PREDICTORS OF PAIN REDUCTION FOLLOWING MANUAL THERAPY IN PATIENTS WITH TEMPOROMANDIBULAR DISORDERS: A PROTOCOL FOR A PROSPECTIVE OBSERVATIONAL STUDY

Supplementary file 1 - Candidate predictors

Demographical variables

Participants' demographic variables [age, gender, education] will be collected at baseline from open hospital records and patient interview.

Age

Age is a significant factor in TMD incidence and prevalence. Lipton et al. found different age-specific prevalence for face/jaw pain: 6.5% in aged 18-34, 5.0% in 35-54 years old, 4.0% in 55-74 years old and 3.9% in people > 74 year old, showing a prevalence reduction across the lifetime[1]. By contrast, data from the OPPERA study[2] showed a 40% increased risk for TMD among individuals aged 25-34 years and a 50% increased risk for TMD among individuals aged 35-50 years.

Gender

Women are 1.5-2 times more likely to develop TMD than men[3-5]. Currently, there is no study examining the extent of recovery from TMD in men and women. Nevertheless, gender is a significant factor to be considered.

Education

The National Centre of Health and Statistic (NCHS)[6] found that the differences in jaw pain prevalence among different educational groups are minimal. On the other hand, there is evidence that people with lower levels of education adopt maladaptive coping strategies, including a tendency to catastrophize about their pain[7]. As a result, the education levels will be collected as candidate predictor of outcome by classifying education into three categories: basic education, intermediate education and university-level education.

General health variable

EuroQol Five Dimension Scale, 5-level [EQ-5D-5L]

According to Kapos et al.[8], health-related quality of life can be a significant factor influencing treatment outcome for TMD. The results showed that a higher health-related quality of life predicted lower TMD pain intensity at an 8 year follow-up. Health-related quality of life will be measured using the Italian version of the EQ-5D-5L [www.euroqol.org]. This instrument transforms different health states into a single value with range 0-1 where 1 is perfect health, and it measures the patient's own judgement about his/her health outcome through a visual analogue scale range 0–100, representing respectively 'worst' to 'best' imaginable health state[9]. The EQ-5D-5L, with 5 possible responses to each item, has increased inter-observer [ICC 2,1 0.57] and test-retest [ICC 2,1 0.69] reliability compared to the previous EQ-5D-3L[10]. Additionally, it has less ceiling effects [20.8% reduction] and adequate convergent validity when compared with the WHO-5 [Spearman rank 0.38-0.51][11].

Sleep quality

It is known that chronic pain patients may suffer from poor sleep quality, even if it is difficult to draw a causal relation[12]. Consequently, sleep quality will be assessed as a candidate predictor because of its possible role among other factors in the transition from acute to chronic pain. Sleep quality will be evaluated through an 11-point Numerical Rating Scale [NRS], where 0 is 'the best possible sleep' and 10 is 'the worst possible sleep'. This scale owns moderate psychometric properties in fibromyalgia patients to assess current sleep quality [over the previous 24 hour period] with a symptom diary[13]. We will use the 0-10 NRS to assess average sleep quality, related to the preceding 6-months at baseline[14], although no psychometric properties have previously been reported for this recall period.

Psychosocial features

Psychosocial factors are known to influence TMD onset and chronicity[15]. Psychological distress is significantly linked to a greater severity and persistence of TMD pain[16]. Moreover, depression and high levels of stress are significantly more common in people with chronic TMD[17-18]. In addition, there is agreement about the predictive strength of psychosocial factors in primary care among different musculoskeletal pain conditions[19-20].

<u>The Hospital Anxiety and Depression Scales [HADS]</u>

The Italian version of the HAD[21] will be utilised to investigate depression, anxiety and manifestations of somatic symptoms[22]. This scale consists of two subscales [anxiety: HADS-A; depression: HADS-D] with 7 items and a total score from 0 to 21, with a higher score indicating elevated levels of anxiety and depression[23].

HADS has been studied in different groups confirming adequate to excellent internal

consistency of HADS-A [0.68-0.93] and HADS-D [0.67-0.90][23]. In a coronary heart disease sample, the standard measurement of error was 1.37 for anxiety and 1.44 for depression; the minimal detectable change was 3.80 for anxiety and 3.99 for depression[24]. The HADS has excellent concurrent validity in comparison to other depression/anxiety scales[23].

Coping Strategies Questionnaire 27 [CSQ-27]

Forssell et al.[25] found that a low perceived ability to control pain increases the risk for poor prognosis of TMD pain at one year regardless of the type of treatment. The Italian version of the CSQ-27[26] will be used to provide an indication of coping strategies used by participants when they are in pain. This 27-item questionnaire contains six domains to assess the strategies for coping with pain: *Distraction, Catastrophizing, Ignoring pain sensations, Distancing from pain, Coping self-statements,* and *Praying*. Patients rate the specific strategies for coping with pain using a seven-point Likert scale [for each domain] ranging from 0 "Never do that" to 6 "Always do that", with higher scores indicating greater use[27]. A recent study in a low back pain cohort[28], in which individual items from multiple questionnaires were factorised, suggested that diversion, reinterpreting and cognitive coping clustered together as a single factor, representing coping cognitions; by contrast, catastrophizing clustered with pain-related distress items. The original form was examined in English-speaking subjects and revealed acceptable internal consistency [Cronbach's alpha estimates ranging from 0.72 to 0.86] and satisfying construct validity[27].

Treatment expectation

A positive treatment expectation is considered as a treatment moderator because of its influence on treatment outcome[29]. A positive treatment expectation is predictive of good outcome

because the expectation of benefit (placebo) has a robust effect on pain[30]. In the current study we will investigate treatment expectation following the same protocol used by Puentedura et al[31]. Participants will be asked whether they "Completely disagree", "Somewhat disagree", "Neutral", "Somewhat agree", "Completely agree" with the following statement: "I believe that *manual techniques applied to my jaw* will significantly help to improve my pain". If the participant chooses "completely disagree," "somewhat disagree," or "neutral," there is not a positive expectation that manual therapy applied to craniomandibular structures will significantly help their temporomandibular disorder. If the participant chooses "somewhat agree" or "completely agree," there is a positive expectation that manual therapy applied to craniomandibular structures will significantly help their temporomandibular disorder.

TMD characteristics

Based on previous studies on predictive factors of outcome in TMD patients[8,25,32], pain characteristics [e.g. pain duration, pain intensity, pain location] are good predictors for pain change in the long-term. In addition, across a variety of different conditions, pain features were reported to hold predictive value for pain modulation[19,33-35].

Pain Duration

According to Grossman et al.[32], pain duration could be a significant factor influencing the treatment outcome for TMD. Their results underline the fact that a longer pain duration is associated with a more refractory therapeutic approach. Consequently, the pain duration [measured in "days"] will be collected as candidate predictor of outcome from open hospital records and patient interview.

Pain intensity

As shown in a previous study[32], high levels of pain intensity at baseline in people with TMD, can be associated with no-clinically significant results at a midterm [3-4 months] follow up. Pain intensity will be calculated by averaging ratings of current pain, average pain, and worst pain in the past week using the visual analogue scale (VAS), consisting of a horizontal line measuring 10 cm (without marks), with "no pain" written at the left extremity, and "unbearable pain" written at the right extremity[36]. Patients will be educated to trace a perpendicular line on the horizontal line to intend the pain intensity. The distance from the 0 points will be after measured in millimetres. The VAS is a reliable and valid scale to assess pain intensity[37].

Pain location and extent

Forssell et al.[25] found that a high number of pain conditions increases the risk for poor prognosis of TMD pain at one year regardless of the type of treatment. Comorbid painful areas are common in patients with TMD pain[38]. Therefore, the pain location and the pain extent will be collected as a candidate predictor of outcome. This will be recorded as described in the DC/TMD protocol[16,39-44]. Patients will be asked to complete a pain drawing symbolising the spatial distribution of the pain, over one chart with a frontal view of the body, one with a dorsal view and one with a dental setting (more specific for the jaw and teeth pain). Pain reported in different body areas (e.g., headache, back pain, pelvic pain, neck pain) can be summarised as a count variable. The extent of pain will be calculated as % of the body area by using an image scanning software (ImageJ: Image Processing and Analysis in Java, http://imagej.nih.gov/ij/; Klong Image Measurement: http://www.imagemeasurement.com/experience-image-measurement/pain-assessment-image-measurement)

Central Sensitization Inventory (CSI)[45]

Central sensitization can be present in different pain disorders including low back pain[46], neck pain[47], fibromyalgia[48], and TMD[49]. The Italian version of the Central Sensitization Inventory (CSI)[50] will be used. Part A consists of a 0-100 score for 25 items on current health symptoms with five options ranging from 'never' (0) to 'always' (4). Part B examines previous physician diagnoses among seven different conditions[45]. The CSI has significant test-retest reliability and internal consistency in subjects with and without pain[45]. The Italian version of the CSI showed a satisfactory Cronbach's alpha [0.87][50].

Classification of TMD

Manual therapy could potentially be beneficial for both myogenous and arthrogenous TMD[51]. The TMD type will therefore be collected as a candidate predictor of outcome. As stated in the inclusion criteria, every patient included in the study will be diagnosed according to the Axis I of the Diagnostic Criteria for TMD DC/TMD[39]. Based on these criteria, Peck et al.[52] reported different types of TMD. This Taxonomic Classification of TMD includes four main domains: TMJ Disorders, Masticatory Muscle Disorders, Headache and Associated Disorders. An additional domain, called Mixed TMD (simultaneous presence of TMJ Disorders and Masticatory Muscle Disorders) will be included. For every patient the type of TMD (total of 5 domains) will be collected as candidate predictors from the patient medical records.

Characteristic pain intensity and disability

A greater number of disability days increases the risk of having clinically significant pain one year after an initial assessment[25]. In this study we will use the Italian version of Graded Chronic Pain Scale [GCPS] version 2.0 [www.rdc-tmdinternational.org][53] following the DC/TMD protocol recommendations[39,42,44]. This scale has good internal consistency in temporomandibular pain [Cronbach's alpha of 0.84][54]. The GCPS measures the facial pain severity over the preceding 6-months by unifying pain intensity and pain-related disability. The characteristic pain intensity score [range: 0-100] is the mean of three pain intensity measurements: 'at the present time' and 'worst pain' and the 'average' pain over the preceding 6 months. The disability status is measured with a 0-6 point score derived from a combination of the number of disability days and the disability level [range: 0-100; limitation given by pain in performing activities of daily living]. Based on these scores, the participant's chronic pain and disability status can be classified into one of the five ordinal categories of chronic pain severity[55].

Oral Behaviour

People with abnormal oral behaviours with scores above 25 in the Oral Behaviours Checklist [OBC] are 75% more likely to develop TMD than individuals with a score below 17[42,44,56]. Parafunctional habits could play a significant role in the development and the persistence of TMD pain[58]. In this study we will use the Italian version of the RDC/TMD questionnaire Axis II Oral Behaviours Checklist [www.rdc-tmdinternational.org][42,56] following the DC/TMD protocol recommendations[39,56]. The OBC measures the self-reported frequency over the preceding month of each of 21 activities involving the jaw such as clenching the teeth or bracing the jaw (five ordinal response options, ranging from ''none of the time,'' coded 0, to ''all of the time,'' coded 4). Psychometric properties of this instrument suggest that it is valid, with patient behaviours matching those measured[56,57,59]. Scoring is computed as the sum of the number of items with non-

zero response or as a weighted sum [e.g. the sum of the endorsed frequencies of the respective items][56].

Clinical tests of the TMJ and masticatory muscles

TMJ range of motion

Mobility testing of the TMJ denotes an essential sign of TMD, it is one of the most reliable clinical measures[39]. Grossman et al.[8] examined the preoperative variables of TMD patients with articular disc displacement without reduction that may alter the effects of arthrocentesis on joint effusion. They observed that small maximum interincisal distance influences treatment outcome. As a result, we will use the Maximal Mouth Opening (MMO) without pain as measure of TMJ range of motion. The measurements will be in millimeters and will be taken with a ruler in a neutral craniocervical position [e.g. sitting or supine]. The distance between the incisal edges of the maxillary and mandibular reference teeth, as described in the DC/TMD protocol[44], will be measured. Participants will be asked to open the mouth as wide as they can without feeling any pain, or without increasing any present pain. The tip of the ruler will be located against the incisal edge of the mandibular reference incisor, and the distance to the mesial-distal center of the edge of the maxillary central incisor will be read. The test will be repeated twice if the pain-free opening if less than 30mm[44]. Assessment of mandibular ROM in a neutral craniocervical position obtained good inter- and intra-rater reliability for MMO[60].

TMJ palpation pain:

Pain induced in joints via palpation is a useful clinical test that allows to understand if the provoked pain duplicates or replicates the patient's pain complaint by identifying potential joint

origin[44]. For this palpation, finger pressure is calibrated [1.0 kg], as described in the DC/TMD protocol[44], using a simple hand-held algometer prior to palpation examination. While the participant mandible is in a comfortable position or in a slightly protruded position, the examiner's index finger will be placed just anterior to the tragus of the ear and dorsal to the TMJ with the participant in neutral craniocervical position e.g. sitting or supine. The index finger will press while orbiting around the lateral pole in a circular fashion over the superior aspect of the condyle and then anteriorly [from the 9:00 to the 3:00 position, and then continuing fully around the condyle]. Palpation will last 5 seconds for each pressed point[44]. If a participant complains of familiar pain in at least one pressed point the point score of this test will be 1; if there is no pain at any points the point score of this test will be 0 [range 0-1: no pain =0; pain = 1]. Palpation will be performed in the left and right side. The interexaminer reliability values of TMJ palpation in TMD patients is 0.59 and the specificity values is acceptable [above 0.90][61].

Muscle palpation pain

For this assessment, finger pressure is calibrated to 1.0 kg for masseter muscles and 0.5 kg for lateral pterygoid area and temporalis tendons as described in the DC/TMD protocol[44], using a simple hand-held algometer prior to palpation examination. Pain induced in muscles via palpation is a useful clinical test that allows to understand whether the provoked pain duplicates or replicates the patient's pain complaint by identifying potential muscular origin[44]. Palpation will be performed with the participant in a neutral craniocervical position (e.g. sitting or supine), on the left and right side and will last 5 seconds for each testing point[44]. The inter-examiner reliability values of palpation in TMD patients is 0.59 and the specificity values are acceptable [above 0.90][61]. The feasibility of the lateral pterygoid muscle palpation is controversial. Some authors defined it as a feasible palpation technique[62], and others considered this muscle unaccessible[63]. Therefore, in this

study, this parameter [pain at lateral pterygoid site] will not be considered alone but in combination with pain at other muscular sites.

Lateral pterygoid area: palpation will be performed with a finger pressure calibrated at 0.5 kg (DC/TMD protocol[44]). The palpation will take place as described in FIG.1. If a participant complains of familiar pain during palpation the lateral pterygoid area will be considered as a painful site.

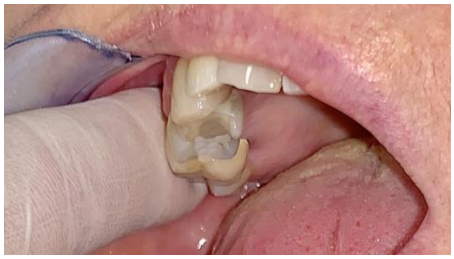


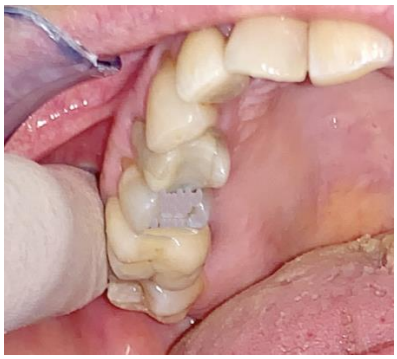
FIG. 1 Lateral pterygoid area: Finger is placed as shown. Palpate the vestibule in posterior-superior-medial direction while the mandible is omolaterally deviated.

Masseter muscle: masseter palpation consists of a sequence of three palpation sites with finger pressure calibrated to 1.0 kg (DC/TMD protocol[44]): origin zone [inferior to the bony margin of the zygomatic process], body zone [in front of ear lobe] and insertion zone [superior to the mandibular angle]. In each zone, the palpation continues until the anterior boundary of the muscle is reached[44]. If a participant complains of familiar pain in at least one pressed point, the masseter muscle will be considered as a painful site.

Temporalis tendon area: the palpation will be performed with a finger pressure calibrated to 0.5 kg (DC/TMD protocol[44]). The palpation will take place as described in FIG.2. If a participant

complains of familiar pain during the palpation the temporalis tendon area will be considered as a painful site.

FIG. 2 Temporalis tendon area: Finger is located against the ascending mandibular ramus while the mouth is slightly open. The palpation direction is superior as far as possible by following the bone surface.



Total score: if a participant complains of familiar pain in at least three of the six examined sites the score will be 1, otherwise it will be 0 [score range 0–1: < 3 sites with familiar pain = 0; ≥ 3 sites with familiar pain = 1][64].

JAw-test

The JAw-test is a clinical test that aims to investigate the immediate effects of four brief intraoral manual therapy techniques on pain and on TMJ range of motion. The participant will be positioned in supine position. Before starting the test, the TMJ range of motion without pain will be measured [MMO - millimeters] with a ruler, as described above, according to DC/TMD protocol[44]. Then the participant will be asked to rate his/her pain through the Verbal Rating Scale (VRS) “at rest”, “during clenching” and “during the maximal opening of the mouth”; an average of the three pain scores will be registered. For this test, finger pressure is calibrated [1.0 kg], in the same way described in the DC/TMD protocol[44], using a simple hand-held algometer prior to

palpation examination.

Participants will be informed with the following words: "*I am going to perform four manual techniques on some muscles and joints in your jaw region. You may feel a little pain, if the pain increases and becomes too intense, let me know, I will reduce the pressure until the pain returns to acceptable levels".*

First technique: Lateral pterygoid area

This techniques will be performed on the most painful side. While one hand stabilizes the participant's head on the least painful side, the other hand will be used to apply pressure over the lateral pterygoid area as described above and in accordance with the DC/TMD protocol[44]. In this position, compression [1.0 kg] is applied for 30-60 seconds.

Second technique: Temporalis tendon area

This techniques will be performed on the most painful side. While one hand stabilizes the participant's head on the least painful side, the other hand (index finger) will be used to apply pressure over the Temporalis tendon area as described above and in accordance with the DC/TMD protocol[44]. In this position, compression [1.0 kg] is applied for 30-60 seconds.

Third technique: Mylohyoid area

The participant will be instructed to open the mouth to let the examiner's finger reach the mylohyoid area in a central position on the mylohyoid raphe. The other hand of the examiner will reach the same area using a finger through an extraoral approach. In this position a combined compression (1.0 kg) will be applied for 30-60 seconds.

Fourth technique: TMJ mobilization

An intraoral ventral and caudal anterior glide [mobilisation grades I and II] of both the TMJs will be performed for 30 seconds as described by Cleland et al.[65]

Final scores:

After the tests, the TMJ range of motion without pain will be measured [MMO - millimeters] with a ruler, as described above, according to DC/TMD protocol[44]. Then the participant will be asked to rate his/her pain using the Verbal Rating Scale (VRS) "at rest", "during clenching" and "during the maximal opening of the mouth"; an average oh this three pain scores will be registered. If a participant shows only an improvement in pain [average score VRS pre-test > average score VRS post-test] the score will be 1; if a participant shows only an improvement of TMJ mobility [MMO pre-test < MMO post-test at least 2 millimeters] the score will be 1; if a participant shows improvements in both pain and TMJ mobility, the score will be 2; if a participant shows no improvements the score will be 0 [Score range 0-2: 0 = no change; 1 = VRS improvement or MMO improvement; 2 = improvement of both].

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