J Oral Med Oral Surg 2021;27:37
https://doi.org/10.1051/mbcb/2021012

https://www.jomos.org

JOMOS
Journal of Oral Medicine and Oral Surgery

Original Article

Widespread bodily pain is not associated with the presence of painful TMJ osteoarthritis: a case control study

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(Received: 11 February 2021, accepted: 19 April 2021)

Keywords: Temporomandibular joint / osteoarthritis / widespread pain / comorbid bodily pain conditions / CBCT

Abstract – Purpose: Temporomandibular Joint Arthralgia (TMJA) in the absence of osteoarthritis has not been thoroughly studied. We aimed to investigate the presence of comorbid bodily pain conditions (CBPC) in patients with TMJA with and without TMJOA and hypothesized that TMJOA is not associated with a higher presence of CBPC. **Methods:** This is a retrospective study involving patients at the University of North Carolina Orofacial Pain Clinic between 2010 and 2014 with TMJA according to the RDC/TMD criteria [1]. Cases fulfilled the Ahmad classification for TMJOA [2], and had TMJA (TMJA+OA), while controls had TMJA only (TMJA-OA). Data was collected from reports of Cone-Beam Computerized Tomography (CBCT). CBPC were self-reported. **Results:** Twenty-eight cases (TMJA+OA) and 25 controls (TMJA-OA) were included. The mean age of cases and controls ($P = 0.027$) and mean pain duration differed ($P = 0.031$). However, the gender distribution ($P = 0.552$), mean pain intensity ($P = 0.381$), mean number of painful muscles upon palpation ($P = 0.759$) and mean number of CBPC ($P = 0.575$) were not different. At least one CBPC was reported by 68% cases and 72% control subjects ($P = 0.743$). **Conclusions:** In this group of patients with TMJA, the presence of CBPC was high and not associated with the presence of TMJOA. This finding suggests that CBPC and TMJOA occur independently.

Introduction

Temporomandibular disorders (TMD) encompass a group of conditions involving the Temporomandibular Joints (TMJ), the masticatory musculature, and associated structures [3]. Approximately 60–70% of the general population reported one symptom of TMD, with 25% of individuals seeking treatment for their symptoms [4]. The incidence rate of TMD is reportedly 4% per annum [5]. Based on the Research Diagnostic Criteria for TMD (RDC/TMD), the overall prevalence of TMD was 45.3% for muscle disorders, 41.1% for disc displacements, and 30.1% for TMJ disorders [6]. The etiopathophysiology of TMD is multifactorial and includes genetic risk determinants, psychosocial factors, pain amplification states, and environmental contributing factors [7].

TMJ arthralgia (TMJA) is defined as pain of joint origin that is affected by jaw movement, function, and/or parafunction, and replication of this pain occurs with provocation testing of the TMJ [3]. Etiologic factors contributing to TMJA include anatomical susceptibility of tissue to trauma, polyarthritic diseases, joint laxity, and oral parafunctional activities [8]. TMJA is a common symptom of TMJ osteoarthritis (TMJOA), which is characterized by deterioration of the articular tissue and the presence of osseous changes [3].

The pathophysiology of TMJOA involves a sustained inflammatory process induced by metabolic or mechanical factors, which initiates a cascade of biomechanical changes and immune responses, resulting in degradation of the cartilage and bony remodeling [9]. The radiographic diagnosis of TMJOA is challenging due to the superimposition of anatomical structures in the preauricular region [10]. Computerized Tomography (CT) is generally recognized as the gold standard for TMJOA diagnosis [2,11]. According to Ahmad *et al.*, the diagnostic criteria for TMJOA categorized osseous changes into 3 categories, namely normal, indeterminate, or affected with OA [2]. The prevalence of TMJOA ranged from 30.1% to 50.8%, with higher prevalence in women between 40 and 50 years old [12]. Subtypes of TMJOA based on etiology include inflammatory, traumatic, autoimmune, and degenerative [13]. The course of TMJOA is benign and of slow progression, and in animal models' pain was present during the

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initial stages of the disease [14]. In addition to pain, other signs, and symptoms of TMJOA include restriction in joint function and joint crepitus [15].

Although commonly reported, the nature of the association between TMJA and TMJOA is not straightforward. A review of the Cone Beam CT (CBCT) data of 440 TMJs revealed that although the majority (65.9%) of the condyles with surface erosions were associated with TMJA, a third of TMJOA were painless [16]. In a case control study using three dimensional surface models of mandibular condyles comparing 29 patients with TMJOA and 36 healthy controls, Cevidanes *et al*. reported that although there was a statistically significant positive correlation between the extent of resorption on specific joint surfaces (of OA joints) and the pain intensity and duration, examination of the global morphologic scores for the severity of TMJ osseous resorption revealed poor correlation with pain intensity and duration [17]. In an analysis of the clinical data and CBCT images of 30 patients with painful TMJOA, Palconet *et al*. also reported that the maximum condylar change correlated poorly with pain intensity [18]. While painful TMJ osteoarthritis has been extensively studied, TMJ arthralgia in the absence of osteoarthritis has not received the same level of scrutiny [17,18]. In 2017, Khawaja *et al*., in a TMJ magnetic resonance imaging (MRI) study, reported no correlation between TMJ effusion (in 80 TMJs) and arthralgia [19]. When the complaint is TMJ pain, whether TMJOA is the cause of that pain remains to be determined.

Numerous studies have reported on the comorbidity of widespread bodily pain and TMD [20–23]. In a group of TMD patients, the presence of widespread pain was associated with 1.7 comorbid pain conditions compared to 0.3 comorbid conditions in its absence ($P < 0.001$) [22]. The presence of pain outside the masticatory system is a known risk factor for the development of TMD [23]. In fact, studies evaluating the relationship between TMD and its co-morbidities have identified a correlation between the frequency/severity of the co-morbidity and TMD [24]. Irrespective of the peripheral bodily pain location, comorbid bodily pain conditions (CBPC) are probably regulated by similar pathways of vulnerability with central sensitization as one of the major themes [25]. Because TMD is highly associated with comorbid bodily pain conditions (CBPC), TMJ arthralgia may represent a manifestation of the central sensitization phenomenon, *i.e.*, deep tissue hyperalgesia, in the absence of joint inflammation associated with OA. In this study, we investigated the presence of CBPC in patients with TMJA in the presence and absence of TMJOA. We hypothesized that in patients with TMJA, the presence of TMJOA is not associated with a higher presence of CBPC.

Methods

This is a retrospective cross-sectional case-control study involving consecutive patients who sought treatment at the University of North Carolina (UNC) Orofacial Pain Clinic between 2010 and 2014. This study was reviewed and approved by the University of North Carolina at Chapel Hill Institutional Review Board (IRB 15-3226) and is in compliance with the Declaration of Helsinki. The inclusion criteria included a diagnosis of TMD according to the RDC/TMD criteria, the presence of TMJA, and the radiographic interpretation report of the TMJ CBCT performed using the CareStream 9300 (Carestream Dental, Atlanta GA). Three Oral Radiology Faculty were involved in the radiographic interpretation of the TMJ CBCTs, and data was extracted from their reports. Based on the CBCT studies (using the criteria established by Ahmad *et al*.) and clinical examination, we identified cases (TMJA+OA) and controls (TMJA-OA). The radiographic criteria defines the presence of OA as condylar deformation due to subcortical cyst, surface erosion, osteophyte, or generalized sclerosis; and a normal condyle as the normal relative size of the condylar head, no subcortical sclerosis or surface flattening, and no deformation due to subcortical cyst, surface erosion, osteophyte, or generalized sclerosis [2]. Exclusion criteria included TMJOA secondary to underlying medical conditions (such as rheumatoid arthritis), history of TMJ surgery, TMJ pathology other than TMJOA, condyles classified as indeterminate for OA (*i.e.*, neither OA nor normal condyle), and incomplete data.

Data collected also included information regarding gender, age, pain intensity and duration, the number of painful sites in the head and neck upon palpation, and the presence and number of CBPC. TMJA was determined based on self-reported pain, on a verbal pain rating scale where '0' was 'no pain' and '10' was 'the worst pain imaginable', in one or both TMJ(s). Pain duration was determined by self-reported onset of pain. Painful sites in the head and neck were determined upon digital palpation with 1 pound finger pressure for the TMJs lateral capsule and TMJs posterior border; and to 2 pounds of pressure on predetermined areas including bilateral masseter, temporalis, sternocleidomastoid, occipitalis, paracervical, trapezius, and the cervical spine. Examination of all participants was done by one Orofacial Pain specialist following the standardized RDC/TMD examination method. CBPC, such as low back pain and fibromyalgia, were self-reported during a clinical interview.

The sample size was calculated based on Chen *et al*. where patients with TMD and wide palpation tenderness had a higher number of comorbid pain conditions when compared with patients with TMD without wide palpation tenderness (2.25 ± 1.5 versus 1.2 ± 0.6 respectively, $P < 0.001$) [26]. This yielded a sample size of 28 subjects in each group, assuming alpha of 0.05 (two-sided) and power at 90%. The quantitative variables were presented as mean and standard deviation, mean (SD), whereas categorical and variables were presented as frequency and percentage, n (%). Chi-square test was used to compare gender and presence of different comorbid pain conditions including headache, sinus pain, gastrointestinal pain, back pain, generalized osteoarthritis and other pain condition between the 2 groups. One-way ANOVA test was employed to compare age and pain characteristics. Logistic regression was used to test association and calculate odds ratios and confidence intervals for gender, age, pain duration, pain intensity, number of painful sites in the head and neck,

Table I. Description of the controls (TMJA-OA) and cases (TMJA+OA).

Characteristics	TMJA-OA (n = 25)	TMJA+OA (n = 28)
Female (%)	15 (60)	19 (68)
Males (%)	10 (40)	9 (32)
Mean age in years (SD)	35.8 (±19)	46.8 (±16)
Mean duration of arthralgia in months (SD)	26.2 (±33)	75 (±107)
Mean pain intensity (SD)	5.2 (±2.23)	5.7 (±1.99)
Mean number of painful muscles upon palpation (SD)	9.24 (±4.6)	9.6 (±4.9)
Mean number of comorbid bodily pain condition (SD)	1.08 (±0.86)	1.25 (±1.26)

TMJA: Temporomandibular Joint Arthralgia; OA: Osteoarthritis; SD: Standard Deviation.

Table II. Logistic regression of the controls (TMJA-OA) and cases (TMJA+OA).

Characteristics	OR	CI	P value
Female (%)	1.40	0.45–4.34	0.552†
Males (%)			
Mean age in years (SD)	1.03	1.00–1.07	0.027‡
Mean duration of arthralgia in months (SD)	1.01	0.99–1.02	0.031‡
Mean pain intensity (SD)	1.12	0.86–1.46	0.381‡
Mean number of painful muscles upon palpation (SD)	1.01	0.90–1.14	0.759‡
Mean number of comorbid bodily pain condition (SD)	1.15	0.69–1.92	0.575‡

OR: Odds Ratio; CI: Confidence Interval; SD: Standard Deviation; TMJA: Temporomandibular Joint Arthralgia; OA: Osteoarthritis.
†Chi-square.
‡Anova.

and number of bodily pain conditions. Statistical significance was set at $P < 0.05$. The STATA SE 14 was used for statistical analyses.

Results

Records from 333 consecutive patients were reviewed and 53 fulfilled the inclusion and exclusion criteria. Twenty-eight patients met the criteria for cases (TMJA+OA) and 25 patients met the criteria for controls (TMJA-OA) (Tab. I). A total of 280 patients were excluded because of the following reasons: absence of CBCT (143), presence of TMJ pathology other than OA (83), condyles classified as indeterminate for OA (43) [2], and insufficient data (11). Cases (TMJA+OA) were significantly older than controls (TMJA-OA) ($P = 0.027$) and had longer mean pain duration ($P = 0.031$, Tab. II). However, the gender distribution ($P = 0.552$), mean pain intensity ($P = 0.381$), mean number of painful muscles upon palpation ($P = 0.759$) and mean number of CBPC ($P = 0.575$) were not statistically significantly different between the cases and controls (Tab. II).

The type of CBPC reported by cases and controls were very similar and included headache, sinus pain, gastrointestinal pain, back pain, generalized osteoarthritis, and others (Tab. III). The number of cases (68%) and controls (72%), who reported at least one CBPC were similarly high ($P = 0.743$, Fig. 1). Furthermore, the report of at least 2 CBPC was not statistically significant between cases and controls ($P = 0.993$, Fig. 2).

Discussion

In this group of TMD patients with TMJA, the presence of CBPC was high and not associated with the presence of TMJOA, suggesting that these two entities occurred independently. In both cases and controls, the pain duration and intensity, the number of painful muscles upon palpation, and the number of bodily pain conditions were similar, suggesting that the pain experience was perhaps better explained by central pain processing. This is consistent with the current understanding of OA pain processing mechanisms involving not just peripheral but also central components [27]. This may imply that in TMJOA, central pain processes probably accounted for some aspects of the TMJA pain experience, in addition to the local inflammatory joint pain. The results of this study could explain why previous studies did not find a consistent correlation between TMJOA and pain intensity [17–19]. Such findings have important treatment implications, underscoring the importance of addressing the presence of widespread pain in patients presenting with seemingly localized TMJOA. Clinicians need to probe for the presence of pain in other parts of the body and

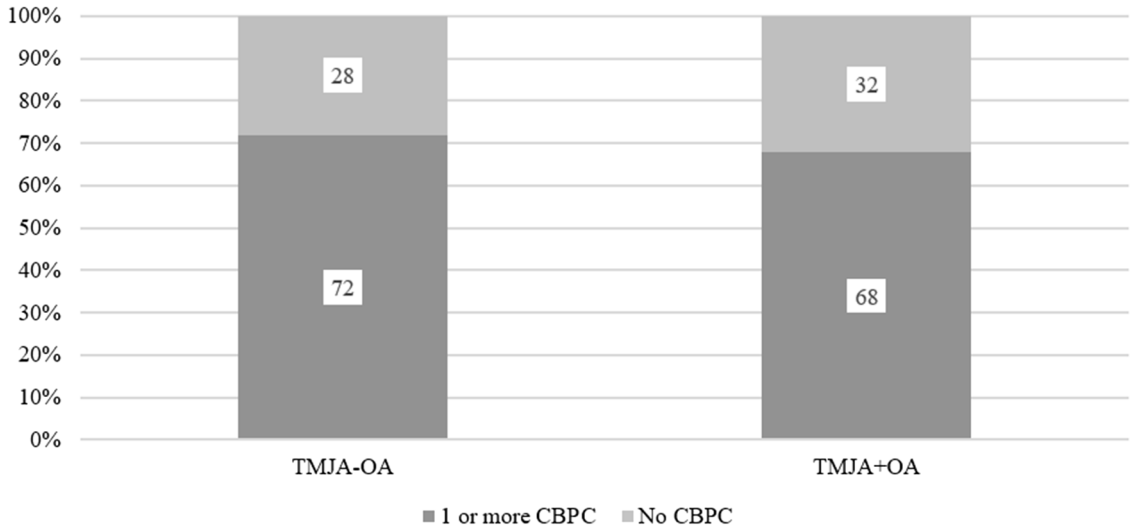

Fig. 1. Percentage of Subjects Reporting 1 or more Comorbid Bodily Pain Condition in cases (TMJA+OA) compared to controls (TMJA-OA) ($P = 0.743$). CBPC: Comorbid Bodily Pain Condition; TMJA: Temporomandibular Joint Arthralgia; OA: Osteoarthritis.

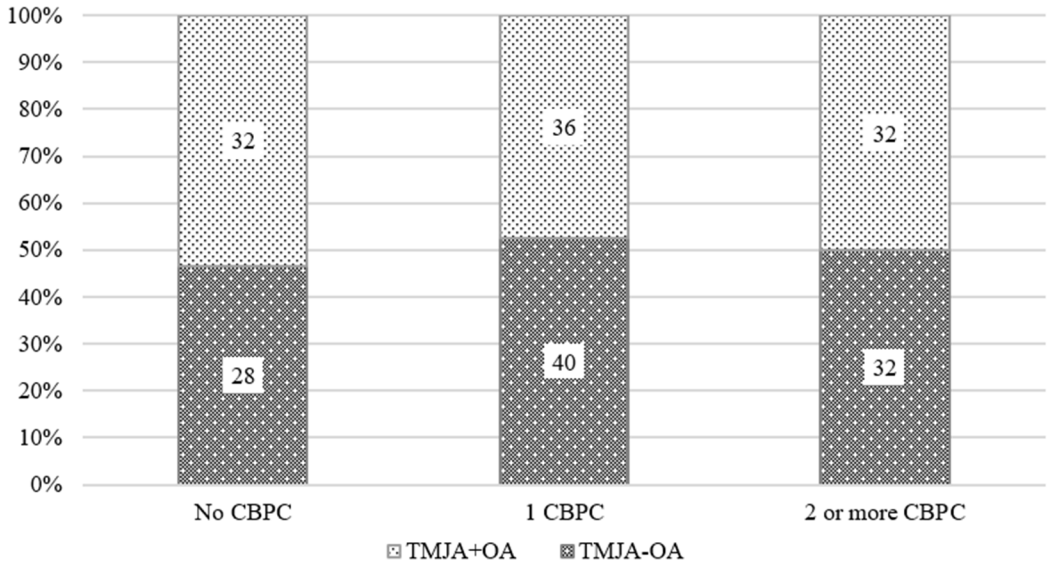

Fig. 2. Percentage of Subjects Reporting 2 or more CBPC in cases (TMJA+OA) and controls (TMJA-OA), compared to those reporting 1 CBCP or no CBPC ($P = 0.933$). CBPC: Comorbid Bodily Pain Condition; TMJA: Temporomandibular Joint Arthralgia; OA: Osteoarthritis.

address the need for concurrent management of widespread pain. Future research needs to investigate the influence of widespread pain on the prognosis of TMJOA, including its effect on localized TMJOA treatment modalities, such as arthrocentesis and joint injections.

Limitations are inherent in retrospective studies. Potential bias from self-report information based on recall cannot be excluded. Age matching was not performed (the mean age of the cases was about 10 years older than the mean age of the controls). This is a group of patients seeking treatment at a tertiary Orofacial Pain Clinic, and therefore, the chronicity and severity of TMD symptoms may not be generalizable. The radiographic interpretation of the TMJ CBCT reports was performed by three Oral Radiology Faculty but without calibration, and the intra-rater and inter-rater reliability were not verified.

On a positive note, the diagnosis of TMJA was based on the validated RDC/TMD criteria, and the diagnosis of TMJOA was made based on CBCT imaging rather than clinical signs [28]. In addition, this is one of only a few studies which has investigated a specific subtype of TMD, namely TMJOA, in conjunction with widespread bodily pain.

Table III. Types of Comorbid Bodily Pain Conditions (CBPC) reported by controls (TMJA-OA) and cases (TMJA+OA).

CBPC	TMJA-OA (n = 25)	TMJA+OA (n = 28)	P value
Headache (%)	10 (40)	10 (36)	0.748†
Sinus Pain (%)	2 (8)	5 (18)	0.290†
Gastrointestinal pain (%)	2 (8)	7 (25)	0.999†
Back pain (%)	5 (20)	2 (7)	0.168†
Generalized osteoarthritis (%)	2 (8)	6 (21)	0.173†
Other pain conditions (%)	2 (8)	2 (7)	0.906†

OR: Odds Ratio; CI: Confidence Interval; SD: Standard Deviation; TMJA: Temporomandibular Joint Arthralgia; OA: Osteoarthritis.
†Chi-square.

While this study suggests that the presence of comorbid pain conditions in TMD patients is not associated with TMJOA, other factors such as psychosocial stressors and sleep disturbances have repeatedly been identified to play an important role. Chen *et al.* reported that the presence of TMD with widespread palpation tenderness was associated with increased somatic symptoms [22]. A cluster analysis of 1031 chronic TMD cases and 3247 TMD-free controls revealed three subgroups, namely the adaptive, pain-sensitive, and global symptoms clusters, with the latter cluster showing both increased psychological distress and more comorbid pain conditions [26]. Stress can clearly influence the perception and experience of pain [26]. Poor sleep quality was notably associated with and promoted the development of TMD [29,30]. Future studies addressing these multidimensional factors need to examine their impact on pain associated with TMJOA.

The pathophysiology of pain in TMJOA is as complex as its diverse clinical presentation. Many factors modulate the pain experience. Understanding the association of chronic painful TMJOA with widespread pain will lead to improved assessment and management strategies.

Conclusion

In this group of TMD patients with TMJA, the presence of CBPC is high and not associated with the presence of TMJOA.

Funding

Dr. Daniela Vivaldi was supported by the National Institute of General Medical Sciences of the National Institutes of Health [grant number T32GM086330]. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interests

Neither the authors, nor any member of our immediate family, have a financial relationship or interest (currently or within the past 12 months) with any entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients. Dr. Daniela Vivaldi was supported by the National Institute of General Medical Sciences of the National Institutes of Health [grant number T32GM086330]. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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