Clinical Paper
TMJ Disorders

Axis II psychosocial findings predict effectiveness of TMJ hyaluronic acid injections

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D. Manfredini, L. Favero, A. Del Giudice, S. Masiero, E. Stellini, L. Guarda-Nardini: Axis II psychosocial findings predict effectiveness of TMJ hyaluronic acid injections. Int. J. Oral Maxillofac. Surg. 2013; 42: 364–368. © 2012 International Association of Oral and Maxillofacial Surgeons. Published by Elsevier Ltd. All rights reserved.

Abstract. The objective was to investigate the correlation between levels of depression, somatization, and pain-related impairment, as assessed by the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMDs) axis II, and the treatment outcome of a cycle of five weekly injections of hyaluronic acid immediately following arthrocentesis. 57 consecutive patients with a diagnosis of temporomandibular joint (TMJ) osteoarthritis according to the RDC/TMD underwent the treatment protocol and a follow-up assessment at 6 months. Axis II findings were assessed as potential predictors of improvement in visual analogue scale (VAS) values at the end of the observation period with respect to baseline. The percentage of VAS improvement at the end of treatment was inversely related to all the psychosocial variables. The best fitting model identified pain-related impairment ($p < 0.001$) and disability points ($p < 0.001$) as the most significant predictors of VAS changes. The percentage of variance in the outcome variable explained by the significant predictors was high (R^2 70.5%). All the RDC/TMD axis II psychosocial scores (depression, somatization, and pain-related impairment levels) were inversely correlated with therapeutic outcome. The clinical relevance of these findings is important, since psychosocial diagnosis may be even more important than physical evaluation in terms of prognostic impact.

The treatment of temporomandibular joint (TMJ) disorders is based on symptom management by means of conservative approaches, which allow good outcomes in the majority of patients. Most patients describe a favourable natural course of the disease,[1,2] with self-limiting and fluctuating symptoms that often seem to respond well to unspecific treatments.[3] Some patients with Temporomandibular Disorders (TMDs) develop chronic pain within the TMJ area, representing a challenge for pain clinicians, especially because of the concurrent presence of psychosocial disorders and their relationship with pain.

The TMD literature is full of studies describing an association between TMD pain and psychosocial factors, such as depression, somatization, and high impairment in daily life activities.[4–7] Consequently, the standard reference guideline for diagnosis, the Research Diagnostic Criteria for TMD (RDC/TMD), provides a dual-axis biopsychosocial diagnostic approach assessing both the physical (axis I) and psychosocial (axis II) diagnoses.[8] While the axis I diagnoses encompass the different muscle and joint disorders, the axis II system includes instruments for the evaluation of depression, somatization, and pain-related impairment. Much research has been carried out on the epidemiology of TMD,[9] but most treatment

studies have focused only on axis I findings, almost crippling the application of the biopsychosocial model of pain.[10] In particular, some studies suggested that assignment of patients to a specific treatment approach based on axis II findings may be useful in the clinical setting,[11,12] so more studies considering the role of psychosocial factors as prognostic factors are recommended.

The strategy of defining predictors of treatment effectiveness is also important for minor and major TMJ surgery, but studies to identify prognostic factors in TMD pain patients undergoing TMJ arthrocentesis and injections failed to detect predictors of treatment efficacy within the patient's axis I physical findings (e.g. baseline pain levels and location).[13,14] Thus, it could be hypothesized that the importance of psychosocial factors as predictors of TMJ injections effectiveness is worth exploring.

In the present investigation, a protocol providing a cycle of combined arthrocentesis and TMJ hyaluronic injections, which is thought to be effective in reducing symptoms in most patients with TMJ osteoarthritis,[15] was adopted to investigate axis II psychosocial predictors of its effectiveness. The specific aim of the study was to investigate the correlation between levels of depression, somatization, and pain-related impairment, as diagnosed with the RDC/TMD axis II, and the treatment outcome of a cycle of five weekly injections of hyaluronic acid immediately following arthrocentesis. The null hypothesis was that knowing the axis II scores makes no difference for predicting therapeutic effectiveness.

Materials and methods

Participants were 57 ($N = 57$; 86% females; mean age 53.6 years, range 27–75 years) consecutive patients with a diagnosis of TMJ osteoarthritis according to the Research Diagnostic Criteria for Temporomandibular Disorders version 1.0 (RDC/TMDs Axis I Group IIIb) with pain symptoms lasting for more than 6 months in the absence of any systemic rheumatic disease seeking treatment at the TMD Clinic, University of Padova, Italy. All participants underwent a cycle of five arthrocenteses with injections (one per week) of 1 ml hyaluronic acid (Hyalgan; Fidia, Abano Terme, Italy) according to the single-needle technique described by Guarda-Nardini et al.[16] and a follow-up assessment 6 months after the end of the treatment. All patients were assessed at baseline according to the RDC/TMD axis

II psychosocial assessment to identify potential psychosocial predictors of treatment effectiveness at 6 months.

RDC/TMD assessment

Patients were selected to receive the treatment protocol on the basis of a TMJ osteoarthritis diagnosis according to the RDC/TMD 1.0 guidelines,[8] provided the following signs and symptoms were present: arthralgia (TMJ pain with lateral and/or posterior palpation plus anamnestical reporting of TMJ pain during maximum voluntary mouth opening and/or maximum assisted mouth opening and/or lateral excursions); crepitus sounds; radiological signs of TMJ bone structures abnormalities, such as erosions, sclerosis, flattening, osteophytes, showed by means of imaging techniques (e.g. magnetic resonance imaging).

The RDC/TMD axis II, contains a questionnaire which enables an assessment of chronic pain severity according to the Graded Chronic Pain Scale (GCPS)[17] as well as an evaluation of depression and somatization scores according to the dedicated Symptoms Checklist-90-R scales.[18]

The GCPS was originally developed by Von Korff et al.[17] Its validity has been tested in a large population survey, and the prognostic value has been tested in a 3-year follow-up study in large samples of primary care pain patients, also including TMD pain patients. The GCPS is composed of six items assessed on a 10-point scale, and one item on the number of disability days due to facial pain. These items are suitable for self-reported use and, even though the characteristics of the scale enable measuring pain dysfunction as a continuous variable, the authors have provided hierarchical criteria to grade pain dysfunction into ordinal categories. The scoring criteria are simple to use, and allow categorizing pain patients into five levels of chronic pain grades (0, no disability; 1, low disability, low pain intensity; 2, low disability, high pain intensity; 3, high disability, moderately limiting; 4, high disability, severely limiting).

As for depression and somatization levels, the RDC/TMD axis II enables their assessment by means of the depression and somatization scales of the Symptom Checklist 90-R (SCL-90-R), an instrument originally developed by Derogatis.[18] The choice to include the SCL-90-R depression and somatization scales (SCL-DEP, SCL-SOM; abbreviated to DEP and SOM in the text below) in the RDC/TMD axis for psychosocial assessment provides a

contemporary evaluation of concurrent depressive and non-specific physical symptoms. 31 items were included in axis II, belonging either to the Depression and Vegetative Symptom Scale or to the Somatization Scale, which is used here to evaluate the presence of non-specific physical symptoms, plus seven additional items added to the Depression and Vegetative Symptom Scale. The mean scale score is calculated by summing up the scores of the single items. This makes it possible to rate patients as having normal, moderate or severe levels of impairment in the depression and non-specific physical symptoms scales. On the DEP scale, scores below 0.535 were considered normal, between 0.535 and 1.105 indicated moderate depression, and above 1.105 the presence of severe ongoing depressive disorder. On the SOM scale, including the pain items, scores lower than 0.5 were considered normal, values between 0.5 and 1 indicated moderate somatization, and above 1 severe somatization.

All the clinical RDC/TMD assessments were performed using the standard, internationally accepted Italian version of the RDC/TMD instrument available since 2002 on the RDC/TMD consortium website.[19] The RDC/TMD axis I assessments for the inclusion of the patients in the treatment protocol were performed by the two same trained examiners (DM, LGN), who took part in several previous studies using the RDC/TMD.[9] The same two investigators performed the interventions, while two other clinicians (ADG, CC) recorded pain at chewing using VAS scores (see below) and were responsible for axis II data collection and elaboration. In order to ensure single-blindness of the study design, all axis II and VAS scores were recorded separately on dedicated sheets not containing any information on the patients.

Treatment protocol

The treatment protocol adopted in this study provided five weekly arthrocentesis plus single-needle hyaluronic acid injection. The single-needle injection technique employs the same reference points as used in arthroscopic examination (lateral cantus-tragus) and is a modified version of the classical two needles technique for TMJ arthrocentesis.[16] The skin surface is disinfected with povidone iodine. Local anaesthesia is achieved with mepivacaine 2% (Carbocaine, Sanofi Winthroph, NY, USA). The anaesthetic is first injected into the joint cavity, relaxing this virtual space. Subsequently, the needle is withdrawn

gently to the skin surface, thus anaesthetizing the soft tissues over the joint, too. A single 19 G needle is then placed within the intra-articular space and physiological saline is injected under pressure with the patient in the open mouth position. After the injection, the patient is asked to close the mouth and the fluid is removed with the same injection needle, thus acting as both entry and exit point for the liquid. The injection–ejection process must be performed for up to 10 repetitions (for a total amount of about 40 cm^3), thus allowing elimination of catabolytes present in the synovial fluid. Once arthrocentesis is completed, 1 cm^3 of hyaluronic acid is injected into the joint in 3 s and the needle is removed. This technique has been shown to be as effective as the two-needle approach, and is currently adopted as the standard of reference at the authors' clinic thanks to its reduced invasiveness.[20]

Statistical design

The statistical approach was designed to answer the clinical research question: do axis II psychosocial findings predict treatment effectiveness at 6 months in patients undergoing the five weekly arthrocenteses plus HA injections? To test the null hypothesis that knowing the axis II scores makes no difference for predicting therapeutic effectiveness, an outcome variable for treatment effectiveness (i.e. pain levels at chewing) was assumed as the dependent variable and the axis II scores were assumed as predictors.

Scores in the clinical parameter 'pain on chewing', assessed by means of a VAS from 0 to 10, with the extremes being 'no pain' and 'pain as bad as the patient ever experienced' respectively, were assessed by the same operator at the time of the diagnosis (baseline) and at the time of the 6 month follow-up. Percentage changes in VAS values at the end of the observation period with respect to baseline were assessed to create an outcome variable that was not dependent on the absolute magnitude of VAS scores. This variable was adopted as the dependent variable to be identified in a linear regression model by the following predictors (independent variables) gathered with RDC/TMD axis II psychosocial assessment[8]: depression levels, as based on the SCL-90 depression scale scores; non-specific physical symptoms (somatization, scores (pain items excluded), as based on the SCL-90 non-specific symptoms scale scores); characteristic pain intensity score; disability score; disability points; pain-related impairment, as based on the GCPS scores.

A single variable regression analysis was performed to test the existence of a correlation between the outcome variable and any of the predictors. A cut-off value of $p < 0.10$ was set to screen variables which were related to the treatment effectiveness, and a multiple variable linear regression analysis was performed to identify the significant associations between the predictors (independent variables: depression levels; somatization levels; characteristic pain intensity score; disability score; disability points; pain-related impairment) and the outcome (dependent variable: percentage change in pain at chewing levels) by including only those variables which were significant at $p < 0.10$ at the single variable analysis. Selection was made among the potential predictors of positive outcome using a backward stepwise selection method. R square (R^2) was obtained as an estimation of the variance explained by a summation of the significant psychosocial factors, and represents the amount that the independent variables can differentiate the dependent variable. R^2 represents a numerical expression of the dependent variable's (percentage changes in VAS pain at chewing scores) variance accounted for by the model of the significant predictors. All statistical procedures were assessed with the Statistical Package for the Social Sciences (SPSS 19.0, SPSS Inc., Chicago, IL, USA).

Results

Based on cut-offs suggested in the RDC/TMD guidelines,[8] psychosocial assessment showed that 19.3% of patients reported high pain-related impairment (GCPS grade III or IV), 26.3% showed severe depression scores, and 43.9% severe somatization levels (Table 1). At the end of the 6 month follow-up,

improvement in VAS scores with respect to baseline values was significant (mean change: 64.9% ± 32.2; $t = 13.73$; $p < 0.001$) (Table 2).

At single variable analysis, the percentage of VAS improvement was significantly inversely related with all the psychosocial variables (correlation values ranging from −0.268 to −0.408). The higher the axis II scores the lower the percentage in VAS improvement (Table 3).

Multiple variable regression analysis confirmed that all axis II results are correlated with the percentage of VAS improvement (data not shown). The best fitting model identified pain-related impairment ($p < 0.001$) and disability points ($p < 0.001$) as the most significant predictors of VAS changes. The percentage of variance in the outcome variable explained by the significant predictors was high (R^2 70.5%) (Table 4). Thus, the null hypothesis that knowing the axis II scores makes no difference for predicting therapeutic efficacy was rejected.

Discussion

The present investigation aimed to explore the usefulness of psychometric measures

Table 1. Percentage of patients receiving the different axis II diagnoses.

RDC/TMD axis II diagnoses		Patients (%)
GCPS	0	–
	I	21.1
	II	59.6
	III	14.0
	IV	5.3
SCL-DEP	Normal	52.6
	Moderate	21.2
	Severe	26.3
SCL-SOM	Normal	21.1
	Moderate	35.1
	Severe	43.8

Table 2. Significance of changes in pain at chewing VAS scores from baseline to follow-up assessment (*t* test for paired samples).

Pain at chewing levels	Mean value (±s.d.) ($N = 57$)	Sig.
Baseline VAS scores	6.05 (±2.3)	<0.001
Follow-up VAS scores	2.33 (±2.3)	

Table 3. Mean values in the psychometric measures and single variable correlation with percentage of improvement in pain at chewing VAS scores.

Variable	Mean value (±s.d.) ($N = 57$)	Correlation with treatment effectiveness	Sig.
Depression	0.76 (±0.72)	−0.324	0.016
Somatization	0.94 (±0.63)	−0.268	0.048
Characteristic pain intensity	63.27 (±21.78)	−0.408	0.002
Disability score	31.69 (±27.73)	−0.328	0.015

Table 4. Significant predictors in the final best-fitting regression model.

Outcome variable	Significant predictors	*p* value	Beta (95% C.I.)	Model's R^2 (%)
% change in pain at chewing VAS pain levels	GCPS scores	<0.001	38.4 (30.5–46.3)	70.5
	Disability points	<0.001	16.5 (8.1–25.0)	

included in the RDC/TMD axis II as predictors for treatment outcome in TMD patients. The treatment protocol adopted was based on a cycle of five weekly arthrocentesis plus hyaluronic acid injections in patients with inflammatory-degenerative disorders of the TMJ (osteoarthritis). The reason for adopting this protocol is that: it has been shown to be effective in reducing average pain levels over various follow-up periods[21,22]; it is more effective than other protocols for arthrocentesis and injections in patients with TMJ osteoarthritis[15]; the choice of the technique for administering arthrocentesis (single needle vs. two needle) does not have a strong influence on treatment effects[20]; and that the effectiveness of the same protocol seems to be influenced only in part by axis I parameters.[14] Thus, it could be assumed that all technique-related factors do not act as confounders in the regression analysis performed to identify psychosocial predictors of treatment effectiveness.

In the present investigation, VAS pain values decreased significantly, and an average pain reduction of 61% at the 6 month follow-up with respect to baseline levels was observed. All psychosocial measures included in the axis II were correlated with treatment effect and parameters related with pain related impairment were the most significant predictors of pain level reduction. The percentage of variance in VAS pain levels explained by psychometric measures was up to 70.5%, which is a much higher value than commonly described in studies depicting multivariate biological models.

The clinical significance of these findings is high, because they explain common observations that TMD treatment is, at least to some extent, unspecific.[23] Several treatment modalities have been shown to be successful at reducing TMD pain in most patients, despite having different mechanisms of action.[24] Notwithstanding that, analyses of failures are lacking in the TMD literature, even if hypotheses were raised that the percentage of patients who do not improve with treatment is similar to the percentage of patients scoring high pain-related impairment levels.[25] The literature includes many studies showing that chronic TMD pain is associated with psychosocial disorders, such as those screened with the RDC/TMD axis II instruments (depression, somatization, pain-related impairment).[5,7,17] Such findings are in line with the well-described relationship between psychosocial factors and pain in several other body areas.[26,27] Whether chronic pain causes psychosocial impairment or whether psychosocial disorders are a major risk factor for chronic pain is still debated, despite this, axis II findings are likely to have a strong impact in the clinical setting, potentially influencing prognosis and therapeutic outcome.

In TMD practice, the need for studying the prognostic impact of psychosocial factors has been supported by several observations that multivariate analysis on the predictability for effectiveness of a cycle of TMJ arthrocentesis and injections showed the presence of bilateral joint pain as the unique factor related to a positive treatment outcome.[14] Such findings were in line with reports showing that the outcomes of arthrocentesis and hydraulic distension of the TMJ are not a matter of simple linearity with any specific clinical or imaging signs.[13,28] This study suggested that a psychosocial assessment of TMD patients may be important as a physical evaluation and that the former may be more important than the latter when predicting treatment effect. This implies that if the external validity of these findings is confirmed with studies on other therapeutic approaches over longer follow-up periods, the clinical relevance of measuring psychosocial impairment cannot be underestimated.[29]

In conclusion, the present investigation assessed the role of RDC/TMD axis II psychosocial measures as predictors of treatment outcome in a group of patients with TMJ osteoarthritis undergoing a cycle of five weekly arthrocentesis plus hyaluronic acid injections. All the psychosocial scores (depression, somatization, and pain-related impairment levels) were inversely correlated with therapeutic outcome. In particular, regression models showed that graded chronic pain severity is the most significant predictor, and that the amount of variance in the measure of pain levels accounted for by the psychosocial predictors is high (up to 70.5%). The clinical relevance of these findings is important, and lies in the fact that a psychosocial diagnosis may be even more important than physical evaluation in terms of prognostic impact.

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