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Risk Factors for Craniomandibular Disorders: Systematic Review and Meta-Analysis.

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ABSTRACT :

Aim : This study aimed to list the different risk factors for cranio-mandibular dysfunctions (CMD), and thus contribute to the creation of a database of the identified risk factors.

Methods : The search strategy was run from September 1,2020 to March 31, 2021. The following electronic databases were searched: Embase, Scopus, Science Direct, PubMed, Cochrane Library. A total of 271 articles were screened by title and abstract, and 29 were assessed by full text. Ten articles met the eligibility criteria and were included in the systematic review.

Results : This study aimed to explore the different risk factors for CMD. Our work targeted articles published between 2011 and 2021, in order to focus on recent scientific research. We divided these factors into 3 categories: general factors, psychosocial factors and dental factors. 5 studies were about general risk factors, 2 were about dental risk factors and 3 were about psychosocial factors.

Conclusion : This systematic review addressed the main risk factors of DCM. The development of a precise classification of risk factors and the determination of the latter will offer practitioners the appropriate choice of treatments, and therefore the possibility of ensuring long-term management.

Key words : Risk Factors, Craniomandibular Disorders, Temporomandibular Joint Disorders

1. Introduction

Craniomandibular disorders or dysfunctions (CMD) are part of the musculoskeletal disorders causing discomfort and pain in a significant category of the population. These disorders include a heterogeneous group of conditions affecting the temporomandibular joint (TMJ), masticatory muscles and/or surrounding tissues [1]. In addition to pain, patients who are affected by these dysfunctions frequently present with limited or asymmetrical mandibular movements and joint noises. The review of the scientific literature highlights genetic, biological and functional factors as predictive and predisposing for the onset and development of CMD. In addition, it is widely assumed that the etiopathogeny of CMD is multifactorial although this is not fully substantiated. [1].

In our context, our interest in DCM was stimulated by two studies on the prevalence of DCM that triggered the curiosity to explore other scientific research questions: the first study [2] involved a sample of 142 students from the Faculty of Dental Medicine of Casablanca. The study found that 52.8% of students have at least one sign of CMD, pain was present in 17.5% of the sample. The second study [3] focused on all patients receiving orthodontic treatment in the dentofacial orthopedic department of the Dental Consultation and Treatment Center of the CHU Ibn Rochd in Casablanca, during the different stages of treatment and over a period of 4 months. Joint noise was found in 14%. Which had a duration of more than a month in 92.9% of cases and less than a month in 7.1% of cases. The pain was periorbital in 22.1% of cases, auricular and angular in 55.5% of cases, perioral in 11.2% of cases and cervical in 11.2% of cases. This pain was considered moderate in 71.54% of cases and severe in 28.4%. [3] Based on these observations, the successful care and long-term management of these disorders requires the identification of possible contributing factors. Thus, a comprehensive diagnostic approach requires clinicians to understand all potential factors related to CMDs. A number of theories have emerged, ranging from muscular and neuromuscular theory to physiological and psychological theories. Nevertheless, none of these theories could clearly explain the mechanisms of CMDs. It turned out that concepts based on a single factor no longer have scientific credibility. In the current state of knowledge, no one can claim to really know the risk factors for CMD. Due to the complexity and multifactorial nature of these disorders, their risk factors have long been the subject of controversy and remain poorly understood [4].

The development of a precise classification of risk factors and the determination of the latter will offer practitioners the appropriate choice of treatments, and therefore the possibility of ensuring long-term management. The objective of this systematic review was to list the different risk factors for CMDs, and thus contribute to the creation of a database of the identified risk factors.

2. METHODS

We carried out a systematic review, that was developed based on a pre-determined protocol, and was reported in line with the updated version of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). [5] This review has been registered in the OSF platform. The registration DOI is as follows: https://doi.org/10.17605/OSF.IO/2HJ5A The inclusion criteria followed the PICO framework as suggested by the PRISMA checklist: [5]

- P: Adult participants (aged >18 years) with a diagnosis of TMD according to the Research Diagnostic Criteria for TMD (RDC/TMD) [6] or any trials with a population reporting signs and symptoms of TMD. [7]
- I: All the studies responding to the boolean equations ((Risk factors [MeSH Terms]) AND (Craniomandibular Disorders [MeSH Terms]); (("Odds Ratio"[Mesh]) AND "Risk Factors"[Mesh]) AND "Temporomandibular Joint Disorders"[Mesh]) chosen and elaborated from these key words (Risk Factors, Craniomandibular Disorders, Temporomandibular Joint Disorders) have been included. All included studies had a comparison group included. Studies with multiple interventions were also included and managed according to the Cochrane Handbook for Systematic Reviews of Interventions.[8]
- O: Only studies allowing the risk factors of CMDs to be determined were included. This through the relative risk (RR) for Cohort studies, the Odds Ratio (OR) for case-control studies, by interpreting the results using confidence intervals. One randomized controlled clinical trial was also included. No restriction on length of studies, assessment time points or setting of study was considered.

All Articles deemed to be expert reports, letters, commentaries, editorials have been excluded.

Articles that did not meet the objectives of our work on the basis of the reading of the abstracts and the critical reading of the full text have been excluded. Articles whose publication date was prior to 2011 have been excluded.

The search strategy was run from September 1,2020 to March 31, 2021. The following electronic databases were searched: Embase, Scopus, Science Direct, PubMed, Cochrane Library. The articles were first selected on their title, then on their abstract and finally on their full text. At each of these sorting steps, articles were kept for their relevance to answering the questions asked and others were, conversely, discarded. This approach allowed us to steadily reduce the number of items and to filter them in order to read only a smaller number of articles in full accordance with our objective.

The extracted data items from the included papers covered:

- Name of authors and year of publication
- Type of study
- Attendees
- Sex
- Middle age
- Follow time
- Risk factors
- OR/RR

Statistical analysis strategy

The revised Cochrane risk of bias tool for randomized trials (RoB 2) to estimate the risk of bias was performed. Reviewers followed the full ROB2 Development Group guidance document. [9] The MERSQI tool was used for the cohort and case-control studies.

3. RESULTS

Figure 1 shows the included studies at each phase of the review. A total of 271 articles were screened by title and abstract, and 29 were assessed by full text. Ten articles met the eligibility criteria and were included in the systematic review. [1,4,6-13]_A total of 10 publications were included in our study:

• 1 randomized controlled clinical trial

• 5 cohort studies

• 4 case-control studies

These studies included more than 53,759 patients with a mean age of 35.8 years and a mean follow-up of 4.6 years. All the characteristics of these studies have been described in Table I.

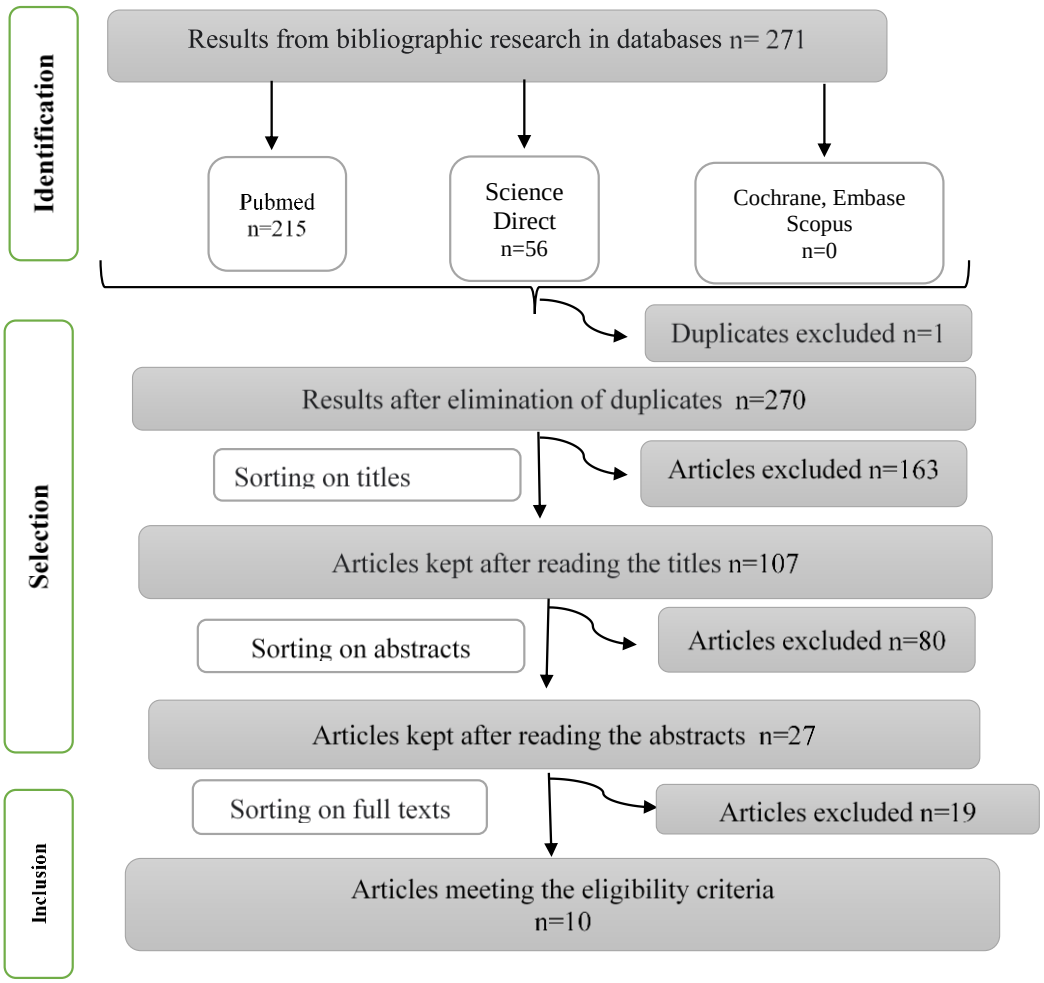


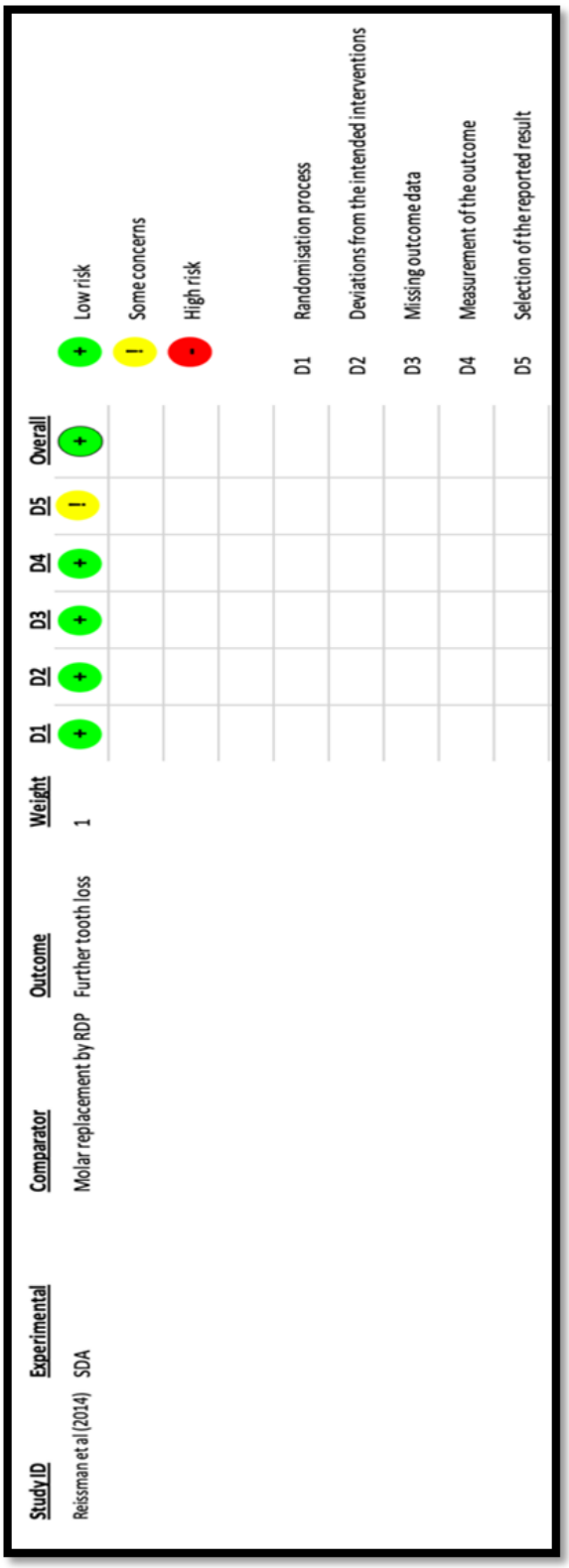
Figure 1. PRISMA flow diagram which included searches of databases [5]

Table I. Characteristics of the studies included

Title	**Author/Year**	**Type of study**	**Sample**	**Gender**	**Age**	**Follow Time**	**Risk Factors**	**Odds /Hazard/ Rate ratio**	**Statistical analysis strategy**	**Conclusion**
Multivariable Modeling of Phenotypic Risk Factors for First-Onset TMD: The OPPERA Prospective Cohort Study [10]	Bair et al., 2013	Cohort study	2737 patients	-	31 years	2,8 years	Sociodemographic and clinical factors, measures of general health, experimental pain sensitivity, autonomic function and psychological distress	**HR :** 1,07 à 1,18	Lasso method, Random drills model	Comorbid pain++ Non-specific orofacial symptoms ++
The randomized shortened dental arch study: temporomandibular disorder pain [1]	Reissmann et al., 2013	Randomized controlled clinical trial	152 patients	82 women, 70 men	59,7 years	5 years	Missing posterior tooth support in patients with short dental arch and patients with temporary denture	OR Self declared: 1.1 OR Clinically verified : 0.7	Student test, Wilcoxon signed rank test, Chi 2 test	Shortened dental arch is not a risk factor
Increased Risk of Temporomandibular Joint Closed Lock: A Case-Control Study of ANKH Polymorphisms [11]	Huang et al., 2011	Case-control study	55 patients	44 women, 11 men	42,6 years	-	ANKH gene polymorphism	**OR** ANKH-OR homozygotes :7,7	Univariate logistic regression method	Polymorphism ANKH-OR is a genetic marker associated with mandible locking
Genetic Variants Associated With Development of TMD and Its Intermediate Phenotypes: The Genetic Architecture of TMD in the OPPERA Prospective Cohort Study [12]	Smith et al., 2013	Cohort study	2737 patients	1630 women, 1107 men	27,1 years	2,8 years	Genetic risk factors	-	Bonferroni method (type of comparison test)	Genetic risk factors linked to clinical, psychological and sensory phenotypes
The risk of temporomandibular disorder in patients with depression: a	Liao et al., 2018	Cohort study	37682 patients	19065 women, 18617 men	39,09 years	7 years	Depression	**HR :** 2,21	Chi 2 test	Patients with depression are more likely to develop CMD (women+)

population-based cohort study[13]										
Association of temporomandibular disorder pain with awake and sleep bruxism in adults [4]	Sierwald et al., 2015	Case-control study	1623 patients	1107 women, 516 men	40,9 years	-	Bruxism (wakefulness and sleep)	OR Awake bruxism: 1.7 OR Sleep bruxism: 1.8 Both combined: 7.7	Chi 2 test, Wilcoxon signed rank test, Student test	Bruxisms (awake and sleep) are interactive, linked to the risk of TMJ pain
Prevalence and Risk Indicators of Temporomandibular Disorder Signs and Symptoms in a Pediatric Population with Spastic Cerebral Palsy [14]	Miamoto et al., 2011	Case-control study	120 patients	73 women, 47 men	10,4 years	-	Body Mass Index (BMI), male gender, severity of malocclusion, mixed dentition	**OR** Presence of BMI : 9,08	Chi 2 test, Fischer test, Logistic regression	Children with BMI have a higher risk of developing CMD
Potential Genetic Risk Factors for Chronic TMD: Genetic Associations from the OPPERA Case Control Study [15]	Smith et al., 2011	Case-control study	1608 patients	663 women, 945 men	31,5 years	5 years	Genetic factors (23 genes)	**OR :** 1,4	Chi 2 test	NR3C1, CAMK4, CHRM2, IFRD1, GRK5, HTR2A and COMT genes contribute to CMDs
Psychological Factors Associated With Development of TMD: The OPPERA Prospective Cohort Study [16]	Fillingim et al., 2013	Cohort study	2737 patients	1630 women, 1107 men	27,1 years	5,2 years	Psychological and somatic factors	**OR :** 1,2 à 1,3	Cox Regression Model, Random Drills Model	Measures of somatic symptoms, perceived stress, prior life events, and negative affect predict CMDs
Depressive and Anxiety Symptoms as Risk Factors for Temporomandibular Joint Pain: A Prospective Cohort Study in the General Population [17]	Kindler et al., 2012	Cohort study	4308 patients	2192 women, 2116 men	49 years	5 years	Anxiety and Depression	**RR :** 2,1	Student test, Chi-square test, Poisson regression model	Anxiety and depression are risk factors. Anxiety related to joint pain Depression related to muscle pain.

The risk of bias of the included studies was assessed by Methodological quality of the randomized trial included with the ROB2 tool (figure 2). The quality of the included observational studies has been summarised in Table II.



SDA: Shortened dental arch, **RDP:** Removable dental prostheses

Figure 2: Individual risk of bias by ROB2 of the randomized controlled trial included in this systematic review

Table II: Measurement of the quality of observational studies included with the MERSQI tool (Medical Education Research Study Quality Instrument)

Domain	**MERSQI Item**	**Score**								
		Cohort Study					**Case-control study**			
		Bair et al (2013)	**Smith et al (2013)**	**Liao et al (2011)**	**Fillingim et al (2013)**	**Kindler et al (2012)**	**Huang et al (2011)**	**Sierwald et al (2015)**	**Miamoto et al (2011)**	**Smith et al (2011)**
Study design	Single group cross-sectional or single group post-test only	-	-	-	-	-	-	-	-	-
	Single group pre-test & post-test	-	-	-	-	-	-	-	-	-
	Nonrandomized, 2 groups	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**
	Randomized controlled trial	-	-	-	-	-	-	-	-	-
Sampling	**No. of institutions studied**									
	1	**0,5**	-	-	-	**0,5**	**0,5**	-	-	-
	2	-	-	-	-	-	-	**1**	-	-
	>2	-	**1,5**	**1,5**	**1,5**	-	-	-	**1,5**	**1,5**
	Response rate, %									
	Not applicable	-	-	-	-	-	-	-	-	-
	<50 or not reported	-	-	-	-	-	-	-	**0,5**	**0,5**
	50-74	-	-	-	-	-	**1**	-	-	-
	≥75	**1,5**	**1,5**	**1,5**	**1,5**	**1,5**	-	**1,5**	-	-
Type of data	**Type of data**									
	Assessment by study participant	**1**	-	**1**	**1**	**1**	-	**1**	-	**1**
	Objective measurement	-	**3**	-	-	-	**3**	-	**3**	-
Validity evidence for evaluation instrument scores	Not applicable	-	-	-	-	-	-	-	-	-
	Content	**1**	**1**	**1**	**1**	**1**	**1**	-		**1**
	Internal structure	**1**	**1**	**1**	**1**	**1**	-	-		**1**
	Relationships to other variables	**1**	**1**	**1**	**1**	-	**1**	**1**	-	-
Data analysis: sophistication	Descriptive analysis only	-	-	**1**	-	-	-	**1**	-	**1**
	Beyond descriptive analysis	**2**	**2**	-	**2**	**2**	**2**	-	**2**	-
Data analysis: appropriate	Data analysis appropriate for study design and type of data	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**
Outcome	Satisfaction, attitudes, perceptions, opinions, general facts	-	-	-	-	-	-	-	-	-
	Knowledge, skills	-	**1,5**	-	-	-	**1,5**	-	-	**1,5**
	Behaviors	-	-	**2**	-	**2**	-	-	**2**	-

	Patient / Health care outcome	**3**	-	-	**3**	-	-	**3**	-	-
Total possible score		**14**	**15,5**	**13**	**15**	**12**	**13**	**11,5**	**12**	**10,5**

General risk factors will be divided into genetic and somatic risk factors:

- **Genetic risk factors**: For Huang et al [11], the ANKH-OR polymorphism was found to be a genetic marker associated with CMDs, more specifically in relation to the locking of the mandible. Smith et al., 2011 [15] report that the HTR2A, COMT, NR3C1, CAMK4, CHRM2, IFRD1 and GRK5 genes have been revealed as new potential genetic risk factors for CMDs.According to Smith et al., 2013 [12], the appearance of CMDs was affiliated with genetic risk factors linked to clinical, psychological and sensory phenotypes.
- **Somatic risk factors**: According to Miamoto et al [14], children with cerebral palsy had a significantly higher risk of developing signs and symptoms of CMDs. Bair et al.,2013 [10] confirm that comorbid pain states, pre-existing pain, and each individual's somatic awareness were factors responsible for the high incidence of CMDs. Fillingim et al., 2013 [16] also concluded that somatic symptoms, as well as pain adaptation and catastrophizing predict the onset of CMDs.

For psychosocial risk factors: The population study that was conducted by Liao et al [13] on the association between depression and CMDs revealed that the risk of diagnosis of CMD was 2.21 to 2.64 times higher in patients presenting with a depressive disorder diagnosed by a physiotherapist.

Kindler et al [17] reported the same findings, confirming that depressive symptoms were more strongly linked to joint pain, and adding that anxiety symptoms are specific to muscle pain. According to Fillingim et al [16], perceived stress, previous life events and negative mood predict the incidence of CMD.

Dental risk factors that were found including:

- **Bruxism:** Sierwald et al [4] reported that when occurring separately, awake bruxism and sleep bruxism were significant risk factors for TMJ pain. In case of simultaneous presence, the risk of pain was even higher.
- **Loss of posterior tooth support**: According to Reissman et al [1], preservation of a shortened dental arch was not a major risk factor for TMJ pain over a 5-year period.

Data synthesis and meta-analysis focused on the overall effect of depression as this was the only exploitable variable: the results of cohort studies on the same factor, depression, were combined. Thus, by studying this association, we were able to show a significant association between depression and CMD with an RR of 2.21.

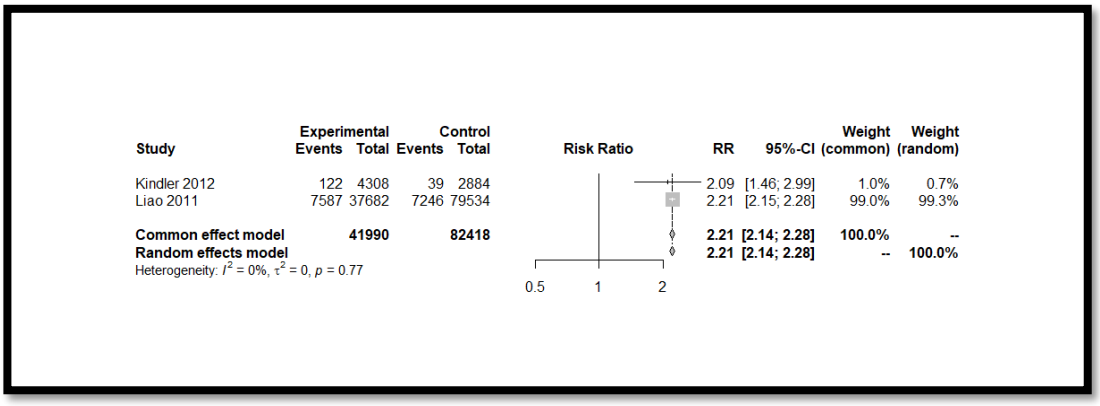


Figure 3: Forest plot of homogeneous studies with similar results

IV. DISCUSSION

This study aimed to explore the different risk factors for CMD. Our work targeted articles published between 2011 and 2021, in order to focus on recent scientific research. We divided these factors into 3 categories: general factors, psychosocial factors and dental factors. 5 studies were about general risk factors, 2 were about dental risk factors and 3 were about psychosocial factors.

Concerning general risk factors, firstly, sex hormones: It has been suggested that pubertal development and related hormonal, physical, and psychosocial changes might influence the genesis, onset, and/or development of CMDs. [18]

The study by LeResche et al [19] revealed that the frequency of TMJ pain increased for both sexes: the prevalence of temporomandibular pain was approximately 4% in prepubertal subjects and 14% in subjects who have completed pubertal development (OR: 1.4-2.0). Weiler et al conducted 2 studies to determine the prevalence of CMDs in athletic and non-athletic adolescents. The 1st study based on adolescent males [20] showed that the CMDs rate was 12% before the growth spurt. This value increased to 71% during the growth spurt, and decreased to 18% after this period. The 2nd study based on

female adolescents [21] showed prevalence of 8.7%, 43.5% and 47.8% in patients before, during and after pubertal growth respectively. The systematic review carried out by Berger et al [22] including 9 articles, of which 2 of them suggested that a high level of oestrogen was associated with an increased prevalence of CMD, while 5 articles established an association between a low oestrogen levels and increased CMD-related pain. Landi et al [23] suggested that certain joint tissues (bones, cartilage, etc.) could be affected by estrogens. These hormones could therefore be involved in the physiopathology of CMD. LeResche et al [24] who examined the association between the use of exogenous hormones and the risk of CMD in postmenopausal women. They concluded that the likelihood of suffering from MCDs was about 30% higher in women receiving estrogen than in those not receiving it. Estrogens affect mRNA replication and Nav1.7 protein expression in trigeminal ganglion sodium channels. This would cause these channels to close and increase the pain response by lowering the TMJ nociceptive threshold. [25] 17-beta-estradiol, being the main estrogen in human beings, could be responsible for the excessive sensitivity of ATM and the development of inflammatory processes at its level. [26]

Regarding the genetic risk factors: The ANKH gene is a human homologue of the murine progressive ankylosis gene, “ank” [27]. The study by Huang et al [11] aimed to establish the relationship between locking of the mandible and ANKH polymorphisms by performing a histological examination of the temporomandibular joint (TMJ) in “ank” mutant mice. This study identified ANKH expression in TMJ synovial cells. Mutations and polymorphisms in the ANKH gene have been found to predispose to mandibular locking in humans and fibrous ankylosis in mice. Tsui et al [27] have shown that the ANKH gene has also been associated with various skeletal and joint abnormalities, including ankylosing spondylitis. Patients with this disease had a higher frequency of internal TMJ derangement, this was also confirmed by the research of Major et al [28]. The OPPERA (Orofacial Pain: Prospective Evaluation and Risk Assessment) study provided further research into genetic influences on CMDs compared to previous studies that targeted one or a few genetic markers. [29] They involved 358 genes, and this was the first large-scale study to assess the genetic mediators of TMJ in both sexes and in all races. The authors observed an association between a few genes and the risk of CMDs: the HTR2A, COMT, NR3C1, CAMK4, CHRM2, IFRD1 and GRK5 genes. The strongest association found was that of the HTR2A serotonin receptor gene rs9316233, where the minor G allele showed a protective effect against ATM risk. Smith et al [15] observed a suggestive association between CMDs and the COMT gene locus, rs174697. Diatchenko et al [30] described three common haplotypes of the COMT gene that predicted low, medium, or high pain sensitivity in Caucasian women. This study showed that the haplotype linked to high pain sensitivity was strongly at high risk for CMDs. The study by Smith et al [12] provided evidence for the existence of several genes contributing to the aetiology of CMDs: the two genes, SCN1A and ACE2 have been associated with the clinical measure of painless orofacial symptoms, one of the predictors of TMD incidence. A polymorphism in the PTGS1 gene has been associated with the psychosocial factor representing global psychological symptoms, a significant predictor of the incidence of CMDs. [12]

For the somatic risk factors: Miamoto et al [14] revealed in their study that patients with cerebral palsy were predisposed to suffer from CMDs. The prevalence of CMDs symptoms in this population was approximately 13.3% and the presence of cerebral palsy was an important risk indicator for this disorder (odds ratio: 9.08; p=0.041), with 9 times more likely for these individuals to have CMD symptoms compared to control subjects. The study by Ortega et al [31] corroborated these results: the frequency of CMD signs observed in the cerebral palsy group (67.6%) was higher than in the control group (25%). The study by Bair et al [10] seeks to find risk factors for CMD using two multivariate statistical methods: the lasso regression method and the random forest method. In general, the results of the lasso model were similar to those of the random forest model. Both models revealed that history of comorbid conditions, body pain, nonspecific orofacial symptoms, and somatic awareness were among the strongest predictors of first-onset CMD. Additionally, one of the strongest predictors of the occurrence of CMD in both models was the number of comorbid conditions reported by the participant. Comorbid conditions included some painful conditions such as fibromyalgia and low back pain, but also other conditions that were not primarily painful (eg, depression and sleep apnea). The results of the multivariate models used by Fillingim et al [16] provided strong evidence that somatic symptoms were the strongest predictor of CMD. According to these authors, the mechanisms by which somatic symptoms increase the risk of CMDs remain unknown. Their theory was based on the fact that somatic symptoms were associated with health behaviors that would increase the risk of CMDs such as parafunctional behaviors (bruxism, nail biting, etc.) or other behavioral changes (sleep disorders, etc. .), which could in turn increase the risk of CMDs. [32]

As regards psychosocial risk factors: The results of the study conducted by Liao et al [13] revealed that the risk of diagnosis of CMD was 2.21 to 2.64 times higher in patients with depressive disorder than in the control group during a follow-up period of 8 years. (HR: 2.21). Slade et al [33] also showed that depression was one of the predictive risk factors for the first appearance of CMDs in healthy women, with a small sample size. This mental disorder modified the effect of genetic polymorphisms on muscle and joint pain [17], and therefore affected the expression of CMD symptoms. For this reason, patients with CMD comorbid with depression were unlikely to improve with dental treatment alone. [34] On the other hand, Aggarwal et al [35] showed that anxiety predicted the development of CMD-related pain in adults. Kindler et al [17] studied the association between depression and anxiety in relation to CMD-related pain. Their results indicated specificity in the relationship between depressive symptoms and joint pain, and the relationship between anxiety symptoms and muscle pain. Depressive and anxiety symptoms trigger muscle over activity and joint inflammation, which would trigger pain. [36] The OPPERA study incorporated a broad assessment of psychological functioning to identify psychosocial risk factors for CMDs. [16] The psychological variables included in this study were: general psychological symptoms, negative mood, post-traumatic stress symptoms, perceived stress and the effect of previous events. A recent study was conducted on the psychosocial impact of COVID-19 on the development of DCMs. [37] All psychological issues related to emergency situations, such as the COVID-19 pandemic, were capable of triggering a chain of events that results in elevated activity of the sympathetic nervous system, and the release of adrenocortical steroids that lead to vasoconstriction muscular. Consequently, the TMJ is affected and symptoms of orofacial pain may appear.

As to dental risk factors, firstly extraction of wisdom teeth: Damasceno et al [38] stated that the association between wisdom tooth extraction and the risk of developing CMDs was based on several factors: the location of the tooth [39] [40], the degree of its impaction [39] [41], use of incorrect surgical technique or lack of mandibular support during extraction of mandibular 3rd molars [39-43], as well as the age and sex. [39,40]. The surgical procedure

and postoperative inflammation affected surrounding tissues, including masticatory muscles, which might contribute to the development of CMD-related pain. [44] After placing the patient in a supine position, the applied forces can be transferred to the TMJ and forced the condyle in a posterior direction, the need to open the jaw for long periods also can cause muscle fatigue, trauma and possibly overloading of one or both TMJs, leading to a process of development of CMDs. [39-41] Dentists often advocate 3rd molar extraction during adolescence, citing benefits such as incomplete roots, better healing, and minimal morbidity. 2 studies [39-40] suggested that the risk of developing CMD may be higher for people under 21 years of age. The relative risk value was slightly higher in this age group (RR: 1.6). Although these disorders were not prevalent in this age group, the high frequency of wisdom tooth extraction results in a 23% risk, indicating that nearly 1/4 of all cases of CMDs in this age group could be related to the extraction of third molars. Huang conducted 2 studies [39-40] where he compared the use of different types of anesthesia during this procedure: local anesthesia, general anesthesia, intravenous sedation and conscious sedation. No significant association was found in these studies. (Relative risk: 1.0)

Concerning bruxism: The systematic review by Manfredini et al [45] identified 20 articles between 1998 and 2008 that reported a link between bruxism and TMJ-related pain. The study by Sierwald et al [4] used 3 models to determine the association between bruxism and CMDs. The 1st model separated daytime bruxism and nighttime bruxism as 2 independent risk factors, with an OR of 2.9 and 2.3 respectively. The 2nd model assumes an interaction between the 2 factors. It turned out that, compared to people reporting only awake bruxism (OR: 1.5) or only sleep bruxism (OR: 1.8), cases reporting having both factors at the same time showed a significant interaction. with an OR of 3.0. The 3rd model included the interaction of the 2 factors and the confounding factors. By multiplying the ORs of awake bruxism, sleep bruxism and that of the confounding factors, they obtained an overall OR of 7.7, which indicates that the risk of pain related to TMJ is considerably increased in the simultaneous presence of awake bruxism and sleep bruxism.

Regarding, loss of posterior tooth support: Tallents et al [46] evaluated the prevalence of missing mandibular posterior teeth and CMDs by comparing symptomatic and asymptomatic patients. They revealed that there was a weak but significant association between the absence of mandibular teeth and the presence of disc dislocation. The results of the study by Wang et al [47] showed the prevalence of CMD increases when the variables of the number of missing posterior teeth and the number of dental quadrants increase, especially in young women. The loss of posterior teeth, especially when the number of teeth lost was low, can lead to secondary changes, including drift and tilting of the remaining teeth. These changes result in a tight bite. The lower the number of missing posterior teeth, the higher the chance that an individual will develop a tight bite. This implies that these individuals have a higher risk of developing CMD. Witter et al [48,49] concluded that the loss of posterior teeth has no effect on the development of CMDs. A shortened dental arch consisting of 3 to 5 posterior teeth ensures long-lasting occlusal stability, and offered sufficient oral comfort for a long period of time. Furthermore, the insertion of removable partial dentures did not prevent CMDs and did not improved oral function. The study by Reissman et al [1] confirmed these statements: the results of their study provided no evidence that replacing missing posterior teeth with removable prostheses reduced the risk of CMD (OR: 0.7). The preservation of a shortened dental arch was not a major risk factor for the development of CMD. The study by Holmlund et al [50] also confirmed that prosthetic replacement of lost molars for the sole purpose of preventing CMD should not be a general principle in treatment planning.

Conflict of interest

The authors declare no conflict of interest.

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