

Relationship between Mediotrusive Occlusal Contacts and Temporomandibular Disorders in Young Adults without Psychosocial Disorders: A Case–Control Study

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ABSTRACT

Aim: Temporomandibular disorders (TMDs) are multifactorial pathologies often associated with pain, muscle dysfunction, and joint alterations. Mediotrusive (MT) occlusal contacts have been implicated in TMDs due to their potential to alter mandibular biomechanics and masticatory patterns. However, the strength of this association, especially in individuals without psychosocial disorders, remains unclear. The aim was to investigate the relationship between MT occlusal contacts and acute TMDs symptomatology in young adults without psychosocial disorders. **Materials and Methods:** This case-control study included 116 university students aged 18–30 years, divided into cases ($n = 58$) with TMDs and controls ($n = 58$) without TMDs. The Diagnostic Criteria for TMDs were used for diagnosis. MT occlusal contacts were evaluated using 12 μ m Arti-Fol tape. Guided lateral mandibular movements were performed to assess their role in TMD symptomatology. Statistical analyses, including Chi-square tests and multivariable logistic regression, were conducted to assess the association between MT contacts and TMDs, adjusting for confounders such as age, gender, angle classification, and retruded contact position to maximum intercuspation (RCP-MI) discrepancies ≥ 2 mm. Statistical significance was set at $P < 0.05$. **Results:** MT occlusal contacts were significantly associated with TMDs ($P = 0.003$). The adjusted odds ratio (OR) for individuals with MT occlusal contacts was 3.70 (95% confidence interval (CI): 1.58–8.66). This association was strongest at short lateral movement trajectories, particularly at 0.5 mm ($P = 0.013$, OR=2.63) and 1 mm ($P = 0.002$, OR=4.56). Class II malocclusion and RCP-MI discrepancies ≥ 2 mm were also significantly associated with TMDs in adjusted models. **Conclusion:** MT occlusal contacts are associated with acute TMDs symptomatology in young adults without psychosocial disorders, particularly during short lateral mandibular movements. However, their predictive value is low, and adaptive mechanisms likely mitigate their long-term effects. This study does not support routine occlusal therapy for managing these contacts in TMD patients. Future longitudinal research should explore chronicity, digital methods for occlusal recording, and the interplay between MT contacts and other etiological factors.

KEYWORDS: Mediotrusive contacts, psychosocial factors (Source: MeSH NLM), temporomandibular joint, temporomandibular joint disorders

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INTRODUCTION

Temporomandibular disorders (TMDs) are functional pathologies with variable prevalences (5–60%).^[1-3] Due to their multicausal nature, variety of signs, symptoms, and different diagnostic forms, TMDs are the subject of research not exclusively in the field of dentistry.^[4] The role of occlusion as an etiology of TMDs has been diluted over the years, first, because it cannot account for all cases of TMDs and, second, because of the biopsychosocial approach (behavioral risk factors, environmental risk factors), is widely accepted by experts in the field of orofacial pain, justifies most cases of TMDs.^[5-9] However, when people are free of psychosocial disorders, one has to wonder whether acute symptoms of TMDs are due to reasons other than somatization.^[6,7] Very little of the chronic symptomatology of TMDs has been attributed to occlusal disturbances, justified by the adaptive capacity of the masticatory system and because in physiological conditions teeth are almost never in contact for 24 h.

Mediotrusive (MT) occlusal contact is an occlusal characteristic that has been associated with TMDs symptomatology, which can alter the masticatory pattern, redistributing occlusal forces, altering the biomechanics of the temporomandibular joint (TMJ) as well as muscle patterns.^[5,10] However, it has not been demonstrated whether MT occlusal contact itself is the origin of joint or muscular symptoms that cannot be overcome by the adaptive capacity of the individual and subsequently present as TMDs in any of its forms.^[11,12]

A consensus statement in 2021 supported the role of MT occlusal contacts (non-working side contacts) in the functionality of the TMJ and considered that MT interferences result in greater pathological effects during the masticatory cycles, produce a predominant or asymmetric side of mastication, alter the muscular effort and lead to TMDs symptoms that may be predominantly acute and disappear in the short term by adaptive intrusion of the teeth.^[10] Other etiological factors may act to predispose, precipitate, and perpetuate TMDs,^[8] with psychosocial factors playing a confounding role in this association which, in studies, is only controlled statistically, leaving aside the fit in the research design.

Currently, conservative approaches to the treatment of TMDs prioritize the evaluation of psychosocial factors, without neglecting anatomical and genetic factors in order to avoid overtreatment due to the multidisciplinary approach.^[13,14] Thus, the evidence available regarding MT occlusal contacts and TMDs highlights that occlusal therapy is not sufficient as a

general solution and even less so to avoid the chronicity of symptoms in patients with perpetuating factors such as psychosocial factors.^[7,13] For this reason, studies that evaluate populations free of these factors are needed to understand whether MT contacts are related to acute symptoms of TMDs. The multifactorial origin of TMDs causes less confusion due to the use of standardized tools such as the Diagnostic Criteria for TMDs (DC/TMD). It is very important for these criteria to be uniform to decrease exposure to unnecessary treatment. Evaluation of oral and dental structures will make dental referrals from other specialists possible.^[15] Therefore, this research aimed to determine the relationship between MT occlusal contact and TMDs in young adults without psychosocial disorders.

MATERIALS AND METHODS

A presented case-control, quantitative study was performed on a population of university students in Lima, Peru, registered between December 2019 and 2020. The study included young adult students between 18 and 30 years of age. Single-stage simple random sampling method was used; each of the individuals in the sampling frame were selected by generating random numbers with statistical software. The sample size was calculated with Epidat 4.2, an algorithm for case-control studies with a confidence level of 95% and a statistical power of 80% (at least 46 individuals in each group). Screening of 212 individuals was performed, 50 of whom were ineligible due to psychosocial disorders, 43 refused to continue in the study, and 3 refused for other reasons. Finally, 116 individuals (58 cases and 58 controls) were eligible [Figure 1].

PROCEDURES AND TECHNIQUES

This study was approved by the Institutional Research Ethics Committee of the Instituto de Medicina Tropical “Daniel Alcides Carrión” of the Universidad Nacional Mayor de San Marcos (CIEI-2020-21), Lima-Peru. Young adults between 18 and 30 years of age who provided signed informed consent were included. The case group included individuals with TMDs symptoms according to the DC/TMD and the control group included subjects without symptoms. The exclusion criteria for both groups were the presence of psychosocial disorders, psychosocial alterations, alterations in mandibular movement, bruxism, fixed or removable prostheses, partially edentulous, the need for orthodontic treatment due to moderate and severe malocclusion according to the criteria of the dental aesthetic index,^[16] Class III individuals, the use of orthodontic appliances and having a history of trauma at the cervicofacial level.

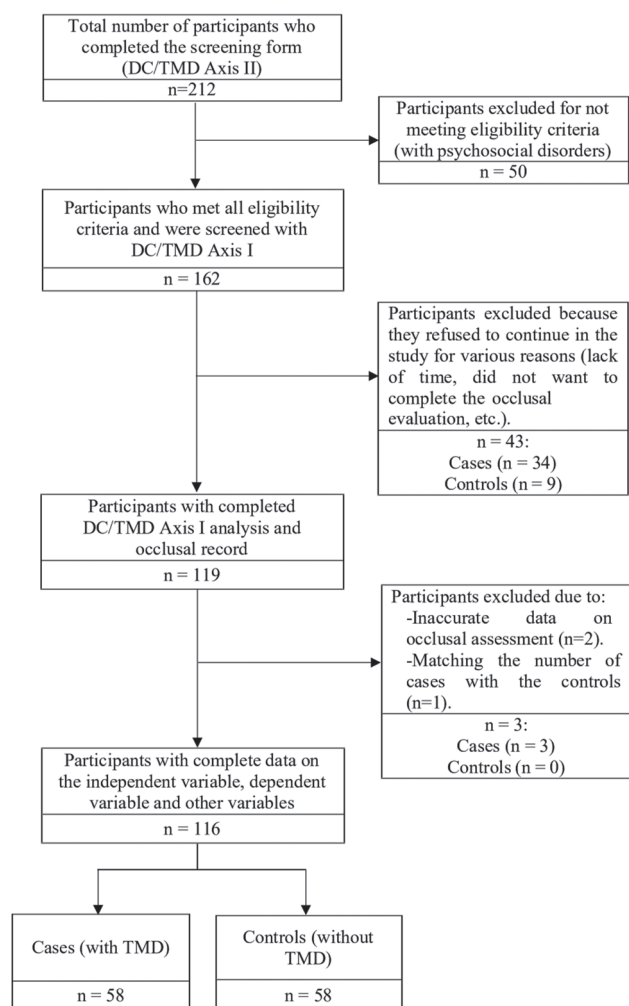


Figure 1: Selection of study participants (own elaboration)

The following instruments were used to evaluate the study participants: DC/TMD—Axis II,^[15,17] which determines psychosocial alterations using the Chronic Pain Grading Scale (version 2.0) that measures chronic pain, the Patient Health Questionnaire (PHQ-4, PHQ-9, PHQ-15)^[17-20] that measures anxiety, depression, and somatization and the Generalized Anxiety Disorders Questionnaire (GAD-7)^[21] that measures anxiety, and a screening card. Any individual with a zero score on the PHQ-4, PHQ-9, and PHQ-15 was considered to be free of psychosocial alteration. In the GAD-7, anyone with a score between 0 and 4 was considered to have no or minimal anxiety.

DIAGNOSIS OF SIGNS AND SYMPTOMS OF TMDs

The sample participants were evaluated for the presence of TMDs with the use of the DC/TMD (Cohen's kappa = 0.82). A hydraulic algometer (Baseline® brand—Made in USA) was used to standardize pressure during intraoral and extraoral

palpation and the DC/TMD—Axis I (examination form and signs and symptoms questionnaire)^[15,22] was used to determine the presence of signs and symptoms of dysfunction, following the diagnostic algorithm proposed by the instrument. The disorders found were divided into three groups (Group I = joint disorders, Group II = muscle disorders, and Group III = headache).

MEASUREMENT OF TOOTH CONTACTS AND OCCLUSAL FEATURES

To record the presence of MT occlusal contacts, 12 µm thick Arti-Fol occlusal recording tapes were used on the non-working side during laterality movements. Each participant was placed in a dental chair with the Frankfort plane as horizontal as possible. Marks were placed on the central incisors with an upper 2B pencil to define displacement phases at 0.5 mm, 1 mm, 2 mm, 2 mm, 3 mm, and bis to bis without mandibular opening and to control the amplitude of the lateral movement; the midline passing interproximally through the lower incisors was taken as a reference.^[23] The examinee was asked to close at maximum intercuspation, to maintain a stable position and pressure before the lateral movement. Then, the Arti-Fol tape was placed on the non-working side to be analyzed during each sliding phase. All occlusal surfaces of the posterior teeth were covered, and the participant was instructed to perform the lateral sliding movement in phases in an operator-guided manner and asked to maintain a constant force during sliding. This procedure was repeated up to three times for each side of the arch in the lateral movement to record contacts in laterotrusion and mediotrusion for accuracy and verification. The values were recorded on a data collection card. The teeth that held the articular tape were recorded as MT contacts if the tooth contacts occurred simultaneously on the MT and laterotrusive side and were considered MT interferences if the contacts occurred only on the MT side.

Sex and age were considered confounding factors, as well as angle classification, the distance from the retruded contact position to maximum intercuspation greater than 2 mm (RCP-MI ≥ 2 mm), and the type of MT contact. Assessment of angle classification was done clinically by observing the relationship between the mesiovestibular cusp of the upper first molar and the mesiovestibular sulcus of the mandibular first molar while the participant was in MIC. The RCP-MI ≥ 2 mm was calculated by means of the mandibular distraction manual.

DATA COLLECTION

The data were collected and immediately registered in an Excel database using double entry. Data were

processed and cleaned in real time to identify and correct implausible values. After screening for TMDs, a 1:1 ratio of cases to controls was chosen and only participants with a complete occlusal examination were considered for inclusion. Cases and controls were chosen based on the outcome variable of interest (presence of TMDs).

STATISTICAL ANALYSIS

The mean and standard deviation were calculated for the variable age, according to the normality of the data. The Chi-square test was used to determine the distribution of individuals according to case and control characteristics. The *t* test for homogeneity of variances was used to compare the means of age. Multivariable logistic regression was applied to investigate the association between MT occlusal contacts and TMDs adjusted for confounders (sex, age, angle classification, and RCP-MI discrepancy ≥ 2 mm). Stata version 17 statistical software was used, were considering a two-tailed hypothesis, a *P* value < 0.05 to be significant and a 95% CI in crude models and adjusted. The OddsPlotty package of R-Studio was used to make the odds plot.

RESULTS

The proportion of females was slightly higher in both the cases and controls groups and the mean age was similar in both groups. There was also a higher prevalence of class I molar individuals in the control group, however, class II individuals were more likely to have some type of TMDs ($P = 0.001$). When the prevalence of MT occlusal contacts was determined, the distribution indicated that those with some types of MT contact were more likely to have TMDs ($P = 0.003$). It should be noted that there was a higher prevalence of MT contacts and MT interferences among the cases [Table 1].

MT occlusal contacts during progressive laterality were significantly associated with TMDs at trajectories of 0.5 mm ($P = 0.013$) and 1 mm ($P = 0.002$) [Table 2]. It is worth mentioning that when they were evaluated in right and left laterality, no matches were found with joint pathologies on the same side of the contact side. Table 3 shows the crude and adjusted odds ratios (OR).

In the crude model, individuals with occlusal MT contacts were 3.12 times (OR = 3.12; 95% CI: 1.46–6.68) more likely to have TMDs compared to those without contacts. In the adjusted model, the strength of

Table 1: General characteristics of the cases and controls (*n* = 116)

Variables		Controls (<i>n</i> = 58)		Cases (<i>n</i> = 58)		<i>P</i>
Gender	Male	27	46.6	28	48.3	0.852
	Female	31	53.4	30	51.7	
Age		22.1 \pm 2.5		21.9 \pm 2.6		0.665
Angle classification	Class I	44	75.9	27	46.6	0.001
	Class II	14	24.1	31	53.4	
RCP-MI discrepancy ≥ 2 mm	No	51	87.9	43	74.1	0.058
	Yes	7	12.1	15	25.9	
MT occlusal contacts	No	39	67.2	23	39.7	0.003
	Yes	19	32.8	35	60.3	
MT occlusal contacts type	MT contacts	9	15.5	23	39.7	0.190
	MT interferences	10	17.2	12	20.7	

All values are mean \pm SD or percent. MT = Mediotrusive, RCP-MI = Retruded contact position to maximum intercuspation

Table 2: Mediotrusive occlusal contact according to trajectory in laterality movements in cases and controls.

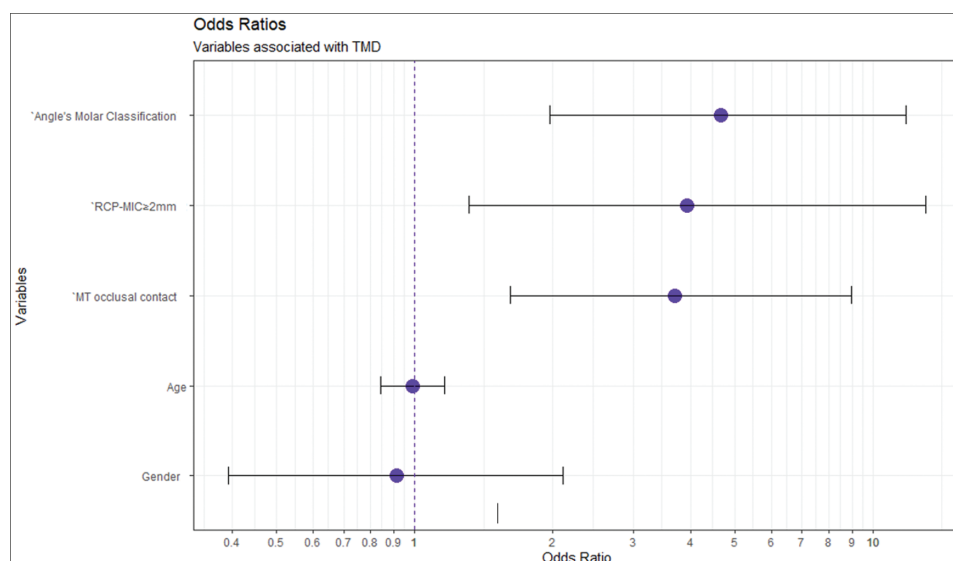
Trajectory	MT occlusal contacts	Controls (<i>n</i> = 58)		Cases (<i>n</i> = 58)		<i>p</i>	OR (95% CI)
0.5 mm	Yes	16	27.6	29	50	0.013	2.63 (1.21 - 5.68)
	No	42	72.4	29	50		
1 mm	Yes	6	10.3	20	34.5	0.002	4.56 (1.67 - 12.44)
	No	52	89.7	38	65.5		
2 mm	Yes	3	5.2	8	13.8	0.113	
	No	55	94.8	50	86.2		
3 mm	Yes	1	1.7	3	5.2	0.309	
	No	57	98.3	55	94.8		
Edge to edge	Yes	0	0	3	5.2	0.243	
	No	58	100	55	94.8		

MT = Mediotrusive, OR = Odds ratio, CI = Confidence interval

Table 3: Crude and multivariable-adjusted odds ratios and 95% confidence intervals for temporomandibular disorders and mediotrusive occlusal contacts

Variables		cOR (95% CI)	<i>p</i>	aOR (95% CI)*	<i>p</i>
Gender	Male	Ref.		Ref.	
	Female	0.93 (0.45–1.93)	0.852	0.91 (0.39–2.11)	0.828
Age		0.96 (0.84–1.12)	0.663	0.99 (0.84–1.16)	0.907
Angle classification	Class I	Ref.		Ref.	
	Class II	3.61 (1.63–7.97)	0.002	4.65 (1.91–11.32)	0.001
RCP-MI discrepancy ≥ 2 mm	No	Ref.		Ref.	
	Yes	2.54 (0.95–6.80)	0.063	3.92 (1.25–12.23)	0.019
MT occlusal contacts	No	Ref.		Ref.	
	Yes	3.12 (1.46–6.68)	0.003	3.70 (1.58–8.66)	0.003

cOR, odds ratio crudo; aOR, odds ratio adjusted for gender, age, angle classification, and RCP-MI discrepancy ≥ 2 mm; *Pseudo $R^2 = 0.16$; CI = Confidence interval, MT = Mediotrusive, RCP-MI = Retruded contact position to maximum intercuspation

**Figure 2: Factors related to TMD**

association increased (OR = 3.70; 95% CI: 1.58–8.66). There was a similar behavior for individuals with molar Class II with ORs showing a tendency to increase on comparing the crude model with the adjusted model. In relation to an RCP-MI discrepancy ≥ 2 mm, the crude model did not show significance, but the OR became significant in the adjusted model (OR = 3.70; 95% CI: 1.58–8.66) [Table 3, Figure 2]. Moreover, the amount of variance in the prevalence of TMDs predicted by the final model was 16% [Table 3].

Table 4 shows the effect modification by sex. Variations in the ORs indicate that men and women with MT occlusal contacts have a similar probability of presenting TMDs. An RCP-MI discrepancy ≥ 2 mm represents a higher risk of causing TMDs in the female group.

DISCUSSION

This study found that MT occlusal contacts are associated with TMDs symptomatology, although with

a low predictive value. Similarly, other publications consider that these contacts during laterality, more than other occlusal factors, have some degree of association with articular and muscular disorders.^[5,10,24–26] However, it has been reported that this relationship is not clinically significant for chronic TMD symptoms, but may be significant for acute transient symptoms.^[10] Studies with electromyography demonstrate that alterations in occlusal contacts may change the pattern and produce painful symptoms at the level of the masticatory muscles,^[27,28] but other studies find that the changes are not significant in relation to non-working side contacts.^[29,30] This is due to resilience and tissue accommodation phenomena or contact wear due to increased mobility between teeth, which explains most cases with the absence of TMDs symptoms and in others, the presence of acute symptoms. On some occasions, if the patient does not manage to adapt completely, the mandibular movement patterns can be permanently altered by parafunctional events in the

Table 4: Multivariable-adjusted odds ratios and 95% confidence intervals for temporomandibular disorders and mediotrusive occlusal contacts by gender

Variables		Male		Female	
		aOR (95% CI)*	<i>p</i>	aOR (95% CI)**	<i>p</i>
Age		0.93 (0.73–1.20)	0.614	1.02 (0.82–1.27)	0.837
Angle classification	Class I	Ref.		Ref.	
	Class II	10.01 (2.31–43.36)	0.002	2.94 (0.88–9.87)	0.080
RCP-MI discrepancy ≥ 2 mm	No	Ref.		Ref.	
	Yes	2.14 (0.33–13.84)	0.426	4.63 (1.02–21.02)	0.047
MT occlusal contacts	No	Ref.		Ref.	
	Yes	4.09 (1.05–15.87)	0.042	3.63 (1.16–11.37)	0.027

aOR, odds ratio adjusted for, age, angle classification, and RCP-MI discrepancy ≥ 2 mm; *Pseudo $R^2 = 0,22$; **Pseudo $R^2 = 0,14$; CI = Confidence interval, MT = Mediotrusive, RCP-MI = Retruded contact position to maximum intercuspation

attempt to eliminate them;^[10] if the adaptive capacity of the individual is exceeded, symptoms of TMJ dysfunction already present can be aggravated.^[10,31,32] These processes would be mediated by genes involved in neurological, endocrine, and inflammatory pathways that would vary according to the degree of adaptability of the individual to the presence, form, and duration of contact.^[33]

However, research on the relationship between MT occlusal contacts and TMJ pathologies has declined, due to reports of strong relationships with psychosocial disorders,^[6–8,34] which led to a trend that was inconsistent with the performance of dental treatments as adjuvant in the resolution of TMDs. Although the failure of many occlusal treatments may be associated with psychosocial disorders, it cannot be ruled out that joint biomechanics may be altered by compressive or tensile occlusal forces on the TM side, because the condyle acts as the fulcrum point causing both the disc and the capsule to be stressed simultaneously.^[35] The elasticity of the disc and its lateral fibers are capable of absorbing the energy of occlusal loads; however, it is possible that the accumulated efforts to achieve stability result in fatigue or plastic deformation of the disc.^[10] These changes occur over a prolonged period of time, where adaptation or aggravation of TMDs symptoms may occur.

On the other hand, much of the evidence does not differentiate between MT interferences and MT contacts, which makes nomenclature difficult when comparing results. MT interferences are more harmful to the TMJ compared to MT contacts, as they are those that cause disocclusion on the laterotrusive side.^[36] In lateral movements performed with higher levels of force, MT interferences can be observed, while with lighter forces, to MT contacts. Although in our study there was a higher frequency of MT contacts than MT interferences in symptomatic individuals in agreement

with Marklund and Wänman,^[36] it is necessary to ask whether, during lateral movement, the force applied by the individual has been homogeneous.

Many studies have shown the low predictive value of MT contacts or interferences is supported by the assertion that the masticatory system is able to adapt asymptotically by the mechanisms already described and, therefore, does not justify occlusal adjustment in the treatment of TMDs.^[5,26,33,37–40] An additional theory supports the idea that MT occlusal contacts would be a direct cause of TMDs,^[39] but it is a hypothesis that is not supported by longitudinal studies. This implies reflecting on the mechanism affecting the TMJ by MT occlusal contacts. An MT interference may change the reaction forces at the condyle level producing tensile stresses as the interference is located more toward the molar area or depending on the magnitude of the interference.^[10] This would produce changes in the condylo-disc relationship of the TMJ through nociceptive and protective co-contraction reflexes. It should be noted that the muscles supporting the joints are the first proprioceptive centers to masticatory stimuli. This indicates that joint dysfunction may be conditioned by these muscle responses.^[41,42] On the other hand, joint instability due to non-working side contacts may hyperactivate the muscles in a compensatory manner resulting in some muscular pathology if there is no tolerance on the part of the individual. In other words, we are referring to a bidirectional relationship.

We found that the frequency of MT occlusal contacts in progressive laterality was found to be associated with distances of 0.5 and 1 mm, both in right and left laterality. This is in agreement with the results of Ogawa *et al.*^[23] and Dodić *et al.*,^[43] who determined that at shorter laterality distances and excursive movements, a greater amount of interference is present. This finding could support the theory that short lateral movements associated with these contacts during mastication may

be catalysts for joint or muscle symptomatology on the same side of the contact. Also, other studies have found that TMDs symptoms were associated with other occlusal characteristics such as molar class II relationship^[44-46] and RCP-MI ≥ 2 mm,^[26,38] similar to the findings of this investigation. Also, in multivariate stratified sampling, we found that males are more likely to present DTM compared to females. This differs from that described by Marchesi *et al.*,^[44] who considered that TMDs are more strongly associated with women, which may be attributed to the fact that in our study we controlled for psychosocial disorders, which, by design, have been mainly associated with women. These findings are relevant and encouraging, as after ruling out psychosocial symptoms, proper occlusal analysis and clinical identification of non-working side interferences using standardized protocols may be important to achieve occlusal and functional stability in a noninvasive manner in order to avoid precipitation of TMDs.

MT occlusal contacts, especially MT interferences, may be associated with acute symptoms, such as loss of occlusal stability, condylar stability, and muscle or joint pain, which together may force the individual to acquire adaptive habits that may be detrimental, such as unilateral chewing, or adaptation through compensatory movements of accommodation, as the TMJ would seek to fulfill its critical life functions.^[32] The inclusion of two fulcrum points may explain alterations in the pivotal condyle of the non-working zone that, together with ligamentous and muscular distension of the pterygoids, could lead to TMDs symptoms in any of its forms.^[47] However, there is no study that can predict the general behavior of the masticatory system in the face of these interferences. Therefore, caution is recommended before using occlusal therapy as a solution to TMDs by eliminating MT occlusal contacts, as they are not capable, by themselves, of reducing the symptomatology of patients with chronic orofacial pain.^[30] Patients with these contacts need to be monitored to prevent acute symptoms from becoming chronic.

The limitations of this study are determined by its cross-sectional design, so causality between MT occlusal contacts and TMDs cannot be affirmed. No complementary examinations or imaging studies were used for the diagnosis of the pathologies, which increases the probability of occurrence of non-differential classification errors, however, it is reduced by the use of a very sensitive and specific tool such as DC/TMD. The inference of the study may be compromised due to internal validity in relation to the inclusion criteria, and

also because of the population where the sample was taken and its size. More efforts are required to control the forces during lateral mandibular movement in order to make the identification techniques more valid. In addition, the measurement of MT occlusal contacts was performed accurately with the use of articulating papers with optimal thickness. Nevertheless, future studies should combine this technique with digital registration to improve its sensitivity in locating contacts or interferences where lateral movements are more functionally reproduced. Future studies should consider following individuals with occlusal contacts in TM in order to clarify the picture of the individual's adaptability or chronicity of TMDs symptoms, considering periodic monitoring of psychosocial factors over time. This could also clarify the hypothesis that DTMs may be predecessors of MT occlusal contacts, clarifying the bidirectional paradigm.

CONCLUSION

MT occlusal contacts are significantly associated with acute TMDs symptoms in young adults without psychosocial disorders, particularly during short lateral mandibular movements. However, their predictive value is limited, likely due to the masticatory system's adaptive capacity in individuals without psychosocial disorders. This study highlights the need for longitudinal research to explore the chronicity of symptoms and the role of digital recording methods in enhancing diagnostic accuracy. While these contacts may contribute to TMDs pathogenesis, routine occlusal therapy for their management is not recommended until stronger evidence supports their causal role in limiting masticatory function.

CONFLICT OF INTEREST

There are no conflicts of interest.

List of Abbreviations

TMDs	Temporomandibular disorders
DC/TMD	Diagnostic Criteria for Temporomandibular Disorders
RCP-MI	Retruded contact position to maximum intercuspation
MT	Mediotrusive; PHQ: Patient Health Questionnaire
GAD	Generalized Anxiety Disorders Questionnaire
CI	Confidence Interval
OR	Odds ratio

PATIENT DECLARATION OF CONSENT

Not applicable.

ACKNOWLEDGEMENT

Not applicable.

AUTHOR CONTRIBUTIONS

YMM and GPC conceived the research idea and participated in the acquisition and analysis. In addition, together with SAM and RWV, they participated in the preparation, editing, and revision of the final manuscript.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study will be accessible by contacting the corresponding author.

ETHICAL POLICY AND INSTITUTIONAL REVIEW BOARD STATEMENT

Approval by Institutional Research Ethics Committee of the Instituto de Medicina Tropical “Daniel Alcides Carrión” of the Universidad Nacional Mayor de San Marcos (CIEI-2020-21).

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