Received: 17 February 2018 | Revised: 1 October 2018 | Accepted: 31 October 2018

DOI: 10.1111/joor.12743

ORIGINAL ARTICLE

WILEY Journal of Oral Rehabilitation

Muscle tenderness score in temporomandibular disorders patients: A case-control study

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Funding information
The authors declare self-funding of the research.

Summary

Background: The total tenderness score (TTS) is commonly used in headache practice and contributes valuable information.

Objective: To assess muscle tenderness scores in patients diagnosed with Temporomandibular disorders (TMD) and analyse their associations with various demographic and clinical parameters.

Methods: Masticatory (MTS), cervical (CTS) and TTSs were analysed in this case-control study among 192 TMD patients and 99 controls. The study included a questionnaire and a clinical examination following RDC/TMD guidelines. Data were analysed using: Pearson's chi-square, analysis of variance, *t* test and Bonferroni post hoc. To examine the factors associated with MTS score in a multivariate manner, a conceptual hierarchical multiple regression model was adopted.

Results: Masticatory and TTS differed between TMD sub-groups and controls. Muscle tenderness was positively associated with: female sex, whiplash history, parafunction, co-morbid pains such as headaches and body pain, pain intensity, onset, frequency and duration. In the conceptual hierarchical multiple regression model, pain onset, frequency and duration, co-morbid pains were mediators in the relationship between TMD diagnosis and MTS.

Conclusion: Muscle tenderness scores were positively associated with TMD disease characteristics and co-morbid pain conditions, which may reflect associations with disease severity. MTS differed between TMD populations and may be used in routine patient workup, to assess MMD severity and changes over time as well as treatments response and as a research tool. MTS can be used as a common methodology to describe both headaches and masticatory muscle disorders and to facilitate interprofessional research and crosstalk between a headache and oro-facial pain practitioners.

KEYWORDS

masticatory muscle disorders, muscle tenderness score, oro-facial pain, temporomandibular disorders

1 | BACKGROUND

The significance of muscle tenderness in painful masticatory muscle disorders (MMD) and tension-type headache (TTH) has long been of interest. Pericranial myofascial tissues are considerably more tender in patients with MMD and headaches such as TTH than in controls, and increased pericranial tenderness is recognised as the most significant abnormal finding.[1,2]

Masticatory muscle disorders are categorised under the "umbrella" term Temporomandibular disorders (TMD), a group of musculoskeletal disorders that involve the temporomandibular joint (TMJ), the masticatory muscles or both.[4] TMD represent the most common chronic oro-facial pain disorder, harming 5%-12% of the population.[4,5] TMDs may severely impact daily life, social and psychological status of patients and their quality of life.[4,6,7]

For diagnosis, the Research Diagnostic Criteria for TMD (RDC-TMD) require the presence of at least three tender muscle sites out of 20 sites.[8] Its revised form (DC/TMD) requires the confirmation of pain locations in the temporalis or masseter muscles only,[4] because these sites have the highest specificity and sensitivity. The DC/TMD states that other masticatory muscles may be examined but their diagnostic sensitivity and specificity have not been established.[4]

Nevertheless, the current DC/TMD classification does not determine MMD severity, changes over time or response to treatment. The ability to determine MMD severity may change the way we approach patient management by enabling different treatment protocols according to TMD severity, such has been done for many chronic diseases such as asthma.[9] Moreover, the clinician will be able to assess changes in TMD severity over time, explain the concept of severity to the patient, assess treatment response in different TMD severity levels and assess TMD severity during research. This led to the question posed by Benoliel and Sharav of what is clinically more important regarding disease severity: how many muscles are involved or how tender they are?.[10]

The muscle tenderness score[11,12] is commonly used in headache practice for the assessment of the severity of pericranial muscle tenderness and contributes valuable information beyond the number of muscles involved.[3,12,17] For example, increased levels of pericranial muscle tenderness evaluated by manual palpation have been demonstrated in chronic tension-type headache patients compared to headache-free controls[18,19] and migraineurs on the symptomatic side.[14] In migraine patients, pressure pain thresholds levels and muscle tenderness scores were negatively correlated.[14] In fact, according to the International Headache Society (IHS), increased pericranial tenderness is the most significant abnormal finding in patients, with any type of tension-type headache.[21] In MMD patients, the tenderness score was found to correlate with the pain scores better than the number of involved muscles and may add further information beyond the number of involved muscles.[10]

Painful disc displacement also correlated with ipsilateral muscle tenderness,[22] and high levels of muscle tenderness correlated with high levels of jaw and neck dysfunction.[23]

There is some overlap between "headache attributed to TMD" and "TTH with pericranial tenderness."[1] Therefore, the establishment of a method describing both entities in terms of muscle tenderness scores and pain characteristics is useful. This will facilitate communication between headache and oro-facial pain practitioners and researchers.

Our primary objective was to assess the total muscle tenderness score (TTS) in the diagnosis of TMD.

Specific objectives of this study were to:

1. Measure the masticatory and total muscle tenderness scores as well as the number of involved muscles in patients with TMD compared to TMD-free controls and across TMD sub-groups.
2. Analyse the associations between various demographic and clinical parameters and the muscle tenderness scores.

We hypothesised that the muscle tenderness scores are positively associated with disease-related outcomes and co-morbid pain conditions. To lessen confounders like ageing and illnesses, we only included young subjects without co-existing mental, psychiatric or physical impairments which improved our ability to evaluate the impacts of other demographic and clinical parameters on muscle tenderness scores. Thus, the study was limited to patients who developed TMD as children or teenagers or in early adulthood.

2 | METHODS

2.1 | Study groups

This is part of a series of papers focusing on the demographic, clinical and behavioural aspects of patients with TMD.[6,24] This case-control study was conducted between 1 March 2011 and 31 January 2013. Data were collected from consecutive individuals referred to the TMD Clinic (a secondary referral centre) at the Department of Prosthodontics, Tel-Hashomer, Israel, with a primary complaint of TMD. This department is a secondary prosthodontics referral centre that coordinates the management TMD patients referred by dentists and physicians from primary clinics all through the country.

Sample size calculation using WINPEPI software[25] determined that at least 256 participants in two groups with 60:40 ratio were needed to provide 90% statistical power to identify a 2.0-point difference in TTS, with alpha set at 0.05, and an estimated standard deviation of 4.4 for the larger group and 5.3 for the smaller group, based on our experience in analysing muscle tenderness scores among oro-facial pain patients.[10]

A total of 100 consecutive, fairly similar in age and sex TMD-free individuals attending a routine dental screening in a primary dental clinic formed the control group.

2.2 | Ethical approval

The study adheres to STROBE guidelines and met the requirements of the Tel Hashomer Institutional Review Board (No. 1000-2010). All

participants signed an informed consent form and received free and unconditional treatment.

2.3 | Inclusion criteria and diagnoses

Inclusion criteria: patients attending for new screenings, aged 18-30 years.

Exclusion criteria for both groups were as follows: drug/alcohol/medications abuse; Fibromyalgia; patients with medical and/or dental emergencies; pregnancy or lactation; mental, psychiatric or physical impairments; co-existing malignant or significant medical conditions; current use of drugs/medications that effect on central nervous system (eg, opioids, tricyclic-antidepressants, anticonvulsants, and/or muscle relaxants).

Temporomandibular disorders was diagnosed according to Axis I of the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD),[8] which was the most accepted diagnostic instrument at the time the study was performed. TMD patients were divided into three diagnostic categories: (a) MMD—masticatory muscle disorders: comprised of Group I muscle disorders (I. a Myofascial pain, I. b Myofascial pain with limited opening) (b) TMJD-isolated disorders of the temporomandibular joint: comprised of Group II (disc displacements: II. a DD with reduction, II. b DD without reduction with limited opening, II. c DD without reduction without limited opening) and Group III (other common joint disorders: IIIa. arthralgia, IIIb. osteoarthritis, IIIc. osteoarthrosis) and (c) TMP—patients with both MMD and TMJ.

Controls, as well as cases, were examined and any of the controls who met the criteria for an RDC/TMD diagnosis were excluded from the study.

2.4 | Data collection

The study included a questionnaire and a clinical examination, performed on both TMD patients and controls, at the first meeting and before treatment. The interviewer administered the questionnaire during the one-on-one consultation, on a standard form. The questionnaire included:

1. personal details: sex (male/female),age in years.
2. History of trauma was assessed using the following questions:
   a Have you had a traumatic event to the head and/or neck? (Yes/No) Details
   b Have you had jaw fractures? Yes/No Details _____
   c Have you had whiplash injury? Yes/No Details _____
3. co-morbid headache (migraine, tension-type headache [TTH], none).The diagnosis of headaches was assessed either from reported medical history or as a result of the patient being diagnosed at our department as part of the patient evaluation process according to the International Classification of Headache Disorders, 3rd edition (beta version).[1] In case, the individual had both types of headaches, the question that was asked to decide what group to place an individual in was as follows: "what is your most frequent headache."
4. parafunctional habits were assessed using the following questions:

Oral habits

1. Do you clench your teeth? Yes/No
2. Do you grind your teeth? Yes/No
3. Do you suffer from sleep bruxism? Yes/No
4. Does your partner report that you suffer from sleep bruxism? Yes/No

2.5 | Pain evaluation

Patients approximated the period since muscle pain began, duration of pain episodes and frequency, and the presence of co-morbid body pain in other body sites. Current pain intensity was rated on a 0-10 verbal pain scale (VPS).

Pain on unassisted mouth opening was assessed on a 4-point ordinal scale: 0 (no pain), 1 (mild), 2 (moderate) and 3 (severe).[6]

2.6 | Clinical examination

Clinical examination was performed in both TMD patients and control subjects, including masticatory and neck muscle tenderness to palpation. Muscle palpation was performed according to the RDC-TMD guidelines. All examinations were conducted by one of two senior authors (A. Zakuto and HS). Prior to the beginning of the study, a training and calibration session was performed for the examiners to ensure mutual agreement, and correct interpretation of the measurements used in the study. All diagnoses were confirmed in the clinic and then re-examined following data tabulation and summary by both senior authors (RB, YS).

Muscle insertions were palpated.[15] Muscles were palpated bilaterally in the same order for all patients. Palpation was performed with small rotational movements of the assessor's second and third fingers during 4-5 seconds.[15] Muscle palpation was performed with about two to three pounds of palpation pressure.[6,26,27] Tenderness to palpation was scored on a 4-point ordinal scale: 0 (no pain), 1 (mild), 2 (moderate) and 3 (severe).[11-14]

Masticatory Muscle Tenderness Score (MTS) was the mean sum of the palpation scores from the masseter and temporalis muscles. Cervical muscles included the following muscles: suboccipital group (as one), sternocleidomastoid and trapezius. Masticatory Muscle Tenderness Score (MTS) and Cervical Muscle Tenderness Score (CTS) were calculated separately, and combined as The Total Muscle Tenderness Score (TTS). The number of tender muscles per patients was also recorded.

2.7 | Data analysis

Statistical analyses were performed using SPSS software version 22.0 (Chicago, IL). Statistical significance was considered as $P < 0.05$.

TABLE 1 Demographic characteristics of the study population

Parameter	Values	Mean age ± SD		*P* value
Study groups (n = 291)	TMD group (n = 192)	21.22 ± 4.01		0.332
	Control group (n = 99)	20.81 ± 1.49		
TMD group (n = 192)	MMD (n = 44)	21.86 ± 5.64		0.356
	TMJ (n = 26)	21.31 ± 3.77		
	TMP (n = 122)	20.97 ± 3.30		
Parameter	**Values**	**Females: (N, %)**	**Males (N, %)**	***P* value**
Study groups (n = 291)	TMD group (n = 192)	113 (58.9%)	79 (41.1%)	0.07
	Control group (n = 99)	47 (47.5%)	52 (52.5%)	
TMD group (n = 192)	MMD (n = 44)	21 (47.7)	23 (52.3)	0.089
	TMJ (n = 26)	13 (50)	13 (50)	
	TMP (n = 122)	79 (35.2)	43 (35.2)	

Numerical variables were presented as means and standard deviations, while categorised variables were presented as frequencies and percentages.

Univariate analyses between muscle tenderness scores and the independent variables were performed according to the data: Pearson's correlation, analysis of variance (ANOVA) or Student's *t* test and Bonferroni post hoc.

To examine the factors associated with MTS score in a multivariate manner, a conceptual hierarchical multiple regression model was adopted.[29] This method employs sequential adjustments from distal to proximal determinants of a health condition, aiming to elucidate their relationships.[29] While conventional multivariable models, such as stepwise logistic regression, are based solely on statistically significant explanatory factors, the hierarchical conceptual analysis adopts a theoretical ordering, based on knowledge about social and biological determinants of disease. The ordering of variables is determined according to the hypothesis that some variables have confounding effects and others have modifying effects. Previous studies have described this analytical approach.[6,29]

3 | RESULTS

3.1 | General description

The TMD group consisted of 192 patients, and the control group had 99 subjects. Eight patients in the TMD group and one in the control were excluded due to missing data.

Table 1 presents the demographic characteristics of the study population. The mean age of the TMD group was 21.22 ± 4.01 years; 79 (41.1%) were males and 113 (58.9%) females. TMP was the most frequent diagnosis (n = 122; 63.5%), followed by MMD (n = 44; 22.9%) and TMJ (n = 26; 13.5%). There were no significant differences in any of the demographic parameters between the TMD diagnoses ($P > 0.05$).

The mean age of the control group was 20.81 ± 1.49 years; 52 (52.5%) participants were males and 47 (47.5%) were females (Table 1).

The TMD and control groups were matched for age and sex ($P = 0.3$ and $P = 0.07$, respectively; Table 1).

3.2 | Tenderness scores

ANOVA analysis and post hoc Bonferroni analysis of MTS, TTS and the number of masticatory and total tender muscles among the study population are presented in Tables 2 and 3, respectively. As expected, MTS, TTS and the number of masticatory and total tender muscles differed between TMD sub-groups and controls ($P < 0.001$ for all muscle tenderness scores; Table 1).

There were no statistically significant differences in these tenderness scores between the controls and the TMJD group ($P = 1.0$; Table 3). Across TMD diagnostic categories, there were no statistically significant differences in these tenderness scores between the MMD and TMP groups ($P = 1.0$; Table 3).

We created two groups within the TMJD group (N = 26):non-painful TMJD (N = 14) and painful TMJD (N = 12). There were statistically significant differences in tenderness scores between painful and non-painful TMJD as following: MTS (0.27 ± 0.34 vs 0.00 ± 0.00, $P = 0.02$, respectively), number of masticatory tender muscles (1.00 ± 1.28 vs 0.00 ± 0.00, $P = 0.02$), TTS (1.08 ± 1.38 vs 0.00 ± 0.00, $P = 0.02$) and number of total (masticatory + cervical) tender muscles (1.00 ± 1.28 vs 0.00 ± 0.00, $P = 0.02$).

3.3 | Tenderness scores demographics and clinical parameters

Univariate analysis of demographic and clinical parameters for the entire study group (N = 291) with statistically significant associations and correlations with the MTS, TTS and the number of masticatory and total tender muscles is presented in Table 4 (ANOVA

TABLE 2 ANOVA analysis of muscle tenderness scores and the number of tender muscles among the study population

Muscle tenderness scores	Study group	N	Mean	SD	*P* value between all groups
MTS	Control	99	0.36	1.14	<0.001
	MMD	44	2.59	2.01	
	TMJD	26	0.50	1.06	
	TMP	122	2.51	2.11	
	Total	291	1.61	2.03	
Number of masticatory tender muscles	Control	99	0.28	0.850	<0.001
	MMD	44	1.84	1.29	
	TMJD	26	0.46	0.980	
	TMP	122	1.68	1.14	
	Total	291	1.12	1.27	
TTS	Control	99	0.47	1.52	<0.001
	MMD	44	3.97	3.95	
	TMJD	26	0.50	1.06	
	TMP	122	3.69	3.50	
	Total	291	2.35	3.31	
Number of total tender muscles (masticatory + cervical)	Control	99	0.38	1.29	<0.001
	MMD	44	2.88	2.60	
	TMJD	26	0.46	0.980	
	TMP	122	2.49	2.04	
	Total	291	1.65	2.14	

analysis for categorical parameters) and Table 5 (Pearson correlations [*R*] analysis for continuous parameters). These include:

1. Female sex ($P < 0.001$ for all muscle tenderness scores).
2. Grinding habit (MTS: $P = 0.002$, TTS: $P < 0.001$, the number of masticatory ($P = 0.045$) and total tender muscles ($P = 0.010$).
3. Increasing levels of pain on opening ($P < 0.001$ for all muscle tenderness scores). According to post hoc Bonferroni test, there were statistically significant differences ($P < 0.05$) in all tenderness scores between patients without pain on opening (none) to those with any level of pain on opening (ie, mild, moderate and severe; <0.001 for all) as well as between mild to moderate pain on opening in the TTS ($P = 0.022$).
4. Co-morbid migraine, followed by TTH (MTS: $P = 0.006$, TTS: $P = 0.022$, the number of masticatory [$P = 0.002$] and total tender muscles [$P = 0.005$]). According to post hoc Bonferroni test, there were statistically significant differences ($P < 0.05$) in the muscles tenderness scores only between patients with migraine to those without headache.
5. Pain scores, including VPS scores, longer onset, duration and more frequent pain episodes ($P < 0.001$ for all muscle tenderness scores), and co-morbid body pains: back + periorbital, followed by: neck + back, neck, periorbital, back and none ($P < 0.001$ for all muscle tenderness scores; Tables 4 and 5).

Whiplash history was positively associated with TTS ($P = 0.006$) and the number of total tender muscles (masticatory + cervical) score ($P = 0.024$), but not with MTS ($P = 0.190$) and the number of masticatory tender muscles score ($P = 0.0228$; Table 4).

Clenching habit was positively associated with all tenderness scores (MTS: $P = 0.010$, the number of masticatory [$P = 0.004$] and total tender muscles [$P = 0.0037$], except for the TTS [$P = 0.071$]; [Table 4]).

3.4 | Results of the conceptual hierarchical multiple regression model for MTS

The univariate analysis demonstrated that the MTS score exhibited similar associations as the TTS score, in agreement with the DC/TMD. Therefore, in the multivariate analysis we have focused on the MTS score. To examine the factors associated with MTS score in a multivariate manner, a conceptual hierarchical multiple regression model was adopted.[29]

Results of the multiple regression model for dichotomized MTS by median are presented in Table 6. Our conceptual modelling assumed that TMD diagnosis was the most distal determinant, while age and sex (1st model), pain characteristics (duration, frequency onset; 2nd model), co-morbid pain conditions such as body pain and headaches (3rd model), and current levels of VPS (4th model) were confounders or mediators in the relationship between TMD diagnosis and MTS. Following this step, the associations between each explanatory variable and MTS were assessed.

TABLE 3 Post hoc Bonferroni analysis of muscles tenderness scores among the study population

Dependent variable	(I) Diagnosis	(J) Diagnosis	Mean difference (I–J)	Std. error	*P* value	95% confidence interval	
						Lower bound	Upper bound
MTS	Control	MMD	−2.22*	0.31	<0.001	−3.06	−1.38
		TMJD	−0.13	0.38	1.000	−1.15	0.88
		TMP	−2.15*	0.23	<0.001	−2.77	−1.52
	MMD	TMJD	2.09*	0.43	<0.001	0.94	3.23
		TMP	0.074	0.30	1.000	−0.74	0.88
	TMJD	TMP	−2.01*	0.37	<0.001	−3.01	−1.01
Number of masticatory tender muscles	Control	MMD	−1.55*	0.19	<0.001	−2.07	−1.04
		TMJD	−0.178	0.23	1.000	−0.80	0.44
		TMP	−1.39*	0.14	<0.001	−1.78	−1.01
	MMD	TMJD	1.37*	0.26	<0.001	0.67	2.08
		TMP	0.16	0.18	1.000	−0.33	0.65
	TMJD	TMP	−1.22*	0.23	<0.001	−1.83	−0.60
TTS	Control	MMD	−3.50*	0.52	<0.001	−4.89	−2.10
		TMJD	−0.02	0.63	1.000	−1.72	1.67
		TMP	−3.22*	0.39	<0.001	−4.26	−2.17
	MMD	TMJD	3.47*	0.71	<0.001	1.57	5.38
		TMP	0.28	0.51	1.000	−1.07	1.63
	TMJD	TMP	−3.19*	0.62	<0.001	−4.86	−1.53
Number of total tender muscles (masticatory + cervical)	Control	MMD	−2.50*	0.33	<0.001	−3.39	−1.60
		TMJD	−0.07	0.41	1.000	−1.16	1.00
		TMP	−2.10*	0.251	<0.001	−2.77	−1.44
	MMD	TMJD	2.42*	0.45	<0.001	1.20	3.64
		TMP	0.39	0.32	1.000	−0.47	1.26
	TMJD	TMP	−2.03*	0.40	<0.001	−3.09	−0.96

*The mean difference is significant at the 0.05 level.

The 1st model adjusted the odds ratio (OR) of MTS dichotomized by median for age and sex, the 2nd model additionally adjusted the OR for pain onset, attack duration and frequency, the 3rd model additionally adjusted for co-morbid pain conditions while the 4th model additionally adjusted for VPS. There was a significant reduction in the OR of MTS, with each step of the model (Table 5): according to the 2nd model by 31.5% (from OR of 2.66 to 1.82), 3rd model by 22.5% (from OR of 1.82 to 1.41) and 4th model by 8.5% (from OR of 1.41 to 1.29). The total reduction of OR of MTS from 1st to 4th model was 51.5% (from OR 2.66 to 1.29). Furthermore, the relationship between MTS and TMD diagnosis lost statistical significance according to the 4th model ($P = 0.160$). The reduction in the OR as well as the loss of significance in the last model suggests that these mediators underlie the differences in MTS when sorted by TMD diagnosis and explained the association. Moreover, as can be seen from Table 6, the Nagelkerke R Square, representing the proportion of the total variability explained by the model, increased with each step of the model (from 35.7% to 67.3%). According to the 4th model, pain duration ($P = 0.007$) and frequency ($P = 0.012$), co-morbid headaches ($P = 0.002$) and body pain ($P = 0.005$) retained their statistical significance with MTS, implying that they are also directly related to higher MTS median scores (Table 5). Finally, the data analysis pathway of this model is illustrated in Figure 1.

4 | DISCUSSION

The main findings of the present study are that pericranial muscle tenderness scores were positively associated with the multiplicity of signs and symptoms. This may reflect the positive associations between the muscle tenderness scores and disease severity as well as co-existing pain conditions. The multivariate conceptual regression model suggests that MTS may be a useful guide for treatment in TMD if taken together with VPS, onset, frequency and duration of pain, and co-morbid pains such as headache and body pain. Only painful TMJD patients, exhibited muscle tenderness scores, suggesting that the difference found between the MMD and the TMJD is due to pain and not due to the diagnosis. These results are in line with the multivariate conceptual regression model for MTS where TMD diagnosis was associated with MTS via parameters related to pain. Therefore, MTS, together with these parameters,

TABLE 4 ANOVA analysis of tenderness scores and the number of tender muscles vs demographic and clinical parameters

		Mean tenderness scores ± SD			
Parameter	**Values**	**MTS**	**Number of masticatory tender muscles**	**TTS**	**Number of total tender muscles (masticatory + cervical)**
Sex	Females	2.0 ± 2.3	1.3 ± 1.3 Number of masticatory tender muscles	3.0 ± 3.8	2.0 ± 2.3
	Males	1.1 ± 1.5	0.8 ± 1.1	1.5 ± 2.2	1.1 ± 1.7
	P	**<0.001**	**0.001**	**<0.001**	**<0.001**
Whiplash	Yes	2.8 ± 2.1	1.8 ± 1.3	6.4 ± 4.6	3.8 ± 2.6
	No	1.5 ± 2.0	1.1 ± 1.2	2.2 ± 3.2	1.6 ± 2.1
	P	0.190	0.228	**0.006**	**0.024**
Clenching habit	Yes	2.0 ± 2.1	1.4 ± 1.3	2.8 ± 3.5	2.0 ± 2.3
	No	1.3 ± 1.9	0.9 ± 1.2	2.1 ± 3.2	1.4 ± 2.0
	P	**0.010**	**0.004**	0.071	**0.037**
Grinding habit	Yes	2.3 ± 2.0	2.4 ± 2.0	3.2 ± 3.2	2.3 ± 2.1
	No	1.4 ± 2.0	1.4 ± 2.0	2.1 ± 3.3	1.5 ± 2.1
	P	**0.002**	**<0.001**	**0.045**	**0.010**
Pain on opening	None	0.7 ± 1.4	0.6 ± 1.0	1.0 ± 2.3	0.8 ± 1.6
	Mild	2.0 ± 1.9	1.5 ± 1.3	2.8 ± 3.0	2.1 ± 2.2
	Moderate	2.9 ± 2.2	1.8 ± 1.2	4.4 ± 4.2	2.9 ± 2.4
	Severe	3.2 ± 2.5	1.8 ± 1.1	4.6 ± 4.1	2.6 ± 1.9
	P	**<0.001**	**<0.001**	**<0.001**	**<0.001**
Co-morbid headache	Migraine	3.4 ± 2.6	2.1 ± 1.4	5.5 ± 4.7	3.6 ± 2.7
	TTH	2.6 ± 1.8	1.8 ± 1.2	3.5 ± 3.4	2.5 ± 2.1
	None	2.0 ± 1.9	1.4 ± 1.2	2.9 ± 3.2	2.1 ± 2.0
	P	**0.006**	**0.022**	**0.002**	**0.005**
Body pain	None	1.2 ± 1.9	0.8 ± 1.1	1.5 ± 2.5	1.0 ± 1.5
	Back pain	1.3 ± 1.6	0.9 ± 1.0	1.7 ± 2.5	1.2 ± 1.5
	Periorbital	2.0 ± 2.6	1.3 ± 1.8	4.4 ± 5.6	2.8 ± 3.7
	Neck pain	2.3 ± 1.7	1.8 ± 1.3	4.2 ± 3.3	3.3 ± 2.8
	Neck + back	2.4 ± 2.2	1.6 ± 1.2	5.8 ± 5.9	3.7 ± 3.3
	Back + Periorbital	4.0 ± 0.0	3.0 ± 0.0	6.0 ± 0.0	5.0 ± 0.0
	P	**<0.001**	**<0.001**	**<0.001**	**<0.001**
Body pain (yes/no)	Yes	2.0 ± 2.1	1.4 ± 1.3	3.2 ± 3.8	2.3 ± 2.4
	No	1.2 ± 1.9	0.8 ± 1.1	1.5 ± 2.5	1.0 ± 1.5
	P	**<0.001**	**<0.001**	**<0.001**	**<0.001**

Statistically significant *P* values ($P < 0.05$).

may be used as follows: (a) to distinguish between mild, moderate and severe MMD cases, (b) to assess changes over time, (c) to explain concepts to the patient, (d) to assess treatment response (e) for research and (f) as a prognostic marker.

Indeed, the present-day concept is that TMD, in particular MMD, is a complicated entity, not only localised to the oro-facial area, but also involving structures beyond the masticatory apparatus.[31] Our findings are also consistent with the findings of the OPPERA study that pain upon palpation of masticatory, neck and body muscles predicted TMD incidence.[31]

The current DC-TMD classification system distinguishes between cases and non-cases but does not establish MMD severity.[27] Currently, we assess MMD severity numerically in terms of pain, using the VPS. However, the VPS is not a specific tool for MMD, and may be used to describe every pain Moreover, pain referral is very common in MMD,[4] and patients may indicate painful sites unrelated to the anatomical origin of the pain. This further emphasises the need for other measures, not just VPS, to assess MMD severity.

Whether pain causes muscle sensitivity or vice versa is currently unclear. Pericranial muscle tenderness may reflect sensitisation of

TABLE 5 Pearson correlations (*R*) of studied parameters with tenderness scores and the number of tender muscles in the study population

		MTS	Number of masticatory tender muscles	TTS	Number of total tender muscles (masticatory + cervical)
Age	Pearson correlation	−0.035	0.006	0.003	0.043
	Sig. (2-tailed)	0.551	0.917	0.964	0.466
	N	291	291	291	291
Frequency of pain episodes	Pearson correlation	−0.411	−0.407	−0.402	−0.402
	Sig. (2-tailed)	**<0.001**	**<0.001**	**<0.001**	**<0.001**
	N	290	290	290	290
Duration of pain episodes	Pearson correlation	−0.382	−0.416	−0.359	−0.359
	Sig. (2-tailed)	**<0.001**	**<0.001**	**<0.001**	**<0.001**
	N	290	290	290	290
Onset of pain	Pearson correlation	−0.290	−0.291	−0.240	−0.240
	Sig. (2-tailed)	**<0.001**	**<0.001**	**<0.001**	**<0.001**
	N	291	291	291	291
Verbal pain scores (VPS)	Pearson correlation	0.605	0.599	0.546	0.546
	Sig. (2-tailed)	**<0.001**	**<0.001**	**<0.001**	**<0.001**
	N	291	291	291	291

Statistically significant *P* values (*P*< 0.05).

TABLE 6 Results of a conceptual hierarchical multiple logistic regression model for MTS

	1st Model—OR adjusted for age and sex		2nd Model—OR additionally adjusted for pain onset, attacks frequency and duration		3rd Model—OR additionally adjusted for co-morbid pain conditions (body pain and headaches)		4th model—OR additionally adjusted for verbal pain scores	
	OR (95% CI[a])	*P*	OR (95% CI[a])	*P*	OR (95% CI[a])	*P*	OR (95% CI[a])	*P*
TMD diagnosis (case vs control)	**2.66** (1.96-3.62)	<0.001	**1.82** (1.35-2.45)	<0.001	**1.41** (1.04-1.91)	0.027	**1.29** (0.90-1.84)	0.160
Duration of pain episodes			0.68 (0.48-0.98)	0.037	0.63 (0.44-0.89)	0.009	0.617 (0.43-0.88)	**0.007**
Frequency of pain episodes			0.63 (0.43-0.95)	0.025	0.55 (0.35-0.85)	0.008	0.56 (0.36-0.88)	**0.012**
Onset of pain			1.18 (0.70-1.97)	0.535	1.51 (0.86-2.67)	0.152	1.53 (0.86-2.72)	0.143
Body pain					3.48 (1.50-8.10)	0.004	3.35 (1.42-7.86)	**0.006**
Co-morbid headaches					4.76 (1.78-12.73)	0.002	4.64 (1.72-12.52)	**0.002**
Current verbal pain scores (VPS)							1.10 (0.88-1.38)	0.397
Nagelkerke *R* square	0.357		0.585		0.671		0.673	

Statistically significant *P* values (*P*< 0.05).

[a]OR of MTS dichotomized by median adjusted for age and sex, additionally adjusted for a pain characteristics (duration, frequency and onset; 2nd model), co-morbid pain conditions (body pain and co-morbid headaches; 3rd model) and for pain intensity (current levels of VPS; 4th model).

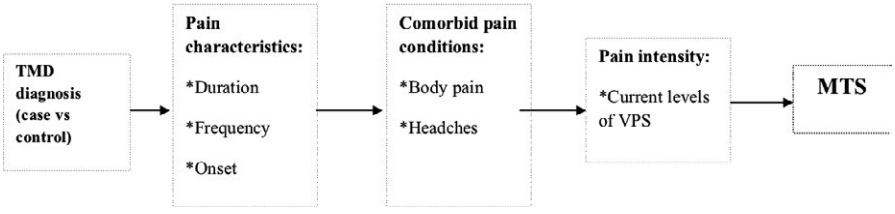

FIGURE 1 A pathway model for TMD diagnosis as a distal determinant affecting the MTS

peripheral nociceptors, or a dysfunction in higher order supraspinal pain modulation systems rather than muscle tissue abnormalities.[32] Trigger points may stimulate the trigeminal nucleus caudalis and trigger a headache attack.[32] Indeed, muscle tenderness was shown to increase during cephalalgic attacks.[33] Furthermore a higher frequency of headaches causes increased muscle tenderness,[34] especially among TTH patients.[35] In agreement, in the present study, higher tenderness scores were positively associated with pain onset, frequency and duration. Moreover, parafunctional habits, such as grinding and clenching, both associated with long-term overuse of peripheral muscles were also positively associated with the muscle tenderness scores (see Table 4). On the other hand, parafunction is considered secondary to muscle pain according to the pain adaptation model.[36]

Interestingly, in the present study, patients with migraine exhibited the highest tenderness scores compared to TTH. Muscle tenderness could be involved in migraine,[3,20] attributed to central sensitisation.[20] Nevertheless, the association between muscle tenderness scores and headaches is particularly seen in TTH, where increased pericranial tenderness is recognised as the most significant abnormal finding, with likely pathophysiological importance.[1] It may be not only responsible for the acute TTH episode but may also trigger central sensitisation, which leads to headache chronicization.[2,3,32]

Although we described our patients presenting with TMD and headache as suffering from "TMD and co-morbid headache," they can also be described as patients with "a headache and co-morbid TMD." An overlap clearly exists between the IHS diagnoses of "TTH with pericranial tenderness" and "Headache attributed to TMD." In fact, TMD-headache comorbidity is bidirectional.[37] The relationship between TMD and headaches may be casual or may involve more complex pathophysiological and evolutionary elements.[37] Both diseases seem to share a common genetic base, and both exhibit peripheral and central sensitisation, manifested by the development of craniofacial allodynia and muscle tenderness to palpation.[1,37] Moreover, the same nociceptive system is involved in both diseases, with chronic painful stimuli originating from trigeminal nerve endings running along common pathways to the central nervous system. Additionally, pain modulation in both diseases involves the thalamus, brainstem nuclei, sensitive cortex and limbic system.[37] Due to these similarities, it may be that MMD represents a facial variant of "TTH with pericranial tenderness" similar to the concept of oro-facial migraine, which had been currently recognised as the facial variant of migraine in the recent edition of the Headache Classification Committee of the International Headache Society.[21] Nevertheless, differences between MMD and TTH exist: unlike TTH, MMD is characterised by unilateral, constant pain, that is present with jaw function. Further studies are needed to explore the TMD-headache comorbidity and overlapping features.

The major strengths of the current study are the large sample size (291 patients) and the uniform protocol utilising the standardised VPS scores and the validated RDC/TMD, allowing comparison with other ethnic groups. We minimised confounders such as ageing and illness. A clinical examination was also performed in the control group, which allows the comparison with subclinical TMD cases. Additionally, TMD and control groups included treatment-seeking patients in the dental setting. Since TMD patients often consult dentists,[4] our control group seems a more valid compared to the general population.[38]

Limitations of this study include the possibility of selection bias of this convenience cohort. However, patients were referred from multiple clinics serving different populations. Due to the case-control study design, we cannot assume causality, and therefore this paper only suggests associations between the variables.

5 | CONCLUSIONS

Routine patient workup should include the MTS, to assess MMD severity and changes over time as well as treatments response and as a research tool. MTS can be used as a common methodology to describe both headaches and MMD and to facilitate interprofessional research and crosstalk between headache and oro-facial pain practitioners.

CONFLICT OF INTEREST

The authors deny any conflict of interest.

AUTHOR CONTRIBUTIONS

Each of the contributors provided substantive intellectual contribution to one or more of the activities related to this manuscript as follows: Galit Almoznino—Corresponding author, the principal investigator, made substantial contributions to the study's conception and design, acquisition of data, and analysis and interpretation of data; drafted the submitted the article and provided final approval of the version to be published. Avraham Zini—analysis and interpretation of data and approved the manuscript. Zakuto Avraham—Data collection of the TMD group and approved the manuscript. Hulio Slutzky—Data collection of the control group and approved the manuscript. Stav Bekker—Interpretation of the results revised and approved the manuscript. Boaz Shay—revised and approved the manuscript. Yaron Haviv—revised and approved the manuscript. Yair Sharav—Interpretation of the results revised and approved the manuscript. Rafael Benoliel—made substantial contributions to the study's conception and design, interpretation of data, drafted, revised and approved the manuscript.

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How to cite this article: Almoznino G, Zini A, Zakuto A, et al. Muscle tenderness score in temporomandibular disorders patients: A case-control study. *J Oral Rehabil*. 2018;00:1–10. https://doi.org/10.1111/joor.12743