Temporomandibular Disorders as Contributors to Primary Headaches: A Systematic Review

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Aims: To systematically review the literature assessing associations between TMDs and primary headaches. **Methods:** Using validated clinical criteria, studies on TMDs and primary headaches published up to January 10, 2023 were identified using six electronic databases. This review adhered to the PRISMA 2020 guidelines and 27-item checklist and is registered on PROSPERO (CRD42021256391). Risk of bias was evaluated using the National Institutes of Health Quality Assessment Toolkits for Observational Cohort and Cross-Sectional Studies. **Results:** Two independent investigators rated 7,697 records against the primary endpoint and found 8 records meeting the eligibility requirements. Migraine was found to be the most common primary headache related to TMDs (61.5%), followed by episodic tension-type headache (ETTH; 38.5%). A moderate association was found for mixed TMDs with migraine and ETTH, with a large sample size and multiple studies included (n = 8). A very low-quality association was found for myalgia-related TMDs with migraine and ETTH (included studies, n = 2). **Conclusion:** The association between TMDs and primary headaches is of great interest given the possible effectiveness of TMD management in reducing headache intensity/frequency in patients with TMDs and headache comorbidity. A moderate association was found for mixed TMDs with primary headaches, in particular migraine and ETTH. However, owing to the overall moderate certainty of evidence of the present findings, further longitudinal studies with larger samples investigating possible associated factors and using accurate TMD and headache category assignment are needed. *J Oral Facial Pain Headache 2023;37:91–100. doi: 10.11607/ofph.3345*

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Recent estimates indicate that chronic pain affects over 30% of people worldwide, severely burdening individual quality of life and finances.[1] As the global population rises and ages, more efforts are needed to improve quality of life and ensure healthy aging so that the additional years of life are spent in good health. Musculoskeletal diseases pose a severe threat in this scenario, limiting physical and mental abilities and functional capacities as well as imposing substantial health and economic burdens on individuals, families, and governments.[2,3]

In this context, temporomandibular disorders (TMDs), which encompass a group of conditions affecting the masticatory muscles, temporomandibular joints (TMJs), and associated musculoskeletal structures of the head and neck,[4] have recently been recognized as the most frequent cause of nonodontogenic orofacial pain. To date, TMDs are the second most common type of musculoskeletal pain after back pain, with a prevalence ranging from 5% to 12%.[5] TMDs are almost twice as prevalent in women as men, and there is evidence that women taking supplemental estrogen or oral contraceptive therapy are more likely to seek treatment for these conditions.[6,7] Symptoms may include decreased mandibular range of motion, masticatory muscle pain, joint pain, associated joint noise during function, and deviation in jaw opening. Although not life threatening, such disorders may impair quality of life,[8,9] and the symptoms may be chronically troublesome. Nevertheless, like many chronic pain syndromes, the biologic pathways related to pain in TMDs have yet to be fully elucidated. Indeed, while acute musculoskeletal pain in the absence of trauma or systemic diseases is likely the result of an overload (eg, prolonged muscle bracing), factors leading to chronic TMD pain are more complex, often involving an interplay of individual vulnerability and iatrogenesis.[10] Furthermore, besides reporting localized pain, impaired jaw movement, and noise during jaw movement, patients with TMDs may also complain of other symptoms, including earache, tinnitus, dizziness, and headache.[11]

The nonnegligible frequency of headache reported by TMD patients has led to the introduction of a subgroup for headache attributed to TMDs as part of the Diagnostic Criteria (DC) for TMD axis diagnoses.[12] The four major groups of primary headaches are currently identified as migraine, episodic tension-type headache (ETTH), trigeminal autonomic cephalalgia, and other primary headaches.[13] Proper management of TMDs may lower nociception, improve sensitization, and reduce the frequency and intensity of primary headaches. However, no direct cause-and-effect relationship between TMDs and headache has been demonstrated, nor is there any clear proof of the DC/TMD entity of a headache attributed to TMDs. Nonetheless, there is emerging evidence that different headaches may co-occur, share common neural circuits, and be reported by patients with TMD symptoms. In such cases, management of the different conditions is best achieved by addressing each symptom individually. To the best of the authors' knowledge, only a very recent systematic review and meta-analysis summarizing existing knowledge on the association between TMDs and headache has been published.[14] The present study aimed to fill this gap in the literature by offering a systematic review of studies investigating the associations among TMDs, TMD subtypes, and different primary headache subtypes, selecting only studies using widely accepted validated clinical criteria for TMDs and primary headaches.

Materials and Methods

Search Strategy and Data Extraction

The present systematic review followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 guidelines, adhering to the 27-item checklist.[15] Separate searches in the US National Library of Medicine (PubMed), Medical Literature Analysis and Retrieval System Online (MEDLINE), Embase, Scopus, Ovid, and Google Scholar databases were performed to find original articles exploring any association between TMDs (exposure) and different subtypes of primary headaches (outcome). The exposure factors were selected to include any indicator(s) of TMDs, while the outcome(s) referred to different primary headache subtypes, selecting only studies using widely accepted and validated clinical criteria for TMDs and primary headaches. The search strategy used in PubMed and then adapted to the other four electronic sources is shown in Appendix Table 1. The literature search covered the time frame from database creation to January 10, 2023. No language limitation was introduced. Two investigators (V.D., M.L.) searched for papers, screened the titles and abstracts of the retrieved articles separately and in duplicate, checked the complete texts, and selected the records for inclusion.

Protocol and Registration

An a priori protocol was established and registered on the PROSPERO database (CRD42021256391) without particular amendments to the information provided at registration. No restrictions were applied to the recruitment settings (home care, hospital, community) or general health status and age of the subjects. Technical reports, letters to the editor, and systematic and narrative review articles were excluded. The following information was extracted by the two investigators (V.D., M.L.) separately and in duplicate in a piloted form: *(1)* general information on single studies (author, year of publication, country, setting, design, sample size, age); *(2)* different TMD subtypes, namely arthralgia-related TMDs, myalgia-related TMDs, and mixed TMDs; and *(3)* different subtypes of primary headache, namely migraine, ETTH, trigeminal autonomic cephalalgia, and other primary headaches. Only studies using validated clinical criteria for TMDs and primary headaches were included. All references selected for retrieval from the databases were managed with the Microsoft Excel software platform for data collection. All duplicate records were excluded. Potentially

Table 1 Selected Studies Investigating TMDs and Primary Headaches (N = 8) and Quality Appraisal Summary

Study	TMD subtypes	Outcome(s)	Design (follow-up)	Participants, n (%)	Age, mean (SD)	Setting(s)
Franco et al,[18] 2010	Mixed	ETTH Migraine	Cross-sectional case-control	158 (15.8 M, 84.2 F)	40.1 y	Community
Gonçalves et al,[19] 2011	Myalgia-related Mixed	ETTH Migraine	Cross-sectional	300 (17.3 M, 82.7 F)	37.84 y (13.03)	Community
Gonçalves et al,[20] 2013	Mixed	Migraine	Cross-sectional	61 (100 F)	38.9 y	Community
Fernandes et al,[21] 2013	Mixed	Migraine ETTH	Cross-sectional	286 (15.7 M, 84.3 F)	37.3 y (12.7)	Community
van der Meer et al,[22] 2017	Mixed	Migraine	Retrospective cohort (8 mo)	203 (26.6 M, 73.4 F)	43.1 y (14.1)	Community
Fenton et al,[23] 2018	Mixed	ETTH Migraine	Cross-sectional	12,626 (77.5 M, 22.5 F)	< 25 to 75+ y	Community
Wieckiewicz et al,[24] 2020	Myalgia-related Arthralgia-related Mixed	ETTH Migraine	Cross-sectional	213 (30 M, 70 F)	37 y (15.82)	Community
Byun et al,[25] 2020	Mixed	Migraine	Longitudinal case-control (2 y)	3.884 (45.1 M, 54.9 F)	40 to 85+ y	Community

Study	Country	Quality assessment	Main Findings
Franco et al,[18] 2010	South America (Brazil)	Moderate	TMDs were associated with increased prevalence rates of primary headache. Migraine was the most common primary headache diagnosis in individuals with TMDs.
Gonçalves et al,[19] 2011	South America (Brazil)	Moderate	TMDs, TMD subtypes, and TMD severity were independently associated with specific headache syndromes and with headache frequency after adjustments. The association required TMDs with a muscular component.
Gonçalves et al,[20] 2013	South America (Brazil)	Low	Women with migraine were more likely to have muscular and articular TMDs, suggesting that both disorders might be clinically associated.
Fernandes et al,[21] 2013	South America (Brazil)	Moderate	The association of sleep bruxism and pain-related TMDs greatly increased the risk for episodic migraine, ETTH, and especially chronic migraine.
van der Meer et al,[22] 2017	Europe (The Netherlands)	High	For migraine, both somatic symptoms and bruxism confounded the initial association found with pain-related TMDs. The findings of this study suggest that there is a central working mechanism overlapping TMDs and primary headaches.
Fenton et al,[23] 2018	North America (United States)	Moderate	Complex patterns of multimorbidity in TMD cases may indicate different underlying mechanisms of association in subgroups or phenotypes, thereby suggesting multiple targets to improve TMDs.
Wieckiewicz et al,[24] 2020	Europe (Poland)	Moderate	Headaches and pain-related TMDs were major problems among the Polish urban population. Headache was a much more frequent problem for participants with pain-related TMDs. Considering the whole population, the relationship between identified TMDs and headache was negligible.
Byun et al,[25] 2020	Asia (South Korea)	High	TMD patients had a higher risk of migraine.

eligible articles were identified by reading the abstract and, if preliminarily selected, reading the full text. Data were cross-checked, any discrepancies were discussed, and disagreements were resolved by a third investigator (F.P.). Last, data extracted from selected studies were structured in tables of evidence.

Quality Assessment Within and Across Studies and Overall Quality Assessment

The methodologic quality of included studies was independently appraised by paired investigators (V.D. and R.S. or M.L.) using the National Institutes of Health Quality Assessment Toolkits for Observational Cohort and Cross-Sectional Studies.[16] The ratings high (good), moderate (fair), and low (poor) were assigned to studies according to the criteria stated in the toolkit. This tool contains 14 questions that assess aspects associated with risk of bias, type I and type II errors, transparency, and confounding factors; ie, study question, population, participation rate, inclusion criteria, sample size justification, time of measurement of exposure/outcomes, time frame,

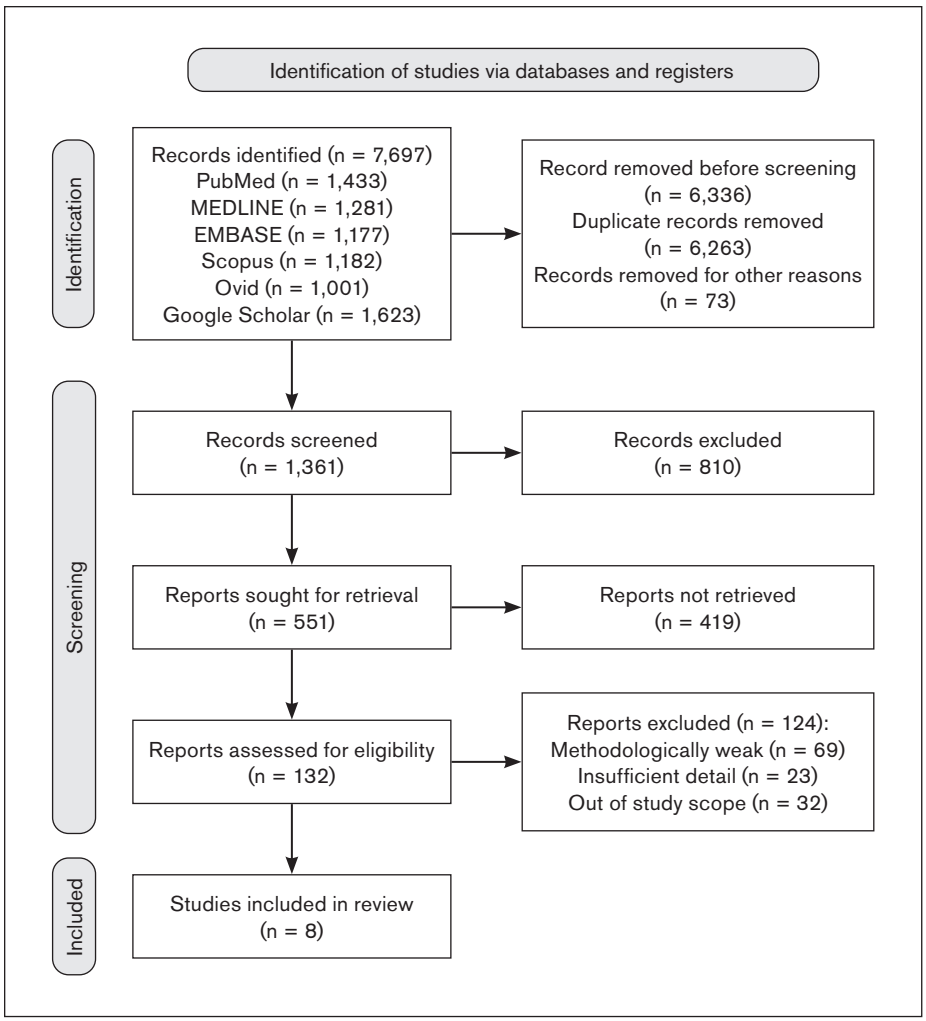

Fig 1 PRISMA flowchart showing study inclusion.

levels of the exposure, defined exposure, blinded assessors, repeated exposure, defined outcomes, loss to follow-up, and confounding factors. Items 6, 7, and 13 do not refer to cross-sectional studies, and so the maximum possible scores for cross-sectional and prospective studies were 8 and 14, respectively. Disagreements regarding the methodologic quality of the included studies were resolved through discussion until a consensus was reached or resolved by a fourth investigator (F.P.). A modified version of the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) rating system was used to assess the overall quality of evidence of the studies included in the present systematic review.[17] The following factors were considered: the strength of association for TMD indicator(s) and different subtypes of primary headaches, methodologic quality/design of the studies, consistency, directedness, precision, size, and (where possible) dose-response gradient of the estimates of effects across the evidence base. Evidence was graded as very low, low, moderate, or high, as used in the GRADE rating system.

Results

The preliminary systematic literature search yielded 7,697 records. After excluding duplicates, 1,361 records were considered potentially relevant and retained for the title and abstract screening. At this stage, 1,229 records were excluded for failure to meet the eligibility requirements. After reviewing the full texts of the remaining 132 records, only 8 met the inclusion criteria and were included in the final qualitative analysis.[18–25] The PRISMA flowchart illustrating the number of studies at each stage of the review is shown in Fig 1. Details of the study design (cohort, retrospective, or cross-sectional), sample size (N) and gender ratio (%), minimum and mean (SD) age, setting (community, hospital, home care), and country are shown in Table 1. All selected studies were in a community setting (100%, N = 8). The American continent led the geographic distribution of selected studies (62.5%, n = 5; 4 from South America and 1 from North America), followed by Europe (25%, n = 2) and Asia (12.5%, n = 1). This finding points

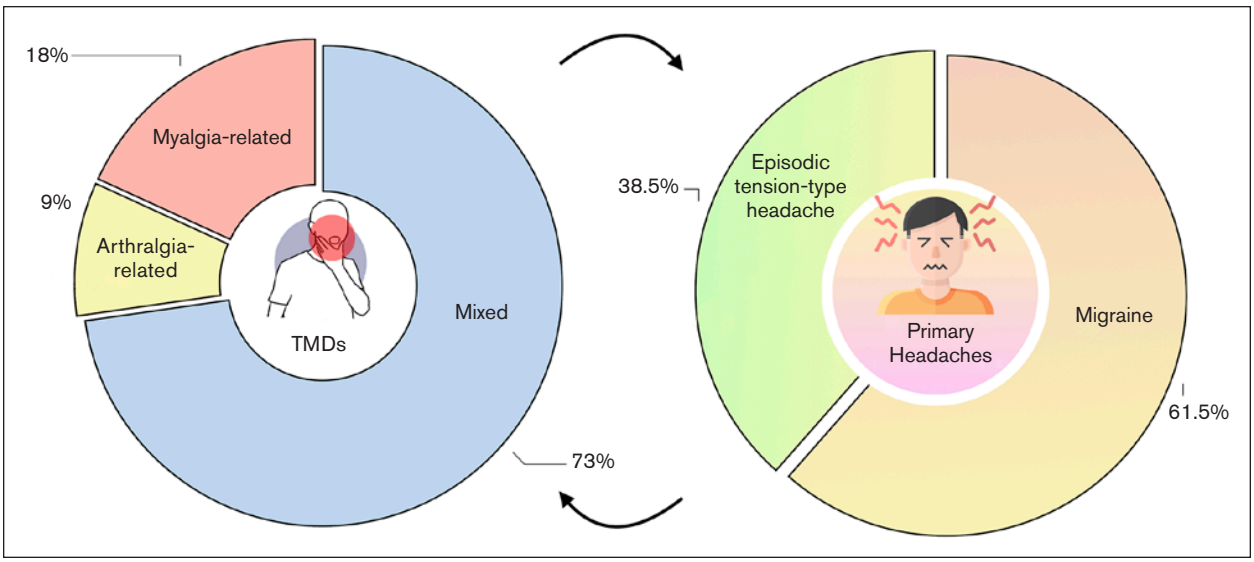

Fig 2 Percentage distribution of TMD subtypes and the two identified subtypes of primary headaches investigated in the selected studies.

to both the lack of homogeneity in geographic distribution and inadequate cross-country representativeness. The mean (SD) age and gender ratio of study participants were recorded where applicable. Among 17,731 subjects, the majority were female (66.2% vs 33.8%). A cross-sectional design (62.5%, n = 5) was more common than case-control (12.5%, n = 2; 1 longitudinal and 1 cross-sectional) or retrospective cohort (12.5%, n = 1) designs.

Subtypes of Primary Headaches, Assessment Tools, and Distribution Across Studies

The percentage distribution and subtypes of the investigated TMDs (arthralgia-related TMDs, myalgia-related TMDs, and mixed TMDs) and the only two subtypes of primary headache found (ie, migraine and ETTH) are shown in Fig 2. Given the multiplicity of the outcomes observed in 5 of the 8 selected studies, a total of 13 outcomes were recorded as denominators when calculating the representativeness of each different subtype of headache outcome. More specifically, 5 studies were found to evaluate two different outcomes each.[18,19,21,23,24] Overall, migraine was found to be the most common (61.5%, n = 8 out of 13), followed by ETTH (38.5%, n = 5 out of 13).

As for the different types of headache assessment tools, the International Classification of Headache Disorders second edition (ICHD-II; 50%, n = 4) was the most frequently adopted, followed by the third edition (ICHD-III; 50%, n = 2), the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; 12.5%, n = 1), and the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM; 12.5%, n = 1).

TMD Assessment Tools and Distribution Across Studies

Given the multiplicity of the exposures observed in 2 of the 8 selected studies, a total of 11 exposures were recorded as denominators when calculating the representativeness of each different subtype of TMDs. More specifically, one study was found to evaluate three different exposures,[24] while another study evaluated two different TMD subtypes.[19] Overall, mixed TMDs were found to be the subtype most commonly related to primary headaches (72.7%, n = 8 out of 11), followed by myalgia-related TMDs (18.2%, n = 2 out of 11) and arthralgia-related TMDs (9.1%, n = 1 out of 11).

Regarding the TMD assessment tools, the Research Diagnostic Criteria for TMD (RDC/TMD; 62.5%, n = 5) was most frequently adopted, followed by the Diagnostic Criteria (DC/TMD; 12.5%, n = 1), the ICD-9-CM (12.5%, n = 1), and the ICD-10-CM (12.5%, n = 1).

Risk of Bias, Overall Quality of Evidence, and Association Between TMDs and Primary Headache Subtypes

Low (n = 1), moderate (n = 5), and high (n = 2) methodologic quality was observed across the 8 included studies (Table 1). An overview of quality ratings within and across studies is shown in Fig 3, highlighting areas with higher or lower risk ratings. Bias was detected predominantly in the domains of sample size justification (selection bias) and blinded assessment

	Study question	Population	Participation rate	Inclusion criteria	Sample size	Exposure prior to outcome	Sufficient time frame	Different levels of exposure	Exposure measures	Multiple exposure	Outcome measures	Blinding of outcome	Loss to follow-up	Confounding
Franco et al[18]	✓	✓	✓	✓	×	–	–	✓	✓	–	✓	×	–	×
Gonçalves et al,[19] 2011	✓	✓	✓	×	×	–	–	✓	✓	–	✓	×	–	✓
Gonçalves et al,[20] 2013	✓	✓	✓	×	×	–	–	✓	✓	–	✓	×	–	×
Fernandes et al[21]	✓	✓	✓	✓	×	–	–	✓	✓	–	✓	×	–	×
van der Meer et al[22]	✓	✓	✓	✓	×	–	–	✓	✓	–	✓	×	–	✓
Fenton et al[23]	✓	✓	✓	✓	×	–	–	✓	✓	–	✓	×	–	✓
Wieckiewicz et al[24]	✓	✓	×	✓	×	–	–	✓	✓	–	✓	×	–	×
Byun et al[25]	✓	✓	×	✓	×	✓	✓	✓	✓	–	✓	×	✓	✓

✓Reported: element reported appropriately in study
× Not reported: element not mentioned in study
– Not applicable: due to study design, element not applicable to report

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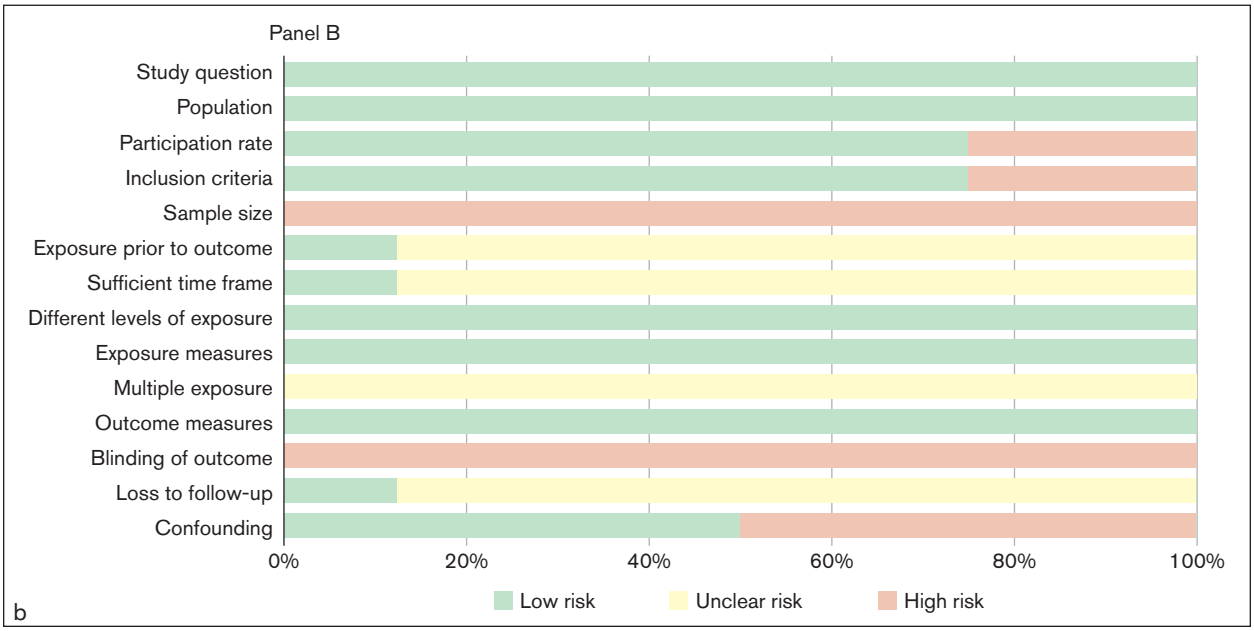

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Fig 3 *(a)* Methodologic quality assessment within studies and *(b)* overall quality assessment across studies.

(detection bias; all 8 [100%] studies were associated with a high risk of bias). Two (25%) studies were associated with a higher risk of bias regarding the participation rate and inclusion criteria, and 5 out of 8 (62.5%) were associated with a prevalent risk of confounding bias (Fig 3b). Using the GRADE approach, the overall quality of evidence was judged to be moderate for the associations for mixed TMDs with migraine and ETTH, with estimates provided, a large sample size, and multiple studies included (n = 8; Table 2). A very low-quality association was found between migraine and ETTH, with estimates provided, a very low number of studies (n = 2), and a small sample size (Table 2). Finally, no association was found for arthralgia-related TMDs with migraine and ETTH, with estimates provided, only one study included, and a very small sample size (Table 2).

Discussion

The present systematic review explored the role of TMDs and TMD subtypes in contributing to different subtypes of primary headache, namely migraine and ETTH, selecting only studies using widely accepted and validated clinical criteria for TMDs and

Table 2 Summary of Findings on Subtypes of TMDs Associated with Migraine and ETTH

TMD subtype	Evidence base	Strength of association	Strength of evidence (GRADE)	Comments
Myalgia-related	Two studies[19,24] (n = 513)	Myofascial TMDs vs ETTH[19]: RR = 4.4, 95% CI = 1.5 to 12.6	⊕ Very low	Very low-quality association with migraine and ETTH, with estimates provided, a very small number of studies, and a small sample size.
		Myofascial TMDs vs migraine[19]: RR = 4.4, 95% CI = 1.7 to 11.7		
		Myalgia vs migraine[24]: OR = 4.17, 95% CI = 2.02 to 8.62		
		Myalgia vs ETTH[24]: OR = 2.56, 95% CI = 1.27 to 5.19		
		Myofascial pain vs migraine[24]: OR = 4.79, 95% CI = 1.88 to 12.22		
Arthralgia-related	One study[24] (n = 213)	Right arthralgia vs migraine: OR = 1.30, 95% CI = 0.56 to 3.04*	⊕ Very low	No association found with migraine or ETTH, with estimates provided, only one study included, and a very small sample size.
		Left arthralgia vs migraine: OR = 0.69, 95% CI = 0.24 to 1.99*		
		Any arthralgia vs migraine: OR = 1.05, 95% CI = 0.46 to 2.41*		
		Right arthralgia vs ETTH: OR = 1.68, 95% CI = 0.75 to 3.76*		
		Left arthralgia vs ETTH: OR = 2.11, 95% CI = 0.90 to 4.95*		
		Any arthralgia vs ETTH: OR = 2.08, 95% CI = 0.97 to 4.42*		
Mixed	Eight studies[18–25] (n = 17,731)	TMDs vs migraine[18]: OR = 2.76, 95% CI = 1.50 to 5.06	⊕⊕⊕ Moderate	Moderate association with migraine and ETTH, with estimates provided, a large sample size, and multiple studies included.
		TMDs vs ETTH[18]: OR = 2.51, 95% CI = 1.18 to 5.35		
		Mixed TMDs vs ETTH[19]: RR = 1.9, 95% CI = 1.3 to 2.7		
		Mixed TMDs vs migraine[19]: RR = 1.9, 95% CI = 1.3 to 2.6		
		TMDs vs chronic migraine[20]: OR = 3.97, 95% CI = 1.53 to 8.94		
		TMDs vs migraine[20]: OR = 3.15, 95% CI = 1.73 to 5.71		
		Painful TMDs vs episodic migraine[21]: OR = 7.0, 95% CI = 3.45 to 14.22		
		Painful TMDs vs ETTH[21]: OR = 3.7, 95% CI = 1.59 to 8.75		
		Painful TMDs vs chronic migraine[21]: OR = 95.9, 95% CI = 12.51 to 734.64		
		Painful TMDs vs probable migraine[22]: OR = 2.2, 95% CI = 1.1 to 4.3		
		TMDs vs migraine (women)[23]: OR = 1.53, 95% CI = 1.38 to 1.71		
		TMDs vs migraine (men)[23]: OR = 1.72, 95% CI = 1.54 to 1.93		
		TMDs vs tension headache (men)[23]: OR = 1.88, 95% CI = 1.34 to 2.63		
		Any pain-related TMDs vs migraine[24]: OR = 4.53, 95% CI = 2.06 to 9.95		
		Any pain-related TMDs vs TTH[24]: OR = 2.80, 95% CI = 1.31 to 5.97		
		TMDs vs migraine[25]: HR = 2.10, 95% CI = 1.81 to 2.44		

RR = risk ratio; OR = odds ratio; HR = hazard ratio.
* Not statistically significant.

primary headaches. Overall, migraine was found to be the most common primary headache subtype related to TMDs (61.5%), followed by ETTH (38.5%). Furthermore, mixed TMDs were found to be the subtype most commonly related to primary headaches (72.7%), followed by myalgia-related TMDs (18.2%) and arthralgia-related TMDs (9.1%). A moderate association was found for mixed TMDs with migraine

and ETTH, with a large sample size and multiple studies. A very low association was found for myalgia-related TMDs with migraine and ETTH. No association was found for arthralgia-related TMDs with migraine and ETTH, with only one study included.

At present, and to the best of the authors' knowledge, only one other very recent systematic review and meta-analysis has been published on the same topic, but adopting a different approach in categorizing TMDs.[14] That study selected eight reports included in their systematic review, limiting the meta-analysis to six studies on pain-related TMDs, which were associated with ETTH and migraine and strongly associated with unspecified headache.[14] Only one article was selected for joint-related TMDs, and a low-quality association with migraine and ETTH was reported.[14] In the present systematic review, selecting only studies using widely accepted and validated clinical criteria for TMDs and primary headaches, there was a moderate association for mixed TMDs with migraine and ETTH; these findings are similar to those reported in the recent systematic review and meta-analysis by Réus et al.[14]

The present findings on TMDs and TMD subtypes and their possible impact on primary headache could be explained by two different but not mutually exclusive hypotheses. The first possible underlying mechanism is continuous stimulation of the trigeminal subnucleus caudalis, a condition occurring in individuals with TMDs, which could influence the frequency and intensity of unspecified headache.[26,27] In migraine patients, TMDs may act as a perpetuating, aggravating, and/or triggering factor.[28] Similarly, in patients with ETTH, TMDs may predispose patients to changes in nociceptive pathways in the brain, especially those related to the pericranial and masticatory muscles.[29,30] The second hypothesis is the activation of brain areas responsible for headache onset, which could explain peripheral symptoms,[29,31] with central sensitization of the trigeminal subnucleus caudalis.[30] A hallmark of trigeminal central sensitization is cutaneous allodynia in the trigeminal nerve distribution. Therefore, TMD pain may reflect a lower peripheral threshold as a result of central changes,[26,27] and central sensitization associated with primary headaches could predispose patients to generalized head, face, and neck pain.

Furthermore, among the possible underlying mechanisms explaining the association between TMDs and primary headaches, central facilitation of nociceptive inputs may be of importance, especially in myalgia-related TMDs. Furthermore, as seen above, some individuals may be predisposed to pain with a shared biologic predisposition, and the association could be coincidental. For example, patients such as migraineurs with TMDs may exhibit greater sensitivity to pain in multiple body areas, suggesting a generalized dysfunction of the nociceptive systems and supporting the concept of a generalized upregulation of nociceptive processing.[32] Moreover, the association between function-related TMDs and headache appeared to be confounded by the presence of somatic symptoms and bruxism,[26,27] suggesting a central working mechanism overlapping these two conditions. Finally, for arthralgia-related TMDs, although lengthy muscular stimulation by parafunction may lower the thresholds of pain sensation in these patients,[32] an independent relationship between occlusal factors and headache cannot be confirmed at present.

Some limitations of the present systematic review must be acknowledged. Owing to the heterogeneity of different variables in TMD assessment and the evaluation of the different primary headache subtypes, a quantitative meta-analysis might be unreliable or limit the analysis to only a single TMD indicator.[14] Other limitations of the present systematic review include the study designs, which were different among the selected studies, with only one longitudinal study featuring short follow-up.[25] Even using the same definition, the statistical survey of TMD indicators associated with different subtypes of headache was different among the studies. Additionally, the number of TMD indicators/primary headache subtypes and the sample sizes varied among studies. Given the original heterogenous labeling, TMD indicators were subjectively grouped into three separate categories, with some degree of overlap between these categories (ie, mixed TMDs).

Conclusions

The present systematic review investigating possible relationships among TMDs, TMD subtypes, and different primary headache subtypes, selecting only studies using validated clinical criteria for TMDs and primary headaches, showed that migraine was found to be the most common primary headache subtype related to TMDs (61.5%), followed by ETTH (38.5%). Furthermore, mixed TMDs were found to be the subtype most commonly related to primary headaches (72.7%), followed by myalgia-related TMDs (18.2%) and arthralgia-related TMDs (9.1%). A moderate-quality association was found for mixed TMDs with migraine and ETTH. A very low-quality association for myalgia-related TMDs with migraine and ETTH was also found. Despite the overall moderate certainty of evidence of the present findings, this topic is of great interest given the possible effectiveness of TMD management in reducing headache intensity and frequency in patients with TMD headache comorbidity.[33] In the near future, further studies on this topic with larger samples and a longitudinal

design, investigating associated and possible confounding factors in depth, and relying on accurate TMD and primary headache category assignment are warranted.

Highlights

- Migraine was found to be the most common primary headache related to TMDs (61.5%), followed by ETTH (38.5%).
- A moderate association was found for mixed TMDs with migraine and ETTH, with a large sample size and multiple studies included (n = 8). A very low-quality association for myalgia-related TMDs with migraine and ETTH (included studies, n = 2) was also found.
- The associations among TMDs, TMD subtypes, and primary headaches may be of great interest given the possible effectiveness of TMD management in reducing headache intensity and frequency in patients with TMDs and headache comorbidity.

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Appendix Table 1 Search Strategy Used in PubMed and MEDLINE and Adapted to the Other Sources According to Selected Descriptors

Strategy	Descriptors used
#1	(migraine[tiab]) OR (headache[tiab]) OR (cephalgi*[tiab]) OR (cephalalgia*[tiab])
#2	(temporomandibular disorders[tiab]) OR (TMD[tiab]) OR (craniomandibular disorders[tiab]) OR (cranio-mandibular disorders[tiab]) OR (temporo-mandibular disorders[tiab]) OR (TMJ[tiab]) OR (TMJD[tiab]) OR (Costen syndrome[tiab])
#3	(review[tiab]) OR (narrative review[tiab]) OR (systematic review[tiab]) OR (editorial[tiab]) OR (perspective[tiab]) OR (letter[tiab]) OR (commentary[tiab])
	#1 AND #2 NOT #3