylar repair and regeneration in adolescents/young adults with early-stage degenerative temporomandibular joint disease: A randomised controlled study. *J Oral Rehabil.* 2019;00:1-11.

**130.** Ok SM, Jeong SH, Ahn YW, Kim YI. Effect of stabilization splint therapy on glenoid fossa remodeling in temporomandibular joint osteoarthritis. *J Prosthodont Res.* 2016;60:301-307.

**131.** Ok SM, Lee J, Kim YI, Lee JY, Kim KB, Jeong SH. Anterior condylar remodeling observed in stabilization splint therapy for temporomandibular joint osteoarthritis. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2014;118:363-370.

**132.** Liu MQ, Chen HM, Yap AU, Fu KY. Condylar remodeling accompanying splint therapy: a cone-beam computerized tomography study of patients with temporomandibular joint disk displacement. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2012;114:259-265.

**133.** Dworkin SF, LeResche L. Research diagnostic criteria for temporomandibular disorders: review, criteria, examinations and specifications, critique. *J Craniomandib Disord.* 1992;6:301-355.

**134.** Comert Kilic S, Kilic N, Sumbullu MA. Temporomandibular joint osteoarthritis: cone beam computed tomography findings, clinical features, and correlations. *Int J Oral Maxillofac Surg.* 2015;44:1268-1274.

**135.** Winocur E, Reiter S, Krichmer M, Kaffe I. Classifying degenerative joint disease by the RDC/TMD and by panoramic imaging: a retrospective analysis. *J Oral Rehabil.* 2010;37:171-177.

**136.** Wiberg B, Wanman A. Signs of osteoarthrosis of the temporomandibular joints in young patients: a clinical and radiographic study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1998;86:158-164.

**137.** Zhao YP, Zhang ZY, Wu YT, Zhang WL, Ma XC. Investigation of the clinical and radiographic features of osteoarthrosis of the temporomandibular joints in adolescents and young adults. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2011;111:e27-34.

**138.** Kuttila M, Niemi PM, Kuttila S, Alanen P, Le Bell Y. TMD treatment need in relation to age, gender, stress, and diagnostic subgroup. *J Orofac Pain.* 1998;12:67-74.

**139.** Ong TK, Franklin CD. A clinical and histopathological study of osteoarthrosis of the temporomandibular joint. *Br J Oral Maxillofac Surg.* 1996;34:186-192.

**140.** Cevidanes LH, Gomes LR, Jung BT, et al. 3D superimposition and understanding temporomandibular joint arthritis. *Orthod Craniofac Res.* 2015;18 Suppl 1:18-28.

**141.** Cevidanes LH, Hajati AK, Paniagua B, et al. Quantification of condylar resorption in temporomandibular joint osteoarthritis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2010;110:110-117.

**142.** Lim MJ, Lee JY. Computed tomographic study of the patterns of oesteoarthritic change which occur on the mandibular condyle. *J Craniomaxillofac Surg.* 2014;42:1897-1902.

**143.** Ko FC, Dragomir C, Plumb DA, et al. In vivo cyclic compression causes cartilage degeneration and subchondral bone changes in mouse tibiae. *Arthritis Rheum.* 2013;65:1569-1578.

**144.** Stegenga B. Osteoarthritis of the temporomandibular joint organ and its relationship to disc displacement. *J Orofac Pain.* 2001;15:193-205.

**145.** Shinoda C, Takaku S. Interleukin-1 beta, interleukin-6, and tissue inhibitor of metalloproteinase-1 in the synovial fluid of the temporomandibular joint with respect to cartilage destruction. *Oral Dis.* 2000;6:383-390.

**146.** Hajati AK, Alstergren P, Nasstrom K, Bratt J, Kopp S. Endogenous glutamate in association with inflammatory and hormonal factors modulates bone tissue resorption of the temporomandibular joint in patients with early rheumatoid arthritis. *J Oral Maxillofac Surg.* 2009;67:1895-1903.

**147.** Yamada K, Fukui T, Tsuruta A, et al. The relationship between retruded contact position and intercuspal position in patients with TMJ osteoarthritis. *Cranio.*

2003;21:240-247.

**148.** He SS, Deng X, Wamalwa P, Chen S. Correlation between centric relation & maximum intercuspation discrepancy and temporomandibular joint dysfunction. *Acta Odontol Scand.* 2010;68:368-376.

**149.** Wang C, Yin X. Occlusal risk factors associated with temporomandibular disorders in young adults with normal occlusions. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2012;114:419-423.

**150.** Visser A, McCarroll RS, Oosting J, Naeije M. Masticatory electromyographic activity in healthy young adults and myogenous craniomandibular disorder patients. *J Oral Rehabil.* 1994;21:67-76.

**151.** Manfredini D, Perinetti G, Guarda-Nardini L. Dental malocclusion is not related to temporomandibular joint clicking: a logistic regression analysis in a patient population. *Angle Orthod.* 2014;84:310-315.

**152.** Selaimen CM, Jeronymo JC, Brilhante DP, Lima EM, Grossi PK, Grossi ML. Occlusal risk factors for temporomandibular disorders. *Angle Orthod.* 2007;77:471-477.

**153.** Zonnenberg AJ, Mulder J. The incidence of centric slides in healthy individuals and TMD patients. *Eur J Prosthodont Restor Dent.* 2013;21:109-113.

**154.** Lila-Krasniqi ZD, Shala K, Pustina-Krasniqi T, Bicaj T, Dula LJ, Guguvcevski L. Differences between centric relation and maximum intercuspation as possible cause for development of temporomandibular disorder analyzed with T-scan III. *Eur J Dent.* 2015;9:573-579.

**155.** Artun J, Hollender LG, Truelove EL. Relationship between orthodontic treatment, condylar position, and internal derangement in the temporomandibular joint. *Am J Orthod Dentofacial Orthop.* 1992;101:48-53.

**156.** Al-Ani Z, Gray RJ, Davies SJ, Sloan P, Glenny AM. Stabilization splint therapy for the treatment of temporomandibular myofascial pain: a systematic review. *J Dent Educ.*

2005;69:1242-1250.

**157.** Machon V, Hirjak D, Lukas J. Therapy of the osteoarthritis of the temporomandibular joint. *J Craniomaxillofac Surg.* 2011;39:127-130.

**158.** Ismail F, Demling A, Hessling K, Fink M, Stiesch-Scholz M. Short-term efficacy of physical therapy compared to splint therapy in treatment of arthrogenous TMD. *J Oral Rehabil.* 2007;34:807-813.

**159.** Mejersjo C, Wenneberg B. Diclofenac sodium and occlusal splint therapy in TMJ osteoarthritis: a randomized controlled trial. *J Oral Rehabil.* 2008;35:729-738.

**160.** Guarda-Nardini L, Masiero S, Marioni G. Conservative treatment of temporomandibular joint osteoarthrosis: intra-articular injection of sodium hyaluronate. *J Oral Rehabil.* 2005;32:729-734.

**161.** Moystad A, Mork-Knutsen BB, Bjornland T. Injection of sodium hyaluronate compared to a corticosteroid in the treatment of patients with temporomandibular joint osteoarthritis: a CT evaluation. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2008;105:e53-60.

**162.** Ekberg EC, Kopp S, Akerman S. Diclofenac sodium as an alternative treatment of temporomandibular joint pain. *Acta Odontol Scand.* 1996;54:154-159.

**163.** Mejersjo C, Hollender L. Radiography of the temporomandibular joint in female patients with TMJ pain or dysfunction. A seven year follow-up. *Acta Radiol Diagn (Stockh).* 1984;25:169-176.

**Table 1. Effect of clinical variables on TMJ OA prognosis and DCI change**

| Variables | | N (%) or Mean (*SD*) | Effect on favorable TMJ OA prognosis | | Change in DCI | | |
|---|---|---|---|---|---|---|---|
| | | | OR (95%CI) | $P^a$ | Initial DCI Mean (*SD*) | Final DCI Mean (*SD*) | $P^b$ |
| Age (years) | | 33.17 (*17.65*) | 1.00 (0.96-1.03) | 0.733 | | | |
| Age group | 10s | 23 (25.84%) | | | 1.60 (*1.91*) | 0.70 (*0.90*) | 0.151 |
| | 20s | 27 (30.34%) | | | 1.34 (*1.74*) | 0.34 (*0.71*) | |
| | 30s | 14 (15.73%) | | | 1.52 (*1.55*) | 0.92 (*1.38*) | |
| | 40s | 6 (6.74%) | | | 1.22 (*1.55*) | 0.11 (*0.31*) | |
| | 50s | 6 (6.74%) | | | 1.40 (*0.92*) | 0.60 (*0.80*) | |
| | 60s≦ | 13 (14.61%) | | | 2.13 (*1.96*) | 1.17 (*1.28*) | |
| Gender | Male | 13 (14.61%) | 0.38 (0.08-1.85) | 0.472 | 1.33 (*1.61*) | 0.90 (*1.57*) | 0.748 |
| | Female | 76 (85.39%) | | | 1.60 (*1.79*) | 0.63 (*0.92*) | |
| F/U period (days) | | 644.58 (*325.71*) | 1.00 (1.00-1.00) | 0.464 | | | |
| CMO (mm) | | 39.43 (*10.55*) | | | | | |
| MMO (mm) | | 43.22 (*9.05*) | | | | | |
| MOL (<38 mm) | No | 64 (71.91%) | 2.05 (0.53-7.87) | 0.182 | 1.67 (*1.91*) | 0.62 (*1.03*) | 0.393 |
| | Yes | 25 (26.97%) | | | 1.30 (*1.32*) | 0.77 (*1.04*) | |
| Pain | No | 39 (43.82%) | 0.73 (0.22-2.35) | 0.119 | 1.34 (*1.69*) | 0.47 (*0.82*) | 0.040* |
| | Yes | 50 (56.18%) | | | 1.74 (*1.82*) | 0.83 (*1.17*) | |
| Noise | No | 63 (70.79%) | 0.30 (0.08-1.09) | 0.156 | 1.42 (*1.71*) | 0.66 (*1.10*) | 0.160 |
| | Yes | 26 (29.21%) | | | 1.91 (*1.86*) | 0.68 (*0.87*) | |
| CO/CR discrepancy | No | 57 (64.04%) | 1.33 (1.08-1.76) | 0.032* | 1.66 (*1.92*) | 0.76 (*1.14*) | 0.838 |
| | Yes | 32 (35.96%) | | | 1.37 (*1.43*) | 0.50 (*0.79*) | |
| Disc displacement | No | 89 (58.60%) | 0.40 (0.10-1.66) | 0.763 | 1.52 (*1.78*) | 0.70 (*1.08*) | 0.529 |
| | Yes | 63 (41.40%) | | | 1.62 (*1.76*) | 0.62 *(0.99*) | |
| Occlusal splint | No | 17 (19.10%) | 1.63 (1.09-2.42) | 0.015* | 1.76 (*2.05*) | 0.76 (*0.90*) | 0.490 |
| | Yes | 72 (80.90%) | | | 1.51(*1.69*) | 0.64 (*1.07*) | |
| Intraarticular injection | No | 68 (76.40%) | 1.49 (0.99-2.23) | 0.057 | 1.62 (*1.90*) | 0.66 (*1.09*) | 0.522 |
| | Yes | 21 (23.60%) | | | 1.36 (*1.23*) | 0.67 (*0.85*) | |
| NSAIDs | No | 44 (49.44%) | 4.34 (0.97-19.50) | 0.011* | 1.48 (*1.86*) | 0.44 (*0.85*) | 0.116 |
| | Yes | 45 (50.56%) | | | 1.64 (*1.66*) | 0.89 (*1.16*) | |
| Initial DCI | | | 7.25 (3.20-16.42) | 0.000* | | | |

F/U, follow-up; CMO, comfortable mouth opening; MMO, maximal mouth opening; CO/CR, centric occlusion/centric relation; NSAIDs, non-steroidal anti-inflammatory drugs; MOL, mouth opening limitation; DCI, destructive change index.

$P^a$, significance analyzed by logistic regression; $P^b$, significance analyzed by repeated measures ANOVA.

$^*p<0.05$

OR, odds ratio; CI, confidence interval.

Nagelkerke $R^2$ (an estimation of total log likelihood) was 0.627.

**Table 2. TMJ OA prognosis according to DCI change**

| Prognosis | N (%) | Initial DCI (*SD*) | Final DCI (*SD*) |
|---|---|---|---|
| Worsened | 27 (17.8%) | 0.33 (*0.54*) | 1.37 (*0.95*) |
| No change | 32 (21.1%) | 0.44 (*1.14*) | 0.44 (*1.14*) |
| Improved | 93 (61.2%) | 2.30 (*1.77*) | 0.54 (*0.93*) |
| Total | 152 (100%) | 1.56 (*1.76*) | 0.66 (*1.04*) |

DCI, destructive change index.

Significance analyzed by repeated measures ANOVA.

## Figure legends

Fig. 1 Evaluation of osteoarthritic changes of the mandibular condyle

Fig. 1a The condylar surface was divided into three sections in the medio-lateral direction between the tangent line on the most medial and lateral point. (M, medial; C, central; L, lateral)

Fig. 1b: The condylar surface was divided into three sections in the antero-posterior direction between the tangent line on the most anterior and posterior point. (A, anterior; M, middle; P, posterior)

Fig. 1c: The condylar surface was divided into nine imaginary sections. (AM, antero-medial; AC, antero-central; AL, antero-lateral; MM, mid-medial; MC, mid-central; ML, mid-lateral; PM, postero-medial; PC, postero-central; PL, postero-lateral)

Fig. 2 The three groups based on longitudinal TMJ OA bone change

Fig. 2a: No change group; Fig. 2b: Improved group; Fig. 2c: Worsened group.

Initial (left) and final (right) CT examination of each image set

Fig. 3 DCI change according to TMJ OA prognosis

DCI, destructive change index.

*P*=0.004, Significance analyzed by repeated measures ANOVA.

Fig. 4 DCI change according to presence of pain

DCI, Destructive change index

*P*=0.04, Significance analyzed by repeated measures ANOVA.

**Figure 1.**

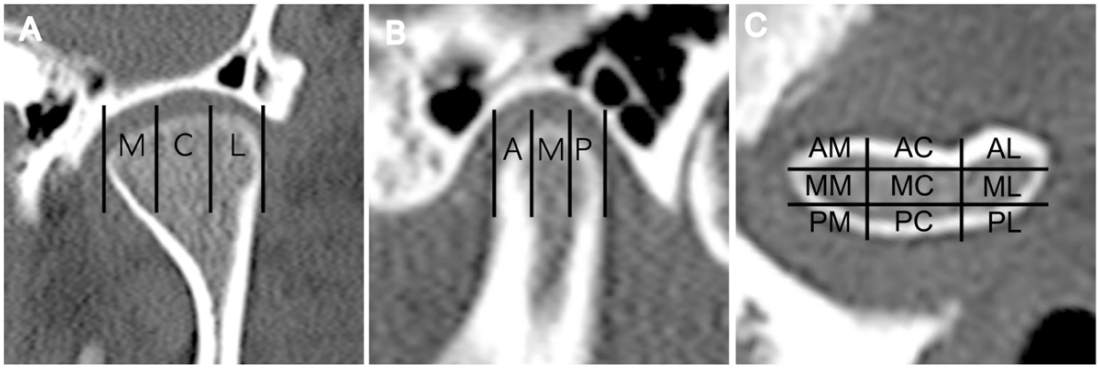


**Figure 2.**

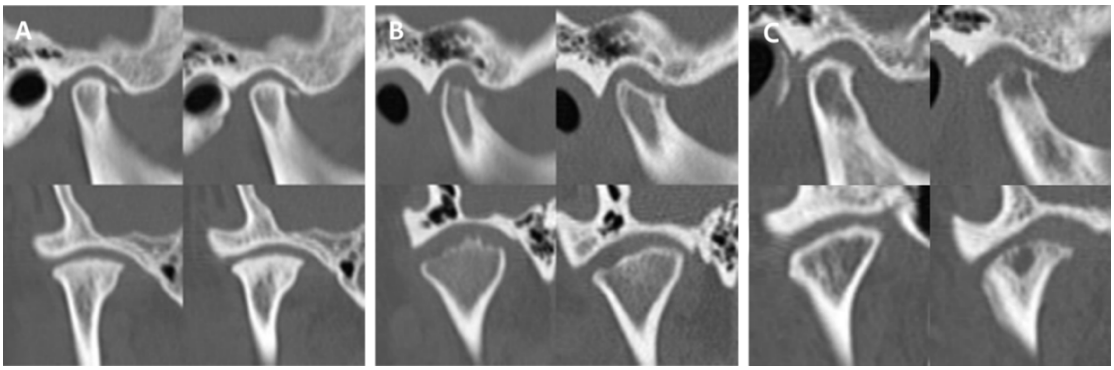


**Figure 3.**

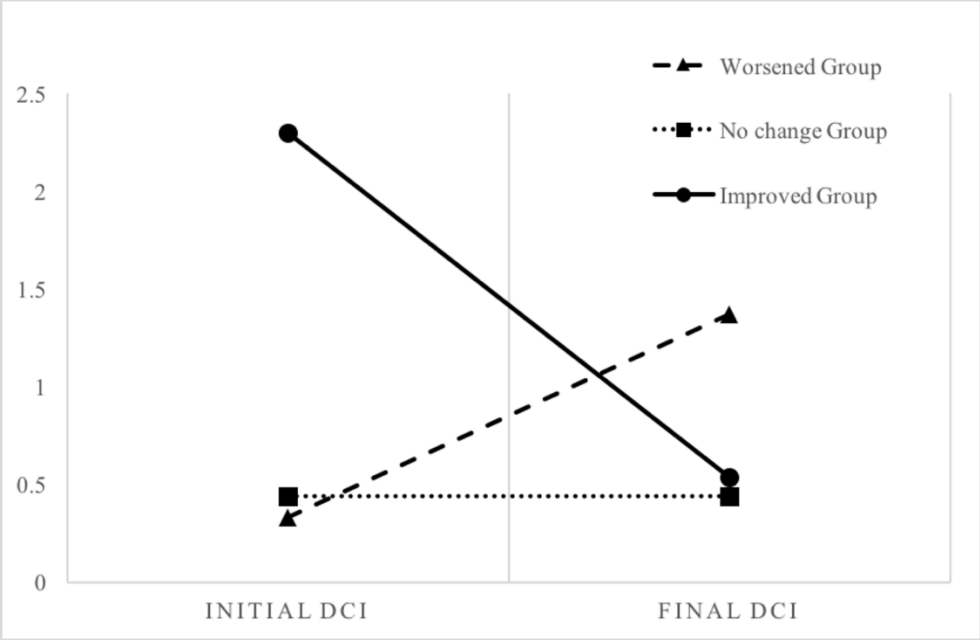
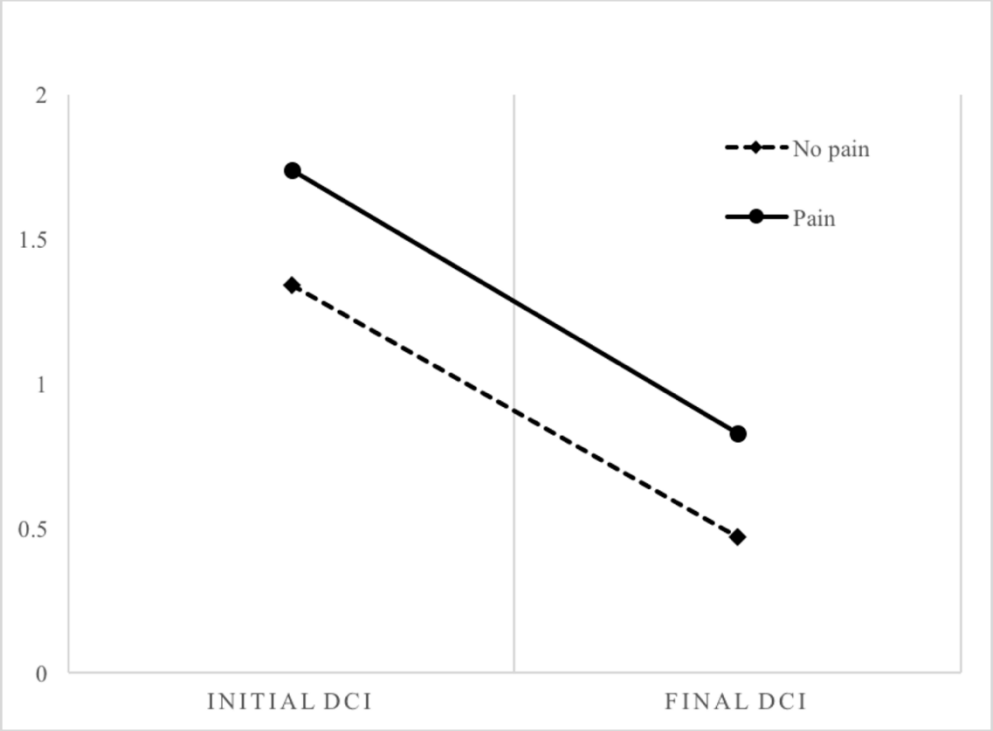

Worsened Group
No change Group
Improved Group
2.5
2
1.5
1
0.5
0
INITIAL DCI
FINAL DCI

**Figure 4.**



국문초록

# 전산화 단층촬영을 바탕으로 한 턱관절 골관절염 변화에 관한 종적 연구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이 연구의 목적은 전산화 단층촬영 (Computed tomography, CT)을 통해 턱관절 골관절염의 종적인 변화 양상을 이해하고 턱관절장애의 다른 임상적 특징이 골관절염의 종적인 변화에 어떤 영향을 미치는지 그 연관성을 확인하기 위한 것이다.

턱관절 골관절염 환자 중 2회 이상 추적 CT를 촬영한 89 명 (여성 76 명, 남성 13 명)의 환자를 대상으로 하였으며, 골관절염에 이환된 관절은 152 관절이고 정상 관절은 26 관절이었다. 평균 추적 기간은 21.47±10.86 개월이며, 대상자의 평균연령은 33.17±17.65 세이다. 성별, 나이, 개구량, 통증, 관절잡음, 중심교합/중심위 부조화, 관절원판 변위, 교합안정장치 치료, 관절강내 주사치료, 비스테로이드성 소염진통제 약물치료 등의 임상적인 정보를 수집하여 분석하였으며, 종적인 CT 영상을 수집하였다. 골파괴의 정도를 파악하기 위하여 CT상 하악과두면을 가상의 9개의 면으로 분할하여 이 중 골파괴성 변화가 나타난 면의

수를 골파괴 지수로 정의하여 판독하였다. 통계분석은 반복분산분석과 회귀분석을 활용하였다.

전반적인 골파괴지수는 1.56에서 0.66으로 감소하여 골파괴의 정도는 추적영상에서 평균적으로 호전되는 것을 확인하였다. 93 관절 (93/152, 61.2%)은 개선되었고 27 관절 (27/152, 17.8%)은 악화되었으며, 32 (32/152, 21.1%) 관절은 변화가 없었다. 통증이 있는 군에서 초기와 마지막 영상의 골파괴 정도가 통증이 없는 군에 비해 유의하게 높았다 (p=0.04). 교합안정장치 치료 그리고/또는 비스테로이드성 소염진통제 약물치료를 받은 경우 턱관절 골관절염의 예후에 유의한 긍정적인 영향을 미치는 것으로 나타났다 (OR 1.63, p=0.015 및 OR 4.34, p=0.011).

이 연구의 결론은 다음과 같다.

1. 턱관절 골관절염은 대부분의 경우 장기적으로 호전되는 경향을 보였다.

2. 골파괴성 변화가 있는 턱관절 골관절염의 피질골이 회복되기까지 평균 약 2년이 걸렸다.

3. 턱관절 골관절염에 통증이 동반되는 경우 골파괴의 정도가 불량한 예후를 보였다.

4. 교합안정장치 치료 그리고/또는 비스테로이드성 소염진통제 복용은 턱관절 골관절염의 개선에 도움이 되었다.

5. 초기에는 경미한 골파괴 정도를 보이는 하악과두도 나중에 악화되는 양상을 보일 수 있으므로 턱관절 골관절염 환자는 반드시 주기적인 추적 영상 관찰이 필요하다.

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**주요어 :** 턱관절장애, 턱관절 골관절염, 전산화단층촬영, 장기 예후, 교합안정장치치료, 비스테로이드성 소염진통제

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