Temporomandibular disorders and cervical spine: a systematic review

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Summary

***Aims*: Temporomandibular disorders (TMD) are a wide group of clinical conditions affecting the temporomandibular joint and the surrounding neuronal and musculoskeletal components. Cervical spine pain (CSP) has been proposed as a risk factor. Thus, the aim of this review is to analyse the available literature to document anatomical, pain and postural association between TMD and cervical spine.**
***Methods*: A systematic review of the literature was performed on TMD and cervical spine, using the following inclusion criteria: studies of any level of evidence, reporting clinical or preclinical results and dealing with the anatomical, pain and postural association between TMD and cervical spine.**
***Results*: A total of n=1150 articles was found. After duplicates exclusion, n=947 articles were selected. At the end of the first screening, following the previously described selection criteria, we selected n=55 articles eligible for full-text reading. Ultimately, after full-text reading, and reference list check, we selected n=25 articles following previously written criteria.**
***Conclusions*: The literature available on the association between TMD and CSP presents major limitations in terms of great heterogeneity. Although a lot of studies focused on the genetic, biomechanical, and radiological background of the disease there is lack of consensus on one or multiple major actors. However, based on our analysis an association between TMD and cervical pain-related symptoms (headache, cervical pain, back pain) can be assumed. More studies are needed to understand the complex and multifactorial genesis of the association.**

Key Words: cervical spine, myofascial, pain, temporomandibular disorders, temporomandibular joint.

Introduction

Temporomandibular disorders (TMD) are a wide group of clinical conditions affecting the temporomandibular joint and the surrounding neuronal and musculoskeletal components (1). TMD prevalence is attested to be higher than 5% (1). Lipton et al. (2) in 1993 reported an evidence of a prevalence between 6 and 12%. Today recent epidemiological studies support an higher prevalence up to 25-30% or even higher (3-6). This group of disease is present in a broad group of ages, with a peak of prevalence in 20-40 aged woman (7). While its wide presence among general population, only 5-10% of patients requires treatment (8).
The etiology is often multifactorial and can be usually be associated with traumatic or atraumatic patient history. While there is evidence of genetic predisposition mainly related to catechol-O-methyltransferase (COMT) low activity, adrenergic receptor polymorphisms (9-11), sexual dysmorphism, probably associated to the distribution of estrogen receptors (12), the exact pathogenesis of the disorder seems to be heterogenous and mainly unknown. Cervical spine pain (CSP) has been proposed as a risk factor to develop TMD. In 1996 De Wijer et al. (13) investigated this relationship in two subgroups of patients: 103 with CSP and 111 with TMD. They reported an overlap of the symptoms and suggested to conduct further studies. Instead, Bevilaqua-Grossi et al. (14) conducted a study in 2007 involv-

ing one hundred woman and they reported how there is a lack of evidence of an higher risk for CSP patients to develop TMD. However, they have confirmed the pathological connection between TMD and CSP: this study demonstrates that TMD patients often develop CSP related symptoms and signs. In addition, TMD seems to be linked with severity of CSP clinical presentation. Even though it could be possible a relationship between TMD and cervical spine disorders (CSD), it is unclear the real association with clinical aspects of disease. The aim of this review is to analyse and report all the up-to-date evidence (1) determining the presence of a clinically relevant association between cervical spine and TMD, (2) identifying risk factors associated with this condition, (3) evaluating anatomical pain and postural association.

Materials and methods

Literature search strategy

This systematic review was conducted according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (15). A comprehensive search was performed on four medical electronic databases (PubMed, Embase, and Cochrane Library) by three independent Authors (E.B., G.C., F.D.) from their date of inception to the 20th of May 2018. Our main aims were: (1) determining the presence of a clinically relevant association between cervical spine and TMD, (2) identifying risk factors associated with this condition, (3) evaluating anatomical, pain and postural association. Articles from the inception of the databases to the 20th of May 2018 were searched using the following key words: [(Temporomandibular disorders OR TMD) AND ("cervical spine OR upper spine")]. The reference lists of all included articles, previous literature reviews on the topic and top hits from Google Scholar were reviewed for further identification of potentially relevant studies and were assessed using the inclusion and exclusion criteria. In addition, a search strategy document was added as supplementary material.

Selection criteria

Eligible studies for the present systematic review included those investigating the use of single-stage surgery for the revision of infected TKA. Primary screening of the titles and abstracts were made using the following inclusion criteria: English language, and studies of any level of evidence published in peer-reviewed journals reporting clinical or preclinical results. Exclusion criteria included: articles written in other languages or studies with a focus on surgical treatment. Additionally, we excluded studies in which data was not accessible, missing, without an available full text, or not well reported. We also excluded all the remaining duplicates, and those with poor scientific methodology, assessed as high risk of bias. Abstracts, case reports, conference presentations, editorials and expert opinions were excluded. The study selection was performed independently by three Authors (E.B., G.C., F.D.), any discrepancies in the selection process were resolved by discussion amongst all the Authors. The senior investigators (P.C. and E.C.) were consulted to revise all the selection process.

Data extraction and criteria appraisal

All data were extracted from article texts, tables and figures. Three independent Authors reviewed each article (E.B., G.C., F.D.). Discrepancies between the four reviewers were resolved by discussion and consensus. The results of every stage of selection were reviewed by the senior investigators (P.C. and E.C.).

Risk of bias and quality assessment

Risk of bias assessment of all *in vivo* selected full-text articles was performed according to the ROBINS-I tool for non-randomized studies (16). The ROBINS-I tool consists of three stage assessment of the studies included. First stage regards the planning of the systematic review, the second stage is the assessment of the common bias possibly found in these studies and the latter is about the overall risk of bias (Supplementary material and Table 1). This assessment used "Low," "Moderate" and "High" as judgement keys: "Low" indicated a low risk of bias, "moderate" indicated that the risk of bias was moderate, and "High" indicated a high risk of bias. *In vitro* and review studies were excluded by the risk assessment. The assessments were performed by 2 Authors (E.B., G.C.,) independently. Any discrepancy was discussed with the senior investigator (E.C. and P.C.) for the final decision. All the raters agreed on the results of every stages of the assessment. Studies that were evaluated at high overall risk of bias were excluded during screening process after discussion with the senior investigator (P.C.).

Statistical methods and analysis

Due to the heterogenous nature of the studies, the different outcomes evaluated, the lack of controlled studies, metanalysis and statistical analysis can not be done. Therefore, descriptive synthesis was undertaken.

Results

Study selection

A total of n=920 articles was found according to the previous described search strategy. Overall, after duplicates exclusion n=798 articles were screened through abstract and title reading after the removal of the duplicates. We selected n=55 articles eligible for full text reading. Ultimately, after full text reading, and reference list check, we selected n=25 articles to the purpose of the present manuscript**.** A PRISMA (15) flow chart of the selection process and screening is provided (Fig. 1).

Supplementary material. Risk of bias assessment using ROBINS-I tool.

Study	Confounding	Selection	Measurement of Intervention	Missing Data	Measurement of Outcomes	Reported Result	Overall
Wu et al.	Moderate	Low	Moderate	Low	Moderate	Low	Moderate
Muñoz-García et al.	Low	Low	Moderate	Low	Moderate	Low	Moderate
Nielsen et al	Low	Low	Low	Low	Low	Low	Low
Plesh et al.	Low	Low	Low	Low	Low	Low	Low
Fejer et al.	Low	Low	Low	Low	Low	Low	Low
Vissher et al.	Low	Low	Low	Low	Low	Low	Low
Munhoz et al.	Moderate	Low	Moderate	Low	Moderate	Low	Moderate
La Touche et al.	Moderate	Moderate	Low	Low	Low	Low	Moderate
De Farias Neto et al.	Moderate	Low	Moderate	Low	Moderate	Low	Moderate
Coskun Benlidayi et al.	Moderate	Low	Moderate	Low	Moderate	Low	Moderate
Greenbaum et al.	Low	Low	Low	Low	Low	Low	Low
Ries et al.	Low	Low	Low	Low	Low	Moderate	Moderate
Halmova et al.	Moderate	Moderate	Low	Low	Low	Moderate	Moderate
Calixtre et al.	Moderate	Low	Low	Low	Low	Low	Low
Da Costa et al.	Moderate	Low	Low	Low	Low	Low	Low
Santander et al.	Moderate	Moderate	Low	Low	Low	Moderate	Moderate
Inoue et al.	Moderate	Moderate	Low	Low	Low	Low	Moderate
Testa et al.	Low	Moderate	Low	Low	Low	Low	Low
Guarda-Nardini et al.	Moderate	Low	Low	Low	Low	Low	Low
Von Piekartz et al.	Moderate	Low	Low	Low	Low	Low	Low

Note: Moderate, the study is sound for a non-randomized study with regard to this domain but cannot be considered comparable to a well-performed randomized trial; Low, the study is comparable to a well-performed randomized trial with regard to this domain.

Included studies

The included articles (13-38) mainly focus on anatomical, postural and pain relationship between cervical spine and TMD. The main findings of the included articles were summarized (Tab. 1).

Of the included studies, one is a cohort study (17), three are prospective studies (18-20), one is an animal study (21), seven are retrospective studies (22-28), two are twin retrospective studies (29, 30), two are cross-sectional studies (31, 32), six are previous reviews (33-39) and three are case-control studies (40-42).

While all the studies analyse the different aspect of the relationship between cervical spine and TMD, the outcome evaluated are heterogenous. However, in order to undertake a descriptive analysis, our primary outcome was pain, both as referred and objectively evaluated during clinical outcome, secondary outcomes were results of patient referred information through surveys and questionnaires as descripted in more details in the studies.

Anatomic

As regards anatomical associations, it is clear how the two regions are linked through muscular, ligamentous and tendinous connections constituting a functional compound who moves as a single unit (43). In addition, what emerges from the recent literature is a possible involvement of common neurological afferences mainly related to C1 and C2 segment which may act as one integrative functional unit to process cutaneous, deep, and visceral nociceptive information from craniofacial and afferent inputs (21).

In a study conducted by de Wijer et al. (13) was concluded that TMD with a myogenous involvement should no longer be viewed as a local disorder of the stomatognathic system and need an evaluation also of cervical spine and shoulder girdle. In 2016, another study (31) involving 86 patients with chronic neck pain or TMD, reported how chronic pain of one of these anatomical regions can spread hyperalgesia and pain in the other one.

Postural

Patient with TMD can often present cervical pain and postural asymmetry in the cranio-cervical area, that influence the general posture of the body and the clinical significance of the temporomandibular disorder (41). A systemic review of the 2009 confirmed

Table 1. The main findings of the included articles are reported.

Study	Study design	Subjects involved	Relationship investigated	Results
Hu, et al.	Animal study	74 nociceptive neurons from 59 adult Sprague Dawley rats	Anatomical	Many C1 and C2 DH nociceptive neurons received mechanosensitive convergent afferent inputs from cervical and craniofacial deep tissues
Muñoz-García, et al.	Cross-sectional study	86 adults with TMD or chronic neck pain (CNP)	Pain hyperalgesia	TMD + CNP participants had more areas of pain and also showed widespread pain hyperalgesia
Nielsen, et al.	Systematic review	56 studies	Genetic	Pain in TMD and CSD seem to be associated by pattern of inheritance
Visscher, et al.	Systematic review	21 studies	Genetic	The literature mainly suggests genetic contributions from candidate genes that encode proteins involved in the processing of painful stimuli from the serotonergic and catecholaminergic system
Plesh, et al.	Retrospective registry study	1,236 monozygotic and 570 dizygotic female twin pairs	Genetic	These preliminary findings suggest that the association between TMD pain and migraine headache in women may be partially due to a modest shared genetic risk for both conditions
Fejer, et al.	Cross-sectional survey	33,794 twins of danish registry	Genetic	Genes play a significant role in neck pain, particularly in women
Vissher, et al.	Twin study	2,238 adult female twins	Genetic	Variation in TMD pain and neck pain can in part be attributed to genes
Landzberg, et al.	Narrative review	8 studies on TMD and a whiplash injury	Anatomic	Patients with TMD and trauma histories display more severe subjective, objective, and psychological dysfunction compared with typical patients with TMDs
Rocha, et al.	Systematic review	22 study	Postural	The relation between TMDs and the head and neck posture is still controversial and unclear
Munhoz, et al.	Retrospective study	50 subjects with (30) and without (20) TMD	Postural	The degree of cervical lordosis was found to correlate to age and TMD degree of severity, suggesting that some pathological features or malocclusion, age or sex, may be more strongly correlated than others with specific posture patterns
La Touche, et al.	Cohort study	29 patients (19 females and 10 males) with myofascial TMD	Posture and pain	The biomechanical relationship between the cranio-cervical region and the dynamics of the temporomandibular joint, as well as trigeminal nociceptive processing in different cranio-cervical postures
De Farias Neto, et al.	Prospective study	56 adult TMD patients	Postural	The symptomatic TMD patients presented a flexion of the first cervical vertebra associated with an anteriorization of the cervical spine (hyperlordosis)

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Coskun Benlidayi, et al.	Retrospective study	60 adult TMD patients	Postural	Patients with TMDs have hypolordotic cervical malalignment (tendency toward kyphosis) regardless of neck pain
Greenbaum, et al.	Case-control study	20 women with myogenic TMD and 20 age matched healthy controls	Anatomical and postural	Potential involvement of the upper cervical joints (c1-c2) in women with myogenic TMD
Ries, et al.	Case-control study	20 TMD patients and 20 controls	Postural and pain	Individuals with TMD presented greater postural asymmetry, and cervical pain demonstrated a potential link with an increase in postural stability
Cuccia, et al.	Review	Narrative review on postural relation between Stomatognathic System (SS) and Body Posture	Posture	According to the literature reviewed there are real correlations between posture and the SS. However, due to the complexity of the factors involved, existing studies have left important gaps in understanding
Halmova, et al.	Retrospective study	98 patients with myofascial TM pain	Pain	It was proved that a combination of simple relaxing and stretching exercises of cervical muscles with a standard method used in the therapy of masticatory muscles is significantly more efficient
Calixtre, et al.	Prospective study	12 women with myofascial TM pain and TMD	Pain	The protocol caused significant changes in pain-free MMO, self-reported pain, and functionality of the stomatognathic system in subjects with myofascial TMD, regardless of joint involvement
Da Costa, et al.	Case-control study	27 subjects with masticatory myofascial pain and 28 controls	Pain	Our results reinforced the clinical interconnection between masticatory and cervical structures, insofar as subjects with masticatory myofascial pain reported greater neck disability, which, in turn, was correlated with regional muscle sensitivity
Morell, et al.	Review of randomized clinical trials	Review on TMD an manual therapy	Pain	There is widely varying evidence that manual therapy improves pain, MMO and PPT in subjects with TMD signs and symptoms, depending on the technique
Santander, et al.	Retrospective study	22 women with TMD and cervical pain with lordosis <20° were included	Posture and pain	The increase in cervical lordosis implies that six months of continuous MAA use, together with a program of postural re-education, promotes the homeostasis of the craniocervical system
Inoue, et al.	Retrospective study	171 TMD subjects	Anatomic and pain	These results indicated painful disk displacement to possibly be correlated with ipsilateral muscle tenderness

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Testa, et al.	Retrospective study	12 subjects with neck pain		People with chronic neck pain display increased activation and altered distribution of masseter muscle activity during a jaw-clenching coordination task. These results provide a greater appreciation of how secondary orofacial pain or temporomandibular disorders may develop in people with neck pain
Guarda-Nardini, et al.	Prospective study	49 TM osteoarthritis patients	Pain	A protocol of TMJ intra articular arthrocentesis and viscosupplementation improved cervical function and reduced disability in patients with concurrent cervical spine pain. These findings add to the complex amount of literature on the relationship between temporomandibular disorders and cervical spine disorders
Von Piekartz, et al.	Cross-sectional survey	99 TMD subjects and 45 controls	Pain	These findings provide evidence that TMD in an acute/subacute pain state is strongly related with certain cervical spine musculoskeletal impairments which suggests the cervical spine should be examined in patients with TMD as a potential contributing factor
Plesh, et al.	Twin study	Data from the 2000-2005 NHIS included information on gender, age, race, ethnicity, education, different common types of pain (specifically TMJMD-type, severe headache/migraine, neck, and low back pains)	Pain	TMJMD-type pain was most often associated with other common pains, and seldom existed alone. Two or more comorbid pains were common. Gender, race, and age patterns for pains with TMJMD-type pain resembled the specific underlying comorbid pain

that there is a probable relationship between the stomatognathic system and the general body posture. The main alteration of subjects with TMD was a cervical extensor muscle tension that can increase the pain perceived, the body posture and the clinical outcome of the patients (38).

Pain
Guarda-Nardini et al. (20) described a reduction of pain after an intra-articular injection with hyaluronic acid into temporomandibular joint (TMJ) in patients with TMJ osteoarthritis and concomitant cervical spine pain. The pain improved in both areas after 3 and 6 months. Patients with chronic neck pain (CNP) and TMD presented more widespread pain, hyperalgesia in different regions of the body than patients with only CNP or only TMD even though psychosocial factors seems to be associated too (31). Pain and posture in the cervical spine/neck region should be assessed prior and after surgery for TMD to further clear this relationship (32). A high-profile study that included 189,977 people in US analysed the pain in subjects with temporomandibular joint and muscle disorder (TMJMD). The 59% of people with TMJMD had two or more comorbid disorders like headache, neck or low back pains. In particular, the 54% of the patients with TMJMD had neck pain (22).

Discussion

Genetic and environmental factors seem to contribute to the pathogenic threshold of the TMD and neck disorders. In particular different twin studies reported strong evidence of this association, even though the underlying mechanism were not investigated (29, 30, 33-35).
The reported evidence of the association between history of whiplash and TMD (36), the anatomical connections (43), the association of the postural alteration affecting TM and cervical spine lack of high profile studies (37). In contrast to this, available evidence seems to support also a postural connection. This relationship could affect the clinical practise and

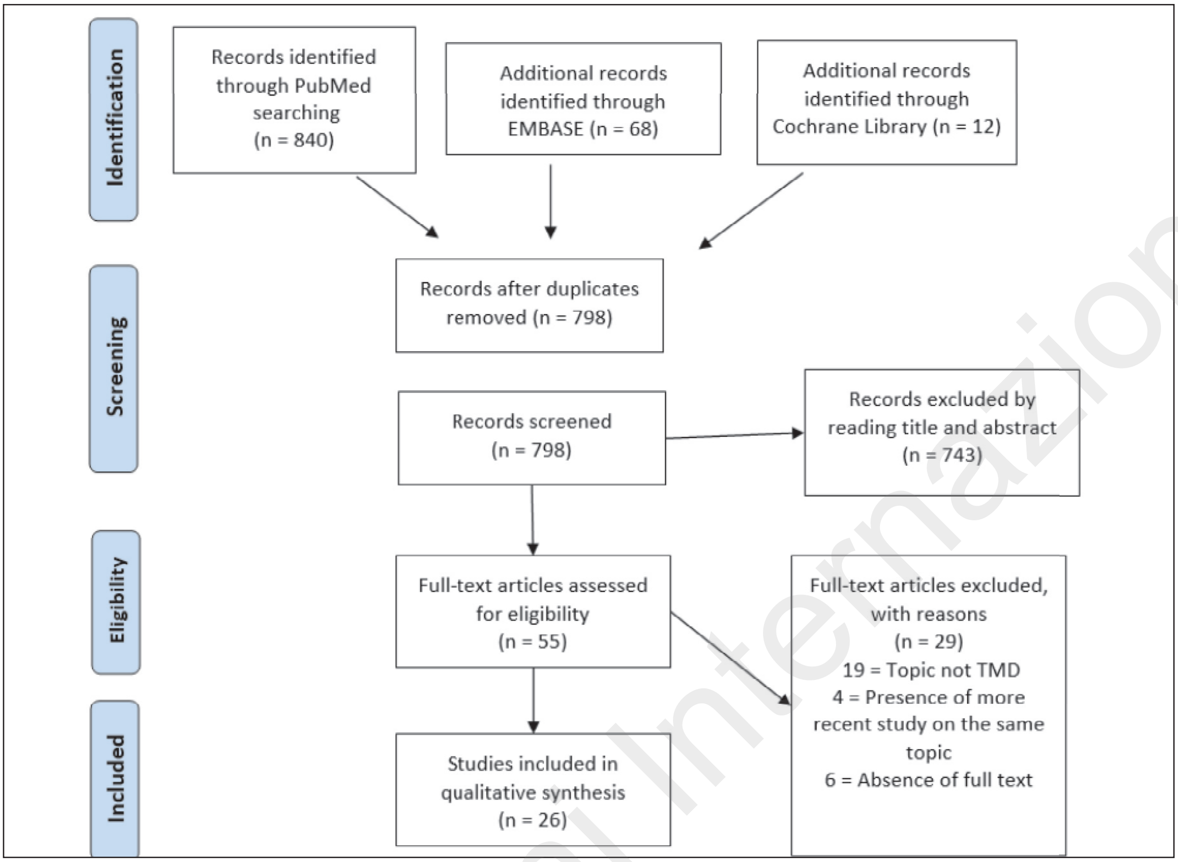

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) flowchart of the systematic literature review.

should be known by al the medical professionals.

A study of 2014 (23) reported how the cervical posture (in particular the degree of cervical lordosis) correlate with the severity of functional pathologies of temporomandibular system (FPTS). Another study held by La Touche et al. (17) confirmed the anatomical relationship by nociceptive innervation of trigeminal nerve and its influence on the relationship between cervical spine and temporomandibular joint. In particular, they reported how cervical posture change affected maximal mouth opening (MMO) and the pressure pain threshold (PPT). Another study of De Farias correlated the symptoms of TMD group patients with a specific cervical posture alteration (i.e. flexion of the Atlas) resulting in an hyper-lordosis of the cervical spine (18). This was further supported by other similar studies on cervical spine lordosis (24) and the cervical ROM in patients with TMD (40).

These alterations are probably the main reason behind the success of rehabilitation therapy in these patients. Indeed, the cranio-cervical rehabilitation, especially if supported by manual therapy, seems to improve the pain in the patients with myofascial temporomandibular disorders (25). In 2016, a study involving twelve women affected by TMD reported significant changes in pain-free maximum mouth opening, self-reported pain, and functionality of the stomatognathic system after being treated with cervical mobilization and stretching technique (19). Another study showed how myofascial pain in patients with TMD affects masticatory and neck muscles (42). In addition, a recent review (39) on manual therapy on myofascial pain in TMD reported a strong evidence of its use in patients with TMD in both head and neck regions.

Another pilot study (26), involving 22 subjects with TMD, showed how the rehabilitation can provide a good effect in the cervical posture after a combination protocol of six months of continuous mandibular advancement appliance (MAA) and a program of postural re-education.

The reported pain is another chapter of the relationship between the temporomandibular joint, and in general the orofacial region, and the cervical or neck/shoulder region.

The results of this literature review seem promising. In particular in one study (27), involving 171 patients with TMD, showed a relationship between the pain in the temporomandibular joint with disk displacement and ipsilateral muscle tenderness in orofacial and neck/shoulder region. The EMG (electromyography) alterations of masseter muscles in people with nonspecific neck pain evidenced how a cervical disease can develop a TMD or orofacial pain (28).

While the rationale behind this relationship is still unclear, we can assume that the anatomical and neurological connections between cervical spine and TMD are clinically significant. TMD seems to be a risk factor to develops myofascial pain, hyperalgesia and chronic neck pain. In addition, TMD seems to intensify CVP and associated symptoms. Studies on posture relationship require more high-profile studies. A complete evaluation of both these clinical conditions must include an accurate physical exam of both regions. Since there is a lack of evidence about of the possible common etiology and pathogenesis of these disorders, we strongly encourage further clinical and molecular studies on patients affected by these disorders.

Abbreviations

TMD, temporomandibular disorders.
CSP, cervical spine pain.
COMT, catechol-O-methyltransferase.
CSD, cervical spine disorders.
MAA, mandibular advancement appliance.
EMG, electromyography.
CNP, chronic neck pain.
TMJMD, temporomandibular joint and muscle disorder.

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