Effects of Clinical Characteristics on Sleep Quality in Patients with Chronic Temporomandibular Disorders

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Research Article

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Abstract

Objectives: We aimed to investigate and compare sleep quality between patients with chronic temporomandibular disorder and healthy controls, and to analyze the association of sleep quality with disease characteristics, obstructive sleep apnea risk factors, and excessive daytime sleepiness.

Methods: Chronic temporomandibular disorder patients (n=503) and 180 age- and sex-matched healthy controls were included, who completed well-organized clinical report and answered questions on sleep quality (Pittsburgh Sleep Quality Index), sleep apnea risk factors (STOP-Bang questionnaire), and excessive daytime sleepiness (Epworth sleepiness scale).

Results: Mean global Pittsburgh Sleep Quality Index scores were significantly higher in the patients (6.25±2.77) than in healthy controls (6.25±2.77) ($p<0.001$). Poor sleep was significantly more prevalent in the patient group (56.9%) than in healthy controls (22.2%) ($p<0.001$). Compared with healthy controls, chronic temporomandibular disorder patients had a higher likelihood of obstructive sleep apnea (STOP-Bang total score ≥3; 7.2% vs. 16.1%; $p<0.01$) and higher excessive daytime sleepiness (Epworth sleepiness scale score ≥10; 12.8% vs. 19.7%; $p<0.05$). Age (odds ratio=2.551; $p<0.001$), female sex (odds ratio=1.885; $p=0.007$), total Epworth sleepiness scale score (odds ratio=1.839; $p=0.014$), and headache attributed to temporomandibular disorder (odds ratio=1.519; $p=0.049$) were the most powerful predictors of poor sleep (global Pittsburgh Sleep Quality Index score ≥5) in chronic temporomandibular disorder patients.

Discussion: Chronic temporomandibular disorder patients had sleep quality impairment. Various factors, including peripheral and central factors, affect the patient's sleep quality. Therefore, in addition to sleep quality and sleep-related problems, the underlying central mechanism for poor sleep quality should be assessed when treating chronic temporomandibular disorder patients.

Introduction

Sleep maintains homeostasis and optimizes various functions across multiple physiologic systems. Good sleep quality is a key factor for good physical health, emotional well-being, brain functioning, daytime performance, and pain control. Humans require both sleep and pain for good health and survival. However, ‘chronic’ pain can lower and deteriorate the quality of life [1-3]. Patients with chronic pain have poorer sleep than healthy controls in terms of sleep latency, sleep efficiency, and awakenings after sleep onset. Reciprocal, bidirectional interactions exist between chronic pain and sleep disorders, deterioration in either of them can ultimately become comorbid conditions [2]. In clinical settings, sleep problems have been found to impact 88% of patients with chronic pain [4]. Contrarily, more than 40% of patients who have sleep-related problems report chronic pain [5]. The prevalence of chronic pain ranges from 10-40% [6], similar to that of sleep disorders, ranging from 10-36% [7].

Temporomandibular disorders (TMDs) are quite common chronic orofacial pain conditions. TMDs are highly prevalent, affecting up to 25% of the population, with a peak incidence at 20-40 years of age, and

1.5-2 times more prevalent in female than in male [8,9]. TMD may promote widespread idiopathic pain, and the etiology of chronic TMD is considered multifactorial. Pain is the most common symptom of TMDs, which can affect areas such as the ears, eyes and/or throat, frequently causing neck pain and headache, and involve musculoskeletal pain, disturbances in mandibular movement, and functional impairment [10]. As the international diagnostic and classification systems for TMD, the research diagnostic criteria for TMD (RDC / TMD) proposed in 1992 is the most popular, and it has been updated to the diagnostic criteria for TMD (DC / TMD) in 2014, and has been subdivided into joint- and muscle-derived TMD pain as well as headache attributed to TMD [11,12]. Sleep quality in patients with TMD decreases as the number of diagnoses of painful TMD increases based on the International RDC / TMD Axis I [13]. Although several studies have been conducted on sleep quality in TMD patients [14-16], few researchers use international RDC / TMD and DC / TMD. Deterioration of sleep quality and impairment of sleep structure occur in a significant proportion in TMD patients and are thought to be a risk factor for maintaining and worsening symptoms, but their impact is not clearly known due to several methodological limitations.

Furthermore, according to the TMD diagnostic subgroups, and the impact on quality of sleep and the symptom severity can vary. TMD patients with muscle-derived or myofascial pain exhibit more advanced stages of depression and somatization than patients diagnosed with TMJ disc displacement, a joint-derived problem [17]. Moreover, TMD patients with headache reported significantly higher levels of pain and mandibular dysfunction than patients with only TMD [18]. Inadequate sleep and deteriorated sleep structures generally increase the risk of developing headaches, worsen headaches, and reduce pain thresholds [19,20]. A close relationship has been suggested among poor sleep quality, headache, and reduced pain thresholds [21]. However, the relationship between sleep and headaches attributed to TMD, especially in chronic TMD conditions, was not thoroughly investigated.

Chronic TMD can present persistent, recurrent, or chronic pain associated with TMJ and/or muscles involved in the masticatory system, which leads to highly disabling. Chronic TMD is also typically related to joint dysfunctions, such as disc displacement with or without reduction [22]. Approximately 90% of TMD patients reported poor sleep quality [16]. Although the etiology underlying the connection of chronic pain and poor sleep remains largely unknown, poor sleep might contribute to TMDs aggravation. TMD patient ratings of poor sleep are associated with increased clinical pain severity and psychological distress [16]. However, there is little evidence to indicate that chronic TMD patients have poor sleep quality, and it is not known which factors affect the sleep quality of chronic TMD patients. Chronic TMD is marked by psychological distress, characteristics of pain amplification mainly presented as hyperalgesia allodynia and hyperalgesia, upregulation of the serotonergic pathway and sleep problems [23].

This cohort study aimed to comprehensively investigate the clinical characteristics and evaluate sleep-related factors to correlate these parameters with poor sleep quality in chronic TMD patients. The Pittsburgh Sleep Quality Index (PSQI) was employed, which is a valid, reliable, and internationally known instrument for assessing self-perceived sleep quality [24]. Compared to objective measurements, such as

polysomnography or oximetry, PSQI addresses a longer time frame. In addition, a comparison of validity with respiratory indices from polysomnographic recordings has been made for PSQI with some degree of success. We described sleep quality differences between chronic TMD patients and healthy controls, investigated subgroup of TMD influences, and studied sleep quality in the full set of diagnostic DC/TMD and RDC/TMD subgroups of Axis I. Chronic TMD has an idiopathic basis in which the pathophysiology mechanism is not well understood. Our findings in this study will support the usefulness of an integrated model of demographics and disease characteristics in explaining sleep quality deterioration in chronic TMD patients.

Methods

Participants

To investigate the research purpose, the authors designed and implemented a retrospective cohort study conducted at the Department of Orofacial Pain and Oral Medicine at Kyung Hee University Dental Hospital of Seoul. The research protocol was reviewed in compliance with the Helsinki Declaration and approved by the Institutional Review Board of the Kyung Hee University Dental Hospital (KHD IRB no. 1804-2). Written informed consent was obtained from all individual participants.

Of the patients who had visited the Department of Orofacial Pain and Oral Medicine between June 1, 2018, and November 30, 2019, the study sample was composed of chronic TMD patients according to inclusion and exclusion criteria. Inclusion criteria were as follows: completed a set of routine TMJ assessments, as well as constructive questionnaires, no treatment of the current episode other than medication, and no history of TMD prior to the present symptoms. Patients who were pregnant or had a history of systemic osteoarthritis, rheumatoid arthritis, other connective tissue diseases, general infection, neurological/neuropathic diseases, and those under 18 years of age were excluded from the study.

TMD Classification

Clinical Evaluation

Clinical evaluation procedures included an oral examination, interview, panoramic radiography, and a comprehensive questionnaire in RDC/TMD criteria [25] and DC/TMD Axis I diagnostic algorithms [26] for TMD diagnoses. A subtype of diagnostics included myofascial pain, disc displacement, arthralgia using RDC/TMD, and headache attributed to TMD based on DC/TMD Axis I diagnostic algorithms.

We diagnosed patients who experienced TMJ pain for more than six months after onset as chronic TMD (cTMD). When the pain persisted more than three to six months, individuals were usually considered in a chronic state [27]. The intensity of TMD pain was measured using a visual analog scale (VAS) (0-10, 10 being the worst possible pain), and symptom duration in the masticatory muscles, TMJ, and adjacent structures were reported in days. Information concerning patient demographics included age, sex, height,

body weight for body mass index (BMI = weight/height^2), and neck circumference were collected by a research assistant.

Sleep Quality Evaluation Using PSQI

PSQI was employed to measure sleep quality. Habitual sleep quality and sleep disturbance in the past month were assessed using the 19-item PSQI, a well-validated self-report questionnaire. The PSQI has seven components that concern subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. Each subscale is weighted equally, scored from 0 (good sleep/no problems) to 3 (poor sleep/severe problems), summing to a global PSQI score (range, 0-21). Higher scores denote worse sleep quality, and a global score >5 has a diagnostic value in distinguishing poor from good sleep [28]. In this study, we investigated sleep quality using PSQI in multidimensional construction.

The risk evaluation of obstructive sleep apnea (OSA) with STOP-Bang

The snoring, tiredness, observed apnea, high blood pressure (STOP)-BMI, age, neck circumference, and male gender (Bang) questionnaire is a validated screening tool for identifying high likelihood for OSA (Chung et al. 2008). The STOP-Bang questionnaire includes eight dichotomous (yes/no) questions related to these clinical features of sleep apnea. For each question, answering “yes” scores 1, a “no” response scores 0, and the total score ranges from 0-8. The exposure of interest was a binary-low or high likelihood for OSA; the low likelihood of OSA: Yes to <3 questions, high likelihood of OSA: Yes to ≥3 questions [29]. All patients were asked to complete the STOP-Bang questionnaire.

Excessive daytime sleepiness measured by ESS

The ESS is a validated clinical tool for the evaluation of excessive daytime sleepiness (EDS) [30]. Unlike other scales, which measure sleepiness at a single time point, the ESS is designed to evaluate the general level of sleepiness. The ESS is an eight-item, self-administered questionnaire designed to provide a measure of the subject’s propensity to fall asleep in a variety of situations. The subject is instructed to answer how likely it is that he/she would fall asleep in those different situations, by giving a score on a 4-point scale (0-3). Thus, the total score (the sum of scores of the eight items) of the ESS ranges from 0-24. The higher the score, the greater the possibility the individual will fall asleep during the daytime. The ESS total scores were dichotomized into scores ≤10 and >10; the latter is considered to be clinically significant EDS [31]. We used a score of 10 or higher on the ESS to measure excessive sleepiness.

Statistical Analysis

The data were analyzed using SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as means and standard deviations (SD), and categorical variables are presented as frequencies and percentages. Differences between groups were examined by using the chi-square test for categorical variables and independent t-test and one-way analysis of variance (ANOVA)

with Tukey post-hoc test for numeric variables. Three questionnaires included in this study were for sleep quality, risk for OSA, and daytime sleepiness. To understand the risk for poor sleep quality, we performed a multiple logistic regression analysis to determine the relative risk for poor sleep (global PSQI score of ≥ 5). In addition, dichotomous variables based on cut-off points of each questionnaire's global scores were used as dependent or independent variables of logistic regression analysis. The high likelihood of OSA (STOP-Bang total score ≥ 3), and EDS (ESS score of > 10) (independent variables), as well as age, sex, and symptom duration, were taken into consideration simultaneously to predict a value of a dependent variable (poor sleep) for cTMD patients. For all analyses, a two-tailed level of statistical significance of a p-value was set at less than 0.05.

Results

General description

In this period, 525 patients who were diagnosed with chronic TMD were included, and 22 patients were excluded because they lacked medical documentations. Finally, 503 patients (mean age: 33.10 ± 13.26 years, 333 females) were designated as the chronic TMD group. One-hundred-and-eighty age- (mean age: 32.77 ± 12.95 years) and sex-matched TMD-free volunteers were designated to the healthy control group.

Table 1 presents the demographic characteristics of cTMD patients compared to healthy controls. Chronic TMD was more prevalent in females (66.2%) than in males (43.8%), and the female:male was 1.51:1. BMI scores were significantly higher in cTMD than in healthy controls (22.32 ± 3.57 vs. 21.45 ± 2.76, p = 0.001), and the mean values were in the normal range. In cTMD patients, the mean VAS score of cTMD patients was 4.89 ± 2.45, and the mean symptom duration was 589.74 ± 1315.01 days.

Differences in Global PSQI Scores and Poor sleep Between TMD group and Controls

Table 2 presents the results of the subjective sleep quality in terms of PSQI score and their comparison of PSQI between cTMD patients and healthy controls. Interestingly, the cTMD patients had higher PSQI global scores and higher frequency of poor sleepers than the healthy controls, which indicates that subjective sleep quality is lower in cTMD patients. PSQI components, including subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, and use of sleep medication, were significantly higher in cTMD patients than in healthy controls (all p < 0.05). The PSQI global scores were significantly higher in cTMD patients than in healthy controls (6.25 ± 2.77 vs. 3.84 ± 2.29, p < 0.001). In other words, subjective sleep quality of the cTMD group was more impaired than the healthy control group. The proportion of poor sleepers was significantly higher in cTMD patients than in healthy controls (56.9% vs. 22.2%, p < 0.001).

A total of 56.9% of cTMD patients were poor sleepers, and the prevalence was significantly higher in cTMD patients than in controls (22.2%) (p < 0.001).

Disease characteristics and their relationship with PSQI in cTMD patients

Table 3 summarizes the clinical factors and subgroups of TMD diagnoses associated with impaired sleep quality. For the cTMD patients, both the PSQI global score was higher (6.56 ± 2.79 vs. 5.65 ± 2.64, $p < 0.001$) and the poor sleeper ratio was significantly higher (62.8% vs. 45.3%, $p < 0.001$) in females than in males. As for age, an increase in age was associated with an increase in PSQI global scores and the occurrence of poor sleep. When we divided TMD patients into subgroups based on their age, the PSQI global scores were significantly higher and the ratio of patients with poor sleep quality was higher in patients in their 30s, 40s, or older as compared with those in their 20s and younger. The PSQI global score of cTMD patients younger than 20 years old was 4.69 ± 2.34, and the poor sleeper ratio was 32.8%, whereas the score in patients in their 40s and older was the highest (7.11 ± 2.90), and 71.6% of them were poor sleepers.

In addition, multiple TMD sub-diagnoses were allowed in one patient, and the PSQI global score was higher when patients were diagnosed with myofascial pain (6.31 ± 2.82 vs. 5.50 ± 1.98, $p = 0.023$) or headache attributed to TMD (6.58 ± 2.85 vs. 5.82 ± 2.60, $p = 0.002$) than in patients without the diagnoses. The majority of cTMD patients simultaneously suffer from pain of myofascial origin (n = 465, 92.4%), arthralgia (n = 355, 70.6%), headache attributed to TMD (n = 285, 56.7%), and disc displacement (n = 278, 55.3%). Therefore, we concluded that it is not appropriate to compare the PSQI global and component scores and presence of poor sleep by subgroup.

Differences in STOP-Bang and ESS Between TMD group and Controls

STOP-Bang total scores were significantly higher in TMD patients than in healthy controls (1.77 ± 1.86 vs. 1.53 ± 0.77, $p = 0.017$) (Table 4). By detail, the proportion of snoring (15.7% vs. 4.4%), high blood pressure (6.4% vs. 1.1%), and age over 50 (15.9% vs. 0.0%) were significantly higher in cTMD patients than in controls (all $p < 0.05$). Of the 503 cTMD patients, 420 (83.5%) had felt tired, 28 (5.6%) had observed sleep apnea, 4 (0.8%) had BMI more than 35 kg/m^2, and 29 (5.8%) had larger neck circumference than the reference (male >17 inches, female >16 inches). The presence of these factors did not differ statistically from the control group. Eighty-one out of 503 cTMD patients (16.1%) had a high likelihood of OSA.

Ninety-nine out of 503 cTMD patients (19.7%) had EDS. Total ESS scores were not significantly different; however, the EDS rate was significantly higher in the cTMD group than in controls (19.7% vs. 12.8%, $p = 0.023$).

PSQI, STOP-Bang, and ESS scores according to the number of TMD/AXIS I diagnosis

When multiple diagnoses according to RDC / TMD and DC / TMD was allowed in one patient, 82.5% of cTMD patients had two or more multiple TMD subgroup diagnoses, and only 17.5% of the patients had one TMD diagnosis. Even, there were 33.8% (n = 170) of patients with four multiple diagnoses. As a result of the ANOVA test, the PSQI global score was significantly higher when cTMD patients had four multiple diagnoses (6.75 ± 2.84) than when they had two multiple diagnoses (5.96 ± 2.65) and three multiple diagnoses (5.90 ± 2.72) ($p = 0.028$) (Figure 1). STOP-Bang total score was not significantly different according to the number of sub-diagnoses. However, in ESS, the ESS total score was significantly higher

when cTMD patients had four multiple diagnoses (7.40 ± 3.79) than when they had only one sub-diagnosis (5.73 ± 3.83) ($p < 0.001$) (Table 5).

Multivariate logistic regression analysis of factors influencing poor sleep quality

Table 6 presents the significant predictors for poor sleep (PSQI > 5) among cTMD patients. To comprehensively examine the risk factors for a poor sleep, multivariate backward stepwise logistic regression analysis of all parameters was performed as the final analysis. The odds ratios (ORs) of each independent variable was interpreted as the change in the incidence of poor sleep in cTMD patients. The increase of age (OR = 2.551, 95% CI = 1.662–3.917) was the most powerful predictor for poor sleep, and female sex (OR = 1.885, 95% CI = 1.193–2.978), ESS total score (OR = 1.839, 95% CI = 1.130–2.993), and sub-diagnosis of headache attributed to TMD (OR = 1.519, 95% CI = 1.014–2.308) were putative risk factors for poor sleep. Whereas BMI, VAS, symptom duration, other sub-diagnoses, except for headache, attributed to TMD, STOP-BANG total score did not reach statistical significance.

Discussion

This is the first study to comprehensively investigate and measure sleep quality with PSQI in chronic TMD patients who were diagnosed based on RDC/TMD and DC/TMD Axis I. Our findings in the present study imply that chronic state TMD patients had poorer sleep than healthy controls, and the magnitude of impaired sleep was associated with increased age, female sex, certain subtypes of TMD diagnosis, including myofascial pain and headache attributed to TMD, and the number of TMD diagnoses in a person. Regarding summary scores and cut-off values of each questionnaire, the presence of EDS was a significant predictor for the poor sleep quality in cTMD patients, whereas the high risk for OSA was not a major predictor.

The cause of chronic TMD is varied, and its localization, and clinical characteristics are vaguer than with acute pain. Chronic TMD is typically associated with joint dysfunctions such as disc displacement with or without reduction [22], and psychological distress [23]. It is difficult to infer a causal relation between sleep and chronic pain; patients with chronic pain commonly suffer from poor sleep quality [32]. Approximately 45.5% of patients with chronic pain suffer from sleep disorders, and older age was significantly associated with pain experience [7]. In this study, 56.9% of the cTMD group met the proposed cut-off of 5 of PSQI for poor sleep, compared to 22.2% of the control group that had impaired sleep. The proportion of TMD patients with poor sleep (56.9%) in our study is higher than the rate reported among adults with TMD (43.3%) in other studies [33,34] but lower than those in other studies involving older TMD patients (69.6-90.0%) [16,35].

The etiology of chronic TMD fundamentally related to peripheral and central factors together. Peripheral factors of TMD include inflammatory processes, including synovitis and myositis, infection, or irritation. Peripheral factors are the main cause of acute pain, but as the pain becomes chronic, the importance of the central factor increases [36]. Central factors include sleep deterioration, impairment of psychological health, and dysfunction of central pain inhibitory system [37,38]. Furthermore, central sensitization is a

key characteristic of chronic pain presented as hypersensitivity, particularly tactile allodynia, hyperalgesia, and enhanced temporal summation [39,40], which commonly presents in chronic TMD patients. As in other idiopathic pain disorders such as fibromyalgia and irritable bowel syndrome, TMD patients frequently present with overlapping signs and symptoms of sleep disorders [41].

Sleep quality of cTMD patients was more impaired by increased age. In the present study, the increase of age (OR = 2.551, 95% CI = 1.662–3.917) was the most powerful predictor for poor sleep, and female sex (OR = 1.885, 95% CI = 1.193–2.978) was followed. In young adults, consolidated sleep at night and wakefulness during the day emerges from a balance between the brainstem, hypothalamus, and midbrain[42]. In older adults, this operation is not effective, and decreased sleep duration, increased sleep latency, impaired sleep quality, shallow sleep, and changes in sleep structure can lead to sustained or deepening pain [43]. In addition, sleep patterns and structures are known to change across the lifespan, with up to 50% of older adults report difficulties initiating and/or maintaining sleep [44]. Chronic sleep disturbances are considered as indications of poor health, vice versa, older adults commonly suffer from pain syndromes, arthritis, hormonal changes, neurodegeneration, psychological distress, cancer, renal and urologic diseases, and medical comorbidities all of which can contribute to sleep disorders [45]. Thus, older adults with cTMD are less likely to get enough rest and recovery through sleep than younger ones.

Female sex was also a major contributor to poor sleep quality in cTMD patients. There is limited recent evidence of interactions among sex, TMD chronicity, and sleep. However, it has been found that females shows higher clinical and experimental pain sensitivity, and worse sleep impairments than males [2]. Few probable causes for poor sleep quality in the female sex may be explained based on sex differences concerning mechanisms of pain of the craniofacial system [46]. Furthermore, contribution of female sex may reflect changes of systems beyond the physical axis of the orofacial area and in line with the biopsychosocial model, blending centrally mediated factors. Especially in postmenopausal female, an increase in sleep problems may be associated with the presence of noticeable hormonal changes, age-associated changes in sleep and psychosocial distress [2]. In clinical research, females reported TMD symptoms, headache, and had muscle tenderness and joint sounds more often than males [47]. It will be crucial to determine whether the effect of sleep on chronic TMD pain, and vice versa, is moderated by key demographic variables, such as age or sex.

EDS was a significant predictor for poor sleep in chronic TMD patients. In our study, EDS was more prevalent in chronic TMD patients than in healthy controls (19.7% vs. 12.8%, $p < 0.05$), and its OR value for poor sleep quality was 1.069. Our EDS prevalence was higher than the prevalence among the general population (12–16%) [48], and lower than 28.57% of TMD patients, the rate previously reported [49]. The discrepancy may have occurred due to differences in age distribution, race, and method of study. In older adults, they are prone to have daytime napping and EDS and the presence of comorbid conditions such as chronic pain, sleep disorders, and frequent nighttime urination breaks [50]. Diminished melatonin secretion and a reduced circadian modulation of rapid-eye-movement sleep and less pronounced day-night differences in the lower alpha activity occurs in the older group [51]. Furthermore, females are more likely than males to have more trouble sleeping at night and experience EDS [52]. Thus, EDS in cTMD

may have different underlying mechanisms of a homeostatic drive for sleep and pain control systems according to age and sex. Hence, it is necessary to consider age-and sex-related differences in cTMD patients to obtain accurate results translation.

Headache attributed to TMD was associated with an increase of PSQI global scores, and a significant predictor for poor sleep. As headaches are a common symptom of accompanying TMD [53], few research has been done on the nature of headache attributed to cTMD. Headache can promote sleep disturbances, and sleep disturbances can also precede or trigger a headache attack [54]. Moreover, sleep deterioration has been associated with an increased risk for headaches, and in individuals with chronic headaches, shorter sleep duration has been associated with more severe pain [55]. Of course, the underlying pathophysiology contributing to the close association and complex relationship among headache attributed to TMD, headache disorders, and sleep disorders are not fully explained. There may be complex bidirectional relationships, and can be explained by peripheral and central sensitization, malfunctions of neuroendocrine, immune, and vascular system, and even gene polymorphism.

Myofascial pain was also associated with poor sleep quality in cTMD patients. Similar to our study, the substantial influence of myofascial pain on poor sleep quality in patients with TMD was documented [56]. Other researchers also observed a higher impact in patients with myogenous complaints than those with disc disorders [57,58]. While joint pain is characterized by a well-defined inflammatory process, chronic muscle pain presents with enigmatic pathophysiologic mechanisms, of which central sensitization is the common factor unifying these conditions [59]. In addition, females have more pain and widespread pain in more body areas than males, which may be related to their worse quality of sleep [60]. Therefore, depending on the subgroup of TMD, the mechanisms by which TMD signs and symptoms occur are different, and further investigation is needed on the effects on sleep quality.

Finally, the quality of sleep was lower in cTMD patients with multiple diagnoses than in patients with a single diagnosis. According to Gil-Martínez et al., patients with mixed pain, having arthrogenous and myogenous origin simultaneously, showed greater craniomandibular and neck disability than patients diagnosed with chronic joint pain or muscle pain only [61]. Patients with headache and TMDs reported significantly higher levels of pain and disability compared to patients with only TMDs [53]. These findings can be interpreted as increasing the number of TMD subgroup diagnoses can increase the severity of TMD symptoms. Overall, chronic TMD symptoms and multiple diagnoses may have a bidirectional cross-correlation, which can impair sleep quality. Chronic TMD, especially myofascial pain, headaches attributed to TMD, and sleep disturbance factors, may share the mechanism of occurrence and exacerbation.

Limitations of this study include the case-control study design, which cannot address a causal direction of effects and suggests only associations/correlations between the variables. A study design with repeated polysomnography (PSGs) may be more powerful in detecting phase-related differences. Instead of using PSG, we used self-assessment measures of sleep due to feasibility and convenience, especially because of our large sample size. PSG is an objective measure of biophysiologic sleep parameters, so we

are planning further studies to expand our findings with PSG. In addition, to get a deeper understanding of the relation between cTMD and poor sleep quality, we need to investigate their biopsychosocial aspects; however, this study did not evaluate psychological distress in patients with cTMD. Further studies on the psychological aspects of cTMD patients are ongoing.

Conclusion

The strength of this study is a comprehensive analysis of how various issues affect poor sleep quality among many factors. Chronic TMD patients suffered more from impaired sleep than healthy control subjects, and poor sleep was associated with multiple comorbid symptoms. Thus, assessing sleep quality should be a routine part of the diagnostic work-up of chronic TMD patients. Furthermore, a multidisciplinary management approach is needed to address all the factors in addition to sleep that modulate pain experience. In the diagnosis and treatment of cTMD, a fragmented field of view is not suitable, and a multidisciplinary approach involving experts in neurology, endocrinology, gerontology, and psychology, in addition to orofacial pain experts, is required. Our results will help to establish strategies for individual treatment and management of cTMD patients.

Declarations

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None.

Conflict of interest

The authors declare no conflict of interest. All authors have read and agreed to the published version of the manuscript.

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Authors' contributions

Y.-H.L. wrote the paper. Y.-H.L. and Q.-S.A contributed to data acquisition, Y.-H.L., and J.-S.A. to both data analysis and interpretation. Y.-H.L., Q.-S.A., and J.-S.A. provided their expertise and contributed to the figures. Y.-H.L. and T.K. provided her expertise and contributed to revisions. All authors have read and agreed to the published version of the manuscript.

Ethics approval and consent to participate: The research protocol was reviewed in compliance with the Helsinki Declaration and approved by the Institutional Review Board of the Kyung Hee University Dental Hospital (KHD IRB no. 1804-2). Written informed consent was obtained from all individual participants.

Availability of data and materials: If there are people requesting data from this study, data can be disclosed in cases upon obtaining KHU_IRB approval.

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Tables

Table 1. Demographic characteristics of chronic TMD patients compared to healthy controls

Parameter	chronic TMD patients (n=503) n (%) or Mean ± SD	Healthy control (n=180) n (%) or Mean ± SD	p-value
Age (years)	33.10 ± 13.26	32.77 ± 12.95	0.771
Sex (Female %)	333 (66.2)	116 (64.4)	0.367
BMI (kg/m2)	22.32 ± 3.57	21.45 ± 2.76	0.001**
VAS	4.89 ± 2.45	-	n.a.
Symptom duration (days)	589.74 ± 1315.01	-	n.a.

The results were obtained from $\chi 2$ test and the mean difference between groups was obtained by t-test.

p-Value significance was set at <0.05. **: p-value <0.01.

TMD: temporomandibular disorder, BMI: body mass index, SD: standard deviation, n.a.: not available.

Table 2. Comparison of Pittsburgh Sleep Quality Index (PSQI) between chronic TMD patients and healthy controls

Parameter	chronic TMD patients (n=503) n (%) or Mean ± SD	Healthy control (n=180) n (%) or Mean ± SD	p-value
PSQI			
Component 1: Subjective sleep quality (0-3)	1.50 ± 0.79	0.59 ± 0.61	< 0.001***
Component 2: Sleep latency (0-3)	0.83 ± 0.97	0.42 ± 0.72	< 0.001***
Component 3: Sleep duration (0-3)	0.72 ± 0.91	0.61 ± 0.79	0.035*
Component 4: Sleep efficiency (0-3)	0.38 ± 0.79	0.11 ± 0.36	< 0.001***
Component 5: Sleep disturbances (0-3)	1.20 ± 0.63	0.45 ± 0.60	< 0.001***
Component 6: Use of sleep medication (0-3)	0.15 ± 0.54	0.04 ± 0.28	0.001**
Component 7: Daytime dysfunction (0-3)	1.41 ± 0.90	1.79 ± 1.04	< 0.001***
PSQI global score (0-21)	6.25 ± 2.77	3.84 ± 2.29	< 0.001***
Poor sleeper (PSQI global score ≥ 5)	286 (56.9)	40 (22.2)	< 0.001***

The results were obtained from $\chi 2$ test and the mean difference between groups was obtained by t-test. p-Value significance was set at <0.05.

*: p-value < 0.05, **: p-value <0.01, ***: p-value <0.001.

TMD, temporomandibular disorder; SD, standard deviation.

Table 3. Descriptive statistics of disease characteristics and their relationship with Pittsburgh Sleep Quality Index (PSQI) in chronic TMD patients

		PSQI		Poor sleepers (> PSQI 5)	
Parameter	**n (%)**	**Global PSQI score**	**p-value**	**n (%)**	**p-value**
Demographics of TMD patients (n=503)					
Age groups					
1. Under 20 years old	61 (12.1)	4.69 ± 2.34	**< 0.001*** **	20 (32.8)	**< 0.001*** **
2. 20-30 years old	208 (41.4)	5.85 ± 2.45	1 < 2,3,4	104 (50.0)	
3. 31-40 years old	93 (18.5)	6.87 ± 2.91	2 < 3,4	61 (65.6)	
4. More than 40 years old	141 (28.0)	7.11 ± 2.90		101 (71.6)	
Sex					
Male	170 (33.8)	5.65 ± 2.64	**< 0.001*** **	77 (45.3)	**< 0.001*** **
Female	333 (66.2)	6.56 ± 2.79		209 (62.8)	
RDC/TMD Axis I diagnosis in TMD patients *(Multiple diagnoses are allowed per patient)*					
Myofascial pain					
[presence]	**465 (92.4)**	**6.31 ± 2.82**	**0.023***	268 (57.6)	0.145
[absence]	**38 (7.6)**	**5.50 ± 1.98**		18 (47.4)	
Disc displacement					
[presence]	278 (55.3)	6.27 ± 2.77	0.862	159 (57.2)	0.928
[absence]	225 (44.7)	6.23 ± 2.78		127 (56.4)	
Arthralgia					
[presence]	355 (70.6)	6.22 ± 2.88	0.888	203 (57.2)	0.448
[absence]	148 (29.4)	6.26 ± 2.72		83 (56.1)	
Headache attributed to TMD					
[presence]	**285 (56.7)**	**6.58 ± 2.85**	**0.002****	**178 (62.5)**	**0.005****
[absence]	**218 (43.3)**	**5.82 ± 2.60**		**108 (49.5)**	

Comparison results of the number (%) between groups performed with $\chi 2$ test and Boneferroni correction.

The mean difference between groups was obtained by post hoc analysis. p-Value significance was set at <0.05.

*: p-value < 0.05, **: p-value <0.01, ***: p-value <0.001.

TMD: temporomandibular disorder, PSQI: Pittsburgh Sleep Quality Index, SD: standard deviation.

Table 4. Comparison of STOP-BANG and ESS components between groups

Parameter	TMD patients (n=503) n (%) or Mean ± SD	Healthy control (n=180) n (%) or Mean ± SD	p-value
STOP-Bang			
Snoring (none =0, yes =1)	**79 (15.7)**	**8 (4.4)**	**< 0.001*** **
Tired (none =0, yes =1)	420 (83.5)	147 (81.7)	0.324
Observed apnea (none =0, yes =1)	28 (5.6)	6 (3.3)	0.163
High blood pressure (none =0, yes =1)	**32 (6.4)**	**2 (1.1)**	**0.002****
BMI more than 35kg/m^2 (none =0, yes =1)	4 (0.8)	1 (0.6)	0.604
Age over 50 (none =0, yes =1)	**80 (15.9)**	**0 (0.0)**	**< 0.001*** **
Neck circumference (male >17 inches, female >16 inches) (none =0, yes =1)	29 (5.8)	7 (3.9)	0.223
Gender (male) (none =0, yes =1)	170 (33.8)	64 (35.6)	0.367
STOP BANG total score (0-8)	**1.77 ± 1.86**	**1.53 ± 0.77**	**0.017***
STOP-BANG total score ≥ 3 (high risk of OSA)	**81 (16.1)**	**13 (7.2)**	**0.001****
Epworth sleepiness scale			
Sitting and reading (0-3)	0.94 ± 0.73	0.91 ± 0.64	0.588
Watching TV (0-3)	0.63 ± 0.67	0.61 ± 0.60	0.751
Sitting, inactive in public place (0-3)	**0.59 ± 0.66**	**0.76 ± 0.73**	**0.007****
As a passenger in a car for an hour without a break (0-3)	**1.19 ± 0.89**	**1.04 ± 0.81**	**0.047***
Lying down to rest in the afternoon when circumstances permit (0-3)	**1.45 ± 0.89**	**1.17 ± 0.84**	**< 0.001*** **
Sitting and talking to someone (0-3)	0.28 ± 0.54	0.33 ± 0.56	0.272
Sitting quietly after a lunch without alcohol (0-3)	1.23 ± 0.85	1.34 ± 0.83	0.107
In a car, while stopped for a few minutes for traffic (0-3)	**0.42 ± 0.63**	**0.54 ± 0.66**	**0.043***
ESS total score (0-24)	6.73 ± 3.62	6.71 ± 3.02	0.952
ESS total score ≥ 10 (Excessive daytime sleepiness)	**99 (19.7)**	**23 (12.8)**	**0.023***

Values are presented as number (%) and mean ± standard deviation. Comparison results of the number (%) between groups performed with $\chi 2$ test and Boneferroni correction. p-Value significance was set at <0.05. *: p-value < 0.05, **: p-value <0.01, ***: p-value <0.001.

TMD: temporomandibular disorder, SD: standard deviation, STOP-Bang: The snoring, tiredness, observed apnea, high blood pressure (STOP)-BMI, age, neck circumference, and gender (Bang), ESS: Epworth sleepiness scale

Table 5. PSQI, STOP-Bang, and ESS scores according to number of TMD/AXIS I diagnosis

	Number of TMD Axis I diagnosis					
	1 (n = 88)	2 (n = 120)	3 (n = 125)	4 (n = 170)	p-value	Post-hoc analysis
PSQI global scores	**6.18 ± 2.77**	**5.96 ± 2.65**	**5.90 ± 2.72**	**6.75 ± 2.84**	**0.028***	**2<4, 3<4**
STOP-Bang total scores	1.90 ± 1.51	1.95 ± 2.82	1.88 ± 1.89	1.49 ± 0.87	0.125	
ESS total scores	**5.73 ± 3.83**	**6.59 ± 3.41**	**6.65 ± 3.60**	**7.40 ± 3.79**	**0.005****	**1 < 4**

Values are presented as mean ± standard deviation. The results were obtained from ANOVA and post-hoc analysis.

p-Value significance was set at <0.05. *: p-value < 0.05, **: p-value <0.01.

TMD: temporomandibular disorder, PSQI: Pittsburgh Sleep Quality Index, STOP-Bang: The snoring, tiredness, observed apnea, high blood pressure (STOP)-BMI, age, neck circumference, and gender (Bang), ESS: Epworth sleepiness scale

Table 6. **Multivariate logistic regression analysis of factors influencing poor sleep (PSQI > 5) among the TMD patients**

	PSQI (≤5) (n=217)	PSQI (>5) (n=286)			95% Confidential interval	
	n (%)	n (%)	p-value	Exp(B)	Lower	Upper
Age [ref.=under average value]	**56 (25.8)**	**141 (49.3)**	**<0.001*** **	**2.551**	**1.662**	**3.917**
Female [ref.= male]	**124 (57.1)**	**209 (73.1)**	**0.007****	**1.885**	**1.193**	**2.978**
BMI [ref.= under average value]	90 (41.5)	139 (48.6)	0.146	1.353	0.900	2.036
VAS [ref.=under average value]	121 (55.8)	168 (58.7)	0.951	1.012	0.685	1.495
Duration [ref.=under average value]	61 (28.1)	73 (25.5)	0.711	0.922	0.600	1.418
Myofascial pain by RDC/TMD [ref.=none]	197 (90.8)	268 (93.7)	0.762	1.125	0.523	2.423
Disc displacement by RDC/TMD [ref.=none]	119 (54.8)	159 (55.6)	0.453	0.829	0.508	1.353
Arthralgia by RDC/TMD [ref.=none]	152 (70.0)	203 (71.0)	0.930	0.976	0.576	1.655
Headache attributed to TMD by DC/TMD	**107 (49.3)**	**178 (62.2)**	**0.049***	**1.519**	**1.000**	**2.308**
STOP-Bang [ref.< 3]	31 (14.3)	50 (17.5)	0.868	1.051	0.584	1.891
ESS [ref.< 10]	**34 (15.7)**	**65 (22.7)**	**0.014***	**1.839**	**1.130**	**2.993**

OR: odds ratio, CI: Confidential interval, ESS: Epworth sleepiness scale

Multiple logistic regression was performed to comprehensively examine the factors affecting poor sleep in cTMD patients. For obtaining significant results, two-tailed level of statistical significance of a p-value was set at less than 0.05. *: p-value < 0.05, **: p-value <0.01, ***: p-value <0.001.

Figures

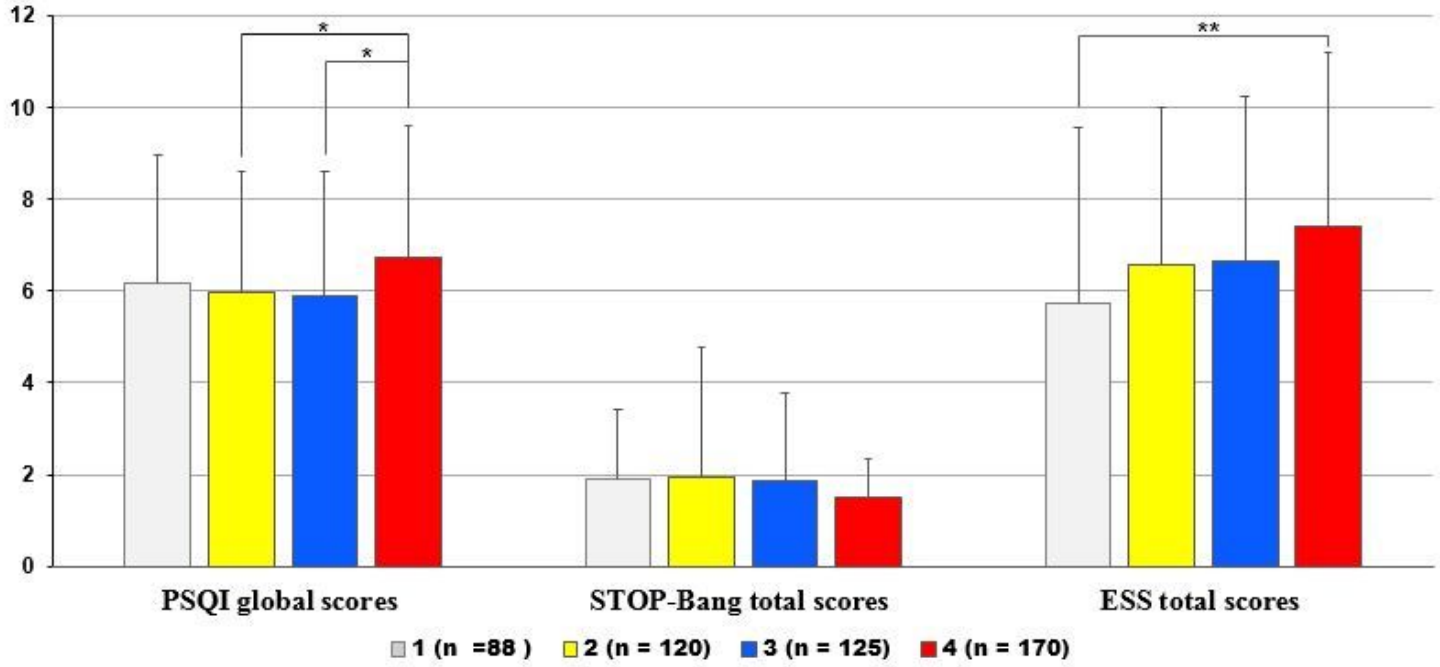

Figure 1

PSQI, STOP-Bang, and ESS scores according to number of TMD/AXIS I diagnosis