



Could Crepitus Be an Indication for Early Temporomandibular Joint Osteoarthritis?

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Purpose: To determine whether crepitus may be a clinical indication for early temporomandibular joint (TMJ) osteoarthritis (OA) and to investigate the correlation between crepitus and the occurrence of TMJ OA with respect to factors, such as patient sex, age, chewing habits, and diagnosis.

Methods: This is retrospective analysis of clinical data for 162 TMJs. The criteria for a joint to be included in this study was a minimum of two cone-beam computed tomography (CBCT) scans performed with no OA observed during the initial scan. The Diagnostic Criteria for Temporomandibular Disorders was used for OA diagnosis. Crepitus was recorded when it was objectively palpated during the follow-up period. Correlations between various patient factors and progression to TMJ OA were calculated using the Pearson's chi-square test. A linear-by-linear association was used to analyze trends of OA progression with increasing age.

Results: Among the 162 joints, 101 progressed to OA and 61 did not. In the joints where crepitus had been present before OA was confirmed at next or last CBCT, OA progressed at a high rate, and especially higher in female and older patients ($p < 0.01$). Patients in the pain-related disorder group with crepitus were observed to have higher rates of OA progression compared to patients in the intra-articular disorder group ($p < 0.01$).

Conclusions: If a patient experiences pain in the TMJs and crepitus, close monitoring through regular CBCT scans is necessary even if there is no evidence of radiologically confirmed OA after the first CBCT.

Key Words: Crepitus; Early osteoarthritis; Temporomandibular joint; The Diagnostic Criteria for Temporomandibular Disorders

INTRODUCTION

Osteoarthritis (OA) is one of the most common diseases that affect the temporomandibular joint (TMJ), causing destructive changes in the bone. In general, TMJ OA is confirmed when subchondral cyst, erosion, generalized sclerosis, and osteophyte are detected on radiographic images

[1]. However, computed tomography (CT) or cone-beam CT (CBCT) cannot detect tissue-related changes, such as damages to articular cartilage. Only when the disease has advanced to the extent that the subcortical layer has been destroyed would it be recognized as OA [2]. Once a bone is damaged, it does not easily recover; therefore, early diagnosis and treatment of TMJ OA are essential in reducing the

degree of joint injury and lowering the risk of possible future OA changes. Early detection of OA is much more complicated than the diagnosis of established OA [3,4]. Patients with early OA who show no radiological signs may go undiagnosed and have a lack of follow-up, thereby leading to continuing deterioration.

TMJ contains fibrocartilage, unlike most joints that contain hyaline cartilage; however, TMJ is similar to other joints in terms of structure and function [5]. Considering the fact that knee OA is often used as an example when describing TMJ OA, it can be argued that using magnetic resonance imaging (MRI) to evaluate cartilage damage and bone marrow lesion may be considered as an appropriate method for early diagnosis of TMJ OA. There have been various studies on the early diagnosis of knee OA using MRI; however, MRIs may be prohibitively expensive despite its possible usefulness [3,6,7].

There are many studies on the clinical features and radiological findings of advanced TMJ OA or temporomandibular disorder (TMD), but there is a lack of research on the clinical manifestations of early TMJ OA. Crepitus, a characteristic sound clinically detected in patients with TMJ OA, is generally thought to occur in the later stages of OA. However, some previous studies on knee OA and TMJ rheumatoid arthritis (RA) have reported that crepitus may be an early clinical indicator of them [8-10]. Therefore, this study aims to determine whether crepitus may be an early clinical indicator of TMJ OA and investigate the association between crepitus and the occurrence of OA, considering various factors about patients, such as sex, age, chewing habits, and diagnosis.

MATERIALS AND METHODS

1. Subjects

All clinical and radiographic data of patients who visited the Department of Oral Medicine at Pusan National University Hospital between June 2013 and December 2016 were retrospectively reviewed. Among the 1,206 patients who underwent at least two CBCT scans, patients with radiographic findings of skeletal deformity, condyle fracture, TMJ tumor, or bilateral TMJ OA at the first CBCT were excluded. The remaining 100 patients did not have TMJ

abnormalities on at least one side.

Among 200 joints (100 patients), 162 joints were investigated—38 joints that showed OA at the first CBCT scan were excluded—and, they were either the ones that progressed into OA on the next or last CBCT scan, or others that did not progress until last CBCT scan. The diagnosis of each joint at the first visit was done by an orofacial pain specialist, and the reading of CBCT was conducted by an oral radiologist.

All patients received conservative treatments, such as medication, behavioral conditioning, and physical therapy. During the follow-up period, CBCT was performed at intervals of a minimum of 6 months and a maximum of 36 months, and the average of intervals is 9.79 ± 5.3 . At first visit, sex, age, diagnosis and chewing habits of each patient were investigated, and the presence or absence of crepitus on charts was studied before being confirmed by next or last CBCT. Among them, 124 were females (76.5%) and 38 were males (23.5%), and the ages ranged from 13 to 83 years (mean age, 29.40 ± 15.46 years). This study was approved by the Institutional Review Board of Pusan National University Dental Hospital (IRB no. PNUDH-2017-027). Written informed consent was obtained from all patients at the first visit.

2. Methods

1) Clinical data collection

Clinical data were studied based on the initial record of age, sex, presence of crepitus, unilateral chewing habit, and diagnosis. The patients were divided into the following three age groups; Group I (11 to 20 years), Group II (21 to 30 years), and Group III (>30 years). The data of crepitus on two groups were collected, and the specific criteria of the data collection are as follows; In Progression-to-OA Group, the existence or non-existence of the detection of crepitus on charts was studied before the OA was observed in the CBCT reading. In No-Progression-to-OA Group, the existence or non-existence of the detection of crepitus on charts was studied until the last visit. Crepitus was expressed as present (P) or absent (A). Crepitus was considered as present when it was objectively palpated at least one time during opening, closing, or right or left lateral or protrusive movement. Subjective reports of crunching, grating, or grinding

sound by patients were not collected while patients were not in the hospital. The diagnosis at first visit was conducted according to Diagnostic Criteria for TMD (DC/TMD). The patients who had visited hospital before DC/TMD was published were diagnosed again, according to DC/TMD based on their chart.

2) OA diagnostic criteria

The CBCT images were taken using Pax-Zenith 3D (Vatech, Hwaseong, Korea). At the time of the first CBCT imaging, TMJ OA was not diagnosed if the images were interpreted as normal, and considered to have no abnormal finding and posterior or anterior position of condyle by experienced oral radiologists. TMJ OA was confirmed when subchondral cyst(s), erosion(s), generalized sclerosis, or osteophyte(s) was observed during CBCT image reading, according to the criteria of OA diagnosis based on DC/TMD [1]. The joints that progressed to OA from the second to the last CBCT were expressed as progression (Pr), and joints not progressed to OA were expressed as no progression (N).

3) Statistical analysis

All statistical analyses were performed using IBM SPSS

Statistics ver. 21.0 software (IBM Co., Armonk, NY, USA). The association between crepitus and the occurrence of OA, considering various factors about patients, such as sex, age, chewing habits, and diagnosis—was calculated using the Pearson's chi-square test. If the expected frequency of the cell was lower than 5, Fisher's exact test was used. A linear by linear association was used to analyze trends of OA progression rate as the age of the patient increases. A p-value of <0.05 was considered statistically significant.

RESULTS

Among the 162 TMJs, 61 (37.7%) progressed to OA and 101 (62.3%) did not.

1. Association between Crepitus and TMJ OA Progression Rate

There was a statistically significant difference in the presence or absence of crepitus between OA-progressed joints and non-OA-progressed joints, with a higher OA progression rate when crepitus was present ($p < 0.01$; Table 1).

Table 1. Correlation between sex and TMJ OA progression

Sex	OA change		Total	χ^2 (p-value)
	Progression	No progression		
Female				
Crepitus				
Presence	16 (64.0)	9 (36.0)	25	7.854** (0.005)
Absent	33 (33.3)	66 (66.7)	99	
Total	49 (39.5)	75 (60.5)	124	
Male				
Crepitus				
Presence	6 (50.0)	6 (50.0)	12	2.754 ^a (0.101)
Absent	6 (23.1)	20 (76.9)	26	
Total	12 (31.6)	26 (68.4)	38	
Total				
Crepitus				
Presence	22 (59.5)	15 (40.5)	37	9.712** (0.002)
Absent	39 (31.2)	86 (68.8)	125	
Total	61 (37.7)	101 (62.3)	162	

TMJ, temporomandibular joint; OA, osteoarthritis. Values are presented as number (%).

The p-value was determined using chi-square test.

^aUsing fisher's exact test.

**p<0.01.

2. Association between Sex, Crepitus and Progression to TMJ OA

Among 162 TMJs, there were approximately three times more female TMJs (124) than male TMJs (38). Among the 38 male TMJs, the rate of joints that progressed to OA was 68.4% and that in females was 65.3%, which showed no statistically significant difference ($p > 0.05$). In males, there was no statistically significant correlation ($p > 0.05$) between OA occurrence and existence and nonexistence of crepitus; however, in females, there was a higher probability of OA progression when crepitus was present ($p < 0.01$; Table 1).

3. Association between Age, Presence or Absence of Crepitus, and Rate of Progression to TMJ OA

The age distribution of the 162 joints is as follows: Group I (11-20 years) had 45 joints (27.8%), Group II (21-30 years) had 73 (45.0%; the largest group), and Group III (>30 years) had 44 (27.2%). The risk of OA increased as age increased, from 26.7% in Group I to 32.9% in Group II, and 56.8% in Group III ($p < 0.01$; Table 2).

There was no statistically significant difference in the rate of progression of OA according to existence and nonexistence of crepitus in Group I; however, there was a statistically significant difference in Group II ($p = 0.044$), and in Group III, when crepitus was present, a higher rate of OA progression was seen ($p = 0.030$).

4. Analysis of OA Progression Rate with Crepitus in Intra-Articular Disorders, and Pain Related Disorders

Initial diagnosis included myalgia, arthralgia, disc displacement with reduction (DD/wR), disc displacement without reduction (DD/woR), and RA according to DC/TMD (including multiple diagnoses; a total $n = 269$). Myalgia was the most common (33.5%; $n = 90$); however, DD/wR was the most common ($n = 52$) among the intra-articular disorders. When all patients were divided into two groups according to existence or absence of OA progression and relative rate of diagnosis names at initial diagnosis was studied, divided into two groups, diagnosis names (myalgia, arthralgia, and normal) showed almost similar distribution regardless of

Table 2. Correlation between age, the presence or absence of crepitus and progression to TMJ OA

Group	OA change		Total	χ^2 (p-value)
	Progression	No progression		
Group I				
Crepitus				
Presence	3 (37.5)	5 (62.5)	8	0.584 ^a (0.661)
Absent	9 (24.3)	28 (75.7)	37	
Total	12 (26.7)	33 (73.3)	45	
Group II				
Crepitus				
Presence	9 (52.9)	8 (47.1)	17	4.043* (0.044)
Absent	15 (26.8)	41 (73.2)	56	
Total	24 (32.9)	49 (67.1)	73	
Group III				
Crepitus				
Presence	10 (83.3)	2 (16.7)	12	4.728 (0.030)
Absent	15 (46.9)	17 (53.1)	32	
Total	25 (56.8)	19 (43.2)	44	
Total				
Age group	61 (37.7)	101 (62.3)	162	9.907** (0.007)
Linear by linear association				8.512** (0.004)

TMJ, temporomandibular joint; OA, osteoarthritis.

Values are presented as number (%).

Group I, 11-20 years; Group II, 21-30 years; Group III, >30 years.

The p-value was determined using the chi-square test.

^aUsing the Fisher's exact test.

* $p < 0.05$, ** $p < 0.01$.

OA progression. The rate of DD/wR was higher in patients whose joint did not progress to OA (21.6%) compared with patients who were diagnosed with OA (14.4%), whereas the rate of DD/woR was significantly higher in patients with OA (15.5%) compared with patients without OA (9.3%; Fig. 1).

There was no statistically significant difference in OA progression between myalgia, arthralgia, DD/wR, and DD/woR, except in normal patients and those with RA. When the rate of crepitus was analyzed according to existence and nonexistence of OA progression, myalgia (p=0.005) and arthralgia (p=0.004) were statistically significant (p<0.01) in the pain-related disorder diagnostic group. There was no statistically significant difference between the crepitus and OA progression rate in the DD/wR and DD/woR intra-articular joint

disorders (Fig. 2).

The sensitivity and specificity of early diagnosis of OA according to the presence of crepitus alone and crepitus within the pain-related disorder group were examined. In the case of crepitus alone, the sensitivity of early diagnosis of OA was 0.36 and the specificity was 0.85. In the pain-related disorder group, the sensitivity of early diagnosis of OA by crepitus was 0.47 and specificity was 0.83. Sensitivity was low and specificity was high compared with DC/TMD values with sensitivity of 0.55 and specificity of 0.61 (Table 3).

5. Association between Chewing Habits and TMJ OA Progression Rate

Among the 147 joints examined for chewing habits in

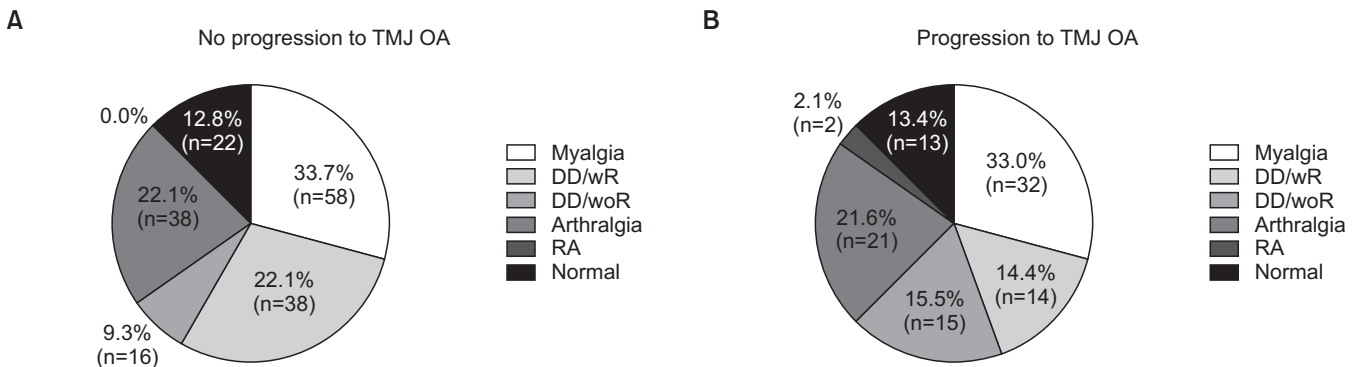


Fig. 1. Percentage of patients according to diagnostic distribution of joints that did or did not progress to osteoarthritis. The rate of DD/wR was higher in patients whose joint did not progress to OA (22.1%, A) compared with patients who were diagnosed with OA (14.4%, B), whereas the rate of DD/woR was significantly higher in patients with OA (15.5%, B) compared with patients without OA (9.3%, A). TMJ, temporomandibular joint; OA, osteoarthritis; DD/wR, disc displacement with reduction; DD/woR, disc displacement without reduction; RA, rheumatoid arthritis. Values are presented as percentage (number).

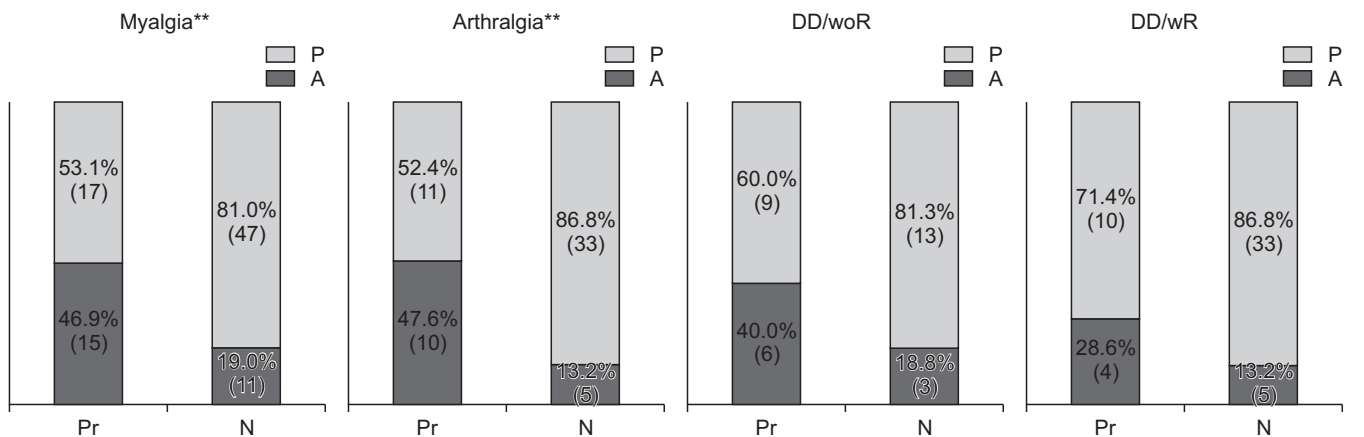


Fig. 2. In each diagnosis, the ratio of presence or absence of crepitus according to osteoarthritis progression. DD/woR, disc displacement without reduction; DD/wR, disc displacement with reduction; P, presence; A, absent; Pr, progression to osteoarthritis (OA); N, no progression to OA. Values are presented as percentage (number). The p-value was determined using the chi-square test. **p<0.01.

Table 3. Sensitivity and specificity of crepitus, crepitus of pain-related disorder, and DC/TMD

Sensitivity and specificity	Crepitus	Crepitus of pain-related disorder group	DC/TMD
Sensitivity	0.36 (22/61)	0.47 (25/53)	0.55
Specificity	0.85 (86/101)	0.83 (80/96)	0.61

DC/TMD, Diagnostic Criteria for Temporomandibular Disorders.

the initial charts, unilateral chewing was noted in 95 (64.6%) and bilateral chewing was noted in 52 (35.4%), showing a ratio of roughly 2:1 for unilateral versus bilateral chewing. Among charts with unilateral chewing, the number of patients chewing on the right and left were very similar (51.6% [n=49] and 48.4% [n=46], respectively). There was no statistically significant association between OA progression rate and chewing habits (unilateral or bilateral), and there was no statistically significant association among OA progression rates in different groups according to age either. Last, there was no statistically significant association between unilateral mastication position and location of OA (data not shown).

DISCUSSION

Crepitus is defined as multiple gravel-like sounds that occur continuously during partial or the complete opening and/or closing movements of the jaw. The noise may be also described as crunching, grating, or grinding, and it is distinct from the discrete sound characteristics associated with clicking [1]. There is a close link between degenerative adaptation and crepitus in OA progression, and previous studies have shown that crepitus is a reliable indication of OA [11-13]. Crepitus is a common finding in advanced OA and may not be associated with pain [13]. However, Lo et al. [8] reported that the higher incidence of subjective crepitus in knee OA was associated with a higher incidence of symptomatic knee OA and that crepitus was a predictor of OA risk factors for symptomatic knee. Hajati et al. [9] reported that bone tissue resorption could be predicted by joint crepitus and plasma glutamate levels in patients with early RA of TMJ. The presence of crepitus was also associated with OA progression in this study, which examined whether crepitus could be a clinical indicator of early TMJ OA (Table 1). In this study, crepitus was palpable in 23% of the patients, similar to the 21% observed in Hajati et al.'s

study [9] and 27% observed in other studies on age-related TMD [14]. In general, there is a higher rate of crepitus in patients with advanced OA. Because this study focused on the early stages of TMJ OA, subjective reports of crepitus by patients were excluded, and that could be the main reason a detection rate of crepitus in this study is similar to that of previous studies.

Previous studies on the relationship of sex and OA reported that females visited clinics for OA treatment more frequently and showed a higher incidence of OA because of hormonal differences [5,15,16]. In this study, the proportion of females who visited the hospital to males was 3:1, but there was no sex difference in the TMJ OA progression. However, there was a difference in OA progression rates of females and males, according to the existence and nonexistence of crepitus (Table 1).

In this study, the patients were divided into the three age groups: Group I included patients up to the age of 20 years when TMJ growth is complete. Previous studies have shown that degenerative changes in the mandibular condyle start at a young age and OA symptoms were first reported in the third decade of life frequently, which includes Group II [17,18]. The rest of the patients were included in Group III. Several previous studies on the link between age and OA concluded that TMJ OA was an age-related disease, with its incidence rate increasing with age. In addition, an autopsy study showed that degenerative lesions were more severe in the older group than in the younger group [15,19-21]. However, other studies found no statistically significant difference in the incidence rates of TMJ OA among age groups. In this study, OA occurred at a higher frequency as age increased in the groups [22]. This was consistent with the results of numerous previous studies. There was no statistically significant difference in OA changes according to the presence of crepitus in Group I, but there was a high association between crepitus and OA progression in Group III. In the age-matched study of crepitus in TMD patients,

the mean age of patients with crepitus was 51.9 ± 14.5 years, which was higher than that of the non-crepitus group (37.9 ± 16.4 years). Similar to this study, it was age-related [14]. It is thought that this result got influenced by synovial fluid. As age increases, the OA changes in TMJ due to lack of synovial fluid increase, and the intra-articular injection of hyaluronic acid was found to be more effective in the elderly group than non-elderly group (Table 2) [23-25].

OA can always occur in joints with excessive loads, but it is most often associated with disc dislocation or perforation. Among internal derangements, DD/woR is known to have relation to OA change [26,27]. In this study, it was also confirmed that the rate of DD/woR was higher than that of the joint that did not progress to OA (Fig. 1). When OA progression according to a presence or absence of crepitus was analyzed, there was no association with intra-articular joint disorders, and there was a high association with pain-related disorders. Crepitus according to the disc position is frequently observed in chronic DD/woR because of the contact of condyle and articular eminence with the destruction of surrounding tissues, such as the retrodiscal tissue. However, because subjects of this study were early OA patients, it was suggested that the incidence of OA in the presence of pain and crepitus was higher than that of crepitus in disc position (Fig. 2). Arthralgia is thought to occur on the joint surface when the muscle loads on the joint. However, because there is no nerve distribution on the joint surface, when the surrounding tissues under pressure are inflamed, the nociceptive receptor sends a signal and pain is felt. Over-expression of these inflammatory cytokines results in an imbalance in the dynamic equilibrium of tissue repair and destruction, which eventually destroys the articular cartilage and bone, causing TMJ OA and resulting in pain originated from the subarticular bone [28-30]. Okeson [31] stated that OA was painful in the early stages and painless as it progressed over time. This supports the finding of a strong correlation between pain and OA incidence in this study [3,4]. Another study examined the correlation between clinical features and MRI results for early detection of knee OA reported that the presence of crepitus and pain history was the first indication of patellofemoral OA [10]. When the sensitivity and specificity of crepitus in predicting OA progression in the pain-related disorder group were examined,

sensitivity was 0.47 and specificity was 0.83. In the DC/TMD OA diagnostic criteria without imaging, the sensitivity compared with original validity was slightly lower, but the specificity pointed 0.83 (Table 3), which was higher than original validity. If only crepitus was considered, sensitivity and specificity were 0.36 and 0.85. When compared with the pain-related group values, the specificity was similar, but the sensitivity was higher. This may be significant in the clinical diagnosis of OA with crepitus, especially with crepitus in the group with pain-related disorder. Therefore, caution is needed when both persistent pain and crepitus are present.

Previous studies on the relationship between unilateral chewing and TMD showed that individuals with unilateral chewing tended to have more TMD signs and symptoms than others. In a study on jaw biodynamic data of patients with chronic unilateral TMD, the side of habitual chewing caused TMD in 71% of patients. Regarding the frequency of unilateral chewing habit, 65% of the subjects surveyed answered that they performed unilateral chewing, similar to previous results [32-34]. In this study, the statistical significance of the relationship between chewing habit (such as unilateral chewing) and OA incidence was investigated with regard to overloading that causes TMJ OA; however, no specificity was found. This difference of results is thought to have relation to the fact that only the relationship among unilateral chewing habit, unilateral chewing position, and occurrence of new OA at the initial visit has been investigated, and unilateral chewing duration, other internal derangements except OA and joints that have already been diagnosed with OA were excluded from the study.

This study has several limitations. First, patients were not controlled to conservative therapy. Second, there was a substantial variation in the retake period of CBCT among patients and the follow-up period (6-36 months). In a previous study of crepitus and symptomatic OA incidence in knee OA, there was no significant relationship found for 1-year follow-up, but a significant relationship was found for 3-year follow-up. Considering these results, further studies need to stabilize the period of observation for patients and timing of CBCT re-imaging. Third, we did not take TMJ MRI imaging for intra-articular disorder diagnosis so, there was the limitation of that diagnosis.

In conclusion, this study focused on crepitus among various clinical symptoms for early diagnosis of TMJ OA. In the joints where crepitus was present before OA was confirmed by CBCT, OA progressed at a high rate, showing a direct correlation with increasing age. When crepitus was present in the pain-related disorder group, it was observed that there was a higher rate of progression to OA. Therefore, in the joints with pain and crepitus, follow-up with CBCT re-imaging is necessary even if there is no evidence of radiologically confirmed OA at the first CBCT. Future studies will require objective measurement of crepitus and various methods for early diagnosis of OA.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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REFERENCES

- 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 Group. *J Oral Facial Pain Headache* 2014;28:6-27.
- Cömert Kiliç S, Kiliç N, Sümbüllü MA. Temporomandibular joint osteoarthritis: cone beam computed tomography findings, clinical features, and correlations. *Int J Oral Maxillofac Surg* 2015;44:1268-1274.
- Das SK. TMJ osteoarthritis and early diagnosis. *J Oral Biol Craniofac Res* 2013;3:109-110.
- Madry H, Kon E, Condello V, et al. Early osteoarthritis of the knee. *Knee Surg Sports Traumatol Arthrosc* 2016;24:1753-1762.
- Robinson JL, Cass K, Aronson R, et al. Sex differences in the estrogen-dependent regulation of temporomandibular joint remodeling in altered loading. *Osteoarthritis Cartilage* 2017;25:533-543.
- Yao W, Qu N, Lu Z, Yang S. The application of T1 and T2 relaxation time and magnetization transfer ratios to the early diagnosis of patellar cartilage osteoarthritis. *Skeletal Radiol* 2009;38:1055-1062.
- Liess C, Lüsse S, Karger N, Heller M, Glüer CC. Detection of changes in cartilage water content using MRI T2-mapping in vivo. *Osteoarthritis Cartilage* 2002;10:907-913.
- Lo GH, Strayhorn MT, Driban JB, Price LL, Eaton CB, Mcalindon TE. Subjective crepitus as a risk factor for incident symptomatic knee osteoarthritis: data from the osteoarthritis initiative. *Arthritis Care Res (Hoboken)* 2018;70:53-60.
- Hajati AK, Näsström K, Alstergren P, Bratt J, Kopp S. Temporomandibular joint bone tissue resorption in patients with early rheumatoid arthritis can be predicted by joint crepitus and plasma glutamate level. *Mediators Inflamm* 2010;2010:627803.
- Schipphof D, van Middelkoop M, de Klerk BM, et al. Crepitus is a first indication of patellofemoral osteoarthritis (and not of tibiofemoral osteoarthritis). *Osteoarthritis Cartilage* 2014;22:631-638.
- Akerman S, Kopp S, Nilner M, Petersson A, Rohlin M. Relationship between clinical and radiologic findings of the temporomandibular joint in rheumatoid arthritis. *Oral Surg Oral Med Oral Pathol* 1988;66:639-643.
- Holmlund AB, Axelsson S. Temporomandibular arthropathy: correlation between clinical signs and symptoms and arthroscopic findings. *Int J Oral Maxillofac Surg* 1996;25:178-181.
- Okeson JP. Management of temporomandibular disorders and occlusion. 7th ed. St. Louis, Mo.: Elsevier Inc.; 2013. pp. 317-361.
- Guarda-Nardini L, Piccotti F, Mogno G, Favero L, Manfredini D. Age-related differences in temporomandibular disorder diagnoses. *Cranio* 2012;30:103-109.
- dos Anjos Pontual ML, Freire JS, Barbosa JM, Frazão MA, dos Anjos Pontual A. Evaluation of bone changes in the temporomandibular joint using cone beam CT. *Dentomaxillofac Radiol* 2012;41:24-29.
- Wang XD, Kou XX, Meng Z, et al. Estrogen aggravates iodoacetate-induced temporomandibular joint osteoarthritis. *J Dent Res* 2013;92:918-924.
- Zhao YP, Zhang ZY, Wu YT, Zhang WL, Ma XC. Investigation of the clinical and radiographic features of osteoarthritis of the temporomandibular joints in adolescents and young adults. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2011;111:e27-34.
- Susami T, Kuroda T, Yano Y, Nakamura T. Growth changes and orthodontic treatment in a patient with condylolysis. *Am J Orthod Dentofacial Orthop* 1992;102:295-301.
- Widmalm SE, Westesson PL, Kim IK, Pereira FJ Jr, Lundh H, Ta-

- saki MM. Temporomandibular joint pathosis related to sex, age, and dentition in autopsy material. *Oral Surg Oral Med Oral Pathol* 1994;78:416-425.
20. Pereira FJ Jr, Lundh H, Westesson PL. Morphologic changes in the temporomandibular joint in different age groups. An autopsy investigation. *Oral Surg Oral Med Oral Pathol* 1994;78:279-287.
 21. 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.
 22. Kim K, Wojczyńska A, Lee JY. The incidence of osteoarthritic change on computed tomography of Korean temporomandibular disorder patients diagnosed by RDC/TMD; a retrospective study. *Acta Odontol Scand* 2016;74:337-342.
 23. Koyama E, Saunders C, Salhab I, et al. Lubricin is required for the structural integrity and post-natal maintenance of TMJ. *J Dent Res* 2014;93:663-670.
 24. Guarda-Nardini L, Manfredini D, Stifano M, Staffieri A, Marioni G. Intra-articular injection of hyaluronic acid for temporomandibular joint osteoarthritis in elderly patients. *Stomatologija* 2009;11:60-65.
 25. Hill A, Duran J, Purcell P. Lubricin protects the temporomandibular joint surfaces from degeneration. *PLoS One* 2014;9:e106497.
 26. Moncada G, Cortés D, Millas R, Marholz C. Relationship between disk position and degenerative bone changes in temporomandibular joints of young subjects with TMD. An MRI study. *J Clin Pediatr Dent* 2014;38:269-276.
 27. Cortés D, Exss E, Marholz C, Millas R, Moncada G. Association between disk position and degenerative bone changes of the temporomandibular joints: an imaging study in subjects with TMD. *Cranio* 2011;29:117-126.
 28. Nishimura M, Segami N, Kaneyama K, Suzuki T, Miyamaru M. Relationships between pain-related mediators and both synovitis and joint pain in patients with internal derangements and osteoarthritis of the temporomandibular joint. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002;94:328-332.
 29. Vernal R, Velásquez E, Gamonal J, Garcia-Sanz JA, Silva A, Sanz M. Expression of proinflammatory cytokines in osteoarthritis of the temporomandibular joint. *Arch Oral Biol* 2008;53:910-915.
 30. Wang XD, Kou XX, Mao JJ, Gan YH, Zhou YH. Sustained inflammation induces degeneration of the temporomandibular joint. *J Dent Res* 2012;91:499-505.
 31. Okeson JP. Management of temporomandibular disorders and occlusion. 7th ed. St. Louis, Mo.: Elsevier Inc.; 2013. pp. 129-169.
 32. López-Cedrún J, Santana-Mora U, Pombo M, et al. Jaw biodynamic data for 24 patients with chronic unilateral temporomandibular disorder. *Sci Data* 2017;4:170168.
 33. Reinhardt R, Tremel T, Wehrbein H, Reinhardt W. The unilateral chewing phenomenon, occlusion, and TMD. *Cranio* 2006;24:166-170.
 34. Jeon HM, Ahn YW, Jeong SH, et al. Pattern analysis of patients with temporomandibular disorders resulting from unilateral mastication due to chronic periodontitis. *J Periodontal Implant Sci* 2017;47:211-218.