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Influence of a Diagnosis of Depression and/or Anxiety on Temporomandibular Joint Treatment - a Retrospective Study

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Abstract

This cross-sectional retrospective study aimed to assess the depression and/or anxiety influence on temporomandibular disorders (TMD) diagnosis and treatment. The primary outcome was temporomandibular joint pain (VAS). The secondary outcomes were: 1) Health-related quality of life (VASLife); 2) Maximal Mouth Opening (MMO); 3) Myalgia degree. Patients were screened through PHQ-2 (depression) and GAD-2 (anxiety) validated questionnaires. A total of 247 patients (202 female), with mean age of 40.51 ± 17.04, were enrolled. 133 patients (53.8%, GAD-2 $\geq$ 3) and 91 patients (38.4%, PHQ-72 $\geq$ 2) were screened positive for anxiety and depression, respectively. The mean pre-treatment pain was 4.25 ± 2.62; VASLife was 6.60 ± 2.36; MMO 37.15 ± 9.50; myalgia degree was 2.22 ± 0.99. A higher psychological distress burden was significantly correlated with VASLife (p=0.040, PHQ-2 $\geq$ 2; p=0.025, GAD-2 $\geq$ 3) and myalgia levels (p=0.013, PHQ-2 $\geq$ 2; p=0.038, GAD-2 $\geq$ 3). Myalgia significantly subsisted post-treatment in patients with anxiety (p=0.038, GAD-2 $\geq$3). The pre-treatment VASLife (OR=1.67; p=0.008) and, in anxious patients, post-treatment myalgia degree (OR=1.89; p<0.001), were determinant factors for reintervention. Depression and/or anxiety were correlated with poor clinical outcomes, particularly in myogenous TMD. To implement multidisciplinary treatment programs for patients reporting a higher disease burden and refractory symptoms, awareness should be raised.

Highlights

1 - A significant association between anxiety and/or depression with myalgia was observed; 2 - Stress and anxiety contribute to parafunctional oral habits and influence muscle pressure pain threshold (PPT) and pain; 3 - Physicians should educate patients on good oral habits and screen and treat underlying associated anxiety and depression; 4 - Depression and/or anxiety influence TMD treatment outcomes, particularly in myogenous TMD, and contribute to intervention; 4 - The presence of co- morbid mental health disorders should warn the physician/surgeon to manage treatment strategies promptly and efficiently in a holistic treatment protocol.

1. Introduction

Temporomandibular disorders (TMD) are heterogeneous conditions related to functional and morphological deformities in the temporomandibular joint (TMJ) and associated structures [1]. TMD is the most common cause of non-dental chronic orofacial pain [2–4]. With an annual incidence rate of 2%, more than 50% of the population report symptoms related to TMD [1, 5], and its prevalence goes beyond 30% [1, 6, 7]. Two main subgroups are recognized: arthrogenous and myogenous TMD[1, 3, 8, 9]. TMD subtypes have specific treatment protocols, starting with conservative options and progressing to other modalities, if required (Dimitroulis, 2013). A change in paradigm advocates minimally invasive options as an early treatment for arthrogenous TMD [8, 10].

In multifactorial TMD etiopathogenesis, biopsychosocial factors play a dominant role. There is a consensual link between TMD and a higher psychopathological burden, particularly for depression and anxiety [4, 5, 9, 11–14].

Stress and anxiety promote neuroendocrine modulation allowing physical and psychosocial adjustment [5, 15, 16]. The biomolecular mechanisms in depression and/or anxiety disorders that trigger the biomechanical alterations in the TMJ are unsure. However, it is thought that depression and anxiety interact with pain-modulating networks and change the perception of pain, resulting in greater awareness of somatic and interoceptive cues [1, 4, 11, 15, 17].

In 2019, Portugal was the European country with the highest prevalence of mental health disorders [18]. In the primary care setting, anxiety and depression prevalence range between 5.4-8.8% and 7.3-13.4%, respectively. In time-constrained clinical environments, brief screening tools such as PHQ-2 and GAD-2 allow timely and accurate screening of these prevalent comorbid mental health disorders [19–21]. Therefore, primarily aiming to assess the association between preexistent depression and/or anxiety and TMD, the following hypotheses were formulated: (1) Are PHQ-2 and GAD-2 scores negatively associated with TMD treatment outcomes? (2) Can some TMD subtypes possibly have a stronger association with depression and/or anxiety? (3) Does a higher psychological burden contribute to the need for intervention?

2. Materials and Methods

2.1. Study Design

A cross-sectional retrospective study included patients treated for TMD from February 2018 to February 2022. The study was carried out on the STROBE guidelines. The study was approved by the ethics committee of Centro Académico de Medicina de Lisboa (CAML) (26.12.2022/311/22). According to current legislation, all enrolled patients were aware of its implications and gave their free terms of consent in writing.

The inclusion criteria were: (1) age >18 years 2) arthrogenous and/or myogenous TMD; 3) conservative treatment without any improvement at least for three months; 4) Dimitroulis Classification between 1-4; 5) indication for one of the following TMD treatments: injection of botulinum toxin; TMJ arthrocentesis; TMJ arthroscopy; TMJ open surgery without alloplastic material. The exclusion criteria were: 1) previous TMJ surgical intervention; 2) impaired cognitive capacity; 3) pregnant or breastfeeding women.

Before the intervention, all participants were examined by the same TMJ surgeon. The variables measured throughout the study were obtained pre and post- treatment: 1) TMJ pain, with a Visual Analog Scale (VAS, 0-10, with 0 corresponding to the absence of pain and 10 maximum insupportable pain); 2) Health-related quality of life (VASLife) through the question: "If you could give a life impact score to your TMJ problem in a 0 to 10 scale, where 0 means no impact and 10 means the maximum impact possible, what would be your score?"; 3) Maximal Mouth Opening (MMO, mm) employing a certified ruler between the incisor's teeth; 4) Myalgia degree (0-3), accordingly with pain intensity in each muscle: 0 = No Pain/Pressure Only; 1 = Mild Pain; 2 = Moderate Pain; 3 = Severe Pain [22]. Myogenous disease, including myalgia, was diagnosed according to a clinical history positive for 1) in the past 30 days, pain in the jaw, temple, in front of the ear, or the ear with examiner confirmation of pain location in the temporalis or masseter muscle and 2) pain modified with jaw movement, function or parafunction and a favorable clinical evaluation for palpation pressure (5 seconds/1kg pressure) in masseter and temporalis muscles as defined in Diagnostic Criteria for Temporomandibular Disorders DC/TMD [23]. Arthralgia was diagnosed through positive history for both criteria: 1) pain in TMJ, in the ear, or front of ear; 2) pain modified with jaw movement, function, or parafunction. Positive examination for arthralgia was reported if it was observed: pain location in the TMJ area and pain on palpation of the lateral pole or around the lateral pole or pain on maximum unassisted or assisted opening, right or left lateral movements, or protrusive movements. The final arthrogenous diagnosis was confirmed with MRI.

Each patient was further categorized, and the decision of which treatment to apply was based on Dimitroulis' TMJ Surgical Classification [24]: Category 1: patients without arthrogenous disease, with TMJ pain associated with myofascial pain. These patients were treated with botulinum toxin injections. Category 2: diagnosis of disc displacement with reduction (DDwR) with joint clicking and intermittent pain or indication of inflammation with normal condyles. These patients were treated with arthrocentesis. Category 3: patients with long-standing closed lock (> 2 months), diagnosis of disc displacement without reduction (DDwoR), absence of clicks, arthrogenous TMD, or synovial chondromatosis. These cases were treated with TMJ arthroscopy. Category 4: radiological signs of changes in condylar morphology such as osteophytes, small subchondral cysts, loss or thinning of cartilage layer, severe displaced and deformed articular discs, including disc perforation. When the disc was salvageable, the patients were treated with discopexy, and a discectomy was performed when unsalvageable.

Independently of the Dimitroulis category, all patients with myalgia grades 2 and 3 received a 155U or 195U botulinum toxin injection in the masticatory muscles (masseter and temporal), respectively. This treatment was performed 10-15 days before the surgery.

All patients were instructed to follow a soft diet for three days after surgery. In addition, five physiotherapy sessions and three speech therapy exercise sessions started 3-5 days after the intervention.

2.1.1. PHQ-2 GAD-2 questionnaires

For each patient, screening for depressive and/or anxiety disorder was assessed in the first consultation through validated PHQ-2 and GAD-2 questionnaires [25,

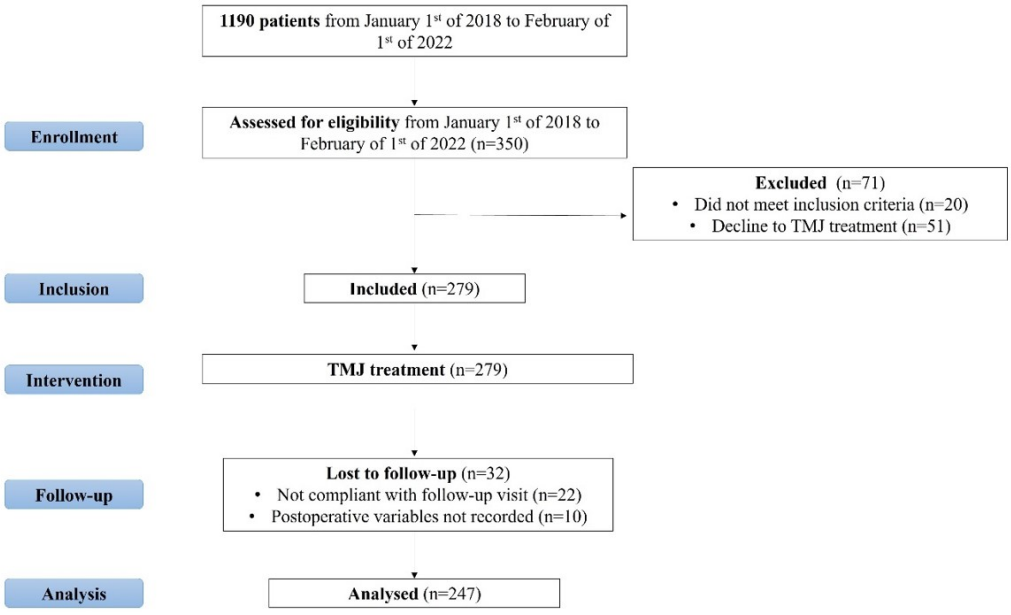

Figure 1. STROBE- flow chart diagram reporting of participant enrolment. TMJ - temporomandibular joint.

26](Kroenke et al., 2003, 2007).

A PHQ-2 cutoff of ≥ 2 was considered likely to be of clinically significant depressive disorder, according to Levis et al. (2020). The authors established sensitivity and specificity of 0.91 and 0.67 for a PHQ-2 score ≥2 and 0.72 and 0.85 for a PHQ-2 score ≥3 20. Accordingly, a diagnostic meta-analysis on PHQ-2 accuracy in the screening of MDD by Manea L. et al. [27] found similar operating characteristics for this lower cutpoint (sensitivity of 0.91, specificity of 0.70) [27]. Bisby M.A. et al [21] also suggested a lower PHQ-2 cut point of ≥2 since it demonstrated optimal sensitivity and specificity. The higher sensitivity results in better case-finding ability, which comes at the expense of lower specificity. To account for the risk of a high rate of false positives and reduced clinical utility, a PHQ-2 score ≥2 should be implemented in settings with a high prevalence of the condition [21, 27]. Considering the high prevalence of depressive symptoms and disorders among the Portuguese population, a cutoff of ≥2 was adopted.

A GAD-2 cutoff of ≥3 suggested clinically significant anxiety disorder [26]. For a cutoff ≥3, GAD-2 has the following operating characteristics: sensitivity and specificity of 86,0% and 83,0% in GAD screening; sensitivity and specificity of 65,0% and 88,0% in any anxiety disorder screening [26]. Patients with a positive screening result for a depressive and/or anxiety disorder received advice on available resources for appropriate treatment and follow-up.

2.1.2. Statistical Analysis

A descriptive analysis of the study was performed through measures, absolute frequencies and mean. The mean was used as a location measure accompanied by its standard deviation (SD) as mean ± SD. The normality analysis was performed for all tests using the Kolmogorov-Smirnov test. Bivariate contingency tables containing the absolute frequency in each possible combination of categorical variables were created. The non-parametric Chi-square test (2) and Fisher's exact test assessed associations between these variables.

The Student T-test or non-parametric Mann-Whitney U Test was used for continuous variables. Multivariable logistic regression analysis was used to assess the impact of depression and anxiety on reintervention treatment. Multivariable analysis was adjusted for: Pre-treatment VASLife; GAD-2; PHQ-2; Post-treatment Myalgia * GAD-2; Post-treatment Myalgia * PHQ-2. P-value <0.05 was considered statistically significant for all analyses. Data were analyzed using SPSS (v26) and graphical representation through GraphPad Prism (v9) software.

3. Results

A total of 247 patients (202 female and 45 male) were enrolled (Figure 1), mean age of 40.51 ± 17.04 years, ranging from 14-88 years (Table 1). The clinical pre-treatment variables evaluated in the study are reported in Table 2. The mean pre-treatment VAS (0-10) was 4.25 ± 2.62, VASLife (0-10) was 6.60 ± 2.36, MMO was 37.15 ± 9.50 (mm), and myalgia degree was 2.22 ± 0.99. The more frequent pre-treatment intra-articular diagnoses were: (1) DDwR (101 patients, 40.9%); (2) DDwoR (93 patients, 37.7%); (3) Osteoarthrosis (OA) (83 patients, 33.6%). Pre-treatment myalgia was identified in 222 (89.9%) patients: I – 24 (9.7%); II – 70 (28.3%); III – 128 (51.8%). One hundred fifty-five patients (37.2%) had arthralgia, and 144

(38.2%) had a disc displacement disorder with pain associated. TMD severity, evaluated using the Dimitroulis Classification, was heterogeneous. Considering the Dimitroulis Classification patients included were staged as following: 18 patients (19.4%) in category 1; 110 patients (44.5%) in category 2; 53 patients (21.5%) in category 3, and 36 patients (14.6%) in category 4. The mean follow-up period was 252.9 ± 278.8 days, ranging from 31 to 1224 days.

Table 1. Demographic data.

Number of patients	247
Sex	**Number of patients (%)**
Female	202 (81.8%)
Male	45 (18.2%)
Age Mean ± SD (range)	40.51 ± 17.04 (18-88)

Table 2. Clinical evaluation.

Pre-treatment VAS (0-10) (mean ± SD)	4.25 ± 2.62
Pre-treatment VASLife (0-10) (mean ± SD)	6.60 ± 2.36
Pre-treatment MMO (mean ± SD)	37.15 ± 9.50
Pre-treatment Myalgia Degree (mean ± SD)	2.22 ± 0.99
Pre-treatment Intra-articular Diagnosis	**Number of patients (%)**
DDwR	101 (40.9%)
DDwoR	93 (37.7%)
OA	83 (33.6%)
Pre-treatment Myalgia Diagnosis	**Number of patients (%)**
Myalgia	222 (89.9%)
I	24 (9.7%)
II	70 (28.3%)
III	128 (51.8%)
Dimitroulis Classification	**Number of patients (%)**
I	48 (19.4%)
II	110 (44.5%)
III	53 (21.5%)
IV	36 (14.6%)
Arthralgia diagnosis	155 (37.2%)
Disc displacement disorder with pain	144 (58.3%)
Follow-up period (days)	252.9 ± 278.2 (31-1224)

The mean GAD-2 and PHQ-2 scores were 2.94 ± 1.78 and 1.33 ± 1.67 (Figures 2 and 3). One hundred thirty-three patients (53.8%, GAD-2 $\geq$3) screened positive for an anxiety disorder, and 91 patients (38.4%, PHQ-2 $\geq$ 2) for depression.

Table 3 summarizes the bivariate analysis of the sociodemographic variables associated with GAD-2 and PHQ-2 status. The mean age was significantly associated with the PHQ-2 rate (P=0.049). However, no significant association was found concerning patients' sex.

The correlation of clinical variables (pre- and post-treatment) with GAD-2 and PHQ-2 status was analyzed (Table 4). There was a statistically positive association between PHQ-2 screening with the following clinical outcomes: pre-treatment VASLife (6.95±2.49; p=0.040), myalgia (reported by 95,6% of the patients with a PHQ-2 score $\geq$2; p=0.011), and myalgia degree (2.43±0.83; p=0.013). For a positive GAD-2, there was a statistically significant association with pre-treatment VASLife (6.92±2.37; p=0.025), myalgia degree (2.35 ± 0.91; p=0.038), and post-treatment myalgia degree (0.67 ± 1.08; p=0.036). For other clinical variables (pre-treatment VAS, MMO and intra-articular diagnosis, post-treatment VAS and MMO, Dimitroulis Classification, arthralgia diagnosis, and disc displacement disorder with pain), no statistically significant differences were found.

Forty patients (16.2%) required reintervention. A multivariable logistic regression predicting patients requiring reintervention was adjusted for the screening measures status (GAD-2 and PHQ-2), pre-treatment VASLife, and post-treatment myalgia degree (Table 5). Although GAD-2 and PHQ-2 alone did not explain the profile of reintervened patients, significance was found for pre-treatment VASLife (odd ratio (OR)=1.67; p=0.008). In addition, the composed variable of post-treatment myalgia degree and GAD-2 status was also significant (OR=1.89; p<0.001).

4. Discussion

The association between psychological disorders, namely anxiety, and depression with TMD has been reported in several studies [11–13, 28, 29]. However, few studies seem to have evaluated the preliminary diagnosis of anxiety and depression on the clinical outcomes of TMD patients and the need for surgical intervention.

Mental health disorders are a significant public health challenge. It has been estimated that almost 14% of Europeans were affected by mental health disorders in 2019. In Portugal, the estimates reach nearly 19%, thereby being the European country with the highest psychopathological burden [18]. Anxiety disorders were the most prevalent (4.69%), followed by depressive disorders (3.79%) [18]. According to the Epidemiological National Mental Health Study (2008-2009), part of the World Mental Health Survey Initiative, in Portugal, anxiety and affective disorders are the most prevalent psychiatric diagnoses, with a prevalence of 16.5% and 7.9%, respectively [30]. Self-reported depressive symptoms reach a 10% prevalence [30]. Vos T. et al [18] reported prevalence values of 8.8% and 4.8% for anxiety and depression, respectively, in the Portuguese population. In our study, 38.4% and 53.8% of the patients screened positive for depression and anxiety, respectively. In line with a previous study in the Portuguese setting [31], the higher prevalence found potentially reflects the consensual association between TMD and psychological distress. A future comparative study using GAD-2 and PHQ-2 in a population not diagnosed with TMD will be required to confirm these data. Although GAD-2 and PHQ-2 are easy

A

GAD-2 (mean ± SD)		2.94 ± 1.78
		Number of patients (%)
GAD-2	0	31 (12.6%)
	1	14 (5.7%)
	2	69 (27.9%)
	3	33 (13.4%)
	4	50 (20.2%)
	5	24 (9.7%)
	6	26 (10.5%)

B

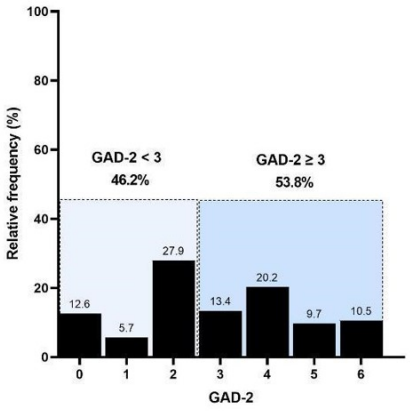

Figure 2. GAD-2 distribution among patients. (A) GAD-2 mean and distribution by the different classifications. (B) Distribution of positive and negative GAD-2.

A

PHQ-2 (mean ± SD)		1.33 ± 1.67
		Number of patients (%)
PHQ-2	0	115 (46.6%)
	1	31 (12.6%)
	2	42 (17.0%)
	3	19 (7.7%)
	4	13 (5.3%)
	5	10 (4.0%)
	6	7 (2.8%)

B

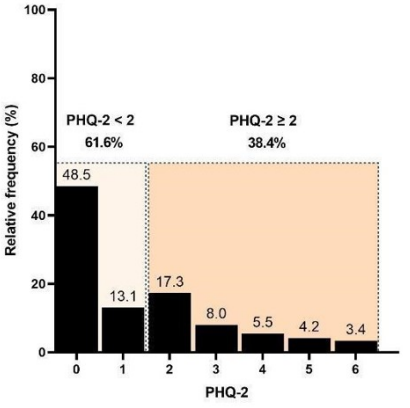

Figure 3. PHQ-2 distribution among patients. (A) PHQ-2 mean and distribution by the different classifications. (B) Distribution of positive and negative PHQ-2.

Table 3. Demographic characteristics according to GAD-2 and PHQ-2 status.

Variable	GAD-2			PHQ-2		
	GAD-2 (0-2)	GAD-2 ≥3	p-value or χ^2; df; p-value	PHQ-2 (0-1)	PHQ-2 ≥2	p-value or χ^2; df; p-value
Sex						
F	92 (80.7%)	110 (82.7%)	0.166; 1; 0.684	120 (82.2%)	72 (79.1%)	0.344; 1; 0.558
M	22 (19.3%)	23 (17.3%)		26 (17.8%)	19 (20.9%)	
Age Mean (mean ± SD)	38.19 ± 24.02	40.71 ± 18.91	0.731	39.11 ± 17.48	43.32 ± 16.74	**0.049**

and reliable clinically validated screening tools, as brief screening measures, a positive result should be complemented with other discriminatory methods or a directed clinical interview [20, 21, 25–27]. In our study, the values obtained could be due to overdiagnosis, and confirmation through other tools is required. If a sequential diagnosis based on PHQ-2 > PHQ-9 and GAD-2 > GAD-7 is implemented, a lower prevalence but a more accurate diagnosis will be obtained. Previous studies, including PHQ-9 and GAD-7 screening tools in patients with TMD or chronic orofacial pain, established depression and anxiety prevalence values of 17-21% (PHQ-9 ≥10) and 15-29% (GAD-7 ≥ 10)[28, 32, 33].

Psychological factors may be prominently relevant in

Table 4. Diagnosis and treatment outcomes according to GAD-2 and PHQ-2 status.

Variable	GAD-2			PHQ-2		
	GAD-2 (0-2)	GAD-2 ≥3	p-value or χ^2; df; p-value	PHQ-2 (0-1)	PHQ-2 ≥2	p-value or χ^2; df; p-value
Pre-treatment VAS (0-10) (mean ± SD)	4.12 ± 2.38	4.37 ± 2.81	0.335	4.06 ± 2.57	4.42 ± 2.68	0.233
Pre-treatment VASLife (0-10) (mean ± SD)	6.25 ± 2.31	6.92 ± 2.37	**0.025**	6.34 ± 2.26	6.95 ± 2.49	**0.040**
Pre-treatment MMO (mean ± SD)	37.40 ± 9.87	36.93 ± 9.21	0.704	37.16 ± 9.90	37.86 ± 8.93	0.589
Intra-articular diagnosis						
DDwR	50 (43.9%)	51 (38.3%)	0.772; 1; 0.380	59 (40.4%)	35 (38.5%)	0.089; 1; 0.765
DDwoR	44 (38.6%)	49 (36.8%)	0.080; 1; 0.777	51 (54.2%)	37 (40.7%)	0.788; 1; 0.375
OA	40 (35.1%)	43 (32.3%)	0.209; 1; 0.647	47 (32.2%)	34 (37.4%)	0.666; 1; 0.414
Myalgia	98 (86.7%)	123 (93.2%)	2.872; 1; 0.090	124 (84.9%)	87 (95.6%)	**6.538; 1; 0.011**
Myalgia degree (mean ± SD)	2.07 ± 1.06	2.35 ± 0.91	**0.038**	2.07 ± 1.07	2.43 ± 0.83	**0.013**
Post-treatment VAS (0-10) (mean ± SD)	0.67 ± 1.59	1.07 ± 2.43	0.614	0.75 ± 1.93	0.73 ± 1.90	0.679
Post-treatment myalgia degree (mean ± SD)	0.46 ± 0.78	0.67 ± 1.08	**0.038**	0.53 ± 0.89	0.57 ± 0.97	0.957
Post-treatment MMO (mean ± SD)	41.00 ± 7.08	40.32 ± 4.67	0.447	40.90 ± 6.24	40.71 ± 5.32	0.836
Dimitroulis Classification						
1	18 (15.8%)	30 (25.8%)	3.36; 3; 0.340	26 (17.8%)	22 (24.2%)	3.436; 3; 0.329
2	55 (48.2%)	55 (41.4%)		72 (49.3%)	34 (37.4%)	
3	27 (23.7%)	26 (19.5%)		28 (19.2%)	21 (18.8%)	
4	14 (12.3%)	22 (16.5%)		20 (13.7%)	14 (15.4%)	
Arthralgia diagnosis	71 (62.3%)	84 (63.2%)	0.020; 1; 0.887	91 (62.3%)	58 (63.7%)	0.048; 1; 0.827
Disc displacement disorder with pain	30 (26.3%)	42 (31.6%)	0.823; 1; 0.364	39 (26.7%)	32 (35.2%)	1.909; 1; 0.167

Table 5. Multivariable logistic regression predicting reintervention treatment adjusted for VASLife, GAD-2, PHQ-2, myofascial pain diagnosis, and post-treatment MT degree.

Variable	OR	95% CI	p-value
Pre-treatment VASLife	1.67	1.14-2.44	0.008
GAD-2	0.93	0.60-1.46	0.759
PHQ-2	0.76	0.42-1.39	0.379
Post-treatment myalgia degree * GAD-2	1.89	1.35-2.64	<0.001
Post-treatment myalgia degree * PHQ-2	0.747	0.49-1.15	0.181

myogenous disease and pain of muscle origin [4, 7, 11, 13]. Psychosocial factors (stressful life events, psychological distress, and pathology) arouse the Central Nervous System, promoting excessive muscle activity [15, 16, 34]. While multiple systems might be affected and influence myofascial pain, the limbic system (LS) and the neurologically related periaqueductal gray are primarily involved in the adjustment of emotions, defensive conduct, and pain modulation [16, 35]. The dynamic motor systems orchestrate the LS response to the perceived environment. Hence, each specific emotion generates certain changes in the body – stress contributes to pain related to muscle tension and trigger point (TrP) formation and perpetuates the body response, causing more stress and pain (hyperalgesia) [6, 16]. Muscular TrP is the critical element of myofascial pain syndrome and is classified as active (ATrP) or latent (LTrP). The latter is defined as the focus of hyperirritability in a taut muscle band and is clinically associated with a local twitch response, tenderness, and/or referred pain upon manual examination [36, 37]. It has been shown that a higher number of LTrP is associated with a higher frequency of depressive symptoms reported by healthy individuals [36]. Likewise, anxiety seems to increase the likelihood of muscle tenderness [38]. In patients with tension-type headaches, the number of ATrPs was associated with the physical burden of headache and trait anxiety levels [39]. Furthermore, the LS outputs also impact autonomic, endocrine, somatic, nociceptive, and immune systems [16]. The autonomic sympathetic nervous system is of primary relevance. A chronically activated fight or flight response leads to neuroendocrine disequilibrium, contributing to muscle hyperactivity and exacerbating perceived pain [16].

Our study has diagnosed many patients with myogenous TMD (89.9%). Depression was significantly associated with myalgia and myalgia degree. The relationship was even more consistent for anxiety, where a significant association was shown for myalgia and post-treatment myalgia degrees. Vedolin G.M. et al [5] have also shown that individuals with myofascial pain TMD reported higher anxiety levels than healthy people. The positive correlation between TMD and psychological factors would anticipate that higher levels of anxiety and depression would lead to a more significant number of tender points, lower MMO, and reduced functionality [5, 11, 13, 14]. However, no significant differences were found for the more objective clinical variables. Changes

in the most subjective physical examination variables (e.g., muscle and joint palpation pain) seem to have the most robust relationship to changes in pain [40]. Stress and anxiety contribute to parafunctional oral habits and influence muscle pressure pain threshold (PPT) and pain. It has been shown that the masticatory muscles PPT of subjects with myofascial pain are markedly lower during stressful events, demonstrating an interaction with stress and anxiety levels [5]. Masticatory muscles may be exceptionally responsive to stressful conditions of personal value [5].

Chronic TMD patients are more frequently diagnosed with muscular TMD and suffer more psychological distress baseline [17, 40]. In our subset of patients requiring reintervention, higher pre-treatment perceived impact on health-related quality of life attributed to TMD (VASLife) and the composed variable of post-treatment myalgia degree and GAD-2 status were predictors of the need for reintervention. Hence, awareness should be raised to identify patients reporting a higher disease burden and whose symptoms subsist after treatment.

Physicians should educate patients on good oral habits and screen and treat underlying associated anxiety and depression. Cognitive behavioral therapy has been proven effective in TMD, particularly of muscular origin, and offers an integrated approach to psychological symptoms [4, 13]. The ultimate objective is to assess further how specific areas of psychological dysfunction influence distinct subtypes of TMD patients to tailor more efficient early intervention and pain management programs [4, 11].

The study's main limitations were the following: (1) not implementing a sequential depression and/or anxiety screening methodology - specificity could be improved by sequentially applying GAD-7 and PHQ-9; (2) were not used tools to make definitive diagnosis according to DSM-5 criteria; (3) the small subset of reintervened patients limited the multivariable prediction model for reintervention; (4) the follow-up period was different between patients; (5) retrospective nature, which introduces potential biases such as establishing causality. This study's retrospective design and single-center data collection introduce several potential biases. Selection bias is a concern, as the sample may not fully represent the broader population of patients with TMD, limiting the generalizability of the findings to other populations or settings. Recall bias is another issue, particularly in how patients reported their symptoms or treatment responses. Additionally, the reliance on self-reported questionnaires like PHQ-2 and GAD-2, despite their validation, may lead to measurement bias if patients underreport or overreport their psychological distress. Although multivariable regression was used to control for some confounding factors, unmeasured confounders may still influence the observed association between psychological distress and TMD outcomes.

The generalizability of the study's findings may be limited by the specific characteristics of the study sample and setting. The predominantly Portuguese patient population, known for a high prevalence of mental health disorders, might influence the applicability of the results to populations with different psychological profiles or healthcare systems. The fact that all patients were treated by the same surgeon in a single institution suggests that the outcomes may reflect practices specific to that clinical setting, which may not be replicated in other centers with different protocols or patient demographics. Furthermore, the study's focus on particular treatment modalities and specific subtypes of TMD, such as myogenous and arthrogenous conditions, may restrict the generalizability of the findings to other forms of TMD or different treatment approaches not covered in this study.

More studies are required to characterize these and other patient-related variables that may influence treatment outcomes and further enhance the profiling of reintervened patients.

5. Conclusion

Despite its limitations, the study established that pre-treatment depression and/or anxiety influence TMD treatment outcomes, particularly in myogenous TMD, and contribute to reintervention. The presence of comorbid mental health disorders should warn the physician/ surgeon to manage treatment strategies promptly and efficiently in a holistic treatment protocol.

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